ABSTRACTS

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Aims and Scope

Mission statement: To advance the scientific basis of human pathology by the publication (encouragement and dissemination) of high quality research (including molecular and translational studies) and thereby contribute to patient care.

Manuscripts of original studies reinforcing the evidence base of modern diagnostic pathology, using immunocytochemical, molecular and ultrastructural techniques, will be welcomed. In addition, papers on critical evaluation of diagnostic criteria but also broadsheets and guidelines with a solid evidence base will be considered. Consideration will also be given to reports of work in other fields relevant to the understanding of human pathology as well as manuscripts on the application of new methods and techniques in pathology. Submission of purely experimental articles is discouraged but manuscripts on experimental work applicable to diagnostic pathology are welcomed. Biomarker studies are welcomed but need to abide by strict rules (e.g. REMARK) of adequate sample size and relevant marker choice. Single marker studies on limited patient series without validated application will as a rule not be considered. Case reports will only be considered when they provide substantial new information with an impact on understanding disease or diagnostic practice.

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OFP-06	Joint Oral Free Paper Session Endocrine Pathology / Head and Neck Pathology
OFP-07	Joint Oral Free Paper Session Digestive Diseases Pathology (GI) / Digestive Diseases (Liver/Pancreas)
OFP-08	Joint Oral Free Paper Session Other Topics (THYM / DEVEL / CARD / HIST / AUT)
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ABSTRACTS

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Oral Free Paper Sessions

OFP-01 Oral Free Paper Session Breast Pathology

OFP-01-001
How can the varied tumour FFPE blocks with HER2 ultra-low influenced on the accurate diagnosis of HER2 in breast cancer
Y. Liu*, J. Li, H. Liu, Y. Ding, S. Wu, J. Shang
*The Fourth Hospital of Hebei Medical University, China

Background & objectives: The inclusion of HER2 ultra-low in DESTINY Breast 06 clinical trial further complicates HER2 detection. This study utilized tumour formalin-fixed paraffin-embedded (FFPE) blocks to evaluate their impacts on breast cancer with HER2 0 (no staining) and HER2 ultra-low under real-world conditions.
Methods: We retrospectively collected 1646 cases of consecutive invasive breast cancer that were surgically treated and diagnosed as HER2 0. Three experienced pathologists reinterpreted these slides and classified them as HER2 0 (no staining) or HER2 ultra-low. All tumour FFPE blocks from 50 consecutive cases were also collected retrospectively. Cohen's Kappa was used for consistency analysis.
Results: Among 1646 cases, 70.5% were HER2 0 (no staining), 29.5% were HER2 ultra-low. HER2 ultra-low was more common in HR+ cases than in HR- cases (32% vs 22.1%). Moreover, we evaluated intra-tumour heterogeneity between them for different number of blocks. Results showed that inconsistent HER2 scores among different FFPE blocks accounted for 60.0%, of which 62.2% and 64.7% had inconsistent HER2 scores among 3 and 4 FFPE blocks, respectively. 82.3% of HER2 ultra-low cases had inconsistent HER2 scores. In simulated daily work scenarios, a multi-FFPE block trial would increase number of 10 patients who could potentially benefit from T-DXd treatment compared with a single FFPE block trial.
Conclusion: Our findings highlighted the significant influence of different FFPE blocks on diagnosing HER2 0 and ultra-low. Inconsistencies in HER2 IHC scores increased as more blocks were tested, highlighting the importance of standardized sample collection and tissue processing protocols. The accurate detection of HER2 0 and ultra-low is highly reliant on the selection of samples and testing factors, while the multi-FFPE blocks testing can avoid underestimation of HER2 status in patients with HER2 ultra-low and ensure the accuracy of HER2 detection.

OFP-01-002
Multi-site European study of a HER2 AI solution as clinical decision-support tool in breast cancer
E. Provenzano*, M. Jimenez-Linan, W. Cope, P. Schouten, A. Vincent-Salomon, A. Gunavardhan, S. Declercq, J. Thomassin, M. Brevet, M. Grinwald, D. Mevorach, R. Ziv, G. Mallel, J. Sandbank, M. Vecsler
*Department of Histopathology, Cambridge University Hospital NHS Foundation Trust and NIHR Cambridge Biomedical Research Centre, Cambridge, United Kingdom

Background & objectives: HER2 is a major predictive biomarker routinely assessed for invasive breast carcinoma (BC). We aimed to determine whether an artificial intelligence (AI) solution contributes to pathologists' standardization and accuracy in interpreting HER2 scores in BC core needle biopsies and excisions
Methods: Two-arm multi-reader study on 839 BC biopsies and excisions, from six different UK and EU centres, compared 14 pathologists ("readers") HER2 scoring performance, each reviewed 50-200 slides, without and with a fully automated AI HER2 solution. Inter-observer agreement and both arms' accuracy compared to ground truth (GT) were analyzed. GT was established by breast expert subspecialists according to ASCO/CAP 2018
Results: Experts' overall inter-observer agreement was 79.3% and for 0/1+/2+/3+ scores it was 86.9%/78.9%/65.6%/94.3%, respectively.
Readers' overall inter-observer agreement was significantly higher when assisted by AI 88.6% [95%CI: 86.3%,90.7%] vs. 76.3% [95%CI: 73.4%,79.1%] without AI ($p < 0.05$), as for HER2 Low 0 vs. 1+/2+/3+ cutoff 95% [95%CI: 93.3%,96.3%] vs. 89.3% [95%CI: 87.0%,91.3%].
Readers with AI had similar accuracy as readers without AI, overall and for HER2 Low cutoff, 81.8% [95%CI: 79.9%,83.6%] vs 80.6% [95%CI: 78.6%,82.5%] and 91.1% [95%CI: 89.6%,92.4%] vs. 90.9% [95%CI: 89.4%,92.2%], respectively.
The AI solution demonstrated high accuracy for HER2 scoring (91.2%) for 0 vs. 1+/2+/3+ and overall (80.9%). A reader feedback survey regarding the solution's usability will also be presented
Conclusion: This study reports an independent multi-site validation of a fully automated AI solution for HER2 scoring in BC. Pathologists supported by AI showed improvements in HER2 scoring consistency, without compromising the sensitivity and overall accuracy. AI solutions, such as the one investigated here, could be used as decision-support tools for pathologists in routine clinical practice, enhancing the reproducibility and consistency of HER2 scoring, thus enabling optimal treatment pathways and better patient outcomes

Funding: Research funding by Ibex Medical Analytics

OFP-01-003
Image analysis-based hormone receptor expression of cancer associated fibroblasts is prognostic in breast cancer: a pilot study
C. Boyaci*, J. Hartman, B. Acs
*Karolinska University Hospital, Karolinska Institute, Sweden

Background & objectives: Cancer-associated fibroblasts (CAFs) represent key elements in the tumour microenvironment, with many preclinical studies demonstrating their association with tumour development and therapy resistance. However, lack of clinical studies examining hormone receptor (HR) expression in CAFs hinders clinical implementation.
Methods: Our cohort comprised 133 patients with immunohistochemically stained slides for estrogen receptor-α (ER) and progesterone receptor (PR). We developed an open-source image-analysis

algorithm in QuPath platform to measure HR expression in CAFs using the training cohort (n=35). We validated the pipeline in standardized hot-spot areas of tumour stroma in the test cohort (n=97) representing all molecular subtypes of breast cancer.
Results: We found that ER in CAFs is expressed in different proportions in different molecular subtypes. Lower "total combined score in Nottingham histological grade" was correlated with higher ER-positivity in CAFs (p=0,009, ANOVA). Using cross-validated thresholds (X-tile software) in the test cohort, the patient subgroup with high ER expression in CAFs had a significantly longer relapse-free survival (p=0,03, log-rank test). The prognostic performance was more robust in subgroup analysis with only luminal A and B patients (p=0,00009, log-rank test). Luminal A cases had a trend to have the highest proportions in ER and PR expression in CAFs without reaching statistically significant result.
Conclusion: The results of our pilot study suggest that the clinical validity of hormone receptor expression in cancer-associated fibroblasts as a potential prognostic biomarker in clinical practice should be investigated in a large population-based breast cancer cohort. Additionally, our results emphasize the importance of focusing on tumour microenvironment in clinical research.

Funding: BA: Swedish Society for Medical Research (Svenska Sällskapet för Medicinsk Forskning)

OFP-01-004
The added value of an artificial intelligence (AI) solution in the identification of microinvasive and T1a carcinomas of the breast
C. Karakas, S. Etöz, S. Goodman, R. Graça-Lopes, J. Sandbank, M. Vecsler, S.J. Schnitt, R. Canas-Marques*
*Anatomic Pathology Department, Champalimaud Foundation, Lisboa, Portugal

Background & objectives: Identification of small foci of invasive breast cancer (BC) is challenging and time-consuming. We assessed the accuracy of an AI solution for identifying microinvasive (MI) and T1a BC associated with DCIS.
Methods: We evaluated 159 digitized H&E slides with DCIS, 97 with invasive foci (85 MI;12 pT1a) and 62 with DCIS only, using an AI solution. Ground truth was established by experienced breast pathologists. AI categorized each slide according to invasive cancer likelihood as high, medium, or low. Cases were enriched for DCIS with potential confounding features (stromal chronic inflammation, lobular involvement).
Results: The AI solution detected malignant lesions in 159/159 cases, 130/159 with high likelihood and 25/159 with medium likelihood. Foci of MI were detected as "invasive" by AI with a high/medium likelihood for invasive carcinoma in 71/85 MI slides (83.5%). Two breast pathologists re-examined the invasive cancer heatmap coverage/points of interest for the 14 slides considered low likelihood by AI and found that AI captured all but 2 MI cases that were obscured by dense stromal chronic inflammation. Thus, the MI detection rate was 83/85 slides (97.6%). For pT1a cases, AI detected invasion in 12/12 slides (100%); 9/12 with high/medium likelihood and 3 slides with low likelihood.
Conclusion: The AI solution demonstrated high performance in detecting MI and pT1a BC, despite co-existent DCIS enriched for potentially confounding alterations. With further studies, this approach holds promise for enhancing diagnostic accuracy and consistency in detection of MI and T1a BC, enhancing pathologist workflow, reducing time spent on identifying small foci of BC, and potentially minimizing the need for IHC. Evaluation of the impact of the AI solution on pathologist time-saving and accuracy is underway, and results will be presented.

OFP-01-005
Cross-platform analysis of MMR deficiency in breast cancer reveals the need for tumour-specific recommendations and guidelines
M. Ivanova*, C. Frascarelli, K. Venetis, G. Cursano, E. Mane, E. Sajjadi, M. Noale, S. Maggi, M. Lombardi, M. Fassan, C. Scatena, E. Guerini Rocco, N. Fusco
*Division of Pathology, European Institute of Oncology IRCCS Milan, Italy
Background & objectives: Breast cancers (BC) with MMR deficiency (dMMR)/microsatellite instability (MSI) are <5%. Although these patients may benefit from immune checkpoint inhibitor (ICI) therapy, no BC-specific testing strategies are currently available. We aimed to assess MMR/MSI testing reproducibility in BC across platforms.
Methods: 1022 BC samples underwent immunohistochemistry analysis for four MMR proteins (MLH1, MSH2, MSH6, PMS2) on three major platforms: Leica (A), Ventana (B), and Dako (C). dMMR was defined by the immunoreactivity loss in any of the markers. Upon biomaterials' availability, dMMR cases were further analyzed using MSI LMR (Promega) kit. Interplatform agreement was evaluated using Cohen's and Fleiss κ coefficients.
Results: dMMR was observed in 22 (2.4%), 57 (6.3%), and 39 (4.3%) cases on platforms A, B, and C, respectively. Platforms A-B and B-C agreements were none (n=10; 1.1%; κ -0.37 and n=15; 1.7%; κ -0.71); A-C agreement was poor (n=17; 1.9% cases; κ 0.15), (p<.001). Overall, the agreement among all platforms was negligible (n=8; 0.9% cases; Fleiss' κ -0.2). MSI analysis of 8 dMMR samples in all three platforms resulted in 5 (62.5%) to be MSI. Additionally, of the 66 dMMR samples identified on at least one platform, only 13 were available for MSI analysis, revealing 3 (23%) MSI cases.
Conclusion: Despite dMMR/MSI is a rare phenomenon in BC, the clinical relevance of this biological condition has become evident following the IC tumour-agnostic approval for all dMMR solid tumours. Our research underscores the challenges in assessing MMR status in BC using methodologies developed for other tumour types and conditions. To accurately identify patients who could benefit from ICI, efforts should focus on developing BC-specific testing recommendations. This includes establishing criteria for retained immunoreactivity and accurately classifying tumours with true dMMR status.

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OFP-01-006
Can artificial intelligence models be color blind: an example in grading breast cancer
L. Dalton*
*Dalton Pathology Research, USA

Background & objectives: The paper introducing Nottingham grading presented images only in black and white (grayscale), from which pathologists learned. A curiosity was if AI could similarly learn from grayscale images. Additionally, use of grayscale provides an advantage of requiring less memory.
Methods: Training set comprised TCGA images from Mayo Clinic, Walter Reed, Roswell Park, and Univ. Pittsburgh (N=196). Images from all other institutions (N=320) formed test set. 250*250 pixel images limited AI predictions to a pleomorphism grade only. Color images were compared to their grayscale counterparts. Using Python, "generic" TensorFlow/Keras-based convolutional neural network models were built.
Results: For each case the fraction of images or tiles predicted as being high grade (FHGT) was unit of measure. Grayscale FHGT was highly correlated with color, showing a Spearman rho of 0.93. With pathologist determined pleomorphism score 3 as response variable, grayscale FHGT had AUC=0.861 [0.8196-0.9018], while color reached 0.845 [0.8041-0.8882]. Of the 220 test cases with corresponding mRNA data, grayscale FHGT had rho=0.46 with MKI67, and color had 0.43. Gradient boosting identified GBP1 as the gene most predictive of color FHGT, and ORC6 for grayscale; both genes are linked to tumour proliferation. The color folder of 113,007 test set PNG images occupied 4.7 GB, whereas grayscale required 2.9 GB.

Conclusion: Is AI color blind? In grading breast cancer, the use of grayscale images showed high correlation with color. Or, using grayscale as a baseline, the addition of color provided no added value, despite requiring 67% more memory. This suggests that AI, as do pathologists, focus on attributes which do not require color. This should be of no surprise to more elderly and wiser pathologists who first learned from the Elston-Ellis paper. Grayscale evaluation alongside color is easy to do.

OFP-01-007

Can complete shaved margin assessment identify a subset of DCIS that can be safely treated by breast conservative surgery alone?

S. Ichihara*, T. Kawasaki, S. Moritani, T. Nakai, M. Ohmori
*Nagoya Medical Center, Japan

Background & objectives: Radiation therapy (RT) for women with ductal carcinoma in situ (DCIS) undergoing breast-conserving surgery (BCS) may be overtreatment. This study was to clarify whether the polygon method identify a subset of DCIS that can be safely treated by BCS alone.
Methods: A key tool of this method is an adjustable mold that prevents the "pancake phenomenon" (Graham 2002) after surgical removal so that the specimen is fixed in the shape of a polygonal prism. Competing risk analysis was used to quantify rates of ipsilateral breast tumour recurrence (IBTR) and contralateral breast cancer (CBC) and to evaluate risk factors.
Results: From 2000 to 2013, we identified 146 DCIS patients undergoing BCS with a contralateral breast at risk. In 100 DCIS patients whose margin was negative by the polygon method, 5 IBTR (3 DCIS and 2 invasive ductal carcinomas [IDC]) and 10 CBC (6 DCIS and 4 IDC) cases were identified during a median follow-up of 7.6 years (range, 0.9-17.4). Ten-year cumulative incidence rate was 5.3% for IBTR, and 13.3% for CBC, respectively. Thus, patients with a negative margin consistently showed at least twofold lower IBTR than CBC despite omission of RT.
Conclusion: Japanese women classified with a negative margin by the polygon method show a very low risk of IBTR and account for approximately half of CBC cases, suggesting the DCIS is eradicated. In this subset of DCIS patients, additional RT is not beneficial. This result also supports the hypothesis that the high proportion of upper outer quadrant carcinomas of the breasts is a reflection of the greater amount of breast tissue in this quadrant.

OFP-01-008

Interassay comparison of four clinically approved HER2 immunohistochemistry assays in primary breast cancer and their metastasis

M.A. Hempenius*, M.C. Zwager, M.A. den Bakker, M. Coster-Heerema, E.G.E. de Vries, C.P. Schröder, N.A. 't Hart, B. van der Vegt
*Department of Pathology and Medical Biology, University of Groningen, University Medical Center Groninngen, Groningen, The Netherlands

Background & objectives: Trastuzumab-deruxtecan has been approved for treatment of advanced HER2-low breast cancer. However, HER2 expression levels might differ between primary tumours and metastases across the various clinically approved HER2 immunohistochemistry (IHC) assays, potentially leading to differences in eligibility for this treatment.
Methods: Tumour samples from 101 patients with metastatic breast cancer participating in the IMPACT-MBC study (ClinicalTrials.gov #NCT01957332) were included in tissue microarrays. Slides were stained in four laboratories using clinically approved antibodies: 4B5/Ultraview, 4B5/OptiView, SP3, and DG44 (Herceptest). HER2 staining was quantified using a CE-IVD-approved image analysis algorithm allowing objective comparison between primary tumours and metastases and between IHC assays.
Results: Ninety-one patients were eligible for analysis. Preliminary results show marked differences between antibodies: DG44 showed 35 (19.2%) IHC HER-low (1+ and 2+) samples out of 182 paired samples from primary and metastatic tumour. 4B5/Ultraview), 4B5/OptiView), and SP3 identified fewer cases but showed greater comparability (19 (10.4%), 22 (12.1%), and 24 (13.2%) samples, respectively). DG44 exhibited the most variability in HER2 scores between the primary tumour and its metastasis, with 28 (30.8%) of the 91 patients receiving a different HER2 score on the metastasis compared to 19 (20.9%) patients for both 4B5/Ultraview and 4B5/OptiView, and 15 (16.5%) for SP3.
Conclusion: HER2 scores vary markedly between different clinically approved HER2 antibodies, both in primary tumours and their corresponding metastasis, and across different antibodies. Especially DG44 deviated from the other antibodies. Discrepancies in testing methods could impact patient selection for Trastuzumab-deruxtecan treatment. Diagnostic HER2 antibody optimisation or alternative predictive testing methods are needed and should be linked with outcome data.

OFP-01-009

Detection of human papillomavirus DNA in basal-like subtype of invasive breast carcinoma: possible pathogenetic role of the virus

G. Tinnirello*, J. Farina, S. Salzano, F. D'Aquila, M. Mazzucchelli, G. La Cava, G. Angelico, A. Santoro, A. Mulè, G. Pannone
*Department of Medical, Surgical Sciences and Advanced Technologies "G.F. Ingrassia", Anatomic Pathology, University of Catania, Catania, Italy., Italy

Background & objectives: The role of oncogenic HPVs in breast cancer development is still debated. The aim of this study is to detect HPV DNA in basal-like carcinomas of the breast, through genotyping and p16 positivity by immunohistochemistry.
Methods: Our cohort consisted of 36 female patients with histologically and immunohistochemically confirmed mammary basal-like carcinoma. As a control group, ten randomly selected cases of invasive ductal G3 NST carcinomas were employed. All cases were investigated by immunohistochemistry for p16 and by DNA PCR. In detail, HPV16-18-31-33-45 DNA genotypes were researched.
Results: 28 cases out 36 showing p16 immunohistochemical overexpression were selected for molecular biology analysis. Amplification of DNA samples showed single HPV DNA infection in 10 cases (HPV16 in 4 cases; HPV18 in 2 cases; HPV45 in 4 cases). Single HPV DNA infection has also been observed in 4 controls of G3 ductal carcinoma NOS and double infection has been reported in only one control (HPV16/HPV18). The overall HR-HPV prevalence was 35,7% in breast basal-like carcinomas.
Conclusion: The results of the present study confirm that HPV DNA can be isolated in breast carcinoma with basal-like phenotype and therefore it might contribute to the carcinogenic process. The investigation of oncogenic gene expression in HPV-related basal-like breast cancer could have a potential value as predictor of neoplastic progression, therapeutic response and clinical outcome. By identifying among basal-like carcinomas, a subgroup characterized by HPV infection (35,7%), this study has shown that high risk HPV could contribute to breast carcinogenesis.

OFP-01-010

Is knowledge of HER3 as a prospective therapeutic biomarker necessary for pathologists?

L. Gao*, Y. Zhang, M. Feng, M. Shen, L. Yang, B. Wei, Z. Zhang
*West China Hospital, China

Background & objectives: HER3, lacking significant kinase activity, commonly partners with HER2 to activate oncogenic pathways, fueling metastasis and resistance in breast cancer. The study assesses HER3 expression and its relationship with HER2, focusing on potential treatments such as anti-HER3 antibodies and ADCs.

Methods: HER3 immunofluorescence assays (IF)were performed on breast cancer cell lines, and 46 invasive breast cancer cases from West China Hospital's Pathology Department were selected for tissue microarrays and immunostained for HER2 and HER3. The cases were categorized into three groups by HER3 expression levels: <25% (Group 1), 25-74% (Group 2), and ≥75% (Group 3), using ASCO/CAP guidelines for interpretation.
Results: IF display shows that SKBR3 and MDA-MB-453 cells exhibit strong positive membrane expression of HER3, as well as T-47D and BT474 cells, while MDA-MB-231 cells show no HER3 membrane expression. Immunohistochemical results indicated that HER3 expression was localized to both the cell membrane and cytoplasm. Notably, all 46 patients included in the study had a poor prognosis, having died or experienced recurrence and metastasis. The results showed that G1(6/46,13%), G2(20/46,43.5%), G3(20/46,43.5%). Additionally, within the subgroup of HER2 overexpression (HER2 3+), 91.7% (22/24) of the tissues demonstrated varying levels of HER3 expression.
Conclusion: We detected membrane expression of HER3 in HER2-overexpressing and Luminal-A/B breast cancer cell lines and used immunohistochemistry to qualitative and localization detection of HER3. In HER2-overexpressing (HER2 3+) tumour tissues, we found a potential correlation between HER3 overexpression and HER2 overexpression. However, whether HER3 expression is associated with disease progression and poor prognosis requires further in-depth analysis. HER3-Dxd has ignited the flames of anti-HER3 therapy, and we need to study HER3 more deeply and extensively in the laboratory.

OFP-01-011
Estrogen-negative invasive lobular carcinoma of the breast: a multicentric clinical-pathological study
S. Marletta*, M. Dello Spedale Venti, V. Idda, P. Vigneri, G. Di Grazia, A. Cremonini, L. Amedei, A. Rizzo, R. Miglio, A. Tafà, A. Baldissera, E. D'Angelo, M.C. Cucchi, A. Maestri, M.P. Foschini
*Division of Pathology, Humanitas Istituto Clinico Catanese, Catania, Italy

Background & objectives: Invasive lobular carcinoma (ILC) accounts for 5-15% of all invasive breast carcinomas (IBCs) and almost invariably expresses estrogen receptors (ER). Albeit rare, ER-negative ILCs have been accustomed to a worse long-term prognosis compared to conventional IBCs with similar immunophenotypes.
Methods: In the present work, we sought to investigate the clinical-pathological features of a series of fifty-seven ER-negative ILCs. The collected samples were studied for their morphological findings and tested with an immunohistochemical (IHC) panel including ER, PR, Ki67, HER2, AR, and GCDFP15. FISH analysis was performed in equivocal HER2 cases at IHC. Follow-up data were recorded from electronic databases.
Results: The patients aged from 37 to 91 years old (median 78). ER-negative ILCs represented the first cancer presentation or a following recurrence in 89% (51/57) and 11% (7/57) of the cases respectively. Some patients (8/57, 14%) underwent neoadjuvant chemotherapy. Histologically, pleomorphic ILCs made up roughly half of the cases (26/57, 47%). A significant percentage of the samples (12/57, 21%) revealed apocrine features. Most tumours (46/57, 81%) belonged to the triple-negative category, whereas the remaining ones (11/57, 19%) were classified as HER2+. During follow-up, a noteworthy proportion of the patients (25/57, 44%) developed either distant metastases (19/57, 33%) or further local recurrences (6/57, 11%).
Conclusion: ER-negative ILCs of the breast are uncommon indeed but frequently display aggressive behavior due to their intrinsic biological characteristics and the lack of response to conventional chemo- and hormone therapy. Our data provide novel insights into this exceedingly rare subset of breast carcinomas, advocating a strict clinical follow-up. Further studies investigating their biological hallmarks and targeting eventual pathogenetic drivers, like, for instance, the apocrine phenotype, are warranted to overall improve patients' clinical management and, ultimately, their outcomes.

OFP-01-012
Subareolar sclerosing ductal hyperplasia shows PI3K pathway alterations
B. Boyraz*, B.D. Robinson, N. Lindeman, S.A. Hoda, J. Solomon
*Weill Cornell Medicine, USA

Background & objectives: Subareolar sclerosing ductal hyperplasia (SSDH) is a distinct type of complex sclerosing hyperplastic lesion first described by Rosen (Cancer, 1987). There have been rare studies investigating SSDH; however, no genetic study has been performed to date.
Methods: Seven SSDH cases diagnosed between 2013-2024 were identified. All were subjected to DNA sequencing using TruSight Oncology 500 panel (523 genes).
Results: All seven patients were female (age range 40 to 74 years, median 46). 5 were in left and 2 in right breast; radiologically all were localized to subareolar region. 4 were excisions and 3 were core biopsies. The lesions ranged from 0.6-1.4 (median 0.7) cm. All showed the characteristic appearance of the lesion, as described, with usual ductal hyperplasia in a densely sclerotic background imparting an "infiltrative" appearance. None of the cases showed atypical hyperplasia or carcinoma. DNA sequencing identified PI3K pathway alterations in all: PIK3CA (n=3, all with p.H1047R and 1 with a second alteration), PIK3R1 (n=3), PIK3C3 (n=1, with concurrent FAT1 mutation).
Conclusion: SSDH shows PI3K pathway alterations similar to those seen in other similar proliferative lesions of the breast (i.e., radial scar, infiltrating epitheliosis) and these lesions may possibly be classified as pre-neoplastic rather than hyperplastic. This finding may explain the rare association of SSDH with atypical hyperplasia/carcinoma.

OFP-01-013
The effect of fixation time on HER2-low status in breast carcinoma
S. Nofech-Mozes*, F. Lu, E. Slodkowska, A. Plotkin, E. Olkhov-Mitsel
*Sunnybrook Health Sciences Centre, Canada

Background & objectives: Optimal tissue fixation is critical for consistent HER2 testing quality. ASCO/CAP advises fixation for 6-72 hours. This audit assesses fixation time adherence and its effect on HER2-low (HER2-L) prevalence in a large academic centre with a reference laboratory.
Methods: The laboratory information system identified all HER2 reports on breast specimens between Jan 2023-Apr 2024. Assessment was carried out by 4 breast pathologists following ASCO/CAP guideline recommendations, aware of the definition and implications of HER2-L category (IHC 1+ or 2+ with a negative FISH result). Cases were classified according to fixation time 6-72h; >72-96h; >96h and unknown fixation time.
Results: Among 2915 breast specimens tested, 2325 (79.8%) were fixed for 6-72h, 300 (10.3%) 72-96h, 15 (0.5%) >96h and 275 (9.4%) unknown. HER2 positivity was 15% (438 cases; 324 IHC3+ and 114 IHC2+/amplified), with 1915 (65.7%) HER2-L and 562 (19.3%) HER2 negative (IHC 0) cases. In HER2 positive cases, 15.2% were fixed for 6-72h, 15.3% 72-96h, 6.7% >96h, and 13.5% unknown. HER2-L cases showed similar variability, with 66.2% fixed 6-72h, 60.0% 72-96h, 66.7% >96h, and 67.6% unknown. Among HER2 negative cases, 18.6% fixed for 6-72h, 24.7% 72-96h, 26.7% >96h, and 18.9% unknown. No significant association was found between the distribution of HER2 scores and fixation time over 72h (P=0.203).
Conclusion: In our reference laboratory, servicing 7 hospitals, the fixation time was known and adherent to ASCO/CAP recommendations in only 80% of breast specimens. In most cases with over-fixation, fixation time was less than 96 hours, likely representing workflow interruptions during statutory holidays. There was no significant difference in HER2-L category between breast specimens and fixation time categories.

OFP-01-014

Comparing HercepTest (GE001) and Ventana HER-2/neu (4B5) in the lower spectrum of HER2 expression

H. Schildhaus*, M. Sierra, C. Koppel, A. Tereshchenko, D. Iievlieva, J. Berg, G. Bänfer, G. Noumsi
*Discovery Life Sciences, Germany

Background & objectives: The performances of HER2 assays across HER2 expression range is relevant in the context of new Anti-HER2 ADCs therapy. Here, we compare two approved HER2 assays in low expressing breast cancer specimens, focusing on discrimination between null expression and "ultra-low".
Methods: Slides from 50 archived FFPE tissues with HER2 expression level from 0 to 2+ as previously determined by 4B5 were tested with the GE001 assay on the DAKO Omnis. Stained slides were scored independently by three pathologists. IHC score 0 were further divided between HER2 null (no staining), and HER2 "ultra-low" (incomplete, faint/barely perceptible staining in ≤10% of tumour cells).
Results: Concordance between 4B5 and GE001 was 56.0% (28/50) when following ASCO/CAP HER2 scoring guidelines. The number of samples reported as HER2 0 was more than doubled with 4B5 when compared to GE001 (25 versus 11). GE001 identified 35% more HER2 1+, and more than twice as many HER2 2+ as 4B5. Among the 10 samples initially classified as HER2 null by 4B5, 7 were scored as HER2 1+ by GE001. Similarly, for 15 cases classified as HER2 "ultra-low" by 4B5, results with GE001 showed: 7 cases scored as HER2 0, 7 cases as HER2 1+, and 1 case as HER2 2+. No differences were found in the HER2 2+ category.
Conclusion: The HER2 "ultra-low" category is not currently recognized as a target for new HER2 anti-ADCs. However, this could change soon depending on the results of ongoing clinical trials. If this becomes the case, HER2 assays must provide supporting evidence on their capability to accurately differentiate HER2 null from HER2 "ultra-low". GE001 seems to exhibit greater sensitivity towards the lower range of HER2 expression compared to 4B5. Additional research is required to understand the biological reasons for these disparities.

OFP-01-015

Tumour stroma characterization for the clinical stratification of HR+/HER2- breast cancer

C. Scatena*, G.N. Fanelli, E. Belcastro, F. Di Cocco, A. Fontana, A. Szumera-Ciećkiewicz, M. Loda, A.G. Naccarato
*University of Pisa, Italy

Background & objectives: Tumour microenvironment (TME) plays a pivotal role in the prognosis and therapeutic response in several types of cancer. Our study aimed to characterize TME cellular composition of HR+/HER2- breast cancer (BC) to gain insight into tumour development and disease progression.
Methods: Tissue Microarrays from 70 HR+/HER2- BC patients have been created. Imaging analysis (HALO®) was used to assess immunohistochemical expression of senescence markers (p16, α-SMA) and collagen (Masson stain). Statistical analysis was performed using GraphPad Prism Software. The study was approved by the local Ethical Committee. The project was partially funded by the 2023 Fellowship Program promoted by Gilead Sciences.
Results: Nuclear p16 expression in stromal cells was significantly higher in the non-metastatic than in the metastatic group (P=0.02). Survival analysis showed that % of α-SMA expression in stromal cells higher than 30 (median value) is indicative of a poor prognosis. In detail, patients with α-SMA expression exceeding 30% exhibit significantly shorter overall survival (Chi-square=6.635 and P=0.0100) compared to those with lower expression levels. Moreover, correlation analysis showed that deposition of collagen (quantified as the area of collagen/total area of tissue core) was associated with the proliferative index of cancer cells (P=0.008).
Conclusion: This study confirms the complexity of TME in BC and proposes novel markers for assessing metastatic risk. Specifically, p16 may not function as inductor of TME senescence, but instead could be degraded through an IL-6-mediated mechanism, as recently proposed. In addition, our data confirm the negative impact of α-SMA on patient survival. As for collagen, further comprehensive investigations are needed to elucidate its potential impact on patient outcomes.

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OFP-02Joint Oral Free Paper Session Gynaecological Pathology / Cytopathology

OFP-02-001

Next generation of interventional pathologists, ultrasound-guided fine needle aspiration / core needle biopsy and rapid on-site evaluation, resident training

H. Torres-Rivas*, L.M. Fernández Fernández, M.L. Berrios Hernández, M.P. González Gutiérrez, N. Zapico Ortiz, J.R. Riera Velasco, J.F. Pérez Fontán, M.d.M. Del Olmo Fernández, K. Villar Zarra
*Hospital Universitario Central de Asturias, Spain

Background & objectives: The role of the interventional pathologist is relatively unknown, and the training of pathology residents in ultrasound-guided interventional procedures for specimen collection is limited in most pathology departments. We present our teaching experience in ultrasound-guided FNA/CNB to pathology residents.
Methods: The training of pathology residents who rotated through the interventional unit of the pathology department and the application of the U-ROSE methodology (Ultrasound-guided FNA/CNB plus Rapid On-Site Evaluation) was systematized and documented over 5 years. The training period was broken down into learning phases, and the number of ultrasound-guided FNA/CNB performed by the resident was recorded.
Results: 19 pathology residents were trained in the U-ROSE methodology, and performed a total of 4003 procedures, with an average of 211 per resident. In 53% of the cases, only 1 pass was performed. The sample was valid in more than 97%. The most frequently biopsied anatomical sites were the thyroid gland (n=2347), followed by the lymph node (n=667), soft tissues (n=663), and salivary glands (n=322). In 10% of the cases, CNB was performed.
Conclusion: The results obtained support the teaching system followed by pathology residents in learning U-ROSE, which is essential to lay the foundations for future interventional pathologists.

OFP-02-002

An institutional experience: comparing risk of malignancy and diagnostic rates with a newly published reporting system for lung cytopathology

X. Jing*, X. Jin, M. Lew, B. Smola, T. Huang
*University of Michigan, USA

Background & objectives: Our institution utilizes diagnostic frameworks similar to those of WHO Reporting System for Lung Cytopathology (WHORSLC) for lung fine needle aspiration (FNA) specimens. This study reports risk of malignancy (ROM) across diagnostic categories for comparison with those of WHORSLC.
Methods: A SNOMED search of the electronic pathology database in our institution (01/2022-12/2023) was conducted to retrieve endobronchial ultrasound (EBUS)-guided lung FNA specimens with concurrent or subsequent surgical biopsies. Cytologic interpretation of these FNA specimens were performed by board-certified cytopathologists using similar diagnostic frameworks to WHORSLC. Diagnostic distribution and ROM across the diagnostic categories were evaluated.

Results: A total of 280 lung cytology specimens were identified. Among which, 62, 45, 33, 15, and 125 were categorized as non-diagnostic, benign, suspicious for malignancy, and malignant, respectively. The corresponding surgical biopsies showed various ROM among these diagnostic categories as follows: 35% (22/62) in non-diagnostic, 20% (9/45) in benign, 57% (19/33) in atypical, 100 (15/15) in suspicious for malignancy, and 100% (125/125) in malignant categories. Lung adenocarcinoma represented a large subset of diagnosed malignancy in non-diagnostic (54%), benign (44%), suspicious for malignancy (66%) and malignant (48%) categories while the atypical category had more metastatic carcinoma and non-carcinoma.
Conclusion: 1. Using diagnostic frameworks similar to the WHORSLC, EBUS-guided lung FNA specimens categorized as malignant or suspicious for malignancy have a higher ROM and concordance with concurrent or subsequent surgical biopsies (100% in our study).
2. Compared to the estimated ROM implied by the WHORSLC, our study resulted in a similar ROM for benign, atypical, and malignant categories while a greater ROM was evident in both non-diagnostic and suspicious for malignancy categories.

OFP-02-003
Relevance of cytopathologist-performed palpation-guided fine needle aspiration in the age of image-guided biopsy
B. Sepodes*, V. Almeida, J.P. Maldonado, J. Pimentel, G. Fernandes
*Unidade Local de Saúde de Coimbra, Portugal

Background & objectives:
Recently, cytopathologists have increasingly utilized ultrasound-guided fine needle aspiration, while palpation-guided aspiration remains prevalent elsewhere. Our objective is to analyze diagnostic and non-diagnostic rates, exploring the influence of lesion characteristics, size, number of passes, and procedural performance on outcomes.
Methods: We retrospectively reviewed medical records encompassing pathologist performed palpation-guided fine needle aspirations between 2021 and 2023. Data were collected on lesion location, size, number of passes, and cytology diagnosis. Diagnostic cytology diagnoses were established based on concordance with histopathologic findings, flow cytometry results, and/or clinical follow-up spanning at least six months. The diagnostic and non-diagnostic rates were evaluated.
Results: A total of 201 cytopathologist-performed palpation-guided fine needle aspirations were included in the analysis. Fine needle aspirations were performed at various anatomical sites, with head and neck sites being the most frequent. Over the three years, the diagnostic rate was 80%, while the nondiagnostic rate was 13%. Scalp lesions exhibited and the highest non-diagnostic rate (29%). Lesion sizes ranged from 0.5 to 12 cm, with lesions smaller than 1 cm demonstrating the highest non-diagnostic rate (33%). The total number of passes ranged from 1 to 5, with the highest non-diagnostic rates observed in cases with one pass (27%) and five passes (29%).
Conclusion: Pathologist-performed palpation-guided fine needle aspiration remains effective, yielding diagnostic results in 82% of cases. However, the diagnostic rate diminishes for lesions smaller than 1 cm, when only one pass is made, and for scalp lesions. Conducting more than four passes did not enhance the diagnostic rate.

OFP-02-004
Intra and interobserver reproducibility in histopathologic diagnosis of follicular neoplasms: how does it affect the rate of malignancy in the "follicular neoplasm" category of the thyroid fine needle aspiration cytology?
A. Noyan*, O. Kurtulan, S. Onder, C. Sokmensuer, Y.G. Guler, H. Avci
*Hacettepe University Department of Pathology, Turkey

Background & objectives: There are discrepancies in diagnoses of thyroid follicular neoplasms (FN) among histopathologists. We aim to investigate the intra-interobserver variability between histopathologists and its impact on the rate of malignancy (ROM) for FN category of thyroid fine needle aspiration (FNA) cytology.
Methods: Cases of thyroid FNA diagnosed as FN with subsequent resection were listed. The representative histopathologic slides in which FNA was performed were reviewed by two endocrine pathologists who signed out the cases initially. The diagnoses were categorized as benign, low-risk neoplasm, and malignant according to the WHO Classification of Endocrine Tumours. Intra and interobserver variability and the ROM were assessed.
Results: Of 60 cases, 27 were initially signed out by reviewer 1, and 33 by reviewer 2. Thirty-two cases were diagnosed as benign, 6 low-risk neoplasms, and 22 malignant. After re-evaluation, 17 (28.3%) cases were re-categorized by reviewer 1 and 24 (40%) by reviewer 2. Cases were re-categorized due to the changes in the interpretation of papillary nuclear features (28.3%), capsular invasion (28.3%), and the interpretation of NIFTP diagnosis (11.6%). The weighted kappa value of intraobserver reproducibility was 0.653 (substantial) and 0.387 (fair) for reviewers, respectively. Interobserver agreement was substantial (kappa value = 0.662). The ROM for initial diagnoses was 36.6%, which changed to 30% and 33.3% for the reviewers respectively.
Conclusion: There was a discernible degree of intra-interobserver variability among histopathologists, attributable primarily to the interpretation of papillary nuclear features and capsular invasion. Although 28.3% of cases were histologically re-categorized, there was only a slight change in the ROM. Thus, the risk of malignancy for the "follicular neoplasm" category of thyroid FNA cytology remained similar despite intra-interobserver variability.

OFP-02-005
Prognostic value of tertiary lymphoid structures in endometrial carcinoma
M. Pradhan*, W. Kildal, L. Vlatkovic, K. Lindemann, K.A. Risan Tobin, G. Kristensen, A. Kleppe, H. A. Askautrud
*Institute for Cancer Genetics and Informatics, Oslo University Hospital, Norway

Background & objectives: Tertiary lymphoid structures (TLS), organized aggregates of lymphoid cells, are reported as an immunological prognostic marker. We have evaluated the prognostic importance of TLS in patients with endometrial carcinoma using L1 cell adhesion molecule (L1CAM) as a surrogate marker.
Methods: The cohort consists of 1228 endometrial carcinoma patients (880 endometrioid and 348 non-endometrioid) treated at Oslo University Hospital between 2006 and 2017. Formalin-fixed and paraffin-embedded tissue samples from the hysterectomy specimens were sectioned and one section was immunohistochemically stained with antibody against L1CAM to evaluate the presence and number of TLS. Sections with $\geq$1 TLS were considered as TLS positive.
Results: Out of 1197 evaluable sections, 911 (76%) sections were TLS negative, while 286 (24%) were TLS positive. In TLS positive sections, the median number was 3 (IQR 1-6). TLS positive patients had a significantly lower risk of recurrence (HR 0.60; 95% CI 0.45-0.8, p<0.001) compared to TLS negative patients in univariable analyses. In molecular subgroups, TLS were more frequently present in tumours with POLE mutation (59%) and MMR deficiency (32%) than in tumours with p53 abnormality (16%) and no specific molecular profile (15%). In patients with MMR deficiency and p53 abnormal tumours, presence of TLS was prognostic with HR of 0.6 (CI 0.37-0.98, p=0.042) and 0.6 (CI 0.68-1.99, p=0.056), respectively.
Conclusion: Evaluation of TLS using L1CAM might provide additional prognostic information for endometrial carcinoma patients with MMR deficiency. A similar indication was observed for patients with p53 abnormality, but further studies are needed to confirm the prognostic value in this subgroup. TLS were predominantly found in POLE mutated and MMR deficient tumours. These findings corroborate with a previous study investigating the correlation and prognostic value of TLS in molecular subgroups using a much smaller patient cohort.

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OFP-02-006

Immunomorphological evaluation of neuroectodermal tissue in immature and mature ovarian teratomas: significance of morphology and role of SOX2 expression

A. Orsatti*, C. Ricci, S. Tenti, G. Tallini, A.M. Acosta, A. De Leo
*University of Bologna School of Medicine, Bologna, Italy, Italy

Background & objectives: Ovarian immature teratoma (IT) is graded by the presence of immature neuroectodermal tissue, challenging to distinguish from mature ependymal tubules/rosettes and cerebellar tissue of mature teratoma (MT). The study aims to define the immunomorphological characteristics of neuroectodermal tissue in teratomas.
Methods: We collected 10 ITs and 50 MTs, 17 of which contained abundant neural tissue including mature ependymal tubules/rosettes. Immunohistochemistry (IHC) for SOX2 was performed to define expression in tissue components of the three germ layers. Immunomorphological characteristics of neuroectodermal tissue (immature and mature) were carefully reviewed according to the study by Robert Scully in 1987.
Results: SOX2 was consistently and strongly positive in both mature (ependymal) and immature neuroectodermal rosettes and immature/mature glia; it was also variably positive in bronchial epithelium, peribronchial glands, salivary glands, and basal squamous epithelial cells. Neuronal cells (including cerebellar granule cells) were consistently negative, as were meningothelial tissue and immature mesenchymal component. SOX2 does not differentiate immature neuroepithelial rosettes from mature ependymal tubules/rosettes. This difference was only based on the identification of the following histological features in immature neuroepithelial rosettes: presence of mitotic activity, apoptosis, necrosis, severe atypia, pseudostratification. Based on the morphology of SOX2-positive rosettes after case review, two cases previously diagnosed as IT were revised and downgraded to MT.
Conclusion: The grading of immature teratoma can be better defined through the identification of SOX2-positive immature neuroectodermal tissue. However, this study shows that SOX2 is also positive in mature ependymal tubules/rosettes and mature glia and is a marker expressed in several tissues. The correct evaluation of immature neuroepithelial tissue is still based on histological features, but SOX2 expression may be useful for differential diagnosis with granular layer of mature cerebellar tissue.

OFP-02-007

Histotype and grade are of prognostic significance only in the No Specific Molecular Profile (NSMP) molecular subtype of endometrial carcinoma

J. Huvila, A. Jamieson, J. McAlpine, B. Gilks*
*University of British Columbia and Vancouver General Hospital, Canada

Background & objectives: Histotype and grade of endometrial carcinoma are used in risk assessment. The aim of this study was to analyze the prognostic significance of grade (low-grade versus high-grade) and histotype (endometrioid, serous, other) within each molecular subtype, with stratification by stage.
Methods: Five different previously reported case series of patients with endometrial carcinoma were investigated separately and then as a combine cohort of 2482 cases. Disease specific survival was compared for tumours of each molecular subtype after stratification of patients into one of four groups: low-grade endometrioid, high-grade endometrioid, serous, and other (all other histotypes e.g. clear cell, dedifferentiated/undifferentiated, mesonephric-like etc.)
Results: In the combined cohort (N=2482) grade and histotype were prognostically significant for tumours of all stages and when just considering stage I tumours. Grade and histotype were not of prognostic significance in POLEmut or p53abn endometrial carcinomas of all stages or within stage I carcinomas. In MMRd endometrial carcinoma, low-grade endometrioid carcinomas were associated with a better prognosis, however low grade was also associated with lower stage, and within stage I tumours grade and hisotype were not of prognostic significance. Grade and histotype were of prognostic significance in NSMP endometrial carcinomas, in both the cohort as a whole and in stage I tumours ($p < 0.001$ for both analyses).
Conclusion: Grade and histotype are not of prognostic significance in p53abn and POLEmut endometrial carcinomas. A high-grade MMRd endometrial carcinoma identified on biopsy is more likely to be advanced stage, compared to a low-grade carcinoma, but histotype and grade are not of prognostic significance in MMRd endometrial carcinomas independent of stage. Histotype and grade are strongly associated with prognosis in NSMP endometrial carcinoma.

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OFP-02-008

Uterine leiomyomas during pregnancy: morphologic, immunohistochemical characteristics, and pitfalls in correlation with outcome

J. Mirkovic*, E. Olkhov-Mitsel, C. Parra-Herran
*Sunnybrook Health Sciences Centre, Canada

Background & objectives: Uterine leiomyomas during gestation often exhibit changes concerning for malignancy, such as increase in size and necrosis. We characterize the full spectrum of morphologic changes seen in uterine leiomyomas excised during pregnancy, focusing on changes attributed to malignant mesenchymal neoplasms.
Methods: Two expert pathologists reviewed 97 specimens (2015-2022) and recorded morphologic features. Immunohistochemistry for ER, Desmin, ALK, Caldesmon, CD10, CyclinD1, PR, p53, ATRX, MTAP, RB, PTEN, HMB45 and MelanA was performed on tissue microarrays (2 cores/tumour). Clinical data, including follow-up information, were obtained from electronic medical records.
Results: Mean age was 37 years (27-55). Mean leiomyoma size was 4.3 cm (0.7-16). With a mean follow-up of 19 months (0-80) none developed malignancy.
Ischemia often mimicked geographic necrosis with sharp border between viable and non-viable tumour (23%), cell ghost outlines (51%) and perivascular preservation (9%). Focal (<30%) myxoid change occurred in 42%, and moderate atypia in 9%. Most cases exhibited no mitoses (74%). Only one case reached 10 mitoses/10-HPF.
Desmin, caldesmon, PR were diffusely positive in 93%, 82% and 61%, while 65% were negative for ER. ALK was positive in 6%, always focal (up to 5% of tumour). p53, ATRX, MTAP, PTEN, RB showed retained/wild-type expression in all cases.
Conclusion: Uterine leiomyomas excised during pregnancy frequently exhibit changes that are attributed to malignant mesenchymal neoplasms (including necrosis that is difficult to subtype, myxoid change, focal expression of ALK, loss of ER staining). Despite this, clinical follow-up revealed no adverse outcomes in this cohort to-date. Pathologists should be aware of these potential pitfalls and avoid a diagnosis of malignancy or uncertain malignant potential (STUMP) in a smooth muscle tumour in the setting of pregnancy.

OFP-02-009

Reproducibility of eosinophilic cells in ovarian serous borderline tumour with BRAFV600E mutation

A. Asaturova*, A. Badlaeva, A. Tregubova, A. Rogozhina, D. Bulanov, N. Lysova
*NMRS for Obstetrics, Gynecology and Perinatology named after V. Kulakov, Russia

Background & objectives: Ovarian serous borderline tumour with BRAFV600E mutation is associated with lower risk of progression to low-grade serous carcinoma. Since eosinophilic cells (ECs) are a marker of above-mentioned mutation, we evaluated the sensitivity and specificity for assessing this histological feature.
Methods: A dataset was consisted of 42 samples of ovarian serous borderline tumours and analyzed for the extent of ECs. The last were characterized by abundant eosinophilic cytoplasm. For BRAFV600E verification mutation status all cases underwent immuhistochemical staining (with anti-BRAF antibody) and genetic profiling by a Sanger sequencing. The accuracy of ECs was measured with sensitivity and specificity.
Results: BRAFV600E mutation was found in 45% serous borderline tumours (19/42). Interobserver reproducibility for estimating the extent of ECs was substantial (κ=0.7). The sensitivity and specificity for predicting BRAFV600E mutation were 78.9% and 91.3%, respectively. Patients with BRAF-mutated tumours were significantly younger than those without mutation (P=0.005) (BRAF-mutated: median age, 33.6y [range: 15 to 79 y]; wild-type: median age, 43.9y [range, 24 to 64 y]). SBTs with mutation were less likely to have non-invasive implants than wild type ones: 11.76% (2/17) versus 33.3% (6/18), respectively. Seven cases have been excluded for incomplete cytoreductive surgery. However, there was no significant difference between frequency of implants in two investigating groups (P=0.228).
Conclusion: Obtained results all suggest that eosinophilic cells in ovarian serous borderline tumours may represent BRAF mutation, so this study can provide prognostic implication and initiate screening genetic test in abovementioned ovarian tumours.

Funding: International Society of Gynecological Pathologists (ISGyP) Young Member Award (research proposal entitled "ArIStOtel: Artificial intelligent-based system for serous ovarian cancer subtyping")

OFP-02-010
Integrated molecular and clinico-pathological study of tubo-ovarian high grade serous carcinoma: HRD status and histological features
R. Ciudino*, T. Maloberti, S. Coluccelli, D. de Biase, G. Tallini, A. De Leo
*Anatomic Pathology - Department of Medical and Surgical Sciences (DIMEC), University of Bologna, Italy

Background & objectives: The aim of the study was to investigate the correlation of tubo-ovarian High Grade Serous Carcinoma (HGSC) tumour morphology, homologous recombination repair (HRR) status, and clinico-pathologic features to identify histopathological and clinical parameters predictive of biological behavior and molecular features.
Methods: Pathologic and immunohistochemical (IHC) characteristics were evaluated in 216 consecutive cases of ovarian carcinoma according to 2020 WHO diagnostic criteria. Intratumoural TILs (iTILs) were counted semi-quantitatively as reported in literature. HRD status was determined by analyzing BRCA1/BRCA2 variants and the "Genomic Scar Score" (GSS) using Amoy HRD focus panel kit and MyChoice HRD-Plus assay. Complete clinical parameters have been collected.
Results: HRD status was positive in 114 (52.8%) cases, including 110 HGSCs and 4 carcinosarcomas. Endometrioid carcinoma, clear cell carcinoma, low-grade serous carcinoma and mesonephric-like carcinoma were HRD negative. In HGSC, HRD positivity was significantly correlated with SET morphology (p<0.0001), higher PCI score (p=0.05) and better clinical outcome. 114 HRD positive tumours included: 28 (24.6%) BRCA1 positive, 25 (21.9%) BRCA2 positive, and 61 (53.5%) tumours BRCA1/2 wild-type. SET tumours showed a statistically significant association with pushing pattern of invasion (p=0.0001), high number intraepithelial TILs (p=0.0001), higher mitotic index (p=0.05) and lower CA-125 levels (p=0.002). No correlation has been observed between site of origin and HRD/BRCA status or tumour morphology.
Conclusion: HRD positive tumours were specifically of high-grade morphology: HGSC and carcinosarcoma. The correlation of molecular status with histological features is important in order to be able to select the cases in which analysis is required. The majority of HGSCs with SET features are HRD tumours independently of BRCA status.

OFP-02-011
Clinical behaviour and gene expression in borderline and malignant brenner tumours
B. Lawson*, M. Luiz Marques-Pibelli, J. Zhang, A. Malpica
*MD Anderson Cancer Center, USA

Background & objectives: Borderline and malignant Brenner tumours are rare entities, with limited data as to behavior and molecular characteristics. This study examined the gene expression profiling of a spectrum of Brenner tumours to characterize potential clinicopathologic and biological differences between these entities.
Methods: Cases of Brenner tumours were identified through retrospective search in laboratory information system between the time period 1/1/1985 to 7/31/2022 for the word "Brenner". Cases were evaluated for diagnosis, patient age, ovarian size, stage, therapy, reported molecular findings, and follow up. Select cases with available FFPE were submitted for HTG gene expression profiling, evaluating 19,308 genes.
Results: 441 cases of Brenner identified, 27 were malignant and 16 borderline. 6 borderline, 4 malignant, and 2 benign were submitted for gene expression. Median age of malignant cases, 60.1 yrs (48-80); borderline, 73.8 (58.4-81.7); and benign, 65.8 (51.7-80). Size was known in n=11, median 12.5 cm (2.3-23.0). 3 genes associated with diagnosis; OR4F17-family and CCDC92B associated with benign (p=0.0000273 and p=0.00248); ZSCAN5B associated with malignant (p=0.0317). RFC3 correlated with age (rho=-0.91, pv < 2e-16). 3 genes correlated with size: HES6 (rho=0.96, p=0.0391), CCDC190 (rho=0.96, p=0.0391), and FAM83E (rho=0.95, p=0.0402). Four immune signatures had higher expression in malignant cases (Interferon gamma IFNG (p=0.012), TLS combined (p=0.024), INF.gamma (p=0.032) and expanded.immune (p=0.048)).
Conclusion: Borderline and malignant Brenner tumours are rare, lacking data as to outcomes or molecular findings. All borderline Brenner tumours were stage 1A at diagnosis, and a single case of recurrence had a focus of microinvasion. Malignant Brenner tumours uncommonly present at high stage, while the majority of cases present at early stage and commonly live with NED. There does appear to significant association with gene expression in relation to multiple aspects of Brenner tumours, including diagnosis, age, and size.

OFP-02-012
Post-radiotherapy endometrial changes should be differentiated from serous endometrial intraepithelial carcinoma
D. Arciuolo*, A. Travaglino, G. Scaglione, N. D'Alessandris, A. Santoro, B. Padial Urtueta, G.F. Zannoni
*Pathology Unit, Department of Woman and Child's Health and Public Health Sciences, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy

Background & objectives: Patients who underwent to chemoradiotherapy may show endometrial reactive atypia which may mimic serous endometrial intraepithelial carcinoma. We aimed to assess the prevalence and morphological/immunohistochemical features focusing on the differential diagnosis between these entities.
Methods: Endometrial histological specimens were assessed for the presence of endometrial reactive atypia in all the cases of patients who underwent to hysterectomy after chemoradiotherapy for locally

advanced cervical cancer. Twenty-two cases of serous intraepithelial carcinoma were used for comparison.
Immunohistochemistry for p53, p16 and Ki67 was performed.
Results: Thirty-six cases out of 244 patients showed endometrial reactive atypia including nuclear enlargement and pleomorphism, clarification or hypercromasia, evident nucleoli, eosinophilic or clear cytoplasm, hobnail changes. The degree of nuclear atypia was similar between endometrial reactive changes and SEIC.
SEIC had a higher mitotic activity and showed a papillary architecture with areas of confluent papillae.
Thirteen and sixteen out of 36 endometrial reactive changes showed, respectively, p53 positivity in most tumour cells- mimicking a mutation pattern- and p16 block-type positivity.
All the SEIC cases were positive for p53 and had block-type p16 positivity.
Mean Ki67 expression was 26.9% in SEIC (range 5-70%) and 8.16% in PoRSEC (range 5-35%).
Conclusion: Our study was the first that assess the morphological and immunophenotypical features of post-chemoradiotherapy endometrial reactive changes.

We found that endometria from patients with LACC can show reactive changes, which may morphologically and immunohistochemically mimic SEIC, in fact there could be an overlap in p53, p16 and Ki67 expression. In such a case, clinical information, low mitotic activity and lack of branching papillae and prominent glandular crowding in reactive changes may be a useful aid.

OFP-02-013
Cytology-based HRD testing and BRCA mutational profiling in a set of ovarian cancer patients
P. Santiago Díaz*, L. Serrano Munné, G. Vargas Parra, I. Vázquez de las Heras, N. Juanpere Rodero, B. Romero Madrid, R. Rueda Miret, A. Quiñonero Inserte, B. Bellosillo Paricio, B. Lloveras Rubio
*Department of Pathology, Hospital del Mar, Barcelona, Spain

Background & objectives: Homologous recombination deficiency (HRD) status assessment in ovarian cancer predicts response to platinum-based chemotherapy and PARP inhibitors. Since tissue availability is often limited, ascitic fluid cytology, readily accessible in early stages, should be considered as an alternative source of material.
Methods: HRD status was assessed in eight positive ascitic cytology samples using DNA isolated from paraffin cell-blocks. Three cases were tested with Myriad MyChoice CDxPLUS Test and five with SOPHiA DDM HRD Solution. BRCA1 and BRCA2 sequencing was conducted on matched paraffin tissue-blocks' DNA in our laboratory, utilizing Illumina platform post PCR-based enrichment with Human BRCA1 and BRCA2 Plus Panel (Qiagen).
Results: Two (25%) cases were HRD positive and two cases (25%) rendered undetermined or non-conclusive results, we hypothesize probably due to low neoplastic cellularity in the sample. Four cases (50%) tested negative. The two HRD positive cases presented with pathogenic BRCA1 and BRCA2 mutations. Consistent BRCA1 and BRCA2 results were found on neoplastic tissue-blocks in our laboratory: BRCA1 c.4484+1G>C and BRCA2 c.8972_8973insCT.
Conclusion: Our data supports considering ascitic cytology samples suitable for HRD testing and BRCA1 and BRCA2 mutation analysis. Further studies are needed to validate the practice of using ascitic cytology as a diagnostic specimen for HRD testing when tissue is not accessible, as it could prove crucial to provide ovarian cancer patients with essential information in an early stage of the diagnostic process.

OFP-02-014
Characterization of recurrent gene amplifications in copy numer-high endometrial cancers
A. Roy*, C. Dagher, N.R. Abu-Rustum, C. Aghajanian, J.J. Mueller, B. Weigelt, M.H. Chui, A. Momeni Boroujeni
*Memorial Sloan Kettering Cancer Center, USA

Background & objectives: The TCGA study of endometrial carcinomas (EC) identified four molecular subtypes, of which copy number-high (CN-H) has the worst prognosis. This study aims to characterize recurrent gene amplifications in CN-H ECs across histotypes and their association with clinical outcomes.
Methods: All CN-H ECs from patients treated at our institution who underwent surgery between 2014 to 2020, had clinical tumour-normal next-generation sequencing, tumour purity ≥20% and coverage above 200x were included. Fold-change and allele-specific copy number analysis was performed and compared to fluorescence in situ hybridization when applicable. Cox regression survival analysis for disease progression and death was performed.
Results: 223 cases were included (75 serous carcinomas, 70 carcinosarcomas, 39 high-grade EC, 39 others). The most frequent amplifications affected *CCNE1* (20.6%), *ERBB2* (15.7%), *MYC* (13.0%), *CDK12* (11.2%) and *AKT2* (9.4%). *CDK12/ERBB2* and *AKT2/CCNE1* co-amplifications were seen in 25 and 15 cases, respectively. Gene amplifications were not associated with histotype.
ERBB2 amplification was associated with higher risk of progression (HR 1.910) and death (HR 2.194). *CDK12/ERBB2* co-amplification also showed an increased risk of progression (HR 1.947) and death (HR 2.065), while *ERBB2* amplification alone was only associated with an increased risk of death (HR 2.547; all p-values <0.05). Other amplified genes were not associated with survival outcomes.
Conclusion: *ERBB2* amplification and co-amplification with *CDK12* are associated with a worse prognosis in CN-H EC across histotypes. Our study suggests that integrating gene copy number alteration information may enhance the prognostic stratification of CN-H EC, a subgroup traditionally associated with poor prognosis. Additional studies with larger cohorts are needed to refine our understanding of these genetic determinants and their prognostic and therapeutic implications.

OFP-02-015
Evaluating the performance of E2F1 and CCNA2 RNA expression, POLE and PPP2R1A/FBXW7 mutation status (ECPPF classifier) in risk stratification of stage I and II endometrioid endometrial carcinoma (EEC) and serous endometrial carcinoma (SEC)
M. Shahi*, N. Kanwar, S. Yadav, J. Gonzalez Bosquet, K. Halling, K. Podratz
*Mayo Clinic, USA

Background & objectives: Despite an overall good prognosis, approximately 15% of stage I and II endometrial cancers (EC) recur. Herein, we compared the performance of standard prognostic stratification tools for endometrial cancer (the TCGA, PORTEC1 and ESMO 2013 criteria) with the ECPPF classifier.
Methods: The Cancer Genomic Atlas (TCGA) data is utilized. Utilizing Five molecular classes were evaluated and correlated with clinical outcomes: 1. PPP2R1Amu/FBXW7mu, 2. E2F1+CCNA2 log2 expression low (L) (<4.75), 3. E2F1+CCNA2 log2 expression high (H) (≥4.75), 4. POLEmut 5. PPP2R1Amu/FBXW7mu and E2F1+CCNA2 log2 expression high. The performance of the TCGA, PORTEC1 and ESMO 2013 criteria are correlated with the clinical outcome.
Results: 177 cases of stage I and II EEC (N=156) and SEC (N=21) were stratified as described above. The 5-year progression free survival (PFS) for E2F1+CCNA2-L, POLEmut, E2F1+CCNA2-H and FBWX7mu/PPP2R1Amu was 95%, 88%, 64%, 65%, and 31%, respectively (p<0.001); corresponding Cox univariate hazard ratios (95% CI) were 1.00 (reference), 0.89, 5.79, 6.42, and 10.22, respectively (P=0.002). The TCGA classifier, PORTEC 2001 and ESMO 2013

criteria failed to achieve statistically significant to stratify the risk or recurrence (p values 0.43, 0.12 and 0.35, respectively).
Conclusion: We present ECPPF as a risk stratification tool which is able to categorize EEC and SEC by clinical outcomes, independent of early stage and histologic grade, suggested that ECPPF might be able to identify early-stage, low grade cases with heightened risk of occult extrauterine disease. This classifier outperforms the TCGTA, PORTEC 2001 and ESMO 2013 in risk stratification of the stage I and II endometrial carcinomas.

OFP-03Joint Oral Free Paper Session Molecular Pathology / Haematopathology

OFP-03-001

The prognostic significance of immune infiltrating cells according to Epstein-Barr virus infection status in classical Hodgkin lymphoma

I. Zawati*, O. Adouni, M. Manai, N. Sadfi, M. Driss, M. Manai
*Department of Immuno-Histo-Cytology, Salah Azaiez Institute, Tunis, Tunisia

Background & objectives: The Epstein-Barr virus (EBV) infects a proportion of classical Hodgkin lymphoma (CHL), frequently harboring an abundant immune cell infiltration. We aimed to explore whether the EBV infection could influence the tumour microenvironment (TME) signature and its prognostic significance.
Methods: We retrospectively conducted an immunohistochemical analysis to evaluate the expression of immune cells' subsets, including CD3+, CD4+, CD8+, FOXP3+, CD20+, and CD68+ and EBV-latent membrane protein 1 (LMP1) in samples from 102 patients with primary CHL. We calculated the ratios CD4/CD8, CD8/FOXP3, CD3/CD68, CD4/CD68, and CD8/CD68 for each patient. Survival rates were calculated using the Kaplan-Meier and Cox regression methods.
Results: EBV-LMP1+ (positivity) was detected in 35 (34%) cases. We found that only the CD8/FOXP3+ ratio was significantly increased in LMP1+ than in LMP1- tumours ($p = 0.027$). Besides, a high CD8/CD68+ ratio was associated with inferior OS in LMP1+ tumours, but with no impact on LMP1- cases. High FOXP3+ T cells were associated with better OS ($p = 0.035$) and tended toward a good prognosis by the Cox model ($p = 0.053$). In the multivariate analysis, only the CD8/CD68+ ratio with B-symptoms tended to be independent prognostic factors for OS in LMP1+ cases (Hazard ratios (HR) = 9.80 (0.56-171.5), $p = 0.11$; HR = 10.28 (1.00-106.0), $p = 0.05$, respectively).
Conclusion: The poorer LMP1+ CHL subgroup exhibited a higher CD8+/FOXP3+ ratio, reflecting probably a cytotoxic signature of the TME. Besides, the current study demonstrated for the first time that the CD8/CD68+ ratio could predict a poor prognosis in LMP1+ CHL tumours, providing more important prognostic information than individual immune cells. Therefore, the CD8/CD68+ may serve as a new potential indicator of LMP1+ CHL clinical outcomes with future immunotherapy applications.

OFP-03-002

Histologic, molecular and clinical characteristics of malignant histiocytosis and outcome: retrospective series of 137 patients

C. Bigenwald, D. Roos-Weil, A. Pages, Z. Hélias-Rdzewicz, C. Copie-Bergman, M. Nashvi, M. Parrens, A. Traverse-Glehen, F. Charlotte, S. Heritier, J. Haroche, J. Donadieu, A. Idbaih, J. Emile*
*Service de Pathologie Hopital Ambroise Paré, France

Background & objectives: Malignant histiocytoses (MH) are tumours of macrophage or dendritic cell (DC) lineage, corresponding to the histiocytic, interdigitating DC, or Langerhans cell (LC)sarcomas of the WHO classification. MH remain poorly understood cancers, for which there are no therapeutic recommendations.
Methods: Cases of MH diagnosed since 2000 were retrieved through the French histiocytosis registry and French lymphoma network. Diagnosis was confirmed by central pathology review. Molecular analysis was performed on DNA extracted from FFPE samples, using either BRAF V600E specific PCR, or NGS. Clinical data were retrospectively collected.
Results: Several histiocyte-rich tumours were excluded during review, while 137 patients were confirmed and included. Median age was 63 years (ICQ: 42-73) and 59% were male. MH was associated in 36% of cases with another hematologic neoplasm (secondary MH). 77% of MH were disseminated. Several organs were involved, lymph nodes being the most frequent. MH were of histiocytic (46%), interdigitating DC (32%), LC (10%) or indeterminate DC (9%) subtypes, or biphenotypic (3%). PTPN11 mutation was present only in primary MH ($p=0.004$). Mutation activating the MAPkinase pathway were more frequent in secondary than primary MH ($p=0.001$). Treatments included surgery, various chemotherapy regiments and targeted therapy (n+26). The 5 years OS was 38%.
Conclusion: MH have a bad prognosis. Localized forms seem to benefit from surgery. No therapeutic strategy had a clear impact on the prognosis of disseminated forms, although BRAF/MEK inhibitors induced significant tumour responses. Molecular and clinical data argue for considering all MH as a unique disease (whatever the subtype), either primary or secondary. Prospective standardized therapeutic and follow-up are necessary to improve the survival of these patients.

OFP-03-003

Gene expression profiling coupled with artificial intelligence: towards a pan-lymphoma classifier

P. Thiebaut*, V. Marchand, F. Drieux, S. Dubois, J. Sabourin, L. Veresezan, P. Ruminy, F. Jardin
*Department of Pathology, Normandy University, Rouen, France

Background & objectives: Lymphoma diagnosis remains a challenge for pathologists, due to the multiplicity of lymphoma subtypes, which widely differ in terms of immunophenotype and molecular profile. Our objective was to provide a single molecular test to assist pathologists in lymphoma diagnosis.
Methods: We evaluated the expression of 137 markers by LD-RTPCR-NGS (100 000 reads/sample) on a 2199 case cohort composed of 17 lymphoma entities. A random-forest-based algorithm was developed to predict lymphoma subtypes, with each case being iteratively extracted and the model trained on the remaining cases. The probability of belonging to each of the 17 entities was calculated for each case.
Results: We observed a high sensibility (often above 90%) of the algorithm where the correct diagnosis was proposed mostly as the first or second hypothesis. The algorithm was particularly effective on small B-cell lymphomas (>90%), large B-cell lymphomas (>98%) and the majority of peripheral T-cell lymphomas (especially T-follicular helper (99%), ALK+ anaplastic large cell lymphoma (97%), NK-T cell lymphoma (92%) and PTCL-NOS (93%)). Specificity and negative predictive value of the test were above 97% in every molecular entity for the algorithm's first hypothesis.
Conclusion: We developed an efficient random-forest algorithm based on gene expression profiling that can help pathologists emit a precise lymphoma diagnosis. This technology is fast, efficient, cost-effective and can be implemented in every pathology laboratory to improve lymphoma diagnosis.

OFP-03-004

Precision in classification: impact of WHO and ICC 2022 criteria on myeloid neoplasms

E.K. Çağdaş*, D. Koyun, S.K. Toprak, M. Özcan, I. Kuzu
*Ankara University Department of Pathology, Turkey

Background & objectives: Myeloid neoplasms with overlapping features, including myelodysplastic syndrome (MDS) and myelodysplastic syndrome/myeloproliferative neoplasia (MDS/MPN), were reclassified according to the 2022 WHO and ICC criteria. We aimed to emphasize the variations in the two classifications and their clinical reflection in our series.
Methods: Seventy-one cases were morphologically examined, and their morphology, clinical presentation, mutation profile were assessed using next-generation sequencing (NGS). Based on the results, each case was diagnosed according to the criteria of the 2022 WHO and ICC classifications. Data analysis was conducted using the SPSS 22.0 (IBM, Armonk, NY, USA) program, with a significance level of $p<0.05$ considered statistically significant.
Results: In a cohort comprising 41 male and 30 female patients with an average age of 62.71±14.00, mutations detected by NGS were categorized by their functions. Epigenetic modifiers were most frequent in CMML, splicing complex genes in MDS, and RAS pathway genes in non-CMML-MDS/MPN cases. Reticulin fibrosis was most frequently observed in non-CMML-MDS/MPN cases and is a poor prognostic factor in MDS cases. The risk stratification for the patients when two classifications were used did not show a major difference in our series, except for one case which had reticulin fibrosis and a low mutation rate, considered as high risk according to WHO but low risk according to the ICC classification.
Conclusion: MDS and MDS/MPN are overlapping hematological neoplasms. NGS is routinely performed in their diagnosis, along with detailed blood analysis, bone marrow tests, and cytogenetics. The current WHO and ICC classifications propose NGS analysis at different steps of the diagnostic algorithm. The prioritizing discrepancy between WHO and ICC classifications can mislead the prognostic stratification and clinical management of these overlapping neoplasms. Although the molecular profile has a high impact on prognosis, specific morphological features such as fibrosis still have prognostic value.

OFP-03-005
In silico analysis of Warburg effect gene alterations and impact on DLBCL outcome
E. Ozsagir*, N. Ozsan, M. Hekimgil, D. Demir
*Ege University Faculty of Medicine Pathology Department, Izmir, Turkey

Background & objectives: The Warburg-effect, a significant topic in cancer research, provides metabolic advantage supporting cancer cell proliferation/survival. This study was to investigate the impact of genetic alterations in glycolysis and oxidative-phosphorylation on clinical outcomes of patients with Diffuse Large B-cell Lymphoma (DLBCL).
Methods: Utilizing NGS data from cBioPortal, we analyzed 1,691 samples/1,658 DLBCL patients across six studies. Genes involved in glycolysis and oxidative-phosphorylation were identified through Reactome. After filtering to include mutation and copy-number-alterations, 433 samples/400 patients were scrutinized in studies (TCGA-MSK). Patients were categorized based on the most frequent genetic alterations in these pathways, and analyzed using Kaplan-Meier, Chi-square compared to unaltered-groups.
Results: The mean age at diagnosis was 67±13years, and 52% were male. PPP2R1A, the most altered gene in glycolysis, was found in 15-patients (4%) and SDHC showed the highest alteration frequency in oxidative-phosphorylation, affecting 10 patients (3%) with, predominantly amplifications and missense-mutations. Significant enrichment of genomic alterations was observed in PPP2R1A-altered group for U2AF2, MYD88, CDKN2A/B, CD79B, SETD1B, IRF4, NOTCH4/3, TBL1XR1, ARID5B; in SDHC-altered group for NCSTN, DDR2, NTRK1, MET, CALR, ALK, SETDB1. Additionally, the unaltered group showed significant enrichment for IHLV3-1, CDKN2A/B-AS1. Alterations in SDHC gene were significantly associated with poorer survival outcomes (p=0.01).
Conclusion: PPP2R1A, a tumour suppressor gene, reduces glycolysis by interacting with MYC. SDHC, encoding a respiratory enzyme, is linked to hereditary cancers and the Warburg-effect. These genomic alterations, especially those related to the Warburg-effect, offer promising therapeutic targets in DLBCL. The results warrant further research into metabolic pathway inhibition as a strategy for DLBCL treatment.

OFP-03-006
The FOXP3/CD68 ratio + CD20 serve as a potential tool for the clinical outcomes of patients with classical Hodgkin lymphoma
I. Zawati*, O. Adouni, M. Manai, N. Sadfi, M. Driss, M. Manai
*Department of Immuno-Histo-Cytology, Salah Azaiez Institute, Tunis, Tunisia

Background & objectives: Immune cells (IC) in the tumour microenvironment (TME) of classical Hodgkin lymphoma (CHL) are critical for anti-tumour efficacy. In this study, we aimed to understand the crosstalk between IC regarding their association with the disease progression.
Methods: Samples from patients with primary CHL were retrospectively included in this study and assessed via immunohistochemistry for the expression of Foxp3, CD8, CD20, and CD68. We tried for the first time to combine three immune markers, notably the combination between the Foxp3/CD68 ratio and CD20 and the combination between Foxp3/CD68 ratio and CD8.
Results: On univariate analyses, the Foxp3/CD68 ratio + CD20 was significantly associated with overall survival (OS) (Hazard ratios (HR) = 2.8 95% confidence intervals (CI) (1.1-7.3), p = 0.032) and on the borderline to be an independent prognostic factor on multivariate analysis (HR = 2.3 95%CI (0.79-6.8), (p = 0.128) using Cox regression model. The Kaplan Meier method demonstrated that the Foxp3/CD68 ratio high + CD20 high was correlated with a good OS (p = 0.047) compared to the Foxp3/CD68 ratio low + CD20 low. However, Foxp3/CD68 ratio + CD8 was not associated with OS (HR = 0.82 95%CI (0.24-2.8), p = 0.025).
Conclusion: We demonstrated for the first time that the Foxp3/CD68 ratio + CD20 had a prognostic significance in CHL, suggesting a crucial role of the combination of these three markers in the disease risk stratification. This finding reflects a dynamic crosstalk between Foxp3, CD68, and CD20 immune cells in the TME, which probably play an important role in the tumour progression of CHL. Further studies will be required to validate our results.

OFP-03-007
Tumour, liquid biopsy, and constitutional microsatellite instability testing using a rapid, low cost, and scalable multiplex PCR and sequencing assay
R. Gallon*, R. Phelps, C. Hayes, R. Hall, P. Herrero-Belmonte, G.M. Borthwick, R. Heer, C. McAnulty, M. Santibanez-Koref, M.S. Jackson, J. Burn
*Newcastle University, United Kingdom

Background & objectives: Tumour microsatellite instability (MSI) analysis informs Lynch syndrome (LS) testing and immune checkpoint inhibitor therapy. Liquid biopsy testing facilitates cancer surveillance. Blood MSI analysis detects constitutional mismatch repair deficiency (CMMRD). Here, we assess a novel MSI assay for each application.
Methods: A multiplex PCR assay was used to amplify, and add sequencing-adapters to, fourteen MSI markers and 22 *BRAF/RAS* mutation hotspots from colorectal cancer (CRC), urothelial cancer (UC), non-neoplastic blood, and cell free urine DNA samples. Amplicons were sequenced using a MiSeq. Tumour/constitutional MSI scores (tMSI/cMSI) were calculated using custom bioinformatics pipelines. Ethical approval: NHS HRA REC reference 13/LO/1514.

Results: The assay was clinically validated for CRC testing, achieving >99% sensitivity and specificity across both tMSI and mutation hotspot analyses. Its use in regional diagnostic service increased annual testing to 97.2% (2466/2536) from 28.6% (601/2104), halved turnaround times from 12 to 6 working days, and identified more patients at-risk of LS (5.5% (139/2536) versus 2.9% (61/2104)) compared to an earlier multi-test pathway. A pilot study of tMSI analysis of postal urine samples from 83 asymptomatic LS carriers detected 4 UC and 1 renal cell carcinoma, facilitating kidney-sparing surgery in 2 patients. Finally, cMSI analysis clearly distinguished 13 CMMRD from 18 control blood samples.
Conclusion: An MSI and mutation hotspot assay using a simple, cheap, and fully automatable methodology enhanced CRC testing and LS screening in clinical service in northern England. The assay is being rolled out to other centres across the UK. It may provide UC surveillance for LS carriers where other options, such as haematuria and urine cytology, are insensitive and unspecific. It can detect the low-level MSI found in constitutional tissues of CMMRD patients, which will complement often uncertain genetic testing.

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OFP-03-008

Geographic disparities and emerging mutation hotspots in ELOC-mutated renal cell carcinomas: a substantial expansion from previous descriptions

T. Cattiaux*, S. Moody, A. Fukagawa, S. Senkin, T. Shibata, L.B. Alexandrov, M.R. Stratton, P. Brennan, B. Abedi-Ardekani
*Genomic Epidemiology Branch, International Agency for Research on Cancer (IARC/WHO), Lyon, France

Background & objectives: ELOC-mutated renal cell carcinoma (RCC), a rare type of RCC resembling clear cell RCC, has been documented in 20 cases, and formally recognized in the WHO 2022 classification. This study presents 10 additional cases, a 50% increase from previous reports.
Methods: This study analyzed 962 clear cell RCC (ccRCC) cases from 11 countries included in the Mutographs cohort and an additional 61 ccRCC cases from a validation group from Japan. IARC/WHO centralized pathology workflow, conducting digital pathology exams on frozen tumour tissues. Whole genome sequencing was performed on all cases, with variant calling using the standard Sanger bioinformatics analysis pipeline.
Results: Previous studies reported 20 cases of ELOC-mutated RCC in various cohorts: 8 in Sato, 3 in The Cancer Genome Atlas, 1 in TRACERx, 5 in MSK-IMPACT and 3 in Batavia. The incidence in Sato cohort (3.3%) exceeded others, where numbers ranged from 0.6% to 1%. Y79 mutations prevailed (17/20).
In our 1023 ccRCC cases cohort, 1% (10) were ELOC-mutated RCC. Rates varied widely by country, with Japan showing a tenfold increase (5.1%, 5/97) compared to others (0.5%, 5/926). Four novel mutation sites were uncovered in ELOC/VHL binding regions, with E92 affected in three cases. Affected cases, mostly young males, had lower tumour mutation burden than other ccRCC cases.
Conclusion: The addition of 10 new cases, alongside the previously documented 20, enriches our understanding of ELOC-mutated RCC's clinical and molecular features. Our findings suggest a fivefold higher incidence in Japan (3.9%, 13/337 combining Mutographs and Sato) compared to other studied countries (<1%), unrelated to the increased prevalence of mutational signature SBS12 recently discovered in Japan. Additionally, our study uncovers four novel mutation sites within the ELOC/VHL binding regions, expanding the known diversity beyond the initial four identified sites.

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OFP-03-009

Comprehensive genomic profiling of intrahepatic and extrahepatic cholangiocarcinoma

P. Vignali*, R. Bruno, A.M. Poma, F. Signorini, C. Vivaldi, V. Genovesi, F. Salani, F. Lorenzo, C. Cremolini, C. Ugolini
*Department of Translational Research and New Technologies in Medicine and Surgery, University of Pisa, Pisa, Italy

Background & objectives: Cholangiocarcinoma (CCA) is a rare biliary tract cancer and can be divided into intrahepatic (iCCA) and extrahepatic (eCCA), according to anatomic location. Here, we aimed to evaluate molecular differences between iCCA and eCCA by performing a comprehensive genome profiling (CGP).
Methods: A retrospective series of primary tumour tissues from 86 CCA underwent pathological revision. Fifty-four (63%) iCCA and 32 (67%) eCCA were selected for CGP by FoundationOne®CDx test. Pathogenic variants were reported, and their prevalence was compared between iCCA and eCCA by using the Fisher exact test; p-value of 0.05 was deemed significant.
Results: Prevalence of pathogenic variants significantly differed between iCCA and eCCA. Particularly, KRAS alterations were more prevalent in eCCA (50%) than iCCA (9.25%) (p=0.00004). Only eCCA harbored ERBB2 (9.37%) and MDM2 (9.37%) amplifications. TERT-promoter mutations were exclusively detected in iCCA (14.8%). Three iCCA (3.5%) had a high tumour mutational burden (TMB, >10 mut/Mb) of which two with microsatellite instability (MSI-H). One eCCA case (3.12%) presented high TMB and MSI-H. No significant differences were reported for the main CCA genes, likely due to the sample size. IDH1 alterations were found in 11% and 6.2%, FGFR2 in 9% and 6.2%, BRAF p.(V600E) in 3.7% and none of iCCA and eCCA, respectively.
Conclusion: Intra- and extrahepatic CCA have distinct clinical and genetic characteristics. Here, we reported a different prevalence of oncogene activating alterations between iCCA and eCCA (e.g., KRAS) that may influence clinical outcome. Moreover, 56 cases had activating alterations (e.g., ERBB2) already targetable in CCA (15% of total cases, 6.2%-eCCA, 20.3%-iCCA) or in other tumours (50% of cases, 81.2%-eCCA, 31.5%-iCCA). Overall, our results confirmed that iCCA and eCCA are separate entities and underlined the importance of CGP in clinical practice.

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OFP-03-010

Enrichment pathways associated with molecular subtypes of ovarian cancer

A. Asaturova*, A. Kobelyatskaya, A. Tregubova, A. Rogozhina, A. Badlaeva
*NMRS for Obstetrics, Gynecology and Perinatology named after V. Kulakov, Russia

Background & objectives: Currently, four main molecular subtypes of high-grade serous ovarian cancer (HGSOC). It was suggested that these subtypes have different survival rate and treatment response. In current research, we have identified the most enriched biological pathways for each of them.
Methods: This study used RNA-Seq data from ovarian cancer samples collected by The Cancer Genome Atlas (TCGA-OV project). The cohort was divided into 4 molecular subtypes: differentiated (DS), immunoreactive (IS), mesenchymal (MS), and proliferative (PS). Enrichment analysis was performed using the STRING network database and KEGG pathways based on lists of differentially expressed genes obtained in our recent study.
Results: We revealed enriched biological pathways in each of HGSOC molecular subtypes. Top-5 pathways in DS: Antigen processing and presentation (hsa04612), Proteasome (hsa03050), Cholesterol metabolism (hsa04979), Rheumatoid arthritis (hsa05323), Phagosome (hsa04145). Top-5 pathways in IS: Allograft rejection (hsa05330), Graft-versus-host disease (hsa05332), Type I diabetes mellitus (hsa04940), Autoimmune thyroid disease (hsa05320), and Antigen processing and presentation (hsa04612). Top-5 pathways in MS: ECM-receptor interaction (hsa04512), AGE-RAGE signaling pathway in diabetic complications (hsa04933), Protein digestion and absorption (hsa04974), Relaxin signaling (hsa04926), and Focal adhesion (hsa04510). Top-5 pathways in PS: Glycosaminoglycan biosynthesis - keratan sulfate (hsa00533) and ganglio series (hsa00604), NF-kappa B signaling (hsa04064), TNF signaling (hsa04668), and Complement and coagulation cascades (hsa04610).
Conclusion: Thus, we identified the top-5 biological pathways associated with each subtype. The top-5 immunoreactive pathways related to the autoimmune component, whereas the mesenchymal subtype pathways covered extracellular matrix and adhesion nodes, which are important during the transition. However, the top-5 pathways in the differentiated and proliferative subtypes are less related to each other.

Funding: International Society of Gynecological Pathologists (ISGyP) Young Member Award (research proposal entitled "ArIStOtel: Artificial intelligent-based system for serous ovarian cancer subtyping")

OFP-03-011

Comprehensive genomic profiling in RAS/BRAF wild type colorectal cancers

G. Martinelli*, R. Bruno, M.M. Germani, F. Signorini, A.M. Poma, C. Cremolini, C. Ugolini
*Surgical, Medical, Molecular and Critical Care Pathology Department, University of Pisa, Pisa, Italy

Background & objectives: In metastatic colorectal cancer (mCRC), different aspects (tumour site and molecular characteristics), influence treatment decision. Comprehensive genome profiling (CGP) is not routine clinical practice for CRC, yet. We aimed to determine the impact of CGP in RAS/BRAF wild-type (WT) mCRC.
Methods: Seventy-seven RAS/BRAF-WT mCRC were retrospectively selected for CGP by FoundationOne®CDx test. In detail, 58 CRC were in the left colon/rectum and 19 were right-sided. Our series included special subtypes: 5 mucinous (2 with signet-ring cell), 8 with a mucinous component, 2 signet-ring type cases. The prevalence of alterations targetable in CRC (level-1) or in other tumours (level-3B) was determined (OncoKB).
Results: CGP detected pathogenic variants in all 77 RAS/BRAF-WT mCRC. Twenty-seven (35%) harbored one or more potentially targetable alterations, of which 17 (63%) were in the left colon/rectum and 10 (37%) in the right colon. All mucinous and 3 with a mucinous component tumour had targetable variants. The most frequent target was PIK3CA (8%). Others were PTEN, MAP2K1, BRCA1, MDM2, CHEK1, BRAF (gene fusion) and amplification in MET and HER2, the latter missed by immunohistochemistry and representing the only level-1 alteration. Tumour mutation burden (TMB) was elevated (>10 mut/Mb) in 9 cases (12%) and linked to microsatellite instability and POLD1 pathogenic mutation in 4 and 1 patients, respectively.
Conclusion: All cases harbored variants in key oncogenes or oncosuppressors and druggable alterations in more than one third of them. Five out of nine patients had a high TMB unrelated to microsatellite instability. TMB may serve as biomarker for immunotherapy-based strategies in mismatch repair proficient/microsatellite stable mCRC. All mucinous CRC presented targetable alterations, deserving deeper investigations about subtype related genetic characteristics. CGP can support clinicians with a biomarker-driven approach for investigational purposes and can also be valuable in routine clinical practice.

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OFP-03-012

If you snooze you lose: early assessment of BRCA mutation in metastatic prostate cancer improves number of patients suitable for PARP inhibitors target therapy

M. Vescovo*, L. Nibid, G. Perrone, D. Righi, G. Sabarese
*Italy

Background & objectives: Low success-rate for NGS analysis in detecting BRCA somatic mutation in formalin-fixed and paraffin-embedded tissue (FFPE) is well known. This is particularly relevant for patients' selection with metastatic prostate cancer that could benefit of PARP-inhibitors target therapy.
Methods: We retrospectively evaluated success rate (SR) of NGS analysis of BRCA mutation in a cohort of 91 FFPE samples collected from 1998 to 2022 at the Anatomical Pathology Unit of Campus Bio-Medico Hospital, Rome and correlated it with length of storage. Molecular testing was performed adopting Myriapod NGS-IL BRCA 1-2 panel. DNA was extracted adopting QIAamp-DNA FFPE Tissue Kit.
Results: Tissue samples were 54 biopsies (liver, bone, prostate, and lymph-node), 34 prostatectomies and 3 TURPs. We classified samples in three groups according to the length of storage: short-time (< 1 year), middle-time (1-2 years), long-term (≥ 2 years) and we correlated it with the SR of NGS analysis of BRCA mutation. Overall, the SR was 50/91 (55%) and it inversely correlated with storage time ($p<0,01$; $r=-0,477$). In detail, success rate was 27/31 (87%) in short-time storage samples, 7/13 (54%) in middle-time samples and 16/47 (34%) in long-term samples. We also found a positive correlation between SR and the DNA fragmentation ($p<0,001$; $R=0,559$) and concentration ($p<0,001$; $R=0,618$) index.
Conclusion: Our study, for the first time, describes the crucial role of storage-time for assessing BRCA mutation in real life clinical practice. A time span longer than 2 years produces significant loss of success rate, leading to a consistent loss of patients that may benefit from PARP inhibitors target therapy.

This study indicates that high-risk prostate cancers should be tested for BRCA mutation at the time of the diagnosis. Liquid biopsy is a feasible alternative for archival-samples.

OFP-04Joint Oral Free Paper Session Neuropathology / Ophthalmic Pathology / Paediatric and Perinatal

OFP-04-001

Infant-type hemispheric glioma: a wide morphological and immunohistochemical spectrum of the disease

M. Senchenko*, L. Papusha, A. Drui, D. Konovalov
*Dmitry Rogachev National Medical Research Center of Paediatric Haematology, Oncology and Immunology, Russia

Background & objectives: Infant-type hemispheric glioma (IGG) is a recently described astrocytic uncertain grade glioma with receptor tyrosine kinase (RTK) fusion. IGG may have different morphological and immunohistochemical features, which can lead to misdiagnosis. In this study we describe 11 cases of IGG.
Methods: The initial morphological diagnosis included: IGG (n=6), desmoplastic infantile glioma (n=2), anaplastic ependymoma (n=1), astroblastoma (n=1), glioblastoma (n=1). Using RNA sequencing fusions of RTK genes were identified in all cases: ROS1 – 4; ALK – 2; NTRK1/2/3 – 5. The DNA methylation profile was consistent with IGG in seven cases (methylation score >0.9). In two cases the score was <0.9.
Results: Histological examination revealed a moderately or highly cellular, well-circumscribed tumour. The neoplastic tissue consisted of spindle-shaped or gemistocytic astrocytes in different proportion. All tumours were highly vascularized with endothelial proliferation in four cases. Tumour cells tended to be perivascular with forming pseudorosettes in some cases. The mitotic activity varied from 2 to >10 per 10 HPF ×400. In one case palisading necrosis was identified. Immunohistochemistry revealed diffuse S100 (n=11), diffuse GFAP (n=8), focal variable GFAP (n=3) expression, Olig2 expression by approximately 50% of cells (n=3), no Olig2 expression (n=7), dot-like EMA expression (n=3), negative reaction with CD34 (n=11) and different neuronal markers in all cases where it was performed.
Conclusion: IGG may have variable morphological appearance and immunophenotype, which can lead to misdiagnosis of desmoplastic infantile glioma, ependymoma, astroblastoma. The importance of accurate diagnosis is determined by the possibility of using targeted therapy among patients with IGG upon identifying the corresponding transcript.

OFP-04-002

Clinicopathologic features of paediatric meningiomas that predict recurrence and mortality: a meta-analysis

K. Heß*, B. Brokinkel, L. Hennig, S. Freitag-Wolf, M. Kalab, C. Röcken, O. Jansen, R. Goldbrunner
*University Hospital Schleswig Holstein, Campus Kiel, Department of Pathology, Kiel, Germany

Background & objectives: Paediatric meningiomas show a more aggressive biological behavior than adult meningiomas, and treatment recommendations are based on small case studies. The aim of our study was to identify clinicopathologic features predictive of recurrence and mortality.
Methods: A PRISMA systemic review and meta-analysis was performed, including articles published between 01/1989 and 03/2023 that focused on paediatric meningiomas. Study heterogeneity was assessed using funnel and forest plots with fixed and random effects models. Histologic and clinical characteristics were evaluated in relation to mortality and recurrence rates using meta-regression.
Results: For the meta-analysis, 45 studies with a total of 883 patients remained for further analysis and interpretation. WHO grade 1-3 tumours were diagnosed in 556 (63%), 153 (17.3%), and 112 (12.7%) patients, respectively. Studies with falx (0.367 (95% CI 0.134, 0.596; p=0.020) and cerebellopontine angle (CPA) meningiomas (0.191 (95% CI 0.051-0.330); p=0.007) showed increased mortality. Studies with falx localization (0.336 (95% CI 0.099-0.573); p=0.005) and age over 10 years (0.751 (95% CI 0.158-1.344; p=0.013) showed an increased recurrence rate. In regression analysis, CPA and falx location were not associated with gender, resection status, radiotherapy or WHO grade.
Conclusion: The present study is the first to demonstrate an association between tumour location, especially CPA and falx, and recurrence and mortality in paediatric meningiomas, probably due to the difficult surgical access and possibly different tumour cell types. Surgical concepts aiming at complete resection are currently being developed for adult meningiomas, which could be prospectively tested and evaluated in paediatric meningiomas with the goal of complete resection, strictly considering perioperative and long-term postoperative complications.

OFP-04-003

Immunohistochemical expression of PAX8 in intracranial hemangioblastomas: a potential diagnostic pitfall

J. Farina*, G. Tinnirello, S. Salzano, G.M.V. Barbagallo, V. Barresi, G. Magro, R. Caltabiano, G. Broggi
*Department of Medical, Surgical Sciences and Advanced Technologies "G.F. Ingrassia", Anatomic Pathology, University of Catania, Catania, Italy

Background & objectives: PAX8 has been traditionally considered a reliable marker of metastatic clear cell renal cell carcinoma, being consistently negative in intracranial hemangioblastomas. As recent studies described some PAX8-positive hemangioblastomas, we investigated the expression of this protein on 23 intracranial hemangioblastomas.
Methods: 23 cases of intracranial hemangioblastomas were retrieved and reviewed to confirm hemangioblastoma diagnosis. Standard immunohistochemical panel for PAX8, CD10, Inhibin-α, S100 and RCC was applied to each case. PAX8 was considered positive when nuclear staining was found. A semiquantitative optical evaluation was performed, based on intensity and extension of staining, and a four-tiered system was created.
Results: In our series, 19 lesions arose in cerebellum and 3 in medulla oblongata. The exact site was not available in 1 case. Immunohistochemistry exhibited strong and diffuse immunoreactivity to Inhibin-α in all cases, while S100 was expressed in 18 cases (80%). All cases were negative for CD10 and RCC. PAX8 immunoreactivity was positive in 9 out of 23 cases (39.1%), with a weak staining pattern in almost all cases (8 out of 9; 88%). Regarding the extension of staining, 7 out of 9 cases showed focal staining (77.8%), whilst in just 2 cases it was more heterogeneous (22.2%).
Conclusion: Although PAX8 has always been considered a reliable marker to distinguish hemangioblastoma (PAX8 -) from metastatic clear cell renal cell carcinoma (PAX8 +), in the present study nearly 40% of intracranial hemangioblastomas were, at least, focally and weakly stained with this antibody. To avoid misdiagnosis between these two entities, especially on small biopsies, we recommend using a broader immunohistochemical panel, including PAX-8, Inhibin-α, CD10, S100 and RCC.

OFP-04-004

The possible role of Wnt/ β-catenin pathway in central neurocytoma

E. Önder, K. Dogan*, G.V. Alkan
*Karadeniz Eregli State Hospital Department of Pathology, Turkey

Background & objectives: Central Neurocytoma (CN) is a rare intraventricular tumour of which molecular features are unclear. Ki67 indices over 4% is associated with aggressive behaviour and these tumours are categorized as Atypical Neurocytoma (ANC). Pathway alteration studies revealed limited results.
Methods: In this study, we aimed to explore the involvement of the Wnt/β-catenin signalling pathway in central neurocytoma by evaluating the immunohistochemical expressions of β-catenin and LEF1. We have documented a total number of 15 central neurocytomas. Among 15 cases, 4 were in the atypical category.

Results: Patient ages were between 11 and 47. Ki67 indices in ACN cases were 7%, 7%, 9%, 15%. β-catenin demonstrated diffuse membranous staining without any nuclear positivity in 12 cases. 3 cases had focal nuclear expression in addition to patchy membranous staining. The nuclear β-catenin positivity was between 3 to 5%. Among these 3 cases, 1 was ACN and showed 5% nuclear positivity. These 3 cases also demonstrated scattered nuclear positivity with LEF1. Nuclear staining with LEF1 was weak and highest in the ACN case with 3% nuclear positivity. There were no additional case staining with LEF1.
Conclusion: The rarity of CN is a limitation to discover its nature. There is no evidence for the possibility of targeted therapies. Still, there are few findings suggesting the involvement of the Wnt/β-catenin pathway. To our knowledge, this is the first study evaluating β-catenin and LEF-1 expressions in CN. Although our findings may suggest some alterations of this pathway, they are limited to make an interpretation. Multicentre studies have great importance in clarifying genetic modifications in CN and the possibility of targeted therapies.

OFP-04-005
MITF discriminates two different populations of tumoural cells with potential therapeutic implications in uveal melanoma
P. Donizy*, J. Pilch, M. Krzyzinski, A. Markiewicz, P. Biecek, B. Romanowska-Dixon, M.P. Hoang
*Department of Clinical and Experimental Pathology, Wroclaw Medical University, Wroclaw, Poland

Background & objectives: Microphthalmia-associated transcription factor (MITF) is a crucial regulator of melanocyte development, proliferation and survival by interacting with prooncogenic and cancer-suppressive pathways. The prognostic role of MITF expression in uveal melanoma has not been studied in a large cohort of patients.
Methods: MITF immunostains were performed on tissue microarrays constructed from paraffin-embedded tissues of 154 uveal melanoma (UM) with no prior therapy. We correlated MITF expression with detailed clinicopathologic variables and patient outcomes. Scoring of MITF immunostain was done using the H-score with further dichotomization into two subgroups with low (H-score <15) and high expression (H-score ≥15) using the Contal-O'Quinley method.
Results: Down-regulation of MITF was observed in 83/154 cases (54%). 71 cases (46%; 71/154) exhibited enhanced MITF expression. Patients with low MITF expression were characterized by shorter cancer-specific overall survival and shorter disease-free survival (p=0.019, p=0.0038, respectively). Down-regulated MITF expression was significantly correlated with presence of distant metastases (p=0.005), BAP1-loss tumours (p=0.023), higher largest basal diameter (p<0.001), and presence of TAMs immune response (p<0.001) with no impact on TILs response. On the other hand, increased MITF expression was correlated with higher mitotic index (p=0.033) and enhanced replicating potential of tumoural cells measured by dTYMK and PARP1 expression (p<0.001).
Conclusion: Decreased MITF expression is associated with aggressive clinical behavior of UM. MITF revealed two subpopulations of UM cells: (1) MITF-low: slowly proliferating UM cells with high invasive potential and characterized by activation of macrophage-related inflammatory phenotype, and (2) MITF-high: fast-replicating and fast-dividing population of cells with immunosuppressive features and lower invasive potential. These findings raise the potential clinical importance of re-induction of MITF expression as a possible therapeutic approach in MITF-low tumours and dTYMK and PARP1 inhibitors in MITF-high UM.

OFP-04-006
Immunohistochemical expression of PRAME correlates with higher metastatic risk and poor prognosis in uveal melanoma: a clinico-pathologic series of 85 cases
M. Failla*, G. Broggi, A. Russo, G. Magro, S. Staibano, R. Caltabiano
*Department of Medical and Surgical Sciences and Advanced Technologies, G.F. Ingrassia, University of Catania, Catania, Italy

Background & objectives: PReferentially expressed Antigen in MElanoma (PRAME) is linked to higher metastatic risks in various cancers, including uveal melanoma (UM). We investigated PRAME expression in a series of UMs to assess its prognostic significance, potentially guiding patient monitoring and treatment strategies.
Methods: We performed a retrospective study on histologic specimens from 85 primary UMs, surgically enucleated. 44 were males and 41 were females (median age: 67 years; age range 29–85). 40 metastasizing UMs and 45 non-metastasizing UMs. PRAME immunohistochemical staining was considered positive if brown chromogen was observed, at least focally, within the tumour cell nuclei.
Results: Of the 85 patients, PRAME expression was present (positive) in 37 and absent (negative) in 48 UMs. Among the 45 primary non metastatic UMs, 14/45 cases (31.1 %) showed a PRAME expression, while the other 31 UMs did not show PRAME expression (68.9 %). In the 40 primary metastatic UMs 23/39 cases (57.5 %) had at least focal PRAME expression, while no PRAME expression was found in the remaining 17/40 UMs (42.5 %). These findings confirm the hypothesis of a significant association between PRAME expression in UM patients and risk of metastasis, and a worse overall survival and disease-specific survival.
Conclusion: Our study corroborates the findings that PRAME expression is an independent risk factor for increased metastatic risk in UM, and it correlates with a poorer disease-specific survival, therefore we suggest using PRAME as an easily detectable and affordable prognostic marker in primary UMs to improve patient stratification by risk of metastasis. Future perspectives of research may explore PRAME as a therapeutic target, potentially revolutionizing metastatic UM treatment and offering a beacon of hope for personalized patient care.

OFP-04-007
Orbital lesions: a 17-year perspective from a tertiary care centre
G. Güngör Sahin*, E. Karatay, B. Bilgic, G. Unverengil, G. Yegen, S. Tuncer, S. Ozturk Sari
*Istanbul University, Istanbul School of Medicine, Department of Pathology, Turkey

Background & objectives: The orbital region encompasses muscles, nerves, adipose tissue, vascular structures, lacrimal glands; rendering it susceptible to various pathological entities including inflammatory lesions, cysts and tumours. Neoplastic lesions manifest as primary or secondary involvement. This study aims to analyze frequency of such lesions using data obtained from tertiary care centre.
Methods: Between 2007 and 2024, a total of 614 orbital lesions were identified. Repeated biopsies from the same patients were excluded from the analysis, with only the most recent resection material considered. Orbital lesions were categorized as: neoplastic and non-neoplastic. Neoplastic lesions were further subcategorized as primary tumours and secondary involvement.
Results: The mean age of the study group was 26 years(range: 1-93). Out of 614 cases,327 were male and 287 were female.116 patients were under 18 years of age. Among adults, neoplastic lesions(63%) were more common, while non-neoplastic lesions including cysts and inflammatory lesions(53%) prevailed among children. The most frequent cystic lesion was dermoid cyst. Neoplastic lesions comprised mesenchymal tumours, lymphomas, salivary gland tumours, metastatic tumours, and secondary infiltration from surrounding areas. Mesenchymal tumours were the most frequent lesions regardless of age, with hemangioma being the most common in adults, while rhabdomyosarcoma predominated in children. Lymphomas, mostly low-grade, followed mesenchymal tumours in frequency. Primary salivary gland

tumours originating from the lacrimal gland were also identified, with the most common subtype being pleomorphic adenoma.
Conclusion: Our analysis of orbital lesions revealed varied prevalence of neoplastic and non-neoplastic entities across different age groups. Neoplastic lesions, predominantly mesenchymal tumours, lymphomas, and salivary gland tumours, exhibited varied prevalence across different age groups, with hemangioma and rhabdomyosarcoma emerging as predominant subtypes in adults and children, respectively. Non-neoplastic inflammatory lesions, notably cysts, were prevalent among paediatric patients. These results highlight the heterogeneous distribution of the orbital lesions.

OFP-04-008
Tumour heterogeneity in uveal melanoma: observation of 5 cases
C. Cacchi*, M. Lammert, D. Jonigk
*University Hospital RWTH Aachen, Institute for Pathology, Germany

Background & objectives: The melanoma of the uvea represents a challenge for ophthalmic oncology. The presence or absence of prognostic morphological, immunhistochemical and molecular parameters in the diagnosis of uveal melanoma is becoming increasingly important.
Methods: From our archives, we wanted to assess in the case of melanomas of the uvea with both spindle-cell and epitheloid morphology the possible presence or absence of heterogeneity of BAP-1 expression and/or monosomy of Chromosome 3. For this we performed immunohistochemistry for BAP-1 and FISH analysis for the presence of Monosomy 3 in five cases.
Results: All cases had a proprtion of spindle and epitheloid tumour cells. Immunohistochemical staining for BAP-1 showed a different reaction (positive/negative) in two out of five cases, being positive in the spindle cell component and negative in the epithelioid component. Interestingly, only one of these two cases showed a discordance in the FISH result for Chromosome 3 monosomy between the two different tumoural-components.
In one out of five cases, although there was a positive immunohistochemical reaction for BAP-1 in one tumour component, both components (spindle cell and epithelioid) showed a monosomy of Chromosome 3.
Conclusion: The limited number of cases and the immunohistochemical method for BAP-1 analysis do not allow for general considerations. However, these initial observations seem to suggest that in evaluating important prognostic factors such as Chromosome 3 monosomy and BAP-1 expression, tumour heterogeneity should be taken into account, perhaps in particular with regard to epitheloid cells.

OFP-04-009
Histopathologic features of biliary atresia and outcome predictors of Kasai portoenterostomy: a 10-year retrospective study of a Philippine cohort
P.M. Dy*, R. Santos, E.M. Yturralde
*Department of Laboratories, Philippine General Hospital, Philippines

Background & objectives: There is a dearth of information regarding the epidemiology of biliary atresia and outcomes of Kasai portoenterostomy (KPE) in the Philippines. Here we describe the histopathologic features of biliary atresia and identify outcome predictors of KPE in a local cohort.
Methods: This is a retrospective cohort study which reviewed all KPEs done in our institution from 2013 to 2023. Review of the pertinent clinical and histologic features was done. Patients were categorized into having favourable or unfavourable outcomes based on a 3-month post-operative serum total bilirubin of more than 2 mg/dL or mortality at 3 months.
Results: A total of 71 patients underwent KPE during the eleven-year period, 41 of which had liver biopsies available for review. Outcomes were available for 28 patients. Fibrosis, ductular reaction, and portal tract cellular infiltrates were consistently present in all samples examined, with varying degrees of portal tract edema and giant cell transformation. Low platelet counts and high AST to Platelet Ratio Index (APRI) scores pre-operatively were associated with a poorer prognosis (p values = 0.0266 and 0.0090, respectively). The presence of visible bile plugs in biopsy samples was the only histologic feature that had a significant correlation with the post-KPE outcome (p value = 0.0119).
Conclusion: This study demonstrated the extensive variability of histologic features in biliary atresia, further emphasizing its heterogeneity and complexity. Identifying significant laboratory and histologic features that can help predict native liver survival is essential in prognostication and in tailoring management goals post-KPE, especially in settings where liver transplant is not readily available. Further studies are needed to contribute to a deeper understanding of the interplay between patient characteristics, both clinical and histopathologic, and treatment outcomes.

OFP-04-010
Comparison of macroscopic evaluation of placental lesions by image analyser software versus human eye: a retrospective study of 23 cases
M. De Brito Pereira*, R. Ilgenfritz, M.E. Vitorino, P. Borralho Nunes
*CUF Descobertas Hospital, Lisbon, Portugal

Background & objectives: Placental macroscopic lesions should be detected and described using an estimated percentage of the involved parenchymal volume. Traditional method relies on visual estimation ("eyeballing"); we compare it to an image software in white/yellow lesions analysis.
Methods: A retrospective review of the macroscopic reports of all placentas received in our institution, during a 1-year interval, was conducted (n=136). Macroscopic findings were reported in 23 cases, mentioning the percentage of white/yellow areas involved. An image software ("Image Colour Summarizer"), which defines the amount of each colour in the image was used for comparison.
Results: The average volume of yellow/ white areas by "eyeballing" was 9.21% ± 3.46 (in a range from 30.00% to 1.00%). The image colour summarizer gave an average volume of 10.47% ± 2.82 (in a range from 22.74% to 1.00%).
The average difference between the image software and the human was 1.26%. In most cases (n=17), the difference was below 10%. In the 6 remaining cases, the difference between manual and software analysis ranged between 22 and 11%. After an expert review of pictures, some cases were reclassified to a value more similar to the image software percentage finding.
Conclusion: The estimation of placental lesions by the human eye is not always reliable, and an objective method for this analysis could be of value for practice.
This software detects the percentage of pixels of one determined colour defined by the pathologist. This same colour can be present in other areas of the placenta and not be necessarily correlated to a lesion.

Better training of a software for this purpose should be pursued in its applicability.

OFP-04-011
Quality assurance review of products of conception cases for chronic histiocytic intervillositis: pre and post COVID-19
O. Greenberg*, W. Parks, K. Chu
*Mount Sinai Hospital - Pathology Department, Toronto, Canada

Background & objectives: Chronic histiocytic intervillositis (CHI) is a rare placental lesion with often severe effects on the foetus. We reviewed products of conception (POC) cases for missed diagnoses of CHI in years prior to and during the COVID-19 pandemic.
Methods: This is a quality assurance retrospective analysis exclusively focusing on POC cases in 2018-2023 (excluding 2019). Total of 6,533 POC cases were retrieved from the pathology archives of MountSinaiHospital, Toronto, Canada. All the cases were reviewed by a perinatal pathologist. When possible histological features of CHI were identified, CD68 and CD3 immunostains were ordered to confirm the diagnosis.
Results: No cases of CHI had been previously identified in these samples. In this review, CHI was identified in 26/6533 cases (0.40%). The baseline rate of CHI from 2018 was 2/874 cases (0.23%). The number of positive CHI cases significantly increased in 2020 and 2021; 8/1295 (0.62%) and 9/1456 (0.62%), respectively. The number of positive CHI cases then decreased for 2022 and 2023; 4/1332 (0.30%) and 3/1576 (0.19%), respectively, effectively returning to baseline.
Conclusion: Due to the high recurrence risk, it is critical to recognize CHI on the evaluation of POCs. Review of POC cases between 2018 and 2022 identified 26 previously undiagnosed cases of CHI. Moreover, the COVID-19 pandemic appeared to have a dramatic effect on number of CHI cases in POCs during 2020-2021. As practicing pathologists may not be accustomed to identifying the microscopic features of CHI, this inexperience may be a potential pitfall in routine examination of POCs.

OFP-04-012
Craniofacial ossifying fibromas in paediatric age group – a case series
P. Panjwani*, P. Bansal, M. Ramadwar, N. Mittal, A. Janu, V. Patil, S. Qureshi
*Tata Memorial Centre, Homi Bhabha National Institute, Mumbai, India

Background & objectives: Ossifying fibromas, the most common benign fibro-osseous lesions (BFOL) in craniofacial bones, are further divided into juvenile trabecular ossifying fibroma (JTOF) and juvenile psammomatous ossifying fibroma (JPOF).
We aim to study the clinico-radiological and histological features of juvenile ossifying fibromas.
Methods: This is a retrospective study of 48 cases diagnosed as BFOL of craniofacial bones, between January 2016 and December 2023 at a tertiary cancer care hospital in India. Of these, 22 cases were diagnosed as juvenile ossifying fibromas. Imaging features were available in 20 cases.
Results: The age range was 1 to 18 years (mean 10 years). The male:female ratio was 15:7. The most common site was maxilla (n-=12), followed by mandible (n=6), ethmoid (n=3) and sphenoid (n=1). On imaging,16 lesions were intramedullary and 4 were cortical. The lesions were expansile, well defined with lytic areas in 16 and sclerotic areas in 4 cases. Histology showed hypercellular stroma with plump spindle cells; with JTOF showing woven lamellar bone trabeculae and JPOF showing cementum and prominent calcification. Two cases showed features of aggressive JTOF with increased mitosis and recurrence after excision. The main differentials included fibrous dysplasia and osteosarcoma. Only 4 cases had recurrence after surgery.
Conclusion: Juvenile ossifying fibromas need to be distinguished from fibrous dysplasia and malignancy. Tumours with aggressive patterns on histology may be a pitfall in diagnosis. A good clinico-radio-pathological correlation helps in correct diagnosis in most cases. Adequate resection is the mainstay of treatment, and does not warrant any adjuvant therapy.

OFP-05Joint Oral Free Paper Session Pulmonary Pathology / Digital and Computational Pathology

OFP-05-001
A semi-automated journey to evaluate tumour stroma ratio and its predictive value in colorectal cancer
A.T. Bol*, E. Öcal, B. Savaş, H. Akbulut, A. Ensari
*Ankara University, Medical School, Pathology Department, Turkey

Background & objectives: Tumour stroma interacts with tumour cells at various differentiation stages and also with microenvironment in colorectal cancers (CRC). This pilot study aims to determine the prognostic impact of tumour-stroma ratio (TSR) and to validate a semi-automated method in evaluating TSR in CRC.
Methods: Within a cohort of 289 CRCs with clinical follow-up, a pilot study was performed on 52 cases. TSR was evaluated on PanCK-stained digitized images, first by eyeballing, then on QuPath software in 3mm2, 30mm2 areas with the highest TSR, besides whole slide images (WSI). By using 50% threshold, the impact of TSR on overall survival (OS) was assessed using Kaplan-Meier survival analysis.
Results: Mean age was 60.7years with a male predominance (62.7%). Mean TSRs were %43.94, %79.42, and %59.33 with eyeballing; %49.13, %83.75, and %65.90 with QuPath, for WSI, 3 mm2, 30 mm2, respectively. The intraclass correlation (ICC) between eyeballing and QuPath was at a good level with values of 0.76, 0.87, and 0.89 for WSI, 3 mm2, 30 mm2, respectively. In cases with lmyphovascular invasion, both by eyeballing and QuPath, TSR was significantly higher in WSI and 30 mm2 areas($p<0.01$). In the 16 cases who died during follow-up, TSR was significantly higher in 30 mm2($p<0.01$-eyeballing, $p=0.03$-QuPath). Overall survival was affected by 30mm2-TSR with 50% threshold for eyeballing ($p=0.02$, HR=4.26), and 65% threshold for QuPath($p=0.04$, HR=3.43).
Conclusion: Recently, TSR is considered a significant determinant of prognosis in CRC. Our results demonstrated that TSR assessment area that best reflects its impact on OS was 30 mm2 area, in which semi-automated QuPath image segmentation method also yielded high concordance with eyeballing. This pilot study supports the use of image segmentation methods, which are becoming increasingly prevalent in line with demand, seems to be feasible, perhaps only with slight adjustments, to provide objective and reproducible results.

OFP-05-002
Histopathological assessment of oesophageal adenocarcinoma precursor lesions with artificial intelligence
M. Botros*, O.J. De Boer, B. Cardenas, E.J. Bekkers, M. Jansen, M. van der Wel, C.I. Sánchez, S. Meijer
*Amsterdam UMC, Amsterdam, The Netherlands

Background & objectives: Histopathological assessment of oesophageal biopsies is crucial in managing patients with Barrett's Oesophagus (BE), yet prone to variability, necessitating reliable diagnostic methods. In this study, we developed an AI system to improve the efficiency and accuracy of diagnosing BE-related dysplasia.
Methods: The AI system was developed with 290 whole slide images (WSIs) and followed a two-stage approach. Firstly, it identifies dysplastic regions and predicts dysplasia grades at a pixel-level. Then, it utilizes these dysplasia scores to generate a slide-level diagnosis. Its performance was compared to an international group of 55 GI pathologists assessing 55 biopsies spanning the spectrum of BE-related dysplasia.
Results: The AI system correctly graded 76.4% of the WSIs, surpassing the median accuracy of 60.9% achieved by the GI pathologists. Despite solely assessing H&E stained slides compared to pathologists who also evaluated p53 immunohistochemical stained slides, the AI outperformed 53 out of 55 participating pathologists. ROC analysis yielded an AUC of 0.94 for predicting dysplasia presence versus absence and that the decision threshold of the AI system can be adjusted to achieve an accuracy of 92.7% (sensitivity: 0.92, specificity: 0.94, PPV: 0.97, NPV: 0.83). Finally, we illustrate case studies that showcase the AI system's ability to precisely identify dysplastic regions within the WSI, contributing to the transparency of our method.

Conclusion: In summary, our AI system demonstrated high accuracy, outperforming 53 of 55 pathologists evaluated. These findings demonstrate that this AI system has the potential to assist pathologists in assessment of BE-related dysplasia. The system's outputs could provide a reliable and consistent secondary diagnosis in challenging cases or be used for triaging low-risk non-dysplastic biopsies, thereby reducing the workload of pathologists, and increasing throughput. Future endeavors may explore integrating assessment of p53 immunohistochemical staining into the system.

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OFP-05-003

A pathplogists' ally - harnessing the potential of artificial intelligence in prostate cancer diagnosis: an analytical validation study

F. Maclean*, C. Petrucco, M. Phang, A. de Souza, M. Peters, A. Kumar, C. Warren
*Douglass Hanly Moir Pathology, Australia

Background & objectives: Prostate carcinoma has a significant worldwide burden, with an expected 85% increase in deaths by 2040. We developed an Artificial Intelligence (AI) model the detects 45 clinical findings despite technical artefacts. This study validates the standalone performance of the model.
Methods: An ensemble AI model was trained on >70,000 H+E stained whole slide images (WSIs) to detect, classify, localise and quantify routine findings across needle core biopsy (NCB) and transurethral resection of prostate (TURP) specimens. WSIs containing a variety of technical factors were included. The efficacy of the AI model was validated against >1700 ground truthed WSIs from distinct patients.
Results: The AI model demonstrated strong performance in the detection and classification of 45 malignant and benign clinical findings across both NCB and TURP WSIs in the presence and absence of technical artefacts. Over 71% of test set slides contained technical artefacts including staining artefacts, air bubbles, and tissue factors including tears, folds, calcification and diathermy artefact, with no significant loss of model performance. Robust results were obtained for identification and segmentation of acinar adenocarcinoma including identification of Gleason patterns 3-5. The model accurately detected cancer mimics including partial atrophy, post-atrophic hyperplasia, adenosis, Cowper's glands and basal cell hyperplasia.
Conclusion: The standalone results of the AI model for prostate NCB and TURP WSIs in the presence and absence of technical artefacts demonstrate reliable classification and localisation of findings. Additionally, the model's performance did not diminish in the presence of known cancer mimics. As the burden of pathological diagnosis of prostate cancer increases, there is a growing need to provide support to pathologists. Utilisation of this AI model may mitigate this burden and growing demands.

OFP-05-004

Swarm learning-based deep learning approach to discriminating autoimmune hepatitis and primary biliary cholangitis with multicentric data

O.L. Saldanha*, A. Gerussi, K. Pfeiffer, G. Cazzaniga, B. Engel, L. Di Tommaso, L. Terracciano, A. Lleo, M.V. Mauro Viganó, C. Rigamonti, D.C. Daniela Cabibi, V.C. Vincenza Calvaruso, V. L'Imperio, M. Carbone, J. Kather
*Else Kroener Fresenius Center for Digital Health, Medical Faculty Carl Gustav Carus, Technical University Dresden, Dresden, Germany

Background & objectives: Distinguishing Autoimmune Hepatitis (AIH) from Primary Biliary Cholangitis (PBC) histologically presents challenges, with florid PBC potentially leading to AIH overestimation and unnecessary immunosuppressive treatment. This study utilises deep learning (DL) pipeline for diagnosis, while Swarm learning (SL) addresses data exchange challenges in computational pathology.
Methods: We compiled three cohorts of digitised liver biopsy slides in a retrospective multicentre study across six European centres. The combined training set comprised 354 cases, with an external validation set of 92 cases. We developed an Artificial intelligence (AI) model, integrating self-supervised learning-based feature extraction and attention-based multiple-instance-learning for whole-slide image analysis. Explainable AI techniques were employed for further output characterization.
Results: Patient-level performance for predicting PBC or AIH was evaluated on external-validation cohort. Models trained on local datasets achieved Area Under the Receiver Operating Characteristic curve (AUROCs) of 0.7086(+/- 0.0447), 0.6305(+/- 0.1172), and 0.7505(+/- 0.1108). Merging the three training cohorts on a central server (merged model) improved prediction to 0.8100(+/- 0.0200). Compared to merged models, the SL model achieved an AUROC of 0.8001(+/- 0.0134), which was not significantly different from the merged model(p=0.6806). The model's predictions were tested against clinico-pathological diagnoses and evaluated for interobserver variability among pathologists using Cohen's kappa. The model emphasises areas with elevated inflammation and interface activity in AIH cases and the absence of lobular inflammation in PBC instances.
Conclusion: Our model represents the first approach to generating quantitative differential diagnoses among PBC-AIH cases, leveraging digital pathology slides without initial expert annotation. This model holds promise in assisting the differential diagnosis of autoimmune liver disease. Nevertheless, tackling computational pathology challenges in liver histology requires extensive datasets from multi-centres to mitigate bias. Overcoming practical, ethical, and legal barriers to data collection is vital. SL offers a solution by serving as an alternative for sharing patient-related data across sites in the future.

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OFP-05-005

Enhancing histopathological research with privacy-preserving swarm learning and advanced image generation techniques

J. Zhu*, O.L. Saldanha, S. Schulz, P. Wienholt, S.U.H. Dar, S. Engelhardt, F. Laqua, B. Baessler, D. Truhn, S. Foersch, J.N. Kather
*Else Kroener Fresenius Center for Digital Health, Medical Faculty Carl Gustav Carus, Technical University Dresden, Dresden, Germany

Background & objectives: Accessing various high-quality histopathology datasets of ccRCC (Clear-Cell-Renal-Cell-Carcinoma) for Artificial Intelligence diagnostic systems is challenging because of data scarcity and ethical concerns. Since current solutions lack data diversity, we aim to create realistic synthetic ccRCC images with generative models and swarm-learning (SL).
Methods: Our approach combines generative models and SL to generate synthetic ccRCC tissue images. We demonstrate this by setting up SL networks and training generative models on three cohorts stored in separate computer systems: TCGA

(The-Cancer-Genome-Atlas-Program, N=510), CPTAC (Clinical-Proteomic-Tumour-Analysis-Consortium, N=420), and internal cohorts(N=720). We assessed the quality of generated images through several quantitative metrics and pathologist feedback, comparing score-based and latent diffusion models.
Results: Preliminary results indicate that the diffusion model can successfully generate synthetic images that closely resemble real histopathological samples (by evaluating with Fréchet Inception Distance, Structural Similarity Index Measure, and Peak Signal-to-Noise Ratio). Quantitative evaluations demonstrate a high degree of similarity between synthetic and real images. Moreover, incorporating synthetic images into diagnostic model training datasets has shown potential for improving model accuracy and robustness. Notably, SL has significantly enhanced the efficiency of the training process. By distributing the dataset and computing across two lab servers, we observed a convergence rate twice as fast as that of centralized learning approaches. This method also mitigates the challenge of data privacy and computational resource consumption.
Conclusion: Our findings show the potential of combining diffusion models with SL for creating synthetic histopathological images. Future efforts will refine the generation process, further validate synthetic images in diagnostics, address survival prediction, and explore more tumour types, including papillary pRCC (Papillary Renal Cell Carcinoma) cases and other clinically relevant parameters through conditional training. We plan to deploy these models in real-world settings, enabling joint training across remote institutes.

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OFP-05-006
DinoBloom: a foundation model for generalizable cell embeddings in haematology
S.J. Wagner*, V. Koch, M. Hehr, S. Kazeminia, J.A. Schnabel, T. Peng, C. Marr
*Helmholtz Munich, Germany

Background & objectives: In haematology, computational models offer significant potential to enhance diagnostic accuracy and workflow efficiency, as samples are still predominantly evaluated manually. However, challenges like small, imbalanced datasets and batch effects hinder the development of robust models and their clinical adoption.
Methods: To address these issues, we introduce DinoBloom, the first foundation model for haematology. We combine a tailored self-supervised pipeline with semi-supervised learning by including losses on cell type and domain to achieve generalizable cell embeddings. DinoBloom is trained on ten diverse datasets with over 3 million white blood cell images from peripheral blood and bone marrow smears.
Results: Four DinoBloom models (small, base, large, giant) are trained to and tested on three various downstream tasks. We achieve a weighted F1-score of 91.8 on cell type classification on peripheral blood smears, 85.7 on bone marrow smears and 93.1 for acute myeloid leukemia subtyping, respectively. With that, our model surpasses both medical and non-medical vision models in cell-level and patient-level classification tasks. We assess the performance on downstream tasks by linear probing, k-nearest neighbor evaluations, and weakly supervised multiple instance learning. The generalization capabilities were evaluated on an external dataset with strong domain shift.
Conclusion: DinoBloom presents a significant advancement in computational haematology, offering better performance on diagnostic tasks with the potential to improve the workflow efficiency using patient embeddings and cell-type quantification. Its superior performance in diverse tasks and robust generalization underscore its potential for clinical adoption. We publish both code and model weights to foster accessibility and facilitate further research in this domain.

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OFP-05-007
Standardization of granulomas in diffuse lung diseases
S. Sato*, Y. Zaizen, J. Augustyniak, S. Berezowska, L. Brcic, A. Carneiro, A. Fabro, A. Hebisawa, I. Kern, R. Koyama, B. Larsen, A. Marchevsky, F. Schneider, S. Kunugi, J. Fukuoka
*Saitama Red Cross Hospital, Japan

Background & objectives: Granulomas are crucial in diagnosing diffuse lung diseases (DLDs). However, the concordance rate among pathologists remains unexplored. This study aimed to clarify the variability in diagnosing granulomas among pathologists and to propose a method for standardization.
Methods: Cases of DLDs diagnosed through multidisciplinary discussion, which featured descriptions of granulomas in the pathological reports, were included in the study. Granulomatous-like candidate images were extracted from the pathological images using whole slide imaging. Thirteen pulmonary pathologists then labeled these candidate images, followed by statistical analysis.
Results: A total of 863 candidate images were extracted from 90 cases, including 41 cases of hypersensitivity pneumonitis (HP), 8 of sarcoidosis, and 4 of granulomatosis with polyangiitis (GPA). Labels for granulomas accounted for 65.9% of the 11,219 (863x13) judgments. In HP, granuloma judgment was applied to only 60.1% of candidate images, with roughly 80% being poorly formed. In contrast, sarcoidosis and GPA showed 93.9%/77.7% for candidate images and 52.0%/60.0% for well-formed/palisading granulomas, respectively. The kappa values for inter-pathologist agreement were 0.43 across all candidates, 0.29 for HP, 0.34 for sarcoidosis, and 0.6 for GPA. Notably, all pathologists labeled some candidate images of HP and GPA cases as having well-formed granulomas.
Conclusion: This study demonstrated for the first time the poor agreement on granuloma judgment in DLDs, which raises concerns since granuloma is a core diagnostic criterion under the guideline for HP, despite the low agreement rate. Additionally, well-formed granulomas, stated as criteria for exclusion, were rare but observed at a consistent frequency in HP and GPA by all pathologists. This underscores the need for further investigation.

OFP-05-008
MTAP deficiency by immunohistochemistry as a new potentially predictive marker in non-small-cell lung cancer (NSCLC)
M. Brune*, L. Roma, O. Chijioke, T. Vlajnic, I. Alborelli, N. Deigendesch, S. Savic, L. Bubendorf
*Institute of Medical Genetics and Pathology, University Hospital Basel, Switzerland

Background & objectives: Loss of MTAP (methylthioadenosine phosphorylase) has been reported in up to 13% of NSCLC. It predicts poor response to immune-checkpoint-inhibitors and serves as putative predictive marker of response to cooperative PRMT5-inhibitors. We investigated the prevalence of MTAP deficiency by immunohistochemistry(IHC).
Methods: MTAP IHC (2G4, Abnova) was assessed in 851 NSCLC samples, including locoregional and metastatic manifestations. We evaluated histological subtype, localization and PD-L1-status. Next generation sequencing (NGS) data were available in 524 cases, analyzed with the OncomineTMPrecision panel (Thermo Fisher) focusing on copy number variations (CNV) of CDKN2A. Additionally, our findings were compared to data from The Cancer Genome Atlas (TCGA).

Results: MTAP deficiency by IHC was found in 20.3% of all samples. It was not associated with the histological subtype, localization, sex or patients' age. There was no significant association between MTAP expression and PD-L1-status or mutations of EGFR, KRAS, BRAF, ERBB2, TP53, METexon14 or CDKN2A. CNV data of CDKN2A – used as surrogate for MTAP loss – were available in 516 cases, of which 107 (20.7%) were MTAP deficient by IHC. MTAP deficiency by IHC was significantly associated with CDKN2A CNV loss (p=0.03). Nevertheless, CDKN2A loss was found in only 28 (26.1%) of 107 specimens with MTAP deficiency. TCGA data analysis revealed MTAP loss in 62/511 NSCLC (12.1%).
Conclusion: 20% of NSCLC in our cohort show MTAP deficiency by IHC. IHC is more sensitive than targeted panel-based NGS to detect MTAP deficiency in NSCLC. The results of ongoing analyses to explore reasons for the lower sensitivity of NGS will be presented at the congress. This study provides evidence that IHC might become the standard method to identify MTAP deficiency in NSCLC as predictive biomarker for treatment with new PRMT5-inhibitors.

OFP-05-009
Proteomic analysis of pulmonary fibrosis associated with lung cancer reveals dysregulation of the apoptotic pathway
C. Guillois*, H. Cazier, E. Guenzi, A. Chassac, P. Mordant, G. Zalcman, A. Mailleux, B. Crestani, A. Cazes, G. Chevreux, N. Poté
*Department of Pathology, Bichat Hospital, France

Background & objectives: The reasons why pulmonary fibrosis (PF) favours lung cancer (LC) remains unknown. Combining Liquid Chromatography Mass Spectrometry (LC-MS/MS) and Mass Spectrometry Imaging (MSI), we compared the proteome of PF tissue samples with and without LC to identify altered signaling pathways.
Methods: 34 Formalin Fixed Paraffin-Embedded surgical samples from patients with PF and LC (LC+, n=17) and without LC (LC-, n=17) were selected. Proteomic profiles of fibrotic areas adjacent to LC in the LC+ group were compared to those of fibrotic areas in the LC- group. Additionally, MSI analysis included ion map, segmentation analysis and in silico digestion.
Results: LC-MS/MS analysis identified 66 out of 4901 proteins differentially expressed between fibrotic areas of LC- and LC+ samples (p<0.001). Pathway analysis suggested the involvement of oxidative stress metabolism and apoptosis, with significant downregulation of four mitochondrial proteins know to regulate apoptosis (BAX, Glutathione Peroxidase, Frataxin, Mitochondrial Fission 1 protein) in fibrotic areas adjacent to LC. Fold changes ranged from 1,65 to 9,2.
After in silico tryptic digestion of mitochondrial proteins, MSI analysis revealed at least 2 unique peptides per protein that were significantly less expressed in LC+ fibrotic areas. Complementary ion map analysis showed a preferential expression of these mitochondrial peptides within the epithelial cells over the mesenchymal cells.
Conclusion: Using an original proteomic approach integrating LC-MS/MS and MSI, we identified 66 proteins differentially expressed between fibrotic areas of PF patients with and without LC. Fibrotic areas adjacent to LC exhibited a significant downregulation of apoptotic-regulating mitochondrial proteins. Interestingly, spatial analysis by MSI suggested that these proteins were expressed by epithelial cells within fibrotic areas. These preliminary results suggest that dysregulation of apoptosis in epithelial cells might be involved in lung carcinogenesis in patients with PF.

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OFP-05-010
Effect of neoadjuvant chemoimmunotherapy on PD-L1 expression in non-small cell lung cancer
S. Stoykova*, L. Chriqui, E. Abdelnour Berchtold, S. Peters, J.Y. Perentes, S. Berezowska
*Department of Laboratory Medicine and Pathology, Institute of Pathology, Lausanne University Hospital and University of Lausanne, Switzerland

Background & objectives: PD-L1 expression is the standard clinical biomarker used to select patients eligible for immunotherapy in non-small cell lung cancer (NSCLC). Here, we evaluate the effect of neoadjuvant chemoimmunotherapy, the novel standard in the neoadjuvant setting, on PD-L1 expression in NSCLC.
Methods: Our retrospective, single centre cohort included 43 patients with stage III and IV NSCLC who underwent neoadjuvant chemoimmunotherapy between 2017 and 2022. Nine patients were excluded due to pathologic complete response. PD-L1 testing on both diagnostic lung biopsy or cytology sample and post-neoadjuvant resection specimen was available in 17/34 patients.
Results: PD-L1 Tumour Proportion Score (TPS) expression pre- and post-neoadjuvant treatment was evaluated according to clinically significant increments: <1%, 1-49% and ≥50%. PD-L1 expression remained unchanged in 8/17 cases (47%), of which 7 with TPS <1%, with 2/7 showing major pathologic response (MPR). No TPS ≥50% was observed in resection specimens. In 7/17 cases (41%), PD-L1 expression was lower in the resection specimens compared to diagnostic biopsies, with 4/7 showing MPR. The 6/17 cases with TPS ≥50% pre-neoadjuvant treatment showed 3 with TPS <1% and 3 with TPS 1-49% in the resection specimens. Only 2/17 cases (12%) presented with an increased PD-L1 expression in the resection specimens (1-40% compared to <1%).
Conclusion: PD-L1 expression in resection specimens after neoadjuvant chemoimmunotherapy was mostly negative, and unchanged negative or decreased compared to the diagnostic pre-neoadjuvant treatment material. Only exceptional cases showed a slightly increased PD-L1 expression in resection specimens, which could be attributed to tumour heterogeneity. Decreased PD-L1 TPS seemed to be associated with MPR, although the low patient numbers preclude any definitive conclusion.

OFP-05-011
CXCR4 expression in tissue samples and circulating tumour cells could play pivotal role as prognostic biomarker in neo-adjuvant treated non-small cell lung cancer
M. Barella*, G. Bertolini, G. Sabella, M. Gentili, B. Bodini, A. Mangogna, V. Lagano, A. Fabbri, D. Lorenzini, T. Beninato, R. Leporati, G. Lo Russo, G. Pruneri, L. Roz, M. Milione
*Department of Diagnostic Innovation, Pathology Unit 1, Fondazione IRCCS Istituto Nazionale dei Tumouri, Milan, Italy

Background & objectives: Neoadjuvant chemotherapy is the primary approach for locally-advanced non-small cell lung cancer (LA-NSCLC). In preclinical models, platinum-based damage has been shown to activate CXCR4-driven dissemination. Our aim was to evaluate CXCR4 expression in tissue samples and circulating tumour cells (CTCs).
Methods: We enrolled 72 patients with LA-NSCLC from 2019 to 2023. Tissue samples were retrieved by pre-treatment biopsy and post-treatment surgery. Immunohistochemistry for CXCR4 (D4Z7W) was performed and evaluated with H-score, accounting as positive any expression. Starting from cryopreserved peripheral blood, CXCR4+ CTCs were enumerated exploiting DEPArray technology. Median value ≥ 5 was set as cut-off for positivity.
Results: Tissue samples were available for 46 and 29 patients in pre- (T0) and post-treatment (T1) settings and were positive for CXCR4 staining in 12 (26,1%) and 13 (44,8%) cases respectively. CTCs were analyzed in 44-T0 and 40-T1 patients' blood samples of which 21 (47,7%) and 24 (60,0%) respectively were positive for CXCR4. No association was identified for CXCR4 positivity between tissue samples

and CTCs. CXCR4+ CTCs were associated with a worse overall survival (OS) in T0 and T1 (p=0,009, p=0,052). Paired T0-T1 tissue specimens were evaluated in 22 patients. H-index increased in T1 setting (p=0,0024) and a worse trend for OS was observed in cases with increased CXCR4 H-index (p=0,1).
Conclusion: CXCR4 membranous expression was increased in both pre- and post-treatment setting showing a trend towards a worse OS. CXCR4+ CTCs represented a negative prognostic factor in both settings confirming the association of CXCR4 with metastatic dissemination as highlighted in preclinical models. No association was identified between CXRC4 positivity in tissue samples and CTCs. Further analyses are needed to fully assess CXCR4 expression in metastasis.

OFP-05-012
One-step nucleic acid amplification (OSNA) assay for nodal analysis in early-stage non-small cell lung cancer: preliminary results
I. Di Stefano*, A. Proietti, G. Romano, C.C. Zirafa, F. Calabrò, S. Pelliccioni, C. Niccoli, F. Melfi, G. Alì
*Surgical, Medical, Molecular and Critical Care Pathology Department, University Hospital of Pisa, Italy

Background & objectives: The significance of nodal micrometastasis in early-stage Non-Small Cell Lung Cancer (NSCLC) remains unclear. We aim to compare the efficacy of One-Step Nucleic Acid Amplification (OSNA) with standard histology and immunohistochemistry in nodal metastasis detection.
Methods: In a prospective study, 24 patients with early-stage NSCLC undergoing minimally invasive robotic surgery were enrolled and randomized into two groups. The first group underwent OSNA analysis for lymph nodes weighing ≥ 25 mg, while the second group underwent standard histopathological examination with CK19 immunohistochemistry to identify nodal metastases. Sensitivity and specificity of both methods were calculated to determine concordance.
Results: A total of 139 lymph nodes from 24 NSCLC patients were examined, 69 in the OSNA group and 70 in the non-OSNA group. All patients had confirmed primary tumour diagnosis, including 20 adenocarcinomas, 3 squamous cell carcinomas, and 1 pleomorphic carcinoma. OSNA detected metastases in two lymph nodes from two different patients out of 69 examined, while the standard method detected metastases in five lymph nodes, all from the same patient. Only OSNA identified a micrometastasis.
Conclusion: In a homogeneous cohort of patients with early-stage NSCLC and without pathological lymphadenopathies, OSNA demonstrates superior sensitivity in detecting lymph node micrometastases compared to conventional methods. These preliminary results suggest the potential of OSNA as a valuable tool in the management of NSCLC, facilitating the identification of patients who may benefit from adjuvant therapy. Further expansion of our case series will strengthen these results.

OFP-05-013
Comprehensive analysis of neurod1, ascl1, pou2f3 and yap1 expression signatures reveal unique lcnec subgroups with guidance for personalized treatment
F. Heijboer*, J. Derks, D. Mustafa, N. Rijnsburger, B. Hermans, L. Hillen, E. Speel, A. Dingemans, J. von der Thusen
*Erasmus MC, The Netherlands

Background & objectives: Large-cell neuroendocrine carcinoma (LCNEC) can be genomically subtyped into SCLC-like and NSCLC-like. NEUROD1, ASCL1, POU2F3 and YAP1 (NAPY) subtypes have been reported for SCLC. We immunohistochemically evaluated NAPY in LCNEC alongside relevant protein expression data (pRb, DLL3, cMYC, TTF1).
Methods: Tissue microarrays from 133 stage I-III resected LCNEC were revised and immunostained for NAPY, pRb, DLL3, cMYC and TTF1. An H-score >10 was considered positive (+), and >50 dominant. Unsupervised clustering and spatial immune RNA profiling using GeoMX Digital Spatial Profiling (DSP) were performed. Clinical data were obtained from the Netherlands Cancer Registry.
Results: ASCL1 was dominant in 26%, and NEUROD1 in 18% of LCNEC. pRb loss was observed in 75%. DLL3, cMYC and TTF1 were positive in 66%, 26%, and 70%, respectively. Unsupervised clustering identified 5 clusters: NEUROD1(high)-ASCL1(high) (10%), ASCL1(high) (22%), POU2F3(high) (5%), YAP1(high) (11%), and NAPY(low) (51%). NEUROD1(high)-ASCL1(high) and ASCL1(high) clusters were correlated with DLL3(high) and high neuroendocrine (NE) marker expression. YAP1(high) was enriched for pRb+. POU2F3(high) and YAP1(high) were NE marker low and DLL3(low). ASCL1(high) showed poorest survival and the highest rate of brain metastases. In the NEUROD1(high)-ASCL1(high)-POU2F3(high)-group, DSP identified four upregulated genes involved in the immune system and/or tumour development.
Conclusion: Five unique LCNEC clusters have been identified: NEUROD1(high)-ASCL1(high), ASCL1(high), POU2F3(high), YAP1(high), and NAPY(low). NE clusters (NEUROD1(high)-ASCL1(high) and ASCL1(high)) were associated with DLL3(high) expression and poor outcome (ASCL1(high)). Compared to the proportion known in SCLC, more NAPY(low) and YAP1(high) and fewer POU2F3(high) cases were identified. Application of transcriptional NAPY markers in LCNEC reflects SCLC-like and NSCLC-like subtyping, potentially allowing for different targeted therapies.

OFP-05-014
Percentage and size of residual viable tumour in lymph node, the performance in estimating pathologic response of lymph node in non-small cell lung cancer treated with neoadjuvant chemoimmunotherapy
D. Lin*, W. Sun
*Beijing Cancer Hospital, China

Background & objectives: Different protocols recommend the percentage of residual viable tumour (RVT%) and metastatic tumour size (MTS) for evaluating lymph node metastasis (LNM) in non-small cell lung cancer following neoadjuvant chemoimmunotherapy. Our aim was to identify superior parameter for LNM evaluation.
Methods: We utilized two cohorts (derivation, n=84; external validation, n=44). In the derivation cohort, we assessed the mean and largest values of MTS and RVT% in LNM, estimating their optimal cutoffs for event-free survival (EFS) using maximally selected rank statistics. Validation was conducted in the external validation cohort. The quality of prognostic factors was evaluated using the Area Under Curve (AUC).
Results: In the derivation cohort, neither the largest MTS (cutoff=6mm, p=0.13) nor RVT% (cutoff=75%, p=0.19) values in LNM were associated with EFS. Optimal cutoffs for EFS were determined to be 4.5mm and 55% for the mean of MTS and RVT%, respectively. In the external validation cohort, RVT% (mean value, cutoff=55%) showed no association with EFS (p=0.99), whereas MTS (mean value, cutoff=4.5mm) was significantly associated with EFS (p=0.015). ypN staging exhibited no association with EFS in either the derivation cohort (p=0.28) or the external validation cohort (p=0.14). The prognostic value of MTS surpassed that of ypN staging in both cohorts, as evidenced by higher AUC values.
Conclusion: The mean value of MTS can effectively serve as a parameter for the pathological evaluation of lymph nodes, with a threshold of 4.5mm, closely linked to EFS. Its prognostic value outperforms that of ypN staging.

OFP-05-015
A comparative analysis of the ESP/QuIP "lung cancer related molecular markers" EQA scheme in non-small cell lung cancer (NSCLC) using different methodologies

M. Ihle*, C. Lindner, K. Ilm, K. Jöhrens, U. Siebolts, S. Merkelbach-Bruse
*Uniklinik Köln, Molekularpathologische Diagnostik, Köln, Germany

Background & objectives: NSCLC accounts for ~85% of all lung cancer. Reliable molecular diagnosis of biomarkers is crucial for treatment decisions. We present the results of the ESP/QuIP EQA for ALK, ROS1, RET fusion and MET ex14 skipping testing in 55 European laboratories.
Methods: QuIP GmbH provided 10 patient-derived FFPE cases of NSCLC to the participants for testing of each biomarker: ALK, ROS1, RET fusions and MET ex14 skipping. Only samples with concordant results in the reference institutes were included in the sample cohort. The anonymized results were reviewed by experts and sent to participants to help improve their diagnostic performance and facilitate benchmarking.
Results: In total, 38 out of 55 participants (69%) successfully participated in the EQA, meaning success for all biomarkers ALK, ROS1, RET and MET ex14 skipping. No specific problem could be detected for a single biomarker. Participants used a wide range of NGS methodologies and bioinformatic solutions and qPCR-assays, showing no correlation to the success rates. Failed samples were further analysed for specific reasons and detailed feedback was provided to the participants.
Conclusion: The high number of participants shows the increasing demand for quality assurance in fusion diagnostics in NSCLC patients. Unsuccessful participants were made aware of the significant consequences of inadequate routine diagnostics for patient care, underlining the importance of regular proficiency testing and continuous monitoring for high quality and accuracy standards.

OFP-06Joint Oral Free Paper Session Endocrine Pathology / Head and Neck Pathology

OFP-06-001
Clinicopathological and epigenetic differences between primary neuroendocrine tumours and neuroendocrine metastases in the ovary

A.V. Verschuur*

*UMC Utrecht, The Netherlands

Background & objectives: Existing literature provides insufficient support to distinguish primary ovarian neuroendocrine tumours (PON) with and without teratomous components from neuroendocrine ovarian metastases (NOM) in patients. This study aims to differentiate NOM from PON using clinical characteristics, immunohistochemistry, and DNA methylation profiles.
Methods: Patients with well-differentiated ovarian neuroendocrine tumours (NET) were identified from electronic records and a nationwide search spanning 1991 to 2023. Clinical characteristics were collected, histologic samples were stained for CDX2, PAX8, TTF1, SATB2, ISLET1, OTP, PDX1 and ARX, and DNA methylation analysis was conducted on NET tissue of ovarian, pancreatic, ileal, and rectal origins (n=16, 22, 10, and 7, respectively).
Results: This study included 71 patients with NOM and 17 with PON. NOM were not associated with teratoma and 78% of NOM were bilateral. All PON were unilateral with nine PON within teratomas (PON-T+). PON without teratoma (PON-T-) showed similar insular growth pattern and immunohistochemistry (CDX2 positivity and ISLET1, ARX and SATB2 negativity) to NOM ($p > 0.05$). Compared to PON-T+, PON-T- showed more frequently ISLET1 positivity, larger tumour size, and older age at diagnosis ($p < 0.05$). Unsupervised analysis of DNA methylation profiles revealed 4/5 of PON-T- clustering together with NOM and ileal NET, while 4/5 of PON-T+ clustered with rectum NET. Chromosome 18 loss was more common in the first cluster.
Conclusion: Presence of teratomous components and lateralization are key in distinguishing between PON and NOM. PON-T- exhibit similar immunohistochemistry, growth pattern, DNA methylation, and chromosome 18 loss to midgut-origin NOM. Therefore, in the absence of a teratoma, the molecular profile suggests a likely midgut-origin NOM. For these patients treatment as for midgut NET might be considered if thorough review of imaging does not reveal a primary tumour.

OFP-06-002
Prevalence and histologic features of multifocal fibrosing thyroiditis in the thyroid gland, a multicentre European study

M.V. Altavilla*, F. Chiarucci, J. Vale, E. Solaroli, A. Repaci, S. Coluccelli, T. Maloberti, A. De Leo, C. Eloy, G. Tallini
*Anatomic Pathology - Department of Medical and Surgical Sciences (DIMEC), University of Bologna, Bologna, Italy

Background & objectives: Multifocal fibrosing thyroiditis (MFT) is an enigmatic entity characterized by multiple fibrotic scar-like lesions, under-recognized and under-reported. Its prevalence is unknown. We analyse for the first time clinicopathologic features and prevalence of MFT in a contemporary routine surgical pathology series.
Methods: MFT cases were collected from the pathology laboratories of Maggiore Hospital in Bologna (Italy) and of IPATIMUP in Porto (Portugal). Cases reviewed included all thyroid resections from Bologna (2017-2023) and from Porto (2021-2022). All slides from Porto were retrieved from the IPATIMUP digital pathology archive and shared virtually for the purpose of the study.
Results: Twenty-seven MFT were identified among 1736 thyroid resections (prevalence 1,5%; 22/1393 from Italy, 5/343 from Portugal). Clinicopathologic features were no different between Italian and Portuguese cases. MFT findings: female patient predominance (23/27,85%); mean age 54.4; most common reason for surgery, thyroid nodule; persistently elevated anti-Thyroglobulin antibodies in a subset of patients; diameter of foci, 1-16 mm (mean 4.0); number of MFT foci, 1-17 per case (mean 4.6); bilateral involvement, 59%; among largest foci, stellate-shaped ones (17/27,63%) predominated over band-like ones (10/27,37%), while peripheral/subcapsular foci (17/27,63%) predominated over central/intraparenchymal ones (10/27,37%); carcinoma, all papillary (PTC), 17/27(63%), most $\leq$10 mm (12/17,70%), many multifocal (9/17,52%); follicular nodular disease, 18/27(67%); thyroiditis, 7/27(26%).
Conclusion: MFT is uncommon, but not exceedingly rare, with a prevalence of approximately 1.5%. There are no clinicopathologic differences between Italian and Portuguese cases. Compared with the largest collection of MFT reported to date, consisting of Dr. Rosai consultation cases (Fellegara&Rosai, AmJSurgPathol.2015), routine MFT cases tend to be larger (4 versus 2 mm), but less multifocal. Also, they have higher proportion of associated PTC and of follicular nodular disease.

OFP-06-003
Syndromic MEN1 parathyroid adenomas consist of multiple clones and subclones

K. Bräutigam*, C. Nesti, P. Riss, C. Scheuba, B. Niederle, T. Grob, A. Di Domenico, M. Neuenschwander, P. Mazal, N. Köhn, R. Trepp, A. Perren, R. Kaderli
*Institute of Cancer Research, Centre for Evolution and Cancer, London, UK, United Kingdom

Background & objectives: Primary hyperparathyroidism with parathyroid tumours is common in Multiple Endocrine Neoplasia Type 1 (MEN1). The nature of these tumours as multi-glandular clonal disease or hyperplasia is still inconclusive. Our study further explores the molecular basis of syndromic MEN1 parathyroid adenomas.
Methods: We examined the histomorphology and protein expression of Menin and p27 in parathyroid adenomas from 25 patients of two

independent, well-characterized MEN1 cohorts. Loss of heterozygosity (LOH) patterns were evaluated using fluorescence in situ hybridization (FISH) in a MEN1-associated parathyroid adenoma. Additionally, next-generation sequencing (NGS) was performed on eleven nodules from four MEN1 patients.
Results: MEN1 parathyroid tumours mostly consist of morphologically distinct nodules. In FISH, centromere 11 loss and MEN1 LOH were much more frequent in the MEN1 adenoma compared to the non-MEN1 adenoma. NGS found known MEN1 gene mutations but no other oncogenic drivers. We observed different second hits of the MEN1 region, i.e. copy number–neutral LOH and biallelic loss, suggesting clonally distinct tumours. Intra-adenomatous subclones had heterogeneous molecular aberrations. In immunohistochemistry, only 9/25 (36.0%) samples were at least partially evaluable. All of those samples showed convincing Menin loss. p27 expression remained intact in about one third of samples.
Conclusion: In MEN1, parathyroid tumours manifest as multiple monoclonal tumours rather than hyperplastic changes. Our findings reveal intra-parathyroidal genetic heterogeneity, suggesting both clonal evolution and multi-clonal origin. Menin loss was consistently observed in all assessable samples. Furthermore, the majority of MEN1 samples exhibited partial absence of p27 protein expression, indicating that p27 immunohistochemistry may not be a reliable indicator for MEN4 in these patients.

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OFP-06-004
Reticulin framework alterations in paragangliomas: do they matter at all?
E. Duregon*, G. Orlando, C. Lopez, A. Vasconi, M. Volante, M. Parasiliti-Caprino, M. Papotti
*Department of Oncology, Pathology Unit, University of Turin, Italy

Background & objectives: Paragangliomas (PGLs) are neuroendocrine neoplasms which lack clinical or histopathological findings predictive of an aggressive/metastatic behavior, thus making them all potentially malignant. This study aims to define the role reticulin framework (RetFr) assessment in the diagnostic workup of PGLs.
Methods: 91 PGLs (82 adrenal and 9 extra-adrenal) fully characterized with genetic, clinical and histopathological information were retrieved from the pathology files of the University of Turin from 1995 to 2022. Reticulin stains of all cases were digitalized, assessed for quantitative and qualitative alterations of the RetFr and then matched with their clinical-genetic profile.
Results: According to the current PGL genetic clustering, 17 cases had gene mutations in VHL and SDHX (Cluster 1), 18 cases in NF1, RET, MAX (Cluster 2) and 56 were sporadic cases. As for adrenocortical tumours, quantitative RetFr (qT-RetFr) alterations were defined as complete nest disruption of the normal paraganglia framework, while qualitative RetFr (qL-RetFr) alterations referred to variations in the nest size in an otherwise intact RetFr. qT-RetFr changes were observed in 41 cases (45%), mostly sporadic (#32, 72%). A novel, predominant (>80%) very small qL-RetFr alteration pattern (1-2 cells/nest) was a feature of 28 cases (31%), significantly associated with mutations of Cluster 1 genes.
Conclusion: Despite remarkable conceptual, biological, genetic and clinical advances, malignancy definition in PGLs remains elusive. This may explain the current lack of effective treatment options for metastatic forms and makes a call for identifying novel targets to stratify and improve the diagnostic, prognostic and therapeutic strategies. Here we show for the first time a link between a qL-RetFr alteration and genetic mutation profile, setting the ground for promising more sophisticated RetFr alteration analyses supported by artificial intelligence algorithms.

OFP-06-005
Tumour grade in medullary thyroid carcinoma: correlation with outcome, molecular analysis and immunomodulation
F. Galuppini*, S. Censi, M. Iacobone, L. Bertazza, S. Barollo, A.P. Dei Tos, C. Mian, G. Pennelli
*Pathology Unit, Department of Medicine (DIMED), University of Padua, Padua, Italy

Background & objectives: The International Medullary Thyroid Carcinoma Grading System (IMTCGS) divides medullary thyroid carcinoma (MTC) into high- and low-grade tumours. The aim of this study was to explore the association between IMTCGS grading, clinical data, molecular status and immunomodulation in sporadic MTC.
Methods: A retrospective cohort study was performed on consecutive sporadic MTCs from patients undergoing initial surgery between January 2000 and January 2022. Clinical, pathological, and follow-up data were collected, tumours were graded, and somatic mutations of RET and RAS genes were analyzed. PD1, PD-L1 and CD8 immunohistochemical analysis were performed. Patient outcomes were based on Ct levels and MTC-related deaths.
Results: The series included 141 consecutive sporadic MTCs.107/14 (76.9%) were classified as low-grade tumours, 32/141 (23.1%) as high-grade. Patients carrying a RET mutation had more aggressive features and shorter disease-specific survival (DSS) ($p = 0.001$). At multivariable survival analysis, only IMTCGS grading was independently associated with DSS ($p = 0.005$). RET mutations, in particular RET-M918T, were more frequent in high-grade MTC (68.8% vs. 29.4% mutated in RET, 46.9% vs. 12.7% mutated in RET-M918T; $p < 0.001$). None of the high-grade tumours was mutated in the RAS gene, but the mutation was present in 11.8% of low-grade tumours. CD8 and PD-L1 expression correlated with high-grade tumours ($p = 0.001$).
Conclusion: IMTCGS grading was associated with DSS independently of other clinical, pathological, molecular factors. Moreover, MTC grading was associated with RET and RAS patterns, which explains, at least in part, the molecular basis of the aggressive behavior of high-grade MTC.

OFP-06-006
Hobnail and tall cell subtypes: clinical and molecular characterization of two aggressive variants of papillary thyroid carcinoma
F. Galuppini*, S. Censi, L. Bertazza, S. Barollo, M. Iacobone, A.P. Dei Tos, F. Vianello, C. Mian, G. Pennelli
*Pathology Unit, Department of Medicine (DIMED), University of Padua, Padua, Italy

Background & objectives: The prognosis of papillary thyroid carcinoma (PTC) is generally excellent, but there are some particularly aggressive subtypes that determine in patients a worse clinical response, with persistence of disease or disease-related death.
Methods: We studied 74 Hobnail PTCs (HOPTC) who underwent thyroidectomy between 2010 and 2021.The presence of mutations in BRAF, TP53 and TERT promoter genes was analyzed. The clinical-molecular characteristics of the patients were compared with those of 173 consecutive patients who underwent surgery for Tall cell PTC (TCPTC) between 2015 and 2021.
Results: HOPTC showed a less marked predilection for female gender, larger size of the primary lesion and stages III and IV compared with TCPTC. However, the higher frequency of negative outcome found in hobnail patients, was not significant. There were no statistically significant differences between the two groups regarding the prevalences of mutations in BRAF and TERT promoter and TP53. However, TERT mutation in TCPTC correlated with greater size of the primary lesion, T4, stage III and perinueral invasion. HOPTC with TERT mutation also, showed greater distribution in more advanced stages. TCPTC with BRAF mutation had larger primary tumour size and stage IV at the diagnosis.

Conclusion: HOPTC is associated with more aggressive clinicopathologic features than TCPTC, so early recognition of this rare form of PTC is crucial. The factors to be paid more attention, as they influence the outcome of HOPTC, are stage, and its constituent parameters, LNR and perithyroidal soft tissue invasion and TERT status.

OFP-06-007

Expression profile differences according to grade in medullary thyroid carcinoma

I. Ruz-Caracuel*, T. Caniego-Casas, T. Alonso-Gordoa, I. Carretero-Cerro, C. Ariño-Palao, A. Santón, M. Rosas, H. Pian, J. Molina-Cerrillo, P. Luengo, J. Palacios
*Pathology Department, Hospital Universitario Ramón y Cajal, Madrid, Spain

Background & objectives: Medullary thyroid carcinoma (MTC) is a rare neuroendocrine neoplasia. A new classification was introduced in 2021 that divides MTC in two grades according to proliferation and necrosis. Our objective was to identify differences in the expression profile between both grades.
Methods: The expression of 760 human mRNAs included in the Tumour Signaling 360 Panel was measured in 21 MTCs (9 high-grade and 12 low-grade) using the NanoString nCounter gene expression platform. qRT-PCR was used to validate the expression of selected genes in 30 MTCs. DLL3 (clone SP347, Roche) immunohistochemistry was quantified in tumour cells in scanned slides using QuPath.
Results: Eight genes, including DLL3, were found differently expressed between high-grade and low-grade MTC. The most significant pathways differentially expressed were DNA damage repair, p53 signaling, cell cycle, apoptosis, and Myc. The expression of DLL3 correlates with ASCL1, an upstream regulator. Subsequently, DLL3 was quantified by digital pathology and tumours with positive DLL3 expression (defined as >1%) were associated with a significantly lower disease-free survival (p=0.035) and overall survival (p=0.014) compared with negative DLL3 tumours. DLL3 positive expression was also associated with the presence of MTC desmoplasia.
Conclusion: High-grade and low-grade MTC have different expression profiles. DLL3 should be explored as a predictor of aggressive disease and poor outcome in MTC.

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OFP-06-008

Interest and relevance of the new 2022 WHO classification to predict the risk of refractory disease in thyroid carcinomas: review of a 238-cases cohort

E. Andre*, L. Mebarki, H. Lasolle, M. Ilie, F. Borson-Chazot, M. Decaussin-Petrucci
*Pathology department, Centre Hospitalier Lyon Sud, Hospices Civils de Lyon, Pierre Bénite, France

Background & objectives: The relevance of the new 2022 WHO thyroid classification to predict clinical evolution is not clearly demonstrated. To evaluate the association between the 2022 WHO and aggressiveness, we studied a large cohort of thyroid carcinomas with follow-up.
Methods: We re-examined 238 differentiated thyroid cancers operated between 2009 and 2017, and considered as advanced stage (stage pT3, pT4 or M1). These cancers had been initially classified according to 2004 WHO criteria. We collected updated diagnosis according to 2022 WHO, and clinical data with a follow-up of at least 5 years. For statistical analysis, we used binomial generalized linear models.
Results: According to the 2022 WHO, we reclassify 27 (11%) cases as NIFTP or UMP-T, 144 (61%) as well-differentiated carcinomas (136 papillary carcinomas, 3 follicular carcinomas, 5 oncocytic carcinomas), and 67 (28%) as high-grade carcinomas (37 high-grade differentiated and 30 poorly differentiated carcinomas). Follow-up revealed 40 (17%) iodo-refractory patients. All the NIFTP and UMP-T had a benign evolution. High-grade carcinomas, new category of the 2022 WHO classification, were significantly associated with iodo-resistance in univariate analysis (p = 0.001). Histological types identified as aggressive (high-grade carcinomas and aggressive subtypes of papillary carcinoma) according to the WHO 2022 classification had a 9-fold higher risk of becoming iodine refractory compared to common histological types.
Conclusion: The results of this study demonstrate that the new 2022 WHO classification is effective in predicting the aggressiveness of thyroid cancers, in particular high-grade carcinomas have a significant higher risk of refractory disease. Physicians need to be alerted to adapt the follow-up and management of these patients.

OFP-06-009

Sinonasal squamous cell carcinoma: a computer assisted image analysis of tumour infiltrating lymphocytes

C. Taverna*, K. Zavaglia, R. Scarpitta, I. Dallan, G. Arcovito, M.A. Hermsen, V.N. Cabal, A. Franchi
*Pathology Unit, Local Hospital ASLAL, Ospedale san Giacomo Novi Ligure, Italy; Department of Health Sciences, University of Eastern Piedmont "Amedeo Avogadro", Italy

Background & objectives: Squamous cell carcinoma is the commonest malignancy of the sinonasal tract (SSCC), occurring either as keratinizing (K-SSCC) or non-keratinizing variants (NK-SCC). Tumour microenvironment (TME) is deeply involved in tumour biology and its role in SSCC has been only partially established.
Methods: FFPE surgical tumour tissue samples of 41 SSCC were retrieved, including 24 K-SSCC and 17 NK-SCC. Ten SSCCs developed from sinonasal papilloma. All tumours were negative for AFF2 immunohistochemistry. HPV typing was performed by DNA pyrosequencing on 27 cases. For TME analysis we immunostained the samples for CD3, CD4, CD8 and FOXP3. Virtual slides were evaluated using QPath software.
Results: Sixteen SSCCs (39%) presented a brisk tumour lymphocytic infiltrate, with no significant difference between K-SSCC and NK-SSCC, and according to HPV status (10 were HPV-positive). Similarly, the number of CD3+, CD4+ and CD8+ lymphocytes per mm2 was not significantly different in the following groups: K-SSCC and NK-SSCC (P=0.09, 0.31, 0.73 respectively), HPV positive and HPV negative SSCCs (P=0.38, 0.79, 0.76 respectively), and SSCCs arising in sinonasal papilloma and de-novo SSCCs (P=0.70, 0.66, 0.72 respectively). K-SSCC presented a higher FOXP3 T-cell infiltrate than NK-SSCC (P<0.001), while there was no difference in the FOXP3 T-cell infiltrate according to HPV status (P=0.59) and between SSCCs arising in sinonasal papilloma and de-novo SSCCs (P=0.42).
Conclusion: The assessment of TME infiltrate in SSCC revealed a significantly higher amount of FOXP3+ lymphocytes in K-SSCC, which account for T-regulatory cells (T-reg). Considering the immune suppressive functions of this subset of lymphocytes, our data suggest that K-SSCCs are more prone to harbor an immunosuppressive TME compared to NK-SSCCs, warranting further studies about the correlation with prognostic features in the two groups. HPV status and origin from sinonasal papilloma do not seem to affect the quality of TME in SSCC.

OFP-06-010

SATB2 is a useful marker to differentiate WNT pathway-altered odontogenic tumours from ameloblastoma and ameloblastic carcinoma

K. Oh*, J. Kim, S. Hong, H. Yoon
*Dankook University, Republic of Korea

Background & objectives: Although WNT pathway-altered odontogenic tumours (WNT-OTs) are molecularly distinct from other odontogenic tumours, they may histologically resemble non-WNT-OTs such as ameloblastoma. This study aims to investigate the utility of immunohistochemical markers for the diagnosis of WNT-OTs.
Methods: Immunohistochemistry for SATB2, CDX2, CD10, and ß-catenin was performed in 19 WNT-OTs (10 benign cystic [calcifying odontogenic cyst], 7 benign solid [dentinogenic ghost cell tumour and adenoid ameloblastoma], and 2 malignant [ghost cell odontogenic carcinoma]) and 18 non-WNT-OTs (7 unicystic ameloblastomas, 7 conventional ameloblastomas, and 4 ameloblastic carcinomas). The sensitivities and specificities of each marker for detecting WNT-OTs were calculated.
Results: All WNT-OTs showed focal to diffuse SATB2 staining (19/19), but all but one non-WNT-OTs were negative for SATB2 (1/18), resulting in a sensitivity of 100% and a specificity of 94.4% for WNT-OTs. About two-thirds of WNT-OTs were positive for CDX2 (12/19), and all non-WNT-OTs were negative for CDX2 (0/18), resulting in a specificity of 100% but a relatively low sensitivity of 63.2%. Although both CD10 and ß-catenin showed 100% sensitivity (19/19), their specificity was low at 16.7% (3/18) and 44.4% (8/18), respectively; nevertheless, CD10 highlighted whorled cellular condensations called morules in most WNT-OTs. In addition, no differences in immunophenotype were found between dentinogenic ghost cell tumour and adenoid ameloblastoma.
Conclusion: This is the first study to demonstrate the immunoreactivity of intestinal markers SATB2 and CDX2 in the epithelial component of odontogenic tumours. SATB2 is a sensitive and specific marker for the diagnosis of WNT-OTs. In addition, the shared immunophenotype between dentinogenic ghost cell tumour and so-called adenoid ameloblastoma suggests their close relationship, supporting the recent finding that the two entities represent a histologic spectrum.

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OFP-06-011

Tumour budding as a negative prognostic marker in sinonasal intestinal-type adenocarcinoma, independent from p53 status and dMMR

V. Maffeis*, S. Puccio, G. Azzarello, L. Laurino, D. Cazzador, D. Politi, E. Emanuelli, G. Spinato, S. Ausoni
*Anatomia Patologica, Azienda Ospedaliera Universitaria Integrata Verona (AOVR); Department of Pathology - Local Health Unit 2 Marca Trevigiana - Treviso, Italy

Background & objectives: Tumour budding (TB) was recently described as negative prognostic marker in sinonasal intestinal-type adenocarcinoma (ITAC), but its role requires further validation. We assessed TB in ITAC, and evaluated its possible association with other biomarkers, such as p53 and MMR status.
Methods: We retrospectively analyzed 32 consecutive FFPE specimens of CK20 and CDX2 positive ITAC, treated in two institutions in Northern Italy. TB was evaluated according to the international recommendations developed for CRC; p53 expression and MMR proteins (MLH1, PMS2, MSH2, and MSH6) were evaluated by immunohistochemistry. Results were stratified using clinical data (4/32 had a relapse and 9/32 died of disease).
Results: Tumour budding was observed in 15/32 (46,9%) ITAC specimens in our previously unpublished cohort. Patients with high TB (>4 buds) have an increased risk of recurrence (p=0,06) and death (p=0,003) compared to those with low TB (≤ 4 buds) (median survival of 13 and 54 months, respectively). On multivariate analysis, TB emerged as an independent prognostic factor net of the stage of disease, and type of therapy received. Occupational exposure to wood and leather dust was not related to the presence of TB. No impact of p53 status as prognostic biomarker was observed and no alterations regarding MMR proteins were found.
Conclusion: The results of the present work provide further significant evidence on the negative prognostic role of TB in ITAC, and underline the need for larger multicentre studies to implement the use of TB in the clinical practice. However, current findings do not seem to support an involvement of p53 status or dMMR in this specific setting.

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OFP-06-012

Biomarkers of different stages in the development of carcinoma of the larynx, identified by in situ spatial profiling of RNA targets

A. Vombergar*, N. Zidar, E. Boštjančič, U. Prosenc Zmrzljak
*Institute of Pathology, Faculty of Medicine, University of Ljubljana, Slovenia

Background & objectives: Most genetic changes in carcinoma of the larynx and hypopharynx occur early, at the level of dysplasia, but genetic event(s) that cause the transition from precancerosis to carcinoma have not been clearly defined yet.
Methods: Our experiment included 11 formalin-fixed paraffin-embedded tissue samples from patients with squamous cell carcinoma (SCC) of the larynx and hypopharynx: normal mucosa, low-grade (LG) dysplasia, high-grade (HG) dysplasia and invasive SCC. We performed multiplex in situ hybridization by Human multi-tissue and cancer gene panel (377 genes) and Xenium technology (10X Genomics).
Results: Using the above-mentioned technology, we were able to identify 25 gene clusters: five clusters showed increased expression in HG dysplasia and invasive SCC, compared to normal mucosa and LG dysplasia, one was decreasing from normal mucosa to LG- and HG dysplasia, and was absent in invasive SCC, one was present only in SCC and three clusters were similarly expressed in normal mucosa, dysplasia and SCC. The remaining 15 identified gene clusters were mostly expressed in the stromal components of the normal mucosa, dysplasia and SCC.
Conclusion: In our preliminary study, we were able to identify candidate genes that might play a significant role in the development of SCC of the larynx and hypopharynx, some of them had been previously recognized as important in cancerogenesis in some tumours (e.g., colon, lung, breast cancers). Multiplex in situ hybridization is a promising new technology for studying cancerogenesis in biopsy tissue samples.

OFP-07Joint Oral Free Paper Session Digestive Diseases Pathology (GI) / Digestive Diseases (Liver/Pancreas)

OFP-07-001

Assessing the application of the margin positive definition in colorectal cancer: a case for greater standardization when reporting oncologically significant margins?

M. Bonert*, E. Ho, A. Naqvi, I. Kak, I. El-Shinnawy, P. Major
*McMaster University, Canada

Background & objectives: The margin positive definition (<=1 mm clearance) in colorectal cancer differs from other cancers. Therefore, we sought to assess whether (1) the definition is consistently applied, and (2) the margin is consistently called by pathologists.

Methods: All colorectal cancers with a synoptic report accessioned 2012-2020 were retrieved from a regional centre. The margin status, surgical clearance, pathologist, surgeon, tumour stage and nodal stage were retrieved from structured free-text reports and reconstructed into categorical data using custom code. Several random subsets were audited to confirm data integrity. Logistic regression (LR) and funnel plots were done with R.
Results: The time period had 2,556 specimens. Margins were positive (Mpos), unknown and negative in 170(6.7%), 8(0.3%) and 2,378(93.0%) cases respectively. In multivariate LR (MLR) margin positive was predicted by pathologist (P=0.0119), tumour stage and nodal stage (both P<0.001); surgeon was non-predictive (P=0.0899). Fourteen pathologists read more than 50 cases each; four were funnel plot (FP) outliers (>95% confidence interval). 47 cases were classified margin negative but had 1 mm clearance (29 cases) or <1 mm clearance (18 cases). The data was recalculated after applying the Mpos definition and the pathologist remained a predictor (P=0.0121) in MLR; however, the FP outliers decreased from four pathologists to two.
Conclusion: Margin call consistency appears to have room for optimization in the local environment. Adopting a tumour primary site independent definition for "positive pathologic margin" (tumour touching marking ink) and a tumour specific definition for "oncologically significant margin present" (defined by a cancer type specific suboptimal clearance distance and/or margin involvement extent – which could change as knowledge/treatments evolve) may be advantageous; the margin positive definition in colorectal cancer may be a potential source of misclassification/suboptimal management.

OFP-07-002
Recommendations for diagnostic and revision strategies in Barrett's oesophagus: results of the Dutch oesophageal pathology panel (DEPP)
Y. Weeda*, L. Brosens, M. Doukas, G. Kats-Ugurlu, J. van der Laan, I. van Lijnschoten, F. Moll, A. Ooms, L. Oudijk, C. van der Post, M. Raicu, W. Timens, M. Visser, M. van der Wel, S. Meijer
*Utrecht, The Netherlands

Background & objectives: Assessing Barrett's oesophagus (BE)-related dysplasia is hampered by high interpathologist variability. Therefore, guidelines advocate expert review. The Dutch oesophageal pathology panel (DEPP) accommodates centralized revision. Analysis of the DEPP review cases may aid in refining current diagnostic and revision strategies.
Methods: Between January 2015 and March 2023, thirteen gastrointestinal pathologists assessed 1018 digitized consecutive panel-revision cases (H&E slides and, when available p53 immunohistochemistry (P53-IHC)). Diagnoses followed Vienna-classification: no-dysplasia, indefinite for dysplasia (IND), low-grade dysplasia (LGD), or high-grade dysplasia (HGD). Expert-panel diagnosis required >75% agreement or a consensus-meeting. Panel diagnosis was compared to referral diagnosis and sub-specified based on initial P53-IHC status.
Results: After expert panel assessment 24.8% of referral diagnoses were downgraded and 21.4% upgraded. IND cases were altered in 73.2% (34.8% downgraded and 38.4% upgraded) and LGD in 34.6% (22.1% downgraded and 12.5% upgraded). Diagnostic shift of review cases was further specified for initial P53-IHC classification into P53-aberrant, P53 wildtype and P53 not-classifiable groups. Of cases with initial P53-aberrant pattern, 11.6% were downgraded and 22.2% upgraded. Of P53 wildtype pattern cases, 33.5% were downgraded and 15.6% upgraded. In P53-not-classifiable cases, 29.4% of cases were both up- and downgraded.
Conclusion: International guidelines advocate review of BE-biopsies. In this study, 46% of referral diagnoses were adjusted after review by the DEPP. When combined with routine P53-IHC, the need for review of dysplasia cases with aberrant P53 expression patterns could potentially be reduced as inter-observer variability is reduced. However, variation in assessment of BE related dysplasia with concurrent wild-type or indefinite p53-IHC remains high and review is recommended.

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OFP-07-003
Tumour immune microenvironment in metastatic and non-metastatic microsatellite unstable colorectal carcinomas
S. Niyazova*, C. Sers, D. Horst, C.M. Krüger, E.P.M. Lorenz, M. Hünerbein, A. von Kirchbach, A. Jarosch
*Charité - Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Institute of Pathology, Berlin, Germany; German Cancer Consortium (DKTK), Partner Site Berlin, and German Cancer Research Center (DKFZ), Heidelberg, Germany

Background & objectives: Microsatellite unstable colorectal carcinomas harbor robust immune responses correlating with favourable prognoses. Still, there are tumours metastasizing, thus leading to poor prognosis. To uncover the immune contexture in MSI-H CRC the immune microenvironment in metastatic and non-metastatic tumours was compared.
Methods: 24 tissue microarrays were produced from formalin-fixed paraffin-embedded patient tumour blocks. The corresponding sections were immunohistochemically stained for 12 immune markers and evaluated based on counting positive immune cell staining in different tumour regions, e.g. invasive margin and centre. The immune cell proportions were statistically compared in both groups. The patients' clinical data were collected based on medical records.
Results: There are significantly higher CD3+ cell numbers in the non-metastatic group (Mann Whitney-U $p < 0{,}001$). There are also significantly higher CD56+ cell numbers in the non-metastatic group ($p < 0{,}001 – 0{,}007$). For IDO1+ cells there are significantly higher numbers in the metastatic group ($p = 0{,}002$). Immunoscores for a combination of CD3+ and CD8+ cell proportions were calculated showing significantly higher numbers in the non-metastatic group ($p < 0{,}001$). Immunoscores were additionally calculated for IDO1, FoxP3 and PD-L1 and correlated with each other resulting in positive correlations between the Immunoscores of CD3/CD8 and IDO1, FoxP3 and PD-L1 each ($p < 0{,}001$, Spearman's $p = 0{,}318 – 0{,}545$).
Conclusion: There are significant differences in the number of immune cells between the metastatic and non-metastatic group of microsatellite unstable colorectal carcinomas. A connection between a low lymphocyte infiltration and metastatic potential seems consistent. A higher number of IDO1+ cells in the metastatic group suggests immunosuppression in further progressed tumours. This positive correlation between T cells and immunosuppressive immune markers potentially indicates adaptive immune resistance, yet, it remains to be elucidated how this is compatible with differences between the two groups.

OFP-07-005
Foundation of combine-and-conquer strategy in gastric and gastro-oesophageal junction adenocarcinomas (GA/GEJA): human epidermal growth factor receptor 2 (HER2) and programmed death-ligand 1 (PD-L1) expression in distinct tumour subclones
A.R. Coelho*, I. Gullo, M. Baptista Freitas, D. Leitão, L. Águas, C. Oliveira, A. Polónia, J. Gomes, C. Albuquerque Reis, H. Oliveira Duarte, F. Carneiro
*Pathology Department, São João Local Health Unit, Porto, Portugal

Background & objectives: In advanced GA/GEJA, HER2 status and PD-L1 expression represent important predictive biomarkers for treatment selection. Combinatorial targeted strategies have shown promising outcomes. In this study we aimed to evaluate HER2 status and PD-L1expression in a thoroughly characterized cohort of GA/GEJA.
Methods: A cohort of GA/GEJA patients treated with curative intent (2015-2017) was selected retrospectively. Clinico-pathological features were collected. HER2-status was evaluated by immunohistochemistry in two tumour sections and by dual-probe in situ hybridization (ISH) in HER2 equivocal (2+) cases. PD-L1 expression was evaluated in HER2-positive (2+/ISH+ and 3+) cases using combined positive score (CPS). IBM SPSS was used for statistical analysis.
Results: The series included 107 patients, with male predominance (n=70/107, 65.4%) and a median age of 68 years (range: 26-93). A minority of patients (n=12/107, 11.2%) harboured GEJA. Nine cases (8.4%) were HER2 positive. HER2 status was not significantly associated with clinicopathological features or survival outcomes. By multivariate analysis, lymph-node status was the only variable associated with worse overall survival (p=0.01). PD-L1 expression, assessed in HER2-positive specimens, was positive in most cases (7/9, 77.8%): CPS<1 in 2/9; CPS≥1<5 in 2/9; CPS≥5 in 5/9 cases. Pathologist-guided region-specific analysis revealed that PD-L1 positive regions were HER2 negative in most of cases (7/9, 77.8%), whereas PD-L1 and HER2-positive areas rarely overlapped (2/9, 22.2%).
Conclusion: In this study we evaluated HER2 status and PD-L1 expression in a thoroughly characterized cohort of GA/GEJA patients to assess the potential eligibility of GA/GEJA patients for the recently approved combinatorial therapies, targeting both HER2 and PD-L1. Our results indicate that the majority of patients harbouring HER2-targetable GA/GEJA may also be candidates for immunotherapy. Additionally, findings of non-overlapping areas of HER2 and PD-L1 biomarker expression, in most cases suggest that such combinatorial strategies could be directed to distinct tumour subclones.

OFP-07-006
Assessment of novel therapeutic treatments in KRAS mutant colorectal cancer using patient-derived organoids
M. Lazzari, D. Liberati, K. Guja-Jarosz, L. Terracciano, C. Esposito, S. Piscuoglio*
*IRCCS Humanitas Research Hospital, Italy

Background & objectives: Colorectal cancer (CRC) arises from mutations in APC, KRAS, and TP53/SMAD2/4. Mutations in the KRAS oncogene activate constitutively KRAS/RAF/MEK/ERK in 35–45% of CRC, favouring tumour progression and metastasis.
Methods: We used patient-derived organoids (PDOs) to better investigate the role of KRAS in tumourigenesis, since knowledge concerning KRAS-targeting in CRC is still missing. We performed a drug screening using a panel of eight compounds targeting the KRAS pathway, first in 2D normal colon mucosa NCM460D cells and in CRC cell lines, including DiFi (KRAS WT), HCT116 (KRASG13D), and LS-174T (KRASG12D).
Results: We tested the 0.1–100 nM and 5 nM–10 uM ranges of drug concentration, and we evaluated the cell viability after 72 hours to calculate the IC50 of each compound. We further repeated the drug screening in KRASG12A, KRASG12D, BRAFV600E, and KRAS WT CRC PDOs, and in spite of CRC PDOs responded to the drug treatment with a similar trend to one of the 2D cell lines, we observed that the IC50 value of each compound was shifted towards a lower effective concentration in CRC PDOs. This demonstrated that PDOs represent a more reliable platform to explore new therapeutic strategies in CRC, since they maintain patient inter- and intra-tumour heterogeneity.
Conclusion: The novel KRASG12D inhibitor MRTX1133 showed an effective IC50 20 times lower (nM) in KRASG12D PDO than in LS-174 cells suggesting PDOS as better model for drug testing. As following step, we plan to validate these data by using scRNA-seq, proteomic analysis and 4i to deepen the KRASG12D in CRC.

OFP-07-007
Could molecular profiling, through unsupervised clustering analysis of GEP-NETs, help in distinguishing the primary site in occult primary neuroendocrine neoplasms?
G. Sabella*, M. Gentili, F. Scalorbi, M. Silvestri, S. Brich, L. Agnelli, A. Vingiani, G. Pruneri, M. Milione
*Switzerland

Background & objectives: Neuroendocrine neoplasms of unknown primary origin are histologically confirmed metastatic disease without an identifiable primary tumour and occur with a poor prognosis. Early localization of the primary site is a fundamental prerequisite for improving the patient's management and prolonging survival
Methods: A cohort of 50 gastro-entero-pancreatic neuroendocrine tumours (GEP-NETs), including pancreatic and ileal primitive and metastases, underwent comprehensive RNA-Seq analysis. Limma identified 35 significantly differentially expressed genes between pancreatic and ileal groups. A custom Nanostring panel for immune profiling was designed based on these genes. Unsupervised clustering analysis was conducted on further 79 GEP-NETs using Ward.D linkage and Euclidean distance metrics
Results: Data from the validation cohort (79 GEP-NETs: 33 pancreatic NETs and 46 ileal NETs, inclusive of both primitive and/or metastases), analyzed through 'unsupervised clustering analyses', distinguished almost three clusters of greater interest.
Conclusion: Our innovative molecular approach led to identification of potential genes enable to distinguish different subtypes of neuroendocrine origin in metastatic setting and led to discovery of genetic footprint between pancreatic and ileal tumours. Within the ileal landscape, it further discriminated between primary and metastatic disease through a specific set of genes

OFP-07-008
Prominent Schlafen 11 expression associates with right-sided, mismatch repair-deficient colorectal carcinomas - a study of 3300 tumours
M. Kaczorowski*, M. Chłopek, O. Daum, M. Michal, A. Kowalik, J. Lasota, M. Miettinen
*Laboratory of Pathology, National Cancer Institute, Bethesda, MD, USA

Background & objectives: Schlafen 11 (SLFN11) regulates cell response to replicative stress and its expression in cancer is associated with sensitivity to various DNA-damaging agents and DNA damage response inhibitors. SLFN11 expression in colorectal cancer (CRC) has not been systematically studied.
Methods: One hundred twenty-four tissue microarrays containing 3300 CRCs were evaluated using Leica automated immunohistochemistry (IHC) and anti-SLFN11 D2 mAb. Diffuse immunoreactivity was validated on whole sections. CRCs with >80% of positive tumour cells were selected and further characterized using IHC and targeted next-generation sequencing (NGS). Limited clinical data were available in all cases.
Results: Diffuse SLFN11 expression was seen in 33 CRCs. The patients were predominantly female (22/33, 67%), with a median age of 67. Twenty-three (70%) tumours were right-sided. Seven (21%) carcinomas were of mucinous subtype and another 12 (36%) had mucinous components. Focal signet ring-cell morphology was present only in 2 (6%) cases. Seven (21%) CRCs were poorly differentiated tumours. IHC analysis of mismatch repair proteins (MMR) showed deficient status in 21/33 (64%) tumours. NGS of 20 tumours revealed driver mutations in BRAF (8/20, 40%), KRAS (5/20, 25%)

and PIK3CA (5/20, 25%) oncogenes. Tumour suppressor genes APC and TP53 harbored pathogenic variants in 30% (6/20) and 20% (4/20), respectively.
Conclusion: CRCs with diffuse SLFN11 expression are characterized by right-sided location, frequent MMR-deficiency, and presence of mucinous morphology. Although SLFN11 expression is rare in CRC, patients with such tumours might benefit from biomarker-informed treatment strategies.

OFP-07-009

EUS-FNB in pancreatic and extra-pancreatic lesions: a 5-year experience highlighting the importance of cell blocks for immunohistochemical analysis and biomolecular testing

S. Marletta*, E. Cavallo, F. Romeo, F. Motta, M. Dello Spedale Venti, G. Leone, L. Gullotti, C. Bonanno, S. Pafumi, C. Carnaghi, G. Magro, G. Bonanno, A. Rizzo
*Division of Pathology, Humanitas Istituto Clinico Catanese, Catania, Italy

Background & objectives: Endoscopic-ultrasound (EUS) sampling has been increasingly employed for approaching deep intra-abdominal processes. Fine-needle biopsy (FNB) has emerged as an alternative option to cytology due to its comparable accuracy and capacity to acquire tissue material for ancillary studies.
Methods: In the present work, we collected a comprehensive series of 372 pancreatic and extrapancreatic EUS-FNB procedures coupled with macroscopic on-site examination and cell block (CB) preparation. Immunohistochemistry (IHC) and biomolecular testing by PCR/NGS were subsequently applied for diagnostic and predictive purposes.
Results: Two-passes EUS-FNB achieved an overall accuracy of 94% with no need for rapid on-site evaluation. Pancreatic ductal adenocarcinoma was the most common diagnosis (107/372, 29%). A noteworthy proportion of the remaining malignancies (23/162, 14%) consisted of much rarer entities, namely 13 metastases and 10 hematological disorders, for which IHC and molecular assays were essential to reach the proper diagnosis and guide clinical management. Biomolecular tests on small EUS-FNBs furnished additional predictive therapeutic information, like c-Myc rearrangement in a gastric lymphoma, c-kit mutations in three GISTs, and IDH1 genetic alternations in a cholangiocarcinoma, among others.

Conclusion: Our findings support an EUS-FNB approach to deep gastrointestinal/peri-gastrointestinal lesions recommending, whenever possible, tissue sample acquisition. The application of IHC and biomolecular testing to CBs significantly helps physicians deal with the most uncommon challenging cases and obtain key predictive prognostic and therapeutic data.

OFP-07-010

Self-supervised learning to predict intrahepatic cholangiocarcinoma transcriptomic classes on routine histology

A. Beaufrère*, T. Lazard, R. Nicolle, G. Lubuela, J. Augustin, M. Albuquerque, V. Priori, N. Théou-Anton, M. Lesurtel, M. Bouattour, K. Mondet, J. Cros, J. Calderaro, T. Walter, V. Paradis

*Department of Pathology, Hôpital Beaujon, Clichy, France
Background & objectives: The transcriptomic classification of intrahepatic cholangiocarcinomas (iCCA) has been recently refined in five classes, associated with survival, but not routinely used in practice. Here, we assessed a self-supervised learning (SSL) model for predicting iCCA transcriptomic classes on whole-slide images (WSIs).
Methods: Transcriptomic classes defined from RNAseq data were available for all samples. A SSL method was used to train our model on a discovery set of 766 biopsy (n=137) and surgical samples (n=109) WSIs from 246 patients in a five-fold cross-validation scheme. The model was validated in TCGA (n= 29) and a French external validation set (n=32) on surgical sample WSIs.
Results: The proportion of the each transcriptomic class in all datasets was as follows : hepatic stem-like (39%), desert-like (5%), tumour classical (12%), Immune classical (22%) and inflammatory stroma (21%) classes. Overall survival was significantly associated with three classes in all cohorts. Our model showed good to very good performance in predicting the four most frequent transcriptomic classes in the discovery set (area under the curve [AUC]: 0.63-0.84), especially for the hepatic stem-like class (AUC 0.84). The model performed equally well in predicting these transcriptomic classes in the two validation sets, with AUCs ranging from 0.76 to 0.80 in the TCGA set and 0.62 to 0.92 in the French external set.
Conclusion: We have developed and validated an SSL model able to predict iCCA transcriptomic classes on WSIs from routine biopsy and surgical samples. This model showed good to very good performance for classifying the four main classes. The ability to predict transcriptomic iCCA classes on routine WSIs could affect patient management by predicting prognosis and guiding the treatment strategy (immunotherapy in inflammatory classes or targeted molecular therapies in hepatic stem-like class).

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OFP-07-011

Reporting residual disease (R0/R1) following pancreatoduodenectomy for pancreatic ductal adenocarcinoma: a joint position statement by the International Study Group for Pancreatic Surgery (ISGPS) and the International Study Group of Pancreatic Pathologists (ISGPP)

A. Farina*, R. Theijse, B. Janssen, L. Lutter, O. Basturk, L. Brosens, I. Esposito, N. Fukushima, V. Henriques, C. Luchini, H. Wang, J. Werner, C. Verbeke, M. Besselink, V. Adsay
*Dpt. of Pathology, Amsterdam UMC, The Netherlands

Background & objectives: Varying definitions are in use to classify residual disease (R0/R1) after pancreatoduodenectomy (PD). Differences mostly focus on which surgical margins and surfaces are considered leading to a significant and undesired variation in R0/R1 rates reported in the literature.
Methods: An international steering group consisting of experienced ISGPS-ISGPP surgeons and pathologists was established. Recommendations are devised based on systematic literature review and multiple consensus meetings while taking current international guidelines into account.
Results: The ISGPS and the ISGPP recommended twofold reporting for residual disease after PD for PDAC including both the "surgical R0" (sR0) and "pathological R0" (pR0). The sR0 includes only the five surgical margins (pancreatic transection plane, stomach/duodenum, jejunum, common bile duct and superior mesenteric artery). The pR0 includes also the three specimen "surfaces" (anterior and posterior pancreatic surfaces and superior mesenteric/portal vein surface). For both sR0 and pR0 a >1mm margin clearance is required, except for the peritonealized anterior pancreatic surface where a 0mm clearance holds. Further recommendations involved standardized reporting of all margins and surfaces and other margins in case of vascular or extended resections.
Conclusion: The joint ISGPS-ISGPP position statement advises to provide both sR0 and pR0 when reporting residual disease after PD for PDAC. Standardized pathology reporting including the individual surgical margins and specimen surfaces will make R0/R1 assessment more reliable and studies comparable.

OFP-07-012

Next-generation sequencing improves diagnostic performances for patients with extrahepatic biliary strictures

A. Brunac*, J. Peron, A. Culetto, K. Barange, L. Buscail, N. Fares, R. Guimbaud, E. Alouani, M. Jaffrelot, D. Grand, C. Basset, J. Selves
*Service d'Anatomie et Cytologie Pathologiques, Institut Universitaire du Cancer de Toulouse - Oncopole, France

Background & objectives: Diagnosis of malignancy in biliary strictures is challenging and requires microscopic examination. Evaluation by brush cytology or biopsies is limited by low sensitivity. Our aim was to investigate feasibility and diagnostic value of targeted Next-Generation Sequencing (NGS) in this setting.
Methods: A prospective cohort of 75 patients with biliary strictures was studied. Two types of samples, brush cytology and biopsies, and two types of preservative solutions, PreservCyt® (Hologic Corp.) and RNAprotect® Cell Reagent (Qiagen) were tested. DNAs were qualified by qPCR and sequenced with a targeted panel containing 48 genes. RNAs were sequenced with a targeted panel containing 98 fusion targets.
Results: Pathological diagnosis classified these strictures as being of non-neoplastic (n=38) or neoplastic (n=37) origin. Sensitivity and specificity were 67.9% and 95.5%, respectively, as on follow-up, eight of the 27 and nine of the 11 initially benign or indeterminate for dysplasia strictures resulted malignant. 97.2% of DNAs from brushings were qualified whereas only 35.6% of DNAs from biopsy supernatants were. Sensitivity and specificity for malignancy of NGS were 80.4% and 80%, respectively. Importantly, the four NGS false positive concern one patient with primary sclerosing cholangitis who underwent several procedures. 15 RNAs from nine patients were sequenced: nine were contributory and only one *EGFR* rearrangement of unknown significance was found.
Conclusion: We demonstrated the feasibility of DNA and RNA sequencing with targeted panels on biliary strictures samples and validated the best preservation conditions for these samples. DNAs from brushings produced better results than DNAs from biopsy supernatants. NGS improved diagnostic performances, especially for strictures classified as "indeterminate for dysplasia" on microscopic examination. Its implementation at the initial diagnosis of biliary strictures could significantly improve clinical management of patients and help in selecting patients for targeted therapies.

OFP-07-013

A novel subgroup of pancreatic neuroendocrine tumours with a highly metastatic potential characterized by PDX1 and CDX2 expression

E. Moser, A. Ura, L. Vogel, K. Steiger, C. Mogler, M. Evert, B. Märkl, K. Scheidhauer, M. Martignoni, H. Friess, A. von Werder, I. Marinoni, A. Perren, G. Klöppel, A. Kasajima*
*Department of Pathology, TUM School of Medicine and Health, Munich, Germany

Background & objectives: Pancreatic NETs (PanNETs) are extremely heterogenous and include alpha-cell like and beta-cell like tumours which correlate strongly with genetic and epigenetic features. The remaining PanNETs are not yet characterized.
Methods: 185 resected PanNETs were clustered based on immunohistochemical expression of the transcription factors ARX, PDX1, ISL1 and CDX2 by Ward´s method. Histology (trabecular-reticulated, trabecular-solid, solid-small nested and solid-large nested), hormone expression (glucagon, PP, Insulin, somatostatin, gastrin, serotonin, calcitonin, ACTH), DAXX/ATRX status, alternative lengthening telomeres (ALT) and clinical features including functionality and patients´ outcome were correlated.
Results: Five subgroups (A1, A2, B, C and D) were identified. A1 (46%) and A2 (15%) were characterized by ISL1+/ARX+/PDX-/CDX2- and ISL1+/ARX+/PDX+/CDX2-, respectively. They showed a trabecular-reticulated pattern, glucagon/PP expression, DAXX/ATRX loss and ALT positivity. Subgroup B (17%, ISL1+/ARX-/PDX+/CDX2-) was characterized by a trabecular-solid pattern, insulin/somatostatin expression, included 15/17 insulinomas, and associated with good prognosis. Subgroup C (15%) was characterized by ISL1-/ARX-/PDX-/CDX2-, a solid-small-nested pattern and serotonin/calcitonin expression. Subgroup D (6%) was characterized by ISL1-/ARX-/PDX+/CDX2+, a solid-large-nested pattern, ACTH/serotonin expression and infrequent DAXX/ATRX loss and ALT positivity. The subgroup D had the shortest 5-year disease free survival rate (38%) compared to the other subgroups and was an independent prognostic factor ($p<0.05$).
Conclusion: We identified a novel subgroup of PanNETs (subgroup D) with PDX1 and CDX2 expression, which showed distinct histology, hormone expression, infrequent DAXX/ATRX loss or ALT positivity, and associates with a high metastatic potential. The tumours differ distinctly from subgroups A1, A2, and B, which are attributable to the alpha or beta cell-like type. The subgroup C consists of heterogenous tumours.

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OFP-07-014

HER2 amplification subtype intrahepatic cholangiocarcinoma exhibits high mutation burden and T cell exhaustion microenvironment

X. Pu*
*China

Background & objectives: This study aimed to establish a uniform standard for the interpretation of HER2 gene and protein statuses in intrahepatic cholangiocarcinoma (ICC). We also intended to explore the clinical pathological characteristics, molecular features, RNA expression and immune microenvironment of HER2-positive ICC.
Methods: We analyzed a cohort of 304 ICCs using immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH) to identify HER2 status. Comprehensive analyses of the clinicopathological, molecular genetic, and RNA expression characterizations of ICCs with varying HER2 statuses were performed using next-generation sequencing. We further investigated the tumour microenvironment of ICCs with different HER2 statuses using IHC and multiplex immunofluorescence staining.
Results: HER2/CEP17 ratio of ≥2.0 and HER2 copy number ≥4.0 ; or HER2/CEP17 ratio of ≥2.0 and HER2 copy number≥6.0 were setup as FISH positive criteria. Based on this criterion, 13 (4.27%, 13/304) samples were classified as having HER2 amplification. The agreement between FISH and IHC results in ICC was poor. HER2-amplified cases demonstrated a higher tumour mutational burden compared to non-amplified cases. No significant differences were observed in immune markers between the two groups. However, an increased density of CD8+CTLA4+ and CD8+FOXP3+ cells was identified in HER2 gene-amplified cases.
Conclusion: HER2 amplification/overexpression are candidates for target-specific therapy in intrahepatic cholangiocarcinoma (ICC). Although the frequency of cases with HER2 amplification is low, there are still a significant number of cases that could be candidates for target-specific therapy. However, there is a lack of correlation between immunohistochemistry and the presence of amplification detected by fluorescence in situ hybridization (FISH). This discrepancy highlights the importance of accurate testing methods to identify patients who may benefit from HER2-targeted therapy in ICC.

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OFP-07-015

Spatial transcriptomics analysis of gallbladder precursor lesions and their progression to gallbladder carcinoma

V. Angerilli*, T. de Bitter, E. Vink-Börger, Y. Doncheva, M. McGuigan, J. Cole, P.R. de Reuver, N.B. Jamieson, I. Nagtegaal, C. van der Post

*Department of Medicine, Surgical Pathology Unit, University of Padua, Padua, Italy

Background & objectives: Biological insights into the stepwise development of gallbladder carcinoma (GBC) are needed to develop tailored approaches for early detection and clinical management. Here, we aimed to elucidate the morphologic and transcriptomic changes that accompany the evolution of GBC from precursors.

Methods: Specimens and clinicopathological data of 670 GBC patients were collected using the Dutch Nationwide Pathology Database and the Netherlands Cancer Registry. All precursors and GBCs were reviewed, and a subset of precursors (n=121) and GBCs (n=71) FFPE tissue underwent whole transcriptomic analysis (GeoMx digital spatial profiler platform [Nanostring]) to investigate differential gene expression across regions of spatially distinct histology.

Results: Precursors were identified in 39.9% of all GBC cases, either intracholecystic papillary neoplasm (ICPNs) (n=170) or biliary intraepithelial neoplasia (BilIN) (n=97). Significant, stepwise differences in gene expression were observed between low-grade dysplasia, high-grade dysplasia, and carcinoma in both carcinogenetic cascades via ICPN or BilIN. Metallothionein family genes were downregulated from low-grade to high-grade dysplasia in both precursors. Wnt signaling pathway genes were activated in BilIN-related carcinogenesis, while ERBB2 upregulation and RB1 and TP53 upstream inhibition were observed in the transition from high-grade to carcinoma in ICPNs. When comparing BilIN and ICPNs, 16 differentially expressed genes were observed, instead, only three differentially expressed genes were found between BilIN- and ICPN-associated GBCs.

Conclusion: In conclusion, our work has improved the current knowledge regarding the molecular events underlying multistep gallbladder carcinogenesis. We showed that ICPNs and BilIN have a different underlying biology and we identified molecular alterations associated with disease progression in the different carcinogenic pathways.

OFP-08 Joint Oral Free Paper Session Other Topics (THYM / DEVEL / CARD / HIST / AUT)

OFP-08-001

Evaluation of diagnostic accuracy of state-of-the-art post-mortem imaging compared to clinical hospital autopsy

H. Hoppe, I. Arnold, N. Lange-Herr, J. Klaus, N. Schwendener, J. Brünig, B. Dislich, M. Trippel, Y. Banz, W. Zech*

*Institute of Forensic Medicine Bern, Switzerland

Background & objectives: The goal of this study was to evaluate if state of the art post-mortem imaging (CT and MRI) can be used as a valid alternative to the classical clinical autopsy.

Methods: Post-mortem imaging (whole-body CT and MRI) was conducted before clinical autopsy on n=120 deceased patients in a prospective study. Imaging findings were compared to autopsy findings. Diagnostic accuracy (sensitivity, specificity, positive predictive value, negative predictive value) was calculated for causes of death and all pathologic autopsy findings for CT only, MRI only and a combined use of CT and MRI.

Results: The overall sensitivity for the correct post-mortem imaging determination of the cause of death was 85 % for a combined use of CT and MRI. Even the combined use of CT and MRI could not visualize certain relevant autopsy findings such as those related to septic shock, certain tumour types (e.g. blood cancers), and small findings in general. For specific causes of death and specific pathologic findings, post-mortem imaging showed high diagnostic accuracy. Such findings were for example acute myocardial infarction (MRI sensitivity 92 %), pulmonary embolism (MRI sensitivity 91 %), pneumonia (CT sensitivity 91 %), metastases (MRI sensitivity 92 %), and aortic dissection (MRI sensitivity 86 %).

Conclusion: Post-mortem CT and/or MRI cannot be used as a general alternative to the classical clinical hospital autopsy. However, if the goal of the post-mortem examination is to confirm or look for specific causes of death or a specific type of pathology, post-mortem imaging can be used as an alternative to autopsy. The combined use of CT and MRI may enhance diagnostic accuracy of some particular findings but the combined use is not always necessary nor useful.

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OFP-08-002

A 2-year review of microbiological testing in paediatric autopsies in a forensic setting

S. Parsons*, J. Fronczek, L. Iles

*Victorian Institute of Forensic Medicine and Monash University, Australia

Background & objectives: Microbiological testing is a routine part of a paediatric autopsy. The VIFM has been performing the same suite of microbiological tests for many years. Review of the results of these tests will allow rationalization and assist to establish future guidelines.

Methods: Review of all paediatric cases under the age of 3 years referred to the VIFM over a 2-year period (July 2018- July 2020). Cases where an internal examination at VIFM and microbiology was performed were included.

Results: 92 cases were available for review. These were divided into bacteriology and Virology testing.

Bacteriology: Blood culture was positive in 25% (23), CSF 1% (1), Spleen swab 6.5% (6), Liver swab 8.6% (8), Middle ears 13% (12) left lung swab 32.6 % (30) and right lung swab 255 (23). Bowel contents did not culture any positive results.

Virology: Nasopharyngeal 38% (35), CSF 11.9 5 (11), Left lung tissue 7.6 % (7), Right lung tissue 7.6% (7) and bowel contents 26% (24).

Conclusion: 12 cases (13%) had an infective cause of death with microbiology being essential for diagnosis. In these cases, multiple samples were positive. Middle ear, spleen and liver swabs did not influence the cause of death in any case. Flavivirus and Alpha virus in the CNS were negative in all cases. The results suggest extensive microbiological testing may not be warranted in all cases and that rationalization of which tests to perform may be warranted.

OFP-08-003

State of decay: the validation and use of autopsy as tool to monitor rates of social isolation in the United Kingdom (UK) - a summary of three years of research

T. Estrin-Serlui*

*Imperial College Healthcare NHS Trust, United Kingdom

Background & objectives: Autopsy has long been used as a tool to monitor populations' physical health, but can it also be used to monitor social health? We present research highlighting the use of autopsy data to examine social isolation rates in the UK.

Methods: Autopsy data was analysed from the one year before and after the UK's first COVID-19 related lockdown. Following this, further data was analysed as part of a meta-review to investigate the association between post-mortem decomposition change and unascertained causes of death. Finally, population data was used to analyse overall trends in unascertained mortality in the UK since the 1970s.

Results: We demonstrate that, controlling for other variables, enforced community social isolation due to COVID-19 restrictions increased the frequency of advanced decomposition seen at autopsy. Our further research demonstrates that around 88% of unascertained causes of death at autopsy are likely a result of advanced decomposition change. To that end, we have then used unascertained deaths as a proxy marker for severely decomposed bodies. We have analysed trends in these unascertained deaths in the UK, demonstrating a more than threefold increase in their frequency starting from the mid-1990s until today, and also demonstrating that males are more than twice as likely to be affected as females.
Conclusion: We have confirmed the link between social isolation and severe post-mortem decomposition by using the COVID-19 pandemic and its associated social restrictions as an inflection point in data analysis. We have also demonstrated that the majority of unascertained causes of death are likely a result of advanced decomposition change. Assimilating these two findings, using publicly available mortality data, we have demonstrated a likely increasing prevalence of severe social isolation in the UK's population, starting from the mid-1990s, mostly affecting males.

OFP-08-004
High relevance of autopsy-based COVID-19 tissue biobanking in anti-SARS-CoV-2 vaccination research
T. Pfeffer*, K. Hofmann, I.M. Klein, C. Schwab, L. Hartmann, A. Marx, M. Werner, O. Schilling, F. Fend, H. Bösmüller, P. Möller, N. Gaisa, A. Stenzinger, T. Longerich, P. Schirmacher
*German Center for Infection Research (DZIF), Tissue Bank at the partner site Heidelberg, Institute of Pathology, University Hospital Heidelberg, Germany

Background & objectives: Since the beginning of the SARS-CoV-2 pandemic, structured and quality assured autopsy-based biobanking has been performed in the context of the COVID-19 Autopsy and Biosample Registry Baden-Württemberg (BW), encompassing the five university pathologies (Heidelberg, Freiburg, Mannheim, Tübingen, Ulm).
Methods: Heidelberg is coordinating site of the consortium, closely cooperates with the Translational Infrastructure Bioresources, Biodata and Digital health (TI-BBD) of the German Center for Infection Research (DZIF), funded by the Ministry of Science, Research and Arts of Baden-Württemberg, Germany in 2020-2024. The main function is structured biobanking and registry assembly to support latest research and facilitate and increase autopsy frequency.
Results: Tissue samples (FFPE, cryopreserved) of all relevant organs are standardized collected from SARS-CoV-2 infected and/or anti-SARS-CoV-2 vaccinated deceased patients. Samples are stored decentraly and harmonized. Sample data including relevant patient datasets, autopsy data, histopathological/radiological characteristics, immunization status, clinical and virological data are recorded in a web-based platform.
Since the beginning of the structured autopsy program, around 12,500 tissue-samples were collected and the supported research projects resulted in >50 publications. While, among others, major findings in latest publication aimed on severe adverse vaccination complications, a longitudinal pathogenicity comparison of virus variants throughout the SARS-CoV-2 pandemic has been performed. Further projects also focus on severe long-COVID cases with histopathological determined lung injures.
Conclusion: Supported by the Ministry of Science, Research and Arts of Baden-Württemberg, the five university pathologies in Baden-Württemberg, Germany, were able to establish a worldwide unique autopsy-based SARS-CoV-2 biomaterial registry and tissue biobanking, which has flagship function and lead to numerous research publications with major contribution to recent medical issues (e.g. changes in severe COVID, post-vaccination myocarditis). This demonstrates the major impact and importance of qualified biobanking in leading research and public health topics.

Funding: Funded by the Ministry of Science, Research and Arts Baden-Württemberg, Germany

OFP-08-005
An in-depth characterization of the natural history of viral myocarditis in a murine coxsackie B3 model
M. Van Hecke*, K. Favere, S. Eens, P. Guns, T. Roskams, H. Heidbuchel
*KU Leuven, Belgium

Background & objectives: Coxsackievirus B3-induced myocarditis in mice is the most used translational model to study viral myocarditis. This study extends the focus of past research from the acute disease pathophysiology to its later stages, encompassing fibrogenesis and arrhythmogenesis associated with worse prognosis.
Methods: C57BL/6J mice received a single intraperitoneal injection with CVB or vehicle as control. Males (n=92) were injected with 5 x 10^5 (regular dose, RD) or 5 x 10^6 (high dose, HD) plaque-forming units of CVB, whereas females received RD only. Clinical, histopathological, molecular and electrophysiological changes were assessed before animals were sacrificed after 1, 2, 4, 8 or 11 weeks.
Results: CVB mice developed disease with a temporary decline in general condition and weight loss, less pronounced in females. Premature mortality occurred in males only. Histology revealed progressive attenuation of myocarditis, with faster resolution in females. The composition of the inflammatory infiltrates was comparable across all groups but changed over time. There was concomitant development of myocardial fibrosis, most pronounced in males. Serum biomarkers of cardiac damage and cardiac expression of remodeling genes were elevated during the acute phase of disease, with less prolonged CTGF gene upregulation in females. In vivo electrophysiology studies demonstrated that ventricular arrhythmias could only be induced in CVB animals, without significant differences between groups.
Conclusion: CVB inoculation in C57BL/6J mice provides a model of acute self-limiting viral myocarditis, with progression to different patterns of myocardial fibrosis. Sex, but not inoculation dose, seems to modulate the course of disease with male animals showing a less favourable disease course and fibrogenesis. Despite enhanced myocardial fibrosis, male animals did not show a higher arrythmia burden, however in vivo electrophysiology in mice remains a challenge.

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OFP-08-006
Automatic quantification of amyloid birefringence in cardiac amyloidosis by digital pathology
A. Pucci, F. Greco, S. Polito, V. Musetti, A. Celi*, V. Castiglione, A. Aimo, G. Vergaro, M. Emdn
*Pisa, Italy

Background & objectives: Automatic quantification of amyloid deposits could improve amyloid evaluation and patient stratification in cardiac amyloidosis (CA). We developed a digital pathology pipeline for quantification of apple-green amyloid birefringence on Congo Red (CR)-stained sections of endomyocardial biopsies (EMBs).
Methods: Twenty EMBs with CA and 10 EMBs with cardiac hypertrophy (CH) and no amyloid were investigated. Amyloid was semi-quantitatively assessed (focal, multi-focal or diffuse depositions) on CR-stained sections under a polarized light microscope by a cardiac pathologist (AP). Whole tissue images of the CR-stained sections were acquired under a polarized light microscope and digitalized together with a bright field image.

Results: Polarized light images were converted into negative images using MATLAB platform to obtain a bright field image, normalized using modified Reinhard normalization and imported into QPath software. Images underwent colour de-convolution and the negative of the apple-green colour was isolated. Intensity threshold on the amyloid channel was applied to detect positive pixels. Total tissue area was calculated by intensity threshold of the bright field image. Birefringence-positive pixel percentage was calculated for each image, a significant difference being observed between CA and CH group; CH cases scored close to zero positive pixels except two with diffuse contraction bands causing false positivity. Results from automatic quantification were mostly comparable with semi-quantitative evaluation.
Conclusion: Current methods for amyloid detection from CR-stained tissue are based on apple-green birefringence under polarized light. The present digital pathology pipeline allowed us for the automatic quantification of amyloid birefringence and its isolation from collagen birefringence in most cases. Under pathologist guidance, automatic amyloid quantification could be applied to improve CA evaluation and could be useful for risk stratification in this clinical setting.

OFP-08-007
Predictors of temporal arteritis: a retrospective analysis of 781 biopsies that includes consideration of the pathologist, surgeon and biopsy length
G. Bidla, A. Naqvi, N. Khalidi, M. Junek, A. Thoma, M. Bonert*
*McMaster University, Canada

Background & objectives: Temporal artery biopsy (TABx) interpretation may depend on the pathologist and amount of tissue. This work sought to examine the role of the health care provider in temporal artery biopsies, in conjunction with biopsy length, patient age and patient sex.
Methods: All TABx reports for cases accessioned at a regional laboratory 2001-2020 were retrieved and diagnostically classified with a string-matching algorithm. Biopsy length was extracted from the gross description. All reports were reviewed to ensure accurate classification of temporal arteritis positive (TApos). Further analysis was done with funnel plots, receiver operator characteristic (ROC) curves, and logistic regression (LR) using R.
Results: The time period had 781 temporal artery biopsies and 137 were called TApos. Funnel plots for providers involved with ≥20 specimens included 14 pathologists with zero 95% confidence interval (95% CI) outliers, and nine surgeons with three 95% CI outliers. 649 cases had an available gross maximal dimension (MAXDIM). A MAXDIM-TApos plot demonstrated lower TApos rates below 2 cm. TApos rate increased with age and was similar for sex. In a LR model for TApos age was significant (p=0.0003); other predictors (surgeon, pathologist, sex, MAXDIM and patient age) were not (p>0.05). ROC curves were plotted and the area under the curve values for a multivariate model/age/surgeon/pathologist/MAXDIM2 were 0.71/0.62/0.61/0.60/0.52 respectively.
Conclusion: The MAXDIM-TApos plot suggest a biopsy length of 2 cm or more may increase biopsy sensitivity. The weak association with surgeon may be dependent on upstream patient selection/referral patterns. Within the limitations of the study, it is reassuring the pathologist in our environment does not appear to be a predictor of the diagnosis of temporal arteritis. Observational data may be useful to make inferences about the diagnostic process and gain a greater understanding of important modifiable parameters.

OFP-08-008
Enhancing amyloid diagnosis via proteomics: from plaque to tissue
A. Vandendriessche*, T.M. Maia, D. Van Haver, I. Kaya, M. Van Der Linden, J. Van Dorpe, A. Dendooven, S. Devos, F. Impens
*Department of Diagnostic Sciences, Faculty of Medicine and Health Sciences, Ghent University, Belgium

Background & objectives: Recent advancements in amyloidosis diagnosis focus on proteomics. We aim to validate mass spectrometry (MS) for clinical use in Belgium, focusing on plaque-typing. Additionally, we explore protein composition changes in surrounding tissue, aiming to gather insights in disease mechanisms.
Methods: We included 173 amyloidosis cases and negative controls (2004-2024). For amyloid typing, Congo-red stained plaques of all cases were collected through laser capture microdissection. Additionally, whole sections of 16 myocardium biopsies (6 ATTR, 10 controls) were obtained for analysis of surrounding tissue. Samples were prepared using refined in-house protocols, followed by timsTOF data-independent LC-MS/MS acquisition and data analysis with DIA-NN.
Results: Our ongoing study on amyloidosis plaque typing showed promising preliminary results, with a small in-house pilot study successfully identifying the origin protein in >90% of cases. Laser capture microdissection revealed minimal material requirement. Further examination comparing our results to immunohistochemical techniques is ongoing. Analysis of whole tissue sections revealed a distinct protein composition profile in ATTR cases compared to controls, including 118 proteins that were uniquely present in affected cases. Additionally, statistical analysis identified nearly 400 significantly up- or downregulated proteins, the former including known ATTR amyloidosis-associated proteins (transthyretin and amyloid signature proteins) as well as other proteins involved in cellular adhesion, cytolysis, proteolysis and immune responses.
Conclusion: Proteomics-based methods for amyloidosis typing show promising results regarding specificity and sensitivity. Our ongoing studies emphasize feasibility of this approach in clinical practice. Additionally, beyond typing, proteomics comparison of ATTR and control samples allowed to study protein changes in tissue surrounding amyloid plaques. This demonstrates the potential of contemporary proteomics in identifying biological processes associated with amyloidosis. Although preliminary results are promising, more research is needed to gain further insight into the molecular mechanisms underlying amyloid deposition.

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OFP-08-009
Theatrum anatomicum: pathology as a spectacle through the ages
H. O'Shea*
*Dublin, Ireland

Background & objectives: To explore the evolution of the 'anatomical theatre' as both an educational space and a public spectacle across the centuries, and how this has manifested itself in the modern era.
Methods: Anatomical dissection has been performed for public audiences across history, with the lines between education and entertainment often being blurred. The first anatomical theatres were established in Renaissance Italy, where dissections were carried out to musical accompaniment and scheduled alongside Carnival. In 17th century London, rambunctious crowds flocked to dissections of criminals – three-day events ending with an elaborate feast.
Results: While such practices have largely been relegated to history, echoes remain, with depictions of autopsy on screen and page continuing to draw large audiences. It is not restricted to the realm of fiction however, with social media becoming a virtual form of anatomical theatre. Videos of dissections are easily accessible and surgical videos have become prevalent, particularly in the sphere of cosmetic procedures, with bite-size clips accompanied by the latest chart-toppers. More literal resurrections of the practice have also occurred, with a public dissection in a Portland hotel by the 'for-profit' company Death Science in 2021 - most worryingly of all, without the consent of the deceased or their family.

Conclusion: Anatomical theatres have played a significant role in the education of healthcare professionals throughout history, with anatomical dissection remaining a cornerstone of medical education. However, in the age of the internet it is perhaps easier than ever to disseminate such imagery inappropriately for the consumption of the public, often under the guise of "education". It is important therefore that the wider medical community continues to uphold ethical standards in order to maintain the dignity of patients and of the deceased.

OFP-08-010

Stroma AReactive Invasion Front Areas (SARIFA) as a new prognostic biomarker in digestive and prostate cancers indicating metabolic reprogramming by tumour cell – adipocyte interaction

B. Grosser, N. Reitsam, P. Grochowski, M. Gross, J. Enke, J. Waidhauser, B. Märkl*
*UK Augsburg, Germany

Background & objectives: Metabolic reprogramming has been established as a new hallmark of cancer. SARIFA, identified histologically by direct contact of tumour cells with adipocytes, is a new prognostic biomarker and indicative of an activation of lipid metabolism in different cancers.
Methods: SARIFA is defined as the direct contact of at least five tumour cells with at least one adipocyte. It has been analysed in gastric – (GC), colorectal – (CRC), pancreatic (PDA) and prostate cancer (PC). Quantitative cut-offs had to be established in PDA and PC, only. Since 2021, 12 case collections have been analysed regarding the prognostic relevance of SARIFA.
Results: In total 5.125 cases have been evaluated (GC: n = 2.103; CRC: n = 2547; PDA: n = 174; PC: n = 301) regarding its SARIFA-status. Depending on the entity, the positivity rates ranged between 15 and 60%. SARIFA correlates with other parameters of the TNM-system and tumour-budding, also. Nevertheless, it could be demonstrated as statistically independent prognostic with particularly strong effects in gastric- and colorectal cancer, with hazard rates ranging between 1.3 and 3.5. In prostate cancer, SARIFA failed significance marginally due to a small size. Bulk and spatial RNA-expression analyses, as well as immunohistochemical staining, revealed an upregulation of lipid metabolism-associated genes and proteins in SARIFA-positive cases.
Conclusion: SARIFA is an easy-to-evaluate biomarker-based solely on H&E histology. It shows remarkable prognostic power, especially in digestive system cancers. All translational investigations suggest a certain biology with metabolic remodeling and upregulation of lipid metabolism. The latter offers a potential therapeutic attempt to attack this metabolism by compounds like metformin, FABP4-, CD36, and CPT1 Inhibitors.

OFP-08-011

MTAP immunohistochemistry and peritoneal mesothelioma: is it really an accurate surrogate for CDKN2A fluorescent in situ hybridization?

A. Quaranta*, F. Fortarezza, A. Marzullo, C. Caporusso, S. Maniglio, F. Pentimone, F. Pezzuto, L. Vimercati, G. Serio, A. D'amati
*Section of Pathology, Department of Precision and Regenerative Medicine and Ionian Area (DiMePRe-J), University of Bari "Aldo Moro", Bari, Italy

Background & objectives: MTAP immunohistochemistry has been proven to be a reliable surrogate for FISH to detect CDKN2A homozygous deletions (HD) only in Pleural Mesothelioma.
We aim to determine whether MTAP IHC could also be applied to the diagnosis of Peritoneal Mesothelioma.
Methods: On 39 Peritoneal Mesothelioma FFPE tissue samples:
CDKN2A copy number status was assessed by FISH using the Zytolight SPEC CDKN2A/CEN9 Dual Color Probe with a 20% cutoff.
MTAP IHC was performed using Antibody Clone 2G4 (Abnova Corp.); cytoplasmic positivity was evaluated using various cutoffs (1%;30%;50%;25%).
Cohen's Kappa was used as a measure of agreement between results from the two techniques.
Results: 25 of 39 cases showed a CDKN2A HD. In 14 of 39 cases no CDKN2A HD was observed.
14 cases of 39 showed no MTAP immunoreactivity. 25 cases displayed variable percentages of immunoreactivity (15%-100%, Mean: 36,4%; Median: 25%).
Cohen's Kappa showed an overall low, non-significant concordance between MTAP IHC and CDKN2A FISH:
MTAP cutoff 1%: Kappa: 0.192;p=0.159.
MTAP cutoff 30%: Kappa: 0.244;p= 0.126.
MTAP cutoff 50%: Kappa: 0.109;p= 0.498.
MTAP cutoff 25% (Median of all values) Kappa: 0.208;p= 0.157.
26 cases represented a true pitfall: 14 cases were completely negative for MTAP but harbored no CDKN2A HD and 12 cases were diffusely positive but retained normal CDKN2A copy number.
Conclusion: Our results raise doubts and questions about the reliability of MTAP immunohistochemistry as a surrogate for CDKN2A FISH in the diagnosis of Peritoneal Mesothelioma.
The discrepancies between our data and those obtained in Pleural Mesothelioma might be due to technical issues or different biological and pathogenetic mechanisms between the pleural and peritoneal forms.

Therefore, we believe that larger, multicentric cohorts might be needed to eventually consider MTAP as a valuable biomarker in the daily diagnostic practice also for Peritoneal Mesothelioma.

OFP-08-012

Optimizing workflow and archiving of slides in a busy pathology laboratory through implementing a slide traceability and archiving system

P. Lund*
*Department of Pathology, Denmark

Background & objectives: Sorting and archiving slides is a time-consuming and demanding task. With a production of more than 900.000 slides a year, the Department of Pathology, Rigshospitalet was looking for a smarter and more efficient way to archive slides with fewer errors.
Methods: On 01.09.2023 the department conducted an observational study with the implementation of a new system to improve traceability, archiving and workflow. The system enables automated scanning, registering, and sorting of slides instead of manually sorting. This means less handling of the slides and a faster pace since there is no longer need for numerical ordering of slides.
Results: Implementing the new system for slide traceability and archiving resulted in a reduction in time associated with archiving slides. This was seen in the decrease of staff-needed hours, from 350 hours in August to 134 hours in January (a decrease of 61,7%). Furthermore, a reduction in time associated with retrieving slides after archiving was achieved.
We experienced a reduction of 3 manual touch points per slide with a scan time of a maximum of 5 minutes per 240 slides. The workflow of archiving slides became more efficient and showed very few problems and errors. After having scanned 368.215 slides, only 239 barcodes required manual entry into the system.
Conclusion: Implementing a system for slide traceability and archiving into a pathology laboratory saves time. As sample volumes increase, slide archiving automation releases staff from the time-consuming task of manually sorting slides into numerical order, which creates more time for crucial activities that support patient care. The system also improves the traceability of slides, making it faster and easier to

precisely locate slides that are needed later for further diagnosis. It also provides lab managers with data to optimize lab workflow.

OFP-08-013

NUT carcinoma of lung/mediastinum: a series of 34 cases of aggressive thoracic tumours from developing nation

R. Kaushal*, R. Khedkar, T. Pai, N. Karnik, A. Janu, V. Noronha, K. Prabhash, J. Agarwal, C. Pramesh
*Tata Memorial Hospital, India

Background & objectives: NUT midline carcinoma (NMC) is a highly aggressive, under-recognised entity characterised by NUT- BRD4/3 fusion. We hereby report the clinicopathological features of 34 cases of NMC of lung/ mediastinum from a single tertiary care oncology centre.
Methods: Cases of NUT carcinoma of the thorax diagnosed between 2015 and 2023(9 years) were retrieved from pathology archives. NUT immunohistochemistry (IHC) using a C52B1 antibody clone (Cell-Signaling-Technologies) was performed in cases of poorly/undifferentiated thoracic tumours, wherein NMC was suspected morphologically. Clinico-radiological details of NUT-IHC-positive cases were recorded, and histopathological features were reviewed.
Results: Thirty-four cases were diagnosed to be NMC, as they expressed diffuse specked nuclear positivity for NUT-IHC, including 26 males and 8 females with median age of 39.76 years (range:12-66 years). Tumour size ranged from 3.8 to 12.6cms (mean 7.53 cms) and located in hilar region(n=11), tracheo-bronchus(n=10), lung(n=8) and mediastinum(n=5). Metastatic disease at presentation was noted in 24/34cases. Histopathologically undifferentiated tumours exhibiting minimal pleomorphism with focal abrupt keratinisation(n=13), cytoplasmic clearing(n=21), spindling(n=5), and neutrophilic infiltration (n=15) were noted. On IHC, AE1/AE3 and p63/p40 were consistently positive in all (except one case), yet expression was focal. BRD4-NUT gene rearrangement by FISH was also demonstrated in one case. Despite multimodality treatment options attempted, outcomes were dismal.
Conclusion: This is one of the largest series on the clinicopathological features of NUT carcinoma of the thorax. Abrupt keratinisation and lack of pleomorphism in an undifferentiated midline tumour are the clues to diagnosis. Increasing awareness among pathologists and using NUT IHC help ascertain the diagnosis of NUT carcinoma in the thoracic region.

OFP-08-014

A preliminary assessment of bap1, mtap, ki67, cd5, cd117 in a thymic carcinoma monocentric cohort

S. Stanca*, I. Di Stefano, V. Aprile, I. Petrini, G. Alì
*Department of Surgical, Medical and Molecular Pathology and Critical Care Medicine, University of Pisa, Pisa, Italy

Background & objectives: Thymic carcinoma represents a rare disease with poor outcome, defined by some overlapping morphological characteristics with B3 thymoma. Based on literature, we evaluated several immunohistochemical (IHC) and molecular markers to better characterize thymic carcinoma in diagnostic and prognostic terms.
Methods: We performed both a preliminary BAP1, mTAP, Ki67, CD5 and CD117 IHC analysis and a fluorescent in situ hybridization (FISH) testing on p16 in a first monocentric cohort of 22 patients (12 males - 10 females) with thymic carcinoma selected at the University Hospital of Pisa from 2014 to 2023.
Results: None of the examined cases showed loss of BAP1 expression. Furthermore, 1 CDKN2A homozygous and 3 homo/heterozygous deletions were highlighted. Interestingly, mTAP, despite the strict proximity of the two gene loci at the level of 9p21.3, was always positive, also in the cases of CDKN2A deletion, showing a concordant expression in 81,82% of patients. Moreover, Ki67 revealed a high response variability between 10 and 75%. CD117 and CD5 exhibited a high co-expression: indeed, CD117 was positive in 86,36% and CD5 in 77,27% of the cases, with a 50-99% and 20-99% protein expression range, respectively.
Conclusion: In conjugation with literature, according to which they are not frequently altered in thymic carcinoma, BAP1 and mTAP do not appear useful markers. However, p16, based on these results, can represent an important diagnostic tool, but a comparative study with thymomas is necessary. These data encourage us to deepen the markers to investigate with consequent correlation with the clinical picture, to extend the series of thymic carcinomas and to peruse the carcinoma-B3 thymoma subtle limen by including a thymoma analysis.

OFP-09 Oral Free Paper Session Dermatopathology

OFP-09-001

Digital spatial profiling yields an activated and B-cell enriched tumour microenvironment in primary melanomas associated with brain metastases

Z. Belcaid*, N. al Amery, S. Najjary, D. Mustafa, J. Kros
*Erasmus MC, The Netherlands

Background & objectives: Brain metastases significantly worsen clinical outcomes in patients with melanoma. Tumour cells exploit immune escape mechanisms to promote tumour progression and metastasis. We therefore characterised the tumour immune landscape in primary skin melanomas from patients with brain metastases.
Methods: We profiled the tumour immune microenvironment of two independent cohorts of primary skin melanomas (N = 30) using a panel of 77 targets of the GeoMx Digital Spatial Profiler (Nanostring technologies). We analysed immune-related proteins in melanomas from patients without metastases, with systemic metastases other than brain, and with brain metastases.
Results: Melanomas from patients without metastases and with brain metastases contained more CD45+ clusters compared to melanomas with other than brain metastases. Melanomas from patients with brain metastases contained a significantly higher expression of CD20 compared to melanomas from patients without metastases and other than brain metastases ($P < 0.05$). Melanomas associated with brain metastases had a significantly higher expression of CTLA-4 and CD27, and a significantly lower expression of IDO1, GITR, CD137 and OX40L compared to melanomas without metastases ($P < 0.05$).
Conclusion: Our study shows that primary melanomas from patients with brain metastases were associated with a higher expression of B-cells with significant differences in expression of co-inhibitory and co-stimulatory markers including CTLA4, CD27, IDO1, GITR, CD137 and OX40L. Our preliminary findings indicate an immune-specific profile of the tumour microenvironment correlated with brain metastases in patients with melanoma.

OFP-09-002

Melanoma of the female genital tract: morphological, clinical and molecular characterization

P. Antonini*, F. Patrizi, A. Muccilli, F. Castiglione, A. De Magnis, A. Santoro, G. Garganese, G. Scambia, G.F. Zannoni, M. Mandalà, D. Massi
*Section of Pathology, Department of Health Sciences, University of Florence, Florence, Italy; Section of Pathology, Department of Diagnostic and Public Health, University of Verona, Verona, Italy

Background & objectives: Female genital tract melanomas (FGT-Ms) are rare and distinct from cutaneous and other mucosal melanomas. Challenges include staging protocols and treatment options. Herein, we investigated the clinical and morphological features of FGT-M including their mutational profile in a multi-centre study.
Methods: This is a retrospective multicentric Italian study of patients diagnosed and treated for FGT-M between 07/2002 and 09/2023 with

median follow-up of 16 months. The clinical and histopathological features were reviewed, and somatic mutations were assessed in FFPE tumour tissues by PCR Real Time and NGS. Progression-free survival (PFS) and melanoma-specific overall survival (OS) were assessed by Kaplan-Meier method.
Results: 41 patients with FGT-M in Stage I-IV, were included, with a median age of 66 years. Tumours originated in the vulva (73.2%), vagina (24.4%), and cervix (2.4%). Most (87.8%) were invasive. KIT was found mutated in 17.6% of cases, predominantly vulvar, BRAFV600E in 2.9%, while NRAS in 6.4%, mainly vaginal. These mutations were mutually exclusive. Radical excision was performed in 68.3% of cases. 20/22 (90%) patients received 1st-line anti-PD1 immunotherapy, 1 (5%) combo-immunotherapy and 1 (5%) target therapy. PFS at 3 months was 50%. Local recurrence was 41%, while systemic recurrences were detected in 24% of cases. Mortality rate was 24.4%, with deaths mostly occurring at 12-18 months from diagnosis.
Conclusion: Our study highlights that FGT-M are a rare and highly aggressive subtype with a unique molecular profile related to the anatomical sub-site. Indeed, immuno-oncologic and targeted therapies show limited benefits due to differing mutation frequencies. Extensive molecular profiling is needed to enable informed treatment choices and deepening out understanding of the multifaced challenges associated with advanced FGT-M integrated management.

OFP-09-003
Basal cell carcinoma of the skin under the age of 40 years: a retrospective study
I. Savic*, J. Pecanac
*Institute of Pathology, Faculty of Medicine, University of Belgrade, Belgrade, Serbia

Background & objectives: Basal cell carcinoma (BCC) of the skin is the most frequent non-melanoma skin cancer. Herein, we analyzed demographic and histopathological characteristics of BCC occurring in individuals under the age of 40 years.
Methods: Biopsy pathohistological reports of patients with BCC at Institute of Pathology, Faculty of Medicine, University of Belgrade between January 1 and December 31, 2022 were retrospectively reviewed. Demographic (sex, age) and pathological characteristics (histopathological subtype, presence of macroscopic ulceration, invasion depth, and status of lateral and deep resection margins), as well as tumour localization, were recorded.
Results: Twenty-three and 1030 cases were ≤40 and >40 years old, respectively. The most common histopathological BCC subtypes were mixed (33.3%) in the younger group and nodular (37.1%) in the older group. The localization of BCC differed between the groups (p=0.003). Ulceration was less common in the younger group (3/21 cases, 14.3% vs. 309/1012, 30.5%) (p=0.14). BCC never invaded tissues deeper than subcutaneous fat in the younger group, whereas in the older group, invasion of the fascia, muscle, cartilage, and bone was recorded in 4%. Deep resection margins were negative in 100% and 91%, and lateral resection margins were negative in 90.9% and 86.5% in the younger and older groups, respectively.
Conclusion: In conclusion, BCC is very rare in individuals under the age of 40 years; however, when present, it shows slightly different localization, histology, and invasion compared with that in older individuals. Further studies are needed to clarify biological differences in BCC in younger individuals.

OFP-09-004
Impact of COVID-19 on clinical findings and histopathological characteristics in cases of cicatricial alopecia: a retrospective cohort study
S. Yağcı*, E. Yağcı, H. Örün, N.D. Özcan, Ö. Özen
*Department of Pathology, Baskent University, Faculty of Medicine, Ankara, Turkey

Background & objectives: This study explores the impact of COVID-19 history on the clinicopathological features of patients diagnosed with cicatricial alopecia conditions such as lichen planopilaris (LPP), fibrosing alopecia in a pattern distribution (FAPD) or frontal fibrosing alopecia (FFA) at our hospital.
Methods: A total of 256 patients diagnosed with LPP, FAPD, or FFA at Baskent University Ankara Hospital, Department of Pathology between January 1, 2020, and May 1, 2023, were retrospectively analyzed. Clinical and histopathological data were compared between patients with and without COVID-19 history. Alopecia exacerbation and treatment response relationships were separately examined. The significance level was set at $p<0.05$.
Results: The median age of 256 patients was 32 years (range 15-83), comprising 140 (54.7%) females and 116 (45.3%) males. Diagnoses included LPP in 124 (48.8%), FAPD in 120 (46.9%), and FFA in 12 (4.7%) patients. Of the patients, 73.2% (131/179) had no COVID-19 history, while 26.8% (48/179) did. Those with COVID-19 history had lower treatment response (p=0.013) and higher alopecia exacerbation rates ($p<0.001$). Logistic regression analysis indicated having a history of COVID-19 was an independent risk factor for poor treatment response (p=0.012, OR: 2.92, 95% CI: 1.26-6.78) and exacerbation of alopecia ($p<0.001$, OR: 16.30, 95% CI: 6.07-43.77); low serum ferritin also associated with exacerbation (p=0.044, OR: 2.67, 95% CI: 1.02-6.97).
Conclusion: Recent literature highlights that hair loss, predominantly of non-scarring types such as telogen effluvium, alopecia areata, or androgenetic alopecia, is associated with COVID-19 in approximately 25% of patients. As our knowledge, this study analytically demonstrates for the first time that COVID-19 may exacerbate symptoms in patients diagnosed with cicatricial alopecia and worsen the response to alopecia treatment.

OFP-09-005
Artificial intelligence applied to a first screening of naevoid melanoma: a new use of fast random forest algorithm in dermatopathology
G. Cazzato*, A. Massaro, A. Colagrande, I. Trilli, G. Ingravallo, N. Casatta, C. Lupo, A. Ronchi, R. Franco, E. Maiorano, A. Vacca
*University of Bari "Aldo Moro", Italy

Background & objectives: Naevoid melanoma (NM), a rare variant of Melanoma that accounts for about 1% of all MM cases, is a constant challenge, and when it is not diagnosed in a timely manner, it can even lead to death.
Methods: For the processes of training, validation and testing, we used a dataset of 18 photomicrographs of NM, originally taken at 1920 × 1088 pixels using a NanoZoomer S60 Digital slide scanner C13210-04 at diverse magnifications (from 4× to 20×). The images were obtained from patients with histologically confirmed diagnoses of NM in the period from January 2010 to December 2022.
Results: Image processing was performed in the self-learning Fast Random Forest analysis, which focused on classifying possible areas of naevoid melanoma. The FRF extracted the probabilistic images from the photomicrographs, highlighting the region where NM is the most probable. This analysis was enhanced via the colour distribution within the 3D RGB colour space, thus estimating the number of pixels contained in each image (pixels with a high probability of classifying a NM region were highlighted in red). The execution of the trained FRF algorithm provides threshold values for the benign cases that are significantly less than 12%, thus proving the efficiency of the algorithm in better identifying dangerous cases.
Conclusion: Such an approach, in our opinion, could be of great assistance in the context of pathology laboratories that have very high volumes of cases and slides, allowing for faster screening of lesions and the initiation of immunohistochemical and, in necessary cases,

molecular investigations that can shorten reporting times and improve diagnostic timelines for patients.

OFP-09-006

Evaluation of Fumarate Hydratase (FH) and 2-Succinocysteine Stainings in cutaneous leiomyomas: an immunohistochemical study

C. Leblebici, B. Noyan Mod*, A. Başkan
*Istanbul Research and Training Hospital, Health Sciences University, Turkey

Background & objectives: Mutations in the fumarate hydratase gene are characterized by hereditary leiomyomatosis and renal cancer syndrome (HLRCC). This study examines the efficacy of immunohistochemistry, specifically fumarate hydratase (FH) and 2-succinocysteine (2SC) markers in detection of FH gene mutations.
Methods: FH and 2SC immunohistochemical stainings were performed on 38 cutaneous leiomyomas in 30 patients diagnosed between 2015 and 2024 in SBU Istanbul Training and Research Hospital. Of these 38 smooth muscle tumours, 16 were angioleiomyomas and 22 were pilar leiomyomas. Cases showing expression loss by FH and/or 2SC were considered fumarate hydratase deficient.
Results: Fourteen smooth muscle tumours excised from the trunk and extremities from 6 patients (2 males and 4 females, aged between 34 and 62 years) were evaluated as fumarate hydratase deficient. As histologic subtype, 13 of these tumours were pilar leiomyomas and one was angioleiomyoma. 3 pilar leiomyoma patients had a history of multiple cutaneous leiomyomas. One of them was male. The remaining two female patients with multiple pilar leiomyomas had previously undergone a hysterectomy due to uterine leiomyomas. Out of 6 patients, 4 underwent renal radiological examinations, and no tumoural lesion was detected.
Conclusion: Especially in patients with multiple pilar leiomyomas, follow-up of patients in terms of HLRCC syndrome is important. However, in our study, we also found a loss of expression of FH or 2SC in solitary pilar leiomyomas or angioleiomyomas. Therefore, immunohistochemical examination of all cutaneous leiomyomas may help identify FH gene mutations.

OFP-09-007

Histopathological clues observed with hematoxylin and eosin staining in cases diagnosed with dermatophytosis

B. Timur*, B. Lebe
*Department of Pathology, Dokuz Eylul University School of Medicine, Turkey

Background & objectives: Periodic Acid Schiff (PAS) stain, effective for detecting fungi's carbohydrate-rich cell walls, is standard for diagnosing dermatophytosis. Its use requires suspected fungal infection or observed histopathological clues. Our aim is to determine histopathological clues observed in skin biopsy diagnosed with dermatophytosis.
Methods: We examined cases diagnosed with dermatophytosis at Dokuz Eylul University Hospital from January 1, 2023, to April 1, 2024, excluding cases involving nails or mucous membranes. We analyzed the histopathological characteristics of 40 cases fitting these criteria, all of which were confirmed by demonstrating fungal hyphae using PAS staining. Features observed in the epidermis and dermis were recorded.
Results: The histopathological features observed in the epidermis are as follows: Spongiosis(10%none; 35%mild; 27,5%moderate; 15%extensive; 7,5%vesiculation),irregulary acanthosis(77.5%), sandwich sign in stratum corneum (62.5%), exocytosis of inflammatory cells(42,5%none; 37,5%lymphocytes; 10%neutrophils, 5%mixt), intraepidermal pustula (47,5%), empty spaces in the stratum corneum(45%), bacteria clusters (25%), parakeratosis(22.5%), epidermal dismaturation(12.5%), orthokeratosis(2,5%), fungal hyphea on H&E staining(5%), psoriasiform hyperplasia(2.5%). The histopathological features observed in the dermis as follows: In all cases, perivascular inflammatory cell infiltration is observed. Inflammatory cell types, including lymphocytes, atypical lymphocytes, eosinophils and neutrophils were present across different cases. Erthyrocyte extravasation (20%) and increased vascularity(65%) were also observed. Two cases couldn't be examined for dermal properties because they only contained the stratum corneum.
Conclusion: Hyphae are hard to detect in H&E stained sections in skin biopsy. In our study, just two cases (5%) showed visible hyphae in the H&E staining. When we observed spongiosis, irregulary acanthosis, sandwich sign and intraepidermal pustula in epidermis, we keep in mind dermatophytosis in differential diagnosis in the skin biopsy. We suggest that applying PAS staining to cases exhibiting certain characteristics can help to confirm the diagnosis, even when not indicated in clinical or differential diagnoses.

OFP-09-008

Diagnostic and prognostic relevance of Spatz-Barnhill criteria for the diagnosis of Spitz nevi

D. Chiba*, N. Ouini, A. Benabdelkader, I. Bahri, S. Ben Tekaya, W. Mokni, B. Sriha, M. Mokni
*Department of Pathology, Farhat Hached Hospital, Sousse, Tunisia

Background & objectives: Spitz melanocytic lesions vary from benign Spitz nevi to spitz melanoma, posing challenges in histological differentiation. Spatz and Barnhill introduced criteria to classify them by metastatic risk. The aim of our work is to evaluate the relevance of these criteria.
Methods: We retrospectively analyzed 6 Spitz nevi diagnosed over the past 5 years and collected follow-up data from our pathology department to determine the diagnostic and prognostic relevance of Spatz-Barnhill criteria.
Results: We enrolled 6 patients, consisting of 4 males and 2 females. The average age of our patients was 6.5 years (range: 1-11 years). The predominant location was the face in 5 patients, followed by the trunk in one patient. Histologically, the tumour measured less than 10 mm in 5 patients. It involved the subcutaneous fat in one patient and displayed a mitotic rate between 0-5/mm2 in all the patients. Ulceration was identified in 3 children. Four of the 6 cases had a low metastatic risk and two had an intermediate risk. None of the patient experienced local or distant metastasis during a follow-up period ranging from 1 to 4 years.
Conclusion: Spitz nevus is an uncommon, melanocytic lesion composed of large, epithelioid and/or spindled cells. It predominantly occurs in children. These lesions are benign; however, their clinical and histological characteristics make them difficult to distinguish from melanoma. This has led to ongoing controversy among clinicians regarding spitz tumours and their diagnostic complexity. According to our experience, the Spatz and Barnhill grading score appeared relevant for predicting the risk of metastasis.

OFP-09-009

Expression of the PRAME immunohistochemical marker in melanocytic lesions: a potential biomarker and its role in differential diagnosis of malignant lesions

B. Noyan Mod*, C. Leblebici
*Istanbul Research and Training Hospital, Health Sciences University, Turkey

Background & objectives: PRAME (Preferentially Expressed Antigen in Melanoma) antibody has been recognized in recent literature as crucial biomarker for differentiating melanoma from benign lesions. This study investigates its diagnostic potential (cutoff 50%-75%) and expression differences across melanoma types and benign melanocytic lesions.

Methods: A total of 145 cases diagnosed in the Pathology Department of Istanbul Training and Research Hospital were included. The cases consist of 52 melanomas, 27 dysplastic nevi, 23 Spitz nevi, 15 compound nevi, 23 blue nevi, and 5 congenital nevi. Selected paraffin blocks were stained with PRAME (EP461). Staining was scored from 0 (no staining) to +4 (75% or more).
Results: In the melanoma-diagnosed group, the proportion of patients with nuclear staining by PRAME exceeding 75% and exceeding 50% was significantly higher than in the non-melanoma group ($p < 0.05$). In our study, using a threshold value of 50% instead of 75% in distinguishing dysplastic nevus, compound nevus, and blue nevus from melanoma leads to an increase in sensitivity without changing specificity. In two atypical Spitz cases, a staining score of +3 was observed; in one dysplastic nevus, the score was +4; and in a melanoma case, there was no staining, indicated by a score of 0.
Conclusion: PRAME is a reliable marker for differentiating benign melanocytic lesions from melanoma, particularly in cases of congenital, compound, and blue nevi. While useful in distinguishing benign from malignant melanocytic lesions, diagnosis should be made on individual case basis, due to potential false positives and negatives. Lowering the positivity threshold from 75% to 50% enhances sensitivity but slightly reduces specificity. This adjustment proves more effective, excluding Spitz lesions, in identifying benign conditions.

OFP-09-010
Association of lymphomatoid papulosis and mycosis fungoides: a retrospective study at a third level hospital
A. Sobrino Prados*, S.A. Galeano Reyes, P.M. Bueno Ortiz, F. Granados Pacheco, K. Martins, M. González Afonso, M.d.C. Camacho García
*CHUIMI, Las Palmas de Gran Canaria, Spain

Background & objectives: Lymphomatoid papulosis (LyP) and mycosis fungoides (MF) represent distinct cutaneous T-cell lymphomas. This study aimed to retrospectively analyze LyP cases, focusing on its association with MF. Additionally, theoretical insights regarding LyP as the heightened risk of secondary lymphomas were incorporated.
Methods: A retrospective study was conducted utilizing the hospital's electronic database in the past decade. Data from patients diagnosed with lymphomatoid papulosis (LyP) were extracted. Detailed clinical information including age, gender, location, and any associated diagnoses were collected. The anatomopathological examination of skin biopsies was performed. Additionally, the number of biopsies required for definitive diagnosis was recorded for each case.
Results: Seven patients with LyP were identified. Among these cases, the demographic distribution included a range of ages and genders. The majority of lessions affected the extremities. Notably, only one patient (Case 5) presented with a concurrent diagnosis of advanced-stage mycosis fungoides. This represented a 14,29% of the cohort. Subtype classification revealed that Cases 1 and 5 were categorized as LyP subtype E, while 6 was classified as LyP type C. Case 4 developed cholangiocarcinoma within a year of LyP diagnosis, leading to mortality. The findings underscore the heterogeneity and clinical significance of LyP manifestations, as well as the importance of thorough pathological evaluation for accurate diagnosis and management
Conclusion: This study highlights the rare association between LyP and MF, underlining the necessity of meticulous dermatopathological assessment for precise diagnosis and management. The observed prevalence of coexisting LyP and MF aligns with existing literature. Given the heightened risk for associated lymphomas, continuous long-term monitoring is recommended to facilitate comprehensive understanding and clinical decision-making.

OFP-09-011
Histomorphometric analysis of metastatic sentinel lymph nodes in melanoma and correlation with regional lymph node dissection status and survival
T. Aydemir*, B. Yaman, G. Serin, T.Akalin
*Turkey

Background & objectives: Sentinel lymph node (SLN) biopsy is important for clinical decision of regional lymph node dissection (RLND) and prognosis. We aimed to investigate the impact of the melanoma SLN metastasis (largest metastatic area, depth and location) characteristics on the RLND status and survival.
Methods: Forty-four melanoma cases with SLN and subsequent RLND were selected. Largest metastatic SLN slide were digitally scanned. The lymph node surface area (LNSA), metastatic area, and depth of metastasis were calculated. Metastatic area at the SLN surface, metastatic area/LNSA ratio, depth of metastasis and locations were statistically compared with the presence of metastasis in RLND and survival.
Results: Eight (18,2%) metastatic cases were observed in RLNDs. Mean follow-up period was 32.5±66.6 (1-107) months, 19(43.18%) cases were died. Mean metastatic area at SLNs were significantly higher (mean: 63.09±97.6 mm2) in cases with positive RLND than in negative cases(p:0.03).
There was no RLND metastasis in cases(n:7) with SLNs metastasis ≤0.1mm2. In cases with SLND metastatic area/LNSA ratio <0.001(n:16) and with SLN metastasis-depth <1 mm, RLND metastasis was not observed (p:0.018-p:0.0046, respectively). There was no difference between survival times.
No relationship was detected between SLN metastasis locations and the status of RLND and survival. The survival rates were 18.2% and the estimated survival time was 31.3±9.3 months(p:0.002) in cases with more than 3 metastatic LNs.
Conclusion: Evaluation of SLN melanoma cases is important for RLND decision and prognosis. There are many SLN tumour burden measurement methods in the literature, but none of them are universally accepted. We found a strong relationship between SLN metastasis depth, metastatic area size and the possibility of metastasis in RLND. Survival times significantly decreased in cases with a total metastatic LN count of three or more. No significant difference was found between SLN metastasis locations and RLND status and prognosis.

OFP-10 Joint Oral Free Paper Session Uropathology / Nephropathology

OFP-10-001
Deep learning-based segmentation of peritubular capillaries in kidney transplant biopsies
D. Van Midden*, L. Studer, M. Hermsen, N. Kozakowski, J. Kers, L. Hilbrands, J. van der Laak
*Radboud University Medical Center, The Netherlands

Background & objectives: An important feature of antibody-mediated rejection (ABMR) is peritubular capillaritis (ptc), defined as the presence of inflammation in peritubular capillaries (PTCs). However, assessing the extent of peritubular capillaritis suffers from interobserver variability and is time-consuming. Automated assessment would offer benefits.
Methods: Kidney transplant biopsies (n=67) were stained with periodic-acid Schiff (PAS), scanned into whole-slide images (WSI) and restrained using anti-CD34-antibody. Guided by the restraining, a pathologist manually annotated over 20,000 PTCs on the PAS-stained WSI. The WSI were divided into a training, validation, and test set which all have a similar distribution of the different morphologies.
Results: For PTCs versus non-PTCs segmentation, a U-Net model (ImageNet pre-trained ResNet50 backbone) was trained with 160,000

patches (512 x 512 pixels, 0.24 µm/pixel) per epoch. For the segmentation task, we computed three different metrics. A Dice score of 71.3% and 98.5%, a Jaccard Index of 56.1% and 97.1%, and a Normalized Surface Dice (NSD) of 73% and 78.7%, for the PTCs versus non-PTCs regions, respectively was achieved. While there was a satisfactory performance in most cases, we observed less accuracy in cases with prominent interstitial changes, such as atrophic tubules and interstitial matrix deposition, which make PTCs less recognizable.
Conclusion: We developed a segmentation model for PTCs in PAS-stained kidney transplant biopsies, which in contrast to healthy tissue also include areas of inflammation and chronic damage. The results highlight the applicability of DL for clinical use to guide pathologist in routine diagnostics. To follow-up on this work, we are currently developing an algorithm for inflammatory cell detection, within the DIAGGRAFT project, as a step towards a more accurate, reproducible scoring of peritubular capillaritis and automated Banff Classification.

OFP-10-002
Macrophage activation in antibody-mediated renal allograft rejection
V. Agrawal*, S. Kamthan, S. Pratap Singh, N. Prasad
*Sanjay Gandhi Postgraduate, India

Background & objectives: M2 macrophages contribute to renal allograft injury. We evaluated the degree of CD163+ (M2) macrophage graft tissue infiltration. Urinary soluble CD163, circulating total, and monocyte-derived microparticles (MMPs) in plasma were estimated and correlated with tissue M2 macrophage infiltration.
Methods: The study included forty-five renal allograft recipients with for-cause graft biopsy, with Antibody-mediated Rejection (ABMR) (n=30) or no evidence of rejection (NER) (n=15), from Jan 2021-Dec 2023, along with fifteen age-matched healthy controls (HC). On immunohistochemistry, CD163 positive cells were counted in glomeruli and tubulointerstitium. Urinary sCD163 was done by ELISA. Flow-cytometry quantified plasma MPs (AnnexinV+) and MMPs (CD14+/ AnnexinV+).
Results: The mean age of renal allograft recipients was 35±9yrs (all males). Mean s.creatinine in ABMR and NER was 3±2.6 and 2±0.5 mg/dl, respectively. ABMR had significantly more glomerular (16.2±13.7/10 glomeruli) and tubulointerstitial (183±108/10hpf) M2 macrophage (CD163+) cell infiltration than NER (4.8±4.7/10 glomeruli; 133.5±108/10hpf). Urinary sCD163 in ABMR was also significantly raised (0.89±0.63ng/ml) than in NER. It was not detectable in healthy controls. Plasma MMPs were elevated in ABMR [25% of total MPs (1.62x104)] as compared to NER [8.2 % of total MPs (1.4x104)] and HC [7.8% of total MPs (1.2x104)]. In ABMR, the glomerular CD163+ cells correlated with urinary sCD163 levels (r=0.350, p=0.050) and circulating MMPs (r=0.526, p=0.002).
Conclusion: We found that renal allograft recipients with ABMR have significantly higher graft biopsy glomerular CD163+ (M2) macrophage infiltration and elevated urinary sCD163 levels than NER. The plasma circulating MMPs were also elevated in ABMR. Our findings suggest that monocyte activation plays a significant role in the pathogenesis and injury in ABMR. Non-invasive markers of monocyte activation can distinguish ABMR from NER in allograft recipients presenting with allograft dysfunction.

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OFP-10-003
Altered glycocalyx sialylation for differential diagnosis of thrombotic microangiopathy (TMA) in renal allografts
J. Schmitz*, W. Dai, A. Tölke, K. Diahovets, K. Niculovic, K. Schmidt-Ott, U. Eisenberger, A. Gäckler, S. Dietrich, K. Schulte, H. Stark, W. Gwinner, J. Menne, A. Münster-Kühnel, J.H. Bräsen
*Nephropathology Unit, Institute of Pathology, Hannover Medical School, Germany

Background & objectives: Thrombotic microangiopathy (TMA) is a severe syndrome affecting native and transplanted kidneys requiring therapeutic action. Antibody-mediated rejection (ABMR) and TMA share morphological similarities, rendering differential diagnosis difficult. Hypothesis: Altered endothelial glycocalyx composition contributes to TMA manifestation and facilitates diagnostic workup.
Methods: To improve the differential diagnosis, we included 227 archival KTX-biopsies from different transplant centres, re-evaluated the original materials (paraffin sections, electron microscopy), performed immunohistochemical and lectin stainings, measurements in ultrastructure and gene expression analyses (NanoString technology). All morphological results were correlated with clinical data. Statistical analyses were performed with IBM SPSS (version 28) and GraphPad Prism (version 10).
Results: Of confirmed TMA cases, 51% had morphological rejection. Patients with ABMR+TMA had significantly worse renal function than patients with pure ABMR. Thrombi were identified in 81% of TMA cases. Most useful histological TMA criteria apart from thrombi were fragmented red blood cells, mesangiolysis and fibrillar appearance of mesangium. Without thrombi, neither morphology, nor immunohistochemistry, ultrastructure or gene expression uncovered a specific difference between ABMR+TMA or without TMA. Biopsies with ABMR+/-TMA showed signifantly reduced sialylation patterns in glomerular endothelial cells and podocytes compared to KTx controls. We observed relevant loss of terminal sialic acid and galactose on endothelial cells in peritubular capillaries which were significantly altered in ABMR+TMA compared to ABMR.
Conclusion: Despite therapeutic interventions, antibody-mediated rejection (ABMR) remains a challenging condition to treat, and its presence especially combined with TMA significantly increases the risk of renal graft loss. Therefore, early detection and prompt specific clinical management of ABMR/TMA are crucial for improved outcomes. Correct diagnosis of TMA with or without ABMR is challenging. Analysis of glycosylation may refine nephropathological diagnosis and thus facilitate correct therapy in these urgent disease states. Glycocalyx preservation/restoration could serve as therapeutic target to prevent rejection/TMA.

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OFP-10-004
Unsupervised learning for labeling globally sclerosed glomeruli
H. Weishaupt*, J. Besusparis, S. Leh
*Haukeland University Hospital, Norway

Background & objectives: Current deep learning models for classifying glomerular lesions in nephropathology are trained almost exclusively in a supervised manner, requiring expert-labeled images. Very little is known about the potential of unsupervised learning for overcoming this bottleneck.
Methods: In a proof-of-concept study, we addressed this open question by focusing on the most fundamental classification task: globally sclerosed versus non-globally sclerosed glomeruli. The clustering performance between the two classes was extensively studied across six labeled datasets (>10000 glomeruli in total) with diverse compositions and histological stains and across the feature embeddings achieved by 30 different pre-trained CNN models.
Results: The study clearly demonstrated that clustering of globally and non-globally sclerosed glomeruli is highly feasible, yielding accuracies of over 95% in most datasets. In addition, the study revealed that: (i) performances differ substantially between different pre-trained CNN models used in the feature embedding step, (ii) the choice of reference image for stain normalization can have an impact on clustering, and (iii) the histological stain and composition of the dataset can drastically

affect the separability of the classes. Specifically, the worst clustering was observed in a periodic acid-silver methenamine (PASM)-stained dataset, in which the pathologist also encountered difficulties labeling cases just based on the visual inspection of the glomerulus itself.
Conclusion: The study demonstrated that an unsupervised learning approach can separate globally and non-globally sclerosed glomeruli with very high proficiency. Further work will be required to expand these experiments towards the clustering of additional glomerular lesion categories. We are convinced that these efforts (i) will open up opportunities for semi-automatic labeling approaches, thus alleviating the need for labor-intensive manual labeling, and (ii) illustrate that glomerular classification models can potentially be trained even in the absence of expert-derived class labels.

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OFP-10-005
PD-L1, ADAR2, and androgen receptor expression in BCG-treated urothelial bladder carcinoma in situ
V. Fiorentino*, C. Pizzimenti, L. Pepe, E. Germanà, G. Ricciardi, W.G. Giordano, F. Pierconti, A. Ieni, V. Ficarra, G. Fadda, G. Tuccari, M. Martini
*Department of Human Pathology in Adult and Developmental Age "Gaetano Barresi", University of Messina, Messina, Italy

Background & objectives: Urothelial bladder carcinoma in situ (CIS) treatment response may be affected by several molecular factors and the immune microenvironment. Our study aims to analyze all of these variables in a cohort of bladder CIS patients.
Methods: A retrospective observational study was performed at Policlinico G. Martino (Messina, Italy), involving tissues from fifty Bacillus Calmette-Guérin (BCG)-treated bladder CISs. Tumour-infiltrating lymphocytes (TILs) as CD4/CD8 ratio, androgen receptor (AR), ADAR1, ADAR2, and PD-L1 expressions were immunohistochemically analyzed, while miR-200a-3p and IFN-gamma were evaluated by qPCR before the treatment. Results were correlated with patients' clinical-biological features and recurrence-free survival (RFS).
Results: High AR levels in CIS had a significant correlation with higher ADAR1 expression, lower ADAR2 expression, a higher PD-L1 Tumour Proportion Score (TPS), a higher CD4/CD8 ratio, the multifocality of CIS, and the presence of high-grade papillary lesions ($p<0.001$). All patients with the aforementioned characteristics had a significant association with a worse RFS ($p<0.0001$). Multivariate and multiple regression analyses confirmed the predictive role of AR, ADAR2, and PD-L1 parameters, especially when all three parameters were combined. Additionally, we demonstrated that patients with lower AR and higher ADAR2 had a significantly higher level of miR-200a-3p and IFN-gamma than those with high AR and low ADAR2 expression ($p=0.002$ and $p=0.0003$, respectively).
Conclusion: Our findings highlight the role of AR in the response to BCG therapy by modulating PD-L1 expression and TILs through the ADAR2, miR-200a-3p, and IFN-gamma pathways. Furthermore, our data provide valuable insights for optimizing BCG therapy in CIS patients, paving the way for other possible combined treatment strategies.

OFP-10-006
High tumour mutational burden is associated with strong PD-L1 expression, HPV negativity, and worse survival in penile squamous cell carcinoma: an analysis of 165 cases
J. Hrudka*, J. Hojný, Z. Prouzová, M. Kendall Bártů, D. Čapka, N. Zavillová, P. Waldauf, R. Matěj
*University Hospital Kralovske Vinohrady, Charles University, 3rd Faculty of Medicine, Czech Republic

Background & objectives: Penile squamous cell carcinoma (pSCC) represents a rare tumour with a diverse prognosis. There is a growing need for additional prognostic markers associated with mutational signatures and the tumour immune microenvironment.
Methods: A retrospective analysis was conducted on a cohort comprising 165 cases of invasive pSCC, using formalin-fixed, paraffin-embedded tumour tissue. The analysis focused on tumour mutational burden (TMB), programmed death ligand 1 (PD-L1) expression, microsatellite instability (MSI), the presence of tumour infiltrating lymphocytes (TILs), and human papillomavirus (HPV) status determined by p16 immunohistochemistry, and traditional histopathological variables.
Results: High TMB (>10 mut/Mb) was found to be associated with strong PD-L1 expression (tumour proportion score/TPS 50-100%) and HPV-negative status. Furthermore, strong PD-L1 expression correlated with HPV negativity, a high abundance of TILs. Notably, high TMB emerged as a significant predictor of shorter overall survival (OS) in both univariate and multivariate analyses, when using a median cut-off value of 4.3 mut/Mb, but not with an arbitrary cut-off of 10 mut/Mb. Low number of TILs was associated with shorter OS and cancer-specific survival in both univariate and multivariate analyses. PD-L1 expression did not exhibit a significant impact on prognosis. Only two cases exhibited MSI high.
Conclusion: These findings lend support to the hypothesis of two distinct etiological pathways in pSCC carcinogenesis: (1) SCC associated with HPV infection, characterized by low TMB, less frequent PD-L1 expression, and lower number of TILs; and (2) SCC associated with chronic inflammation leading to a high mutation burden (high TMB), HPV negativity, increased neoantigen production (e.g., PD-L1), and heightened immune cell infiltration.

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OFP-10-007
Analysis of MicroRNA-371-373 on post-chemotherapy trophoblastic tumours of germ cell tumour origin support a differentiation phenomenon towards teratoma
J. Lobo*, N.T. Tavares, D. Fonseca, C. Jerónimo, R. Henrique, M.T. Idrees, T.M. Ulbright, A.M. Acosta
*Liga Portuguesa Contra o Cancro, Portugal

Background & objectives: Histologic subtypes of trophoblastic tumours (TT) of germ cell origin are rare, occurring mostly after chemotherapy. They are thought to represent a spectrum of "differentiation" between typical choriocarcinoma and cystic TT. Limited data suggests that cystic TTs are equivalent to teratoma.
Methods: Unusual TTs, choriocarcinomas, and postpubertal-type teratomas were manually dissected for RNA extraction for miR-371/miR-372/miR-373 RT-qPCR. RNU48 was used for quality control. TCam-2 cell line was used as positive control. No template controls were included. Results were classified as positive, negative, and in the grey zone.
Results: A total of 7 unusual TTs were assessed (2 unclassified TTs, 2 epithelioid TTs, 2 monophasic choriocarcinomas, and 1 mixed unclassified/cystic TT). RT-qPCR for miR-371a-3p showed that 2 cases were negative (1 epithelioid TT and 1 mixed epithelioid/unclassified TT), 3 cases were in the grey zone (1 monophasic choriocarcinoma, 1 epithelioid TT, and 1 unclassified TT), and 2 cases were positive (1 monophasic choriocarcinoma and 1 unclassified TT). Results for miR-372-3p and miR-373-3p followed the same pattern. A total of 10 chemo-naïve choriocarcinomas were included for comparison. Median levels of miR-371a-3p were significantly higher in choriocarcinomas than in post-chemotherapy trophoblastic tumours ($p=0.0095$). Four mature teratomas were negative.

Conclusion: Unusual TTs demonstrate variable levels of miR371-373 expression, from negative, to clinically indeterminate (i.e., expressed at low levels, "grey zone"), to frankly positive. These results suggest that these neoplasms represent a spectrum, with some demonstrating similarities to teratoma and others being comparable to non-teratoma.

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OFP-10-008

TFEB-altered renal cell carcinoma is morphologically and immunohistochemically challenging entity

K. Pivovarčíková*, J. Rogala, L. Kuthi, M. Slisarenko, B. Rychlý, M. Michal
*Bioptická laboratoř s.r.o., Czech Republic

Background & objectives: TFEB-rearranged renal cell carcinomas (RCCs) (harbouring fusions of the gene TFEB) and TFEB-amplified RCCs (demonstrating amplification of the 6p21 locus harbouring TFEB) are currently encompassed in a group of „TFEB-altered RCCs". The morphologic spectrum and immunohistochemical profile may be challenging.
Methods: The detailed morphological and immunohistochemical study of 18 TFEB-altered RCCs (confirmed by FISH) was performed (including 10 TFEB-rearranged and 8 TFEB-amplified RCCs).
Results: No case showed well defined pseudorosettes.
TFEB-rearranged RCCs: All cases stained for Melan A and Cathepsin K and 7 tumours were positive for HMB45. AE1/3 was positive in 3 cases (only focally). Interestingly, 3 tumours showed reactivity for CD117. 3/8 tumours were negative in PAX8 and no reactivity was detected with actin or desmin.
TFEB-amplified RCC: Four tumours were completely negative for Melan A, and 7/8 tumours negative for HMB45; AE1/3 showed only focal positivity in 4 cases. Cathepsin K and PAX8 stained 7/8 cases. No positivity was detected for CD117, actin or desmin. CK20 positivity was found in 2/3 analysed cases.
Conclusion: In TFEB-rearranged RCCs, confluent and solid growth patterns prevailed. In majority of cases clear cells predominated. Significant proportion of these cases showed morphology which may be confused with clear cell RCC; positive staining for melanocytic markers proved high importance in this differential diagnosis.

In TFEB-amplified RCCs, the predominant growth pattern was papillary/tubulopapillary. All tumours contained predominantly cells with abundant granular eosinophilic cytoplasm. TFEB-amplified RCC are frequently negative for melanocytic markers and may have morphology of „papillary RCC with oncocytic features".

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OFP-10-009

Cytogenomic evaluation of severe oligozoospermia cases undergoing infertility treatment

A. Saraswat*, B.K. Chakrabarty, N. N, S. Venkatesan
*India

Background & objectives: 15 to 30 percent of male infertility is due to genetic factors. There is still a dearth of pan-Indian ethnic data on sperm aneuploidies and chromosomal abnormalities in a therapeutically significant population of infertile male cases presenting with severe oligozoospermia.
Methods: The study included 43 infertile male patients receiving treatment at the Assisted Reproductive Technique (ART) clinic of a tertiary care centre and were detected with severe oligoasthenoteratospermia or oligozoospermia. A competent ART specialist comprehensively assessed all cases, including relevant laboratory parameters. Peripheral blood conventional karyotyping and Sperm Fluorescence in situ hybridisation (FISH) were performed using standard protocols.
Results: A total of 80 infertile male patients having non-obstructive azoospermia or severe oligoasthenoteratospermia / oligozoospermia were examined. Patients with severe oligozoospermia (sperm count < 5 million sperm/mL) or azoospermia (no detectable sperm in the ejaculate) were classified following the recent guidelines. Out of the studied patients, 43 individuals were found to have severe oligozoospermia or oligoasthenoteratospermia. 13.5% of studied azoospermia patients were detected with peripheral blood cytogenetic abnormalities other than polymorphic variation. A Sperm FISH panel was performed for chromosome 13,18,21, X and Y aneuploidies, only for severe oligozoospermia/ oligoasthenoteratospermia cases. The peripheral blood cytogenetics and sperm FISH results related to severe oligoasthenoteratospermia or oligozoospermia patients will be presented.
Conclusion: Due to lifestyle changes, technological advancement, and rapid changes in socio-demographic features in developing countries like India, more couples are availing of ART facilities. Utilisation of ART methods circumvent natural selection and increases the chances of transmission of chromosomal anomalies to the child. The analysis of the cytogenetic abnormalities in the peripheral blood of infertile males and its correlation and effects with sperm chromosomal abnormalities can highlight the male contribution and reproductive outcomes of an altered sperm FISH result.

OFP-10-010

Utilising artificial intelligence to support histopathological diagnosis of needle core biopsies and transurethral resection of the prostate: a clinical validation study

F. Maclean*, A. de Souza, M. Phang, C. Petrucco, M. Peters, C. Warren
*Douglass Hanly Moir Pathology, Australia

Background & objectives: Prostate cancer poses a significant healthcare burden, with a global projected increase to 2.9 million new cases annually by 2040. Concurrently, there's a chronic worldwide pathologist shortage. This study validates an Artificial Intelligence (AI) model as a diagnostic support tool.
Methods: A Multi-Reader Multi-Case (MRMC) study, including 30 pathologists was conducted using an enriched test set of over 1700 H+E stained whole slide images (WSI) representing individual patients. Pathologists interpreted ground truthed test set images, rating their diagnostic confidence in 45 clinical findings from a predefined ontology. A statistical analysis was performed in comparison to the AI model interpretation.
Results: The classification performance of the AI model achieved statistical non-inferiority compared to unassisted pathologists for all 45 findings. Furthermore, statistical superiority was shown for 98% of needle core biopsy (NCB) and 91% of transurethral resection of prostate (TURP) findings. The AI model successfully identified malignancy (AUC 0.97) compared to pathologists (AUC 0.92). In NCB the model identified acinar adenocarcinoma Gleason patterns 3, 4 and 5 with AUCs of 0.96, 0.98, 0.97 respectively, compared to pathologists with AUCs of 0.85, 0.93, 0.81. Other clinical findings where the model outperformed pathologists include cribriform architecture, adenocarcinoma with ductal features, and prognostic factors including intraductal carcinoma, extraprostatic extension, lymphovascular invasion and perineural invasion.

Conclusion: This study validates the performance of the AI model in detection of all included prostate findings on H+E stained WSIs and supports its use as a decision support tool for pathologists in detection of prostate adenocarcinoma and associated findings. Given the projected surge in prostate cancer over the coming years, and the fundamental role pathology has in diagnosis and determination of treatment, this model has potential for great utility.

OFP-10-011

Beyond BRCA: what does assessment of additional homologous recombination and mismatch repair genes in primary and metastatic prostatic adenocarcinoma add?

N.J. Nguyen*, N. Park, E. Olkhov-Mitsel, W. Huang, C. Sherman, M.R. Downes
*Department of Laboratory Medicine and Pathobiology, University of Toronto, Canada

Background & objectives: Prostatic carcinoma (PC) with homologous recombination repair defect (HRD) has shown response to PARP inhibitors. We assessed somatic HRD and mismatch repair (MMR) defects in primary and metastatic PCs to determine the frequency of actionable genes beyond *BRCA1* and *BRCA2*.
Methods: Primary and metastatic PCs that had somatic testing for HRD at our centre (2022-2023) were included. Indications for reflex HRD testing were: global biopsy Grade Group (GG) 3-5, ≥pT3, nodal or metastatic disease. The Oncomine Comprehensive Assay v3 was used. The analyzed genes were *BRCA1, BRCA2, ATM, PALB2, BRIP1, CDK12, CHEK1, CHEK2, RAD51B, RAD51C, RAD51D, MLH1, MSH2, MSH6* and *PMS2*.
Results: 259 primary PCs and 74 metastases. GG distribution of primary PCs was: GG1-2 (0.8%), GG2-20 (7.7%), GG3-93 (35.9%), GG4-36 (13.9%), GG5-107 (41.3%), neuroendocrine-1 (0.4%). Sites of the metastases were: node-20 (27.0%), liver-13 (17.6%), lung-9 (12.2%), neuro-15 (20.3%), bone-6 (8.1%), other-11 (14.9%). Tier 1/2 *BRCA1/BRCA2* mutation was seen in 7/259 (2.7%) primary PCs and 4/74 (5.4%) metastases. Tier 1/2 variants were identified in the additional HR genes in 28/259 (10.8%) primary PCs and 8/74 (10.8%) metastases. Tier 1/2 MMR deficiency was detected in 3/259 (1.2%) primary PCs and 3/74 (4.1%) metastases. There were 2.0 times more *BRCA1/BRCA2* mutations (p=0.251) and 3.5 times more MMR defects (p=0.099) in metastases versus primary PCs.
Conclusion: We reported the frequency of HRD and MMR somatic mutations in a large real-world cohort of consecutive primary and metastatic PCs, providing a realistic estimate of the proportion of patients that could benefit from PARP or immune checkpoint inhibitors. Analysis of HR genes beyond *BRCA1* and *BRCA2* significantly increased the pool of patients that would be eligible for PARP inhibitor trials. *BRCA1/BRCA2* and MMR mutations were more frequent in metastatic lesions suggesting these gene defects to be strong metastatic drivers.

OFP-10-012

Somatic genomic alterations TP53, CDKN2A, ATM, EPHA7, POT1, CHEK1, GRIN2A and EGFR worsen survival in penile squamous cell carcinoma: comprehensive DNA analysis of 146 cases and correlation with patient`s follow-up

J. Hrudka*, J. Hojný, Z. Prouzová, E. Krkavcová, M. Kendall Bártů, J. Dvořák, R. Michálková, D. Čapka, N. Zavillová, R. Matěj, P. Waldauf
*University Hospital Kralovske Vinohrady, Charles University, 3rd Faculty of Medicine, Czech Republic

Background & objectives: Penile squamous cell carcinoma (pSCC) is a rare tumour known for its stagnant mortality rates, psychosexual distress, and highly unpredictable prognosis. The WHO classification differentiates between two types: those associated with human papillomavirus (HPV) and those independent of HPV.
Methods: In our study, we performed thorough next-generation sequencing (NGS) DNA profiling on 146 samples of penile squamous cell carcinoma (pSCC) using a panel comprising 355 genes linked to tumourigenesis. This profiling was then correlated with immunohistochemical markers and prognostic clinical data. Additionally, we conducted a survival analysis focusing on recurrent genomic events identified in at least 10 cases.
Results: Alterations in *TP53, CDKN2A, ATM, EPHA7, POT1, CHEK1, GRIN2A*, and *EGFR* were linked to shortened overall survival (OS). HPV positivity, as diagnosed through both p16 immunohistochemistry and PCR, did not affect survival but was associated with high grade, lymphatic invasion, PD-L1 negativity/weak expression, and low tumour mutational burden (TMB). Alterations in *FAT1, TP53, CDKN2A, ATM, CASP8, HRAS,* and *GRIN2A* were more frequently observed in HPV-independent pSCCs. HPV-associated pSCCs showed an enrichment of *EPHA7* and *CHEK1* mutations. *PIK3CA, FAT1, FBXW7,* and *KMT2D* mutations were associated with high TMB. *NOTCH1, TP53, CDKN2A, POT1, KMT2D, ATM, CHEK1, EPHA3,* and *EGFR* mutations correlated with adverse clinical-pathological features such as stage, tumour budding, lymphovascular invasion.
Conclusion: Recently, there has been an evolving line of research documenting the enrichment of HPV-independent pSCC with high tumour mutational burden (TMB) and programmed death ligand-1 (PD-L1) expression, as well as clusters of genes associated with HPV status. To the best of our knowledge, this study presents the largest cohort of pSCC cases, incorporating comprehensive analysis of molecular, pathological, and clinical factors correlated with patient prognosis.
Funding: This work was supported by the Czech Health Research Council (Grant number NU21J-03-00019).

OFP-11Joint Oral Free Paper Session Soft Tissue and Bone Pathology / Infectious Diseases Pathology

OFP-11-001

Description of FOS alterations in osteosarcoma raises the hypothesis of malignant transformation of osteoblastoma: a multicentric clinico-pathological and molecular study of five cases

C. Bontoux*, H. Reboul, M. Csanyi, C. Bouvier, F. Larousserie, H. Sartelet, F. Bibeau, G. De Pinieux, N. Van Acker, S. Evrard, A. Gomez-Mascard
*IUCT-Oncopole, Toulouse, France

Background & objectives: Recent studies have suggested a potential link between osteoblastoma and osteosarcoma, supporting a malignant transformation process. We aimed to explore the hypothesis of malignant transformation of osteoblastoma to osteosarcoma and to discuss the potential clinical implications of these findings.
Methods: We conducted a multicentric restrospective case-series study within the ResOs network (French National network specialized in pathology and care of bone sarcomas) by collecting clinical, radiological, histological and follow-up data of osteosarcoma suspected to be linked with malignant transformation of osteoblastoma. Immunohistochemistry and molecular analysis (fluorescence in situ hybridization-FISH and next-generation sequencing-NGS) were performed to characterize these tumours.
Results: Five cases were included (3 female and 2 male patients). Median follow-up was 3 years (range:2-7). The median age at diagnostic of osteosarcoma was 35 years (range:13-74). The tumour was located in axial skeleton for 4 patients. All tumours were osteoblastoma-like osteosarcoma subtype. Two patients had a previous history of osteoblastoma diagnosed 11 and 17 years before the diagnosis of osteosarcoma. Four osteosarcoma harboured *FOS* gene rearrangement in FISH including two tumours with characterized fusions by NGS (*FOS::VGLL4* and *FOS::COL5A2*). One patient had *FOS* polysomy in FISH. Two patients relapsed into conventional high-grade

osteosarcoma. All patient with survival data (n=4) were alive at last follow-up.
Conclusion: We present the comprehensive analysis of five cases of osteosarcoma with *FOS* alteration, combining genetic profiling, histopathological evaluation, and clinical data. Our results support the hypothesis of malignant progression of osteoblastoma towards osteosarcoma. This study emphasizes the need to recognize the malignant transformation potential of osteoblastoma and the indolent course of these tumours to improve the management of the patients.

OFP-11-002
USP2 and USP8 fusions define a new subset of myofibroblastic neoplasms
C. Bouvier*, A.C. Marsan-Fratini, A. Meurgey, D. Pissaloux, S. El Zein, G. Pierron, F. Le Loarer, M. Karanian, F. Tirode, N. Macagno
*Timone Hospital, France

Background & objectives: Myofibroblastic neoplasms include nodular fascitis, inflammatory myofibroblastic tumours and myofibromas.
Methods: We retrospectively collected 15 myofibroblastic benign tumours diagnosed in the French Sarcoma Network of pathologists which harboured USP2or USP8 fusions by RNA sequencing.
Results: The most common location was superficial soft tissues of upper limb but 2 cases were intracardiac. The tumours were well circumscribed made of spindle bland cells arranged in fascicles. 2 cases had mild pleomorphism, 2 other cases necrosis. 3 cases had more than 5 mitoses/2mm2 Tumour cells were SMA positive (14/15) and HMGA2 positive (7/15). 10 cases/15 had a USP8 fusion with variable partners. 5 cases had a USP2 :: CBLB fusion. USP8-fused tumours had more frequently a myxoid and or inflammatory stroma while USP2-fused tumours had a hyaline stroma.
Conclusion: This is the first report of USP2 and USP8 fusions in myofibroblastic tumours. Though limited follow-up is available these tumours had no histological features of malignancy. Further studies are required to fully defined the clinical and histomolecular features of this new myofibroblastic tumour.

OFP-11-003
Optical genome mapping detects complex rearrangement patterns in Ewing sarcoma that associate with poor clinical outcome
C. Salguero-Aranda, E. de Álava, J. Diaz-Martin*
*Instituto de Biomedicina de Sevilla (IBiS) - Hospital Virgen del Rocío / CSIC / Universidad de Sevilla / CIBERONC, Spain

Background & objectives: Ewing sarcoma (ES) prognosis is affected by genomic structural variants (SV). Our main aim is the comprehensive characterization of SVs using a cutting-edge cytogenetic method, Optical Genome Mapping (OGM), in order to identify all those alterations in a single assay.
Methods: OGM is a genome-wide mapping technique that detects copy number alterations (CNA), aneuploidies, balanced and unbalanced SV (translocations, inversions, and insertions) in a single assay. We used OGM for profiling a case series of undifferentiated small round sarcomas comprising 19 cases of ES (17 cases EWSR1::FLI1, 2 cases EWSR1::ERG), and 3 cases of ES-like (2 cases BCOR::CCNB3, 1 case EWSR1::NFATC2).
Results: The analysis revealed genomic gains and losses that were concordant with the CNA profiles in our previous studies using SNP arrays. We detected the pathognomonic translocation in all the cases. Interestingly, several ES cases exhibited a pattern of complex looped rearrangements, known as chromoplexy. Conceptually, chromoplexy is an extended version of balanced translocations, which is explained by a catastrophic event producing multiple DNA double-strand breaks. RNA-seq confirmed the expression of transcripts corresponding to additional gene fusions arising from chromoplectic rearrangements. Importantly, cases displaying chromoplexy had a poor clinical outcome. Matched ES samples -primary and lung metastatic tumours- showed a similar SV profile, suggesting a common clonal origin for both lesions.
Conclusion: OGM allows for the accurate identification of clinically relevant SVs providing both diagnostic and prognostic information, and consolidates in a single assay the diagnostic yield of other standard-of-care orthogonal techniques. Therefore, OGM could be considered as first-line molecular test for precision diagnostics of sarcomas. Prospective validation of our results in a larger series of ES cases, would allow designing a refined multiparametric risk score that integrates all those alterations with significant impact on clinical parameters.

OFP-11-004
Primary intraosseous "undifferentiated" sarcomas showing rhabdomyoblastic differentiation: clinicopathological, immunohistochemical and molecular features of 11 ultra-rare tumours
B. Rekhi*, R. Jayan, O.A. Shetty, J. Bajpai, K. Kösemehmetoğlu
*Tata Memorial Centre, India

Background & objectives: Presently WHO subclassifies rhabdomyosarcomas into four subtypes. Primary intra-osseous sarcomas with rhabdomyoblastic differentiation are uncommon, including some characterised by certain clinical and genetic features. This study aimed to evaluate clinicopathological features of 11 primary intra-osseous undifferentiated sarcomas with rhabdomyoblastic differentiation.
Methods: Apart from their location (primarily intraosseous), only those sarcomas were included that displayed skeletal muscle differentiation with immunohistochemical stains, such as myoD1 and or myogenin. Mesenchymal chondrosarcomas showing skeletal muscle differentiation were excluded. Eleven tumours occurred in 7 males and 4 females with age-range of 3-62 years (median=22); median size=12.5 cm in pelvic bones(n=2), femur(n=2), humerus(n=2), maxilla (n=2) tibia(n=2) and fibula (1)
Results: Histopathology showed spindle, round and pleomorphic cells with rhabdomyoblastic differentiation. One tumour showed osteoid matrix, two (fibula and tibia) were diagnosed as embryonal rhabdomyosarcoma, another(maxilla) as alveolar rhabdomyosarcoma and remaining comprised epithelioid and spindle cells. Immunohistochemically, tumours were positive for desmin(11/11), MYOD1(10/10), myogenin(6/10), pan-keratin(4/8, variable), ALK(3/4), synaptophysin(2/2, focal), SATB2(4/5); showed 'dot-like'/membranous MIC2 expression(3/3) and were negative for h-caldesmon(0/3). One tumour showed loss of H3k27me3 (malignant triton tumour-like). EWSR1 and FUS gene rearrangements were detected in 1/8 and 1/2 tumours, respectively. Most patients underwent chemotherapy (7/9), followed by surgery (4/9). Post-neo-adjuvant chemotherapy response was 40-44% in 3 resections. All 9 patients with available clinical details developed metastasis, frequently in lung(n=6), bones(n=4) and lymph nodes(n=5).
Conclusion: These tumours are mostly large-sized, aggressive, suboptimally respond to the defined chemotherapy protocols and need to be distinguished from their mimics namely osteosarcomas, classical rhabdomyosarcomas and Ewing sarcomas which are relatively chemosensitive. There is a scope of newer therapies, including ALK inhibitors for these ultra-rare tumours.

OFP-11-005
Liposclerosing myxofibrous tumour: case series with radiologic-pathologic correlation and review of this infrequent entity
E.M. Pena Burgos*, G. Serra del Carpio, M. Tapia Viñe, E.J. Ortiz Cruz, J.J. Pozo Kreilinger
*Hospital General Universitario Gregorio Marañón, Spain

Background & objectives: Liposclerosing myxofibrous tumour (LSMFT) is a bening fibro-oseous entity that predominantly arises in

the intertrochanteric femoral region. It is a probably fibrous dysplasia related entity. To our knowledge, only 241 cases have been reported in medical literature.
Methods: We report 15 new cases, all adult patients, with a 1:0.9 male-female ratio. All cases arose in femur, fourteen cases in the proximal intertrochanteric region and one case in the distal diaphysis. There were well-defined intraosseous lytic masses with peripheral sclerotic rim, isointense T1-WI and hyperintense on T2–WI, with variable amounts of internal calcifications and fat on radiological studies.
Results: They were histopathologically composed by predominant variable proportions of fibromyxoid stroma, bone tissue (trabecular, pseudopagetoid or psammomatoid patterns), adipose tissue, xantomized cells, micro- and macrocystic spaces, inflammatory cells, hemosiderophages and small hyalinized vessels. Aneurysmal bone cyst changes were observed in one case. The cells were non-atypical, spindled or stellated, with round nuclei, and showed a patchy SATB2 and smooth muscle actin immunoreactivity. No complete correlation between radiological findings and the histopathological ones was found in all cases. Molecular tests (next generation sequencing) revealed GNAS or TP53 mutations in four cases. They were treated with curettage and bone grafting in most cases. Neither local recurrence nor metastases were seen.
Conclusion: LSMFT presents a diagnostic challenge due to its overlapping features with several bone tumours. LSMFT should be included in the differential diagnoses of solitary bone lesions in the femoral intertrochanteric region. It is important to recognize the typical radiological findings and its heterogeneous histopathological components, especially in a small biopsy, to not misdiagnose and overtreat these patients. Clinical, radiological, and histopathological evaluation is essential to reach the correct diagnosis.

OFP-11-006
Mesenchymal chondrosarcoma: a tertiary care centre experience from South India
I. S Nair*, J. K, S. Nair P, N. Radhakrishnan, E. Joy, G. N, V. M, P. T, M. Paul, A. Mathew
*Regional Cancer Centre, Thiruvananthapuram, India

Background & objectives: Mesenchymal Chondrosarcoma is a rare aggressive variant of chondrosarcoma accounting for 2-4% of Chondrosarcomas. Microscopy exhibits biphasic morphology-sheets of undifferentiated small round/spindly cells with islands of hyaline cartilage. Important to recognise this entity due to its poorer prognosis and risk of recurrence.
Methods: A retrospective analysis in our department identified 22 cases of Mesenchymal Chondrosarcoma reported between January 2013 and December 2023.The microscopic, clinicopathological and radiological features were analysed by reviewing hematoxylin and eosin slides and patient charts.
Results: Total cases:22, Included 15 females (68%) and 7 males (32%). Age range-8 to 66 years with median age of 28 years. Ratio of occurrences in bone to soft tissue is 2.7:1.Primary tumour locations: skull bones(n=6,27.3%),lower limbs(n=6,27.3%),pelvis(n=3,13.7%),vertebrae (n=2,9.1%).Other sites were forearm(n=1),soft palate(n=1),chest wall (n=1),paraspinal soft tissue(n=1) and cerebellopontine angle of brain(n=1).Diagnosis was made in histomorphology in 9 cases(41%). MIC2 positivity identified in 8 cases;SOX9 positivity in 6 cases. Two patients had metastasis at time of diagnosis. Five cases showed recurrence in a span of 1-5 years.11 patients underwent surgery followed by chemoradiation.6 cases received neoadjuvant chemotherapy followed by surgery. At median follow up of 26.5 months,4 patients had expired. Two year Overall survival and Disease-free survival is 89.1% and 72.3% respectively.
Conclusion: It is essential to diagnose this entity, especially in Trucut biopsies considering its morphological overlap with other small blue round cell tumours leading to misdiagnosis. Accurate correlation with clinical and radiological features is crucial in diagnosis since it exhibits a strong trend to cause late recurrences.

OFP-11-007
Prognostic value of vessels encapsulating tumour clusters (VETC) in solitary fibrous tumours (SFT). Validation on a retrospective cohort.
A. Bressan*, L. Sama', Ö. Mintemur, L. Ruspi, A. Bertuzzi, P. Colombo, A. Bonometti, F. Cananzi, S. Renne
*Humanitas University, Italy

Background & objectives: SFT are divided based on risk-stratification scores; however, how they metastasize is unknown. In our previous studies, VETC was a possible mechanism of metastasis in sarcomas and prognostic in SFT. We aim to confirm this finding on a larger series.
Methods: SFT cases diagnosed in our Institution from 2000 to 2020 were retrospectively reviewed. VETC was assessed with CD31 immunohistochemistry and defined as a continuous endothelial lining around tumour clusters. We used Bayesian probabilistic modeling to detect small effects and multilevel hierarchical modeling to reduce overfitting. Models were fit using Stan and R. CI were computed with the HPDI method.
Results: Among 76 cases (14 metastatic), 14 showed VETC. VETC was positively associated with metastasis (mean slope: 1.23; CI: -0.09 – 2.53). The probability of metastasis increased with VETC: 0% VETC = 0.19 (CI: 0.13 – 0.26), 30% VETC = 0.26 (CI: 0.16 – 0.39), 60% VETC = 0.34 (CI: 0.17 – 0.53), 100% VETC = 0.45 (CI: 0.17 – 0.74). Follow-up data (n=73) showed that VETC + cases had a worse prognosis with a shorter metastasis-free survival interval (mean HR: 9.94; CI: 1.84 – 17.58).
Conclusion: VETC is confirmed as a potential mechanism for SFT metastasis, with a rising probability of metastasis with increasing VETC. Additionally, VETC's prognostic role in metastasis-free survival is validated. These findings suggest targeting VETC might be a therapeutic approach.

OFP-11-008
CD63 prevents the elimination of cancer cells through macrophages in osteosarcoma
T. Lerbs*, L. Cui, C. Muscat, R. Buettner, G. Wernig
*University Hospital Cologne, Germany

Background & objectives: Metastatic osteosarcoma has a poor prognosis despite multimodal therapies. Unfortunately, immunotherapies have shown only limited efficiency, potentially linked to the tumour microenvironment with rare T cells and abundant macrophages. Here, we investigated the function and the therapeutic potential of CD63.
Methods: We assessed the expression of CD63 via immunohistochemistry and In-situ-hybridization. In vitro, we performed phagocytosis assays with MG63 and 143b cells after deleting CD63. In vivo, we subcutaneously transplanted both cell lines and measured proliferation and macrophage-mediated phagocytosis of cancer cells via flow cytometry. Finally, we transplanted MG63 cells into the tibia to evaluate the occurence of lung metastases.
Results: Immunostaining confirmed the expression of CD63 in osteosarcoma tissue. In vitro and in vivo in an ectopic model, deleting CD63 increased the elimination of cancer cells through macrophages. Additionally, deleting CD63 impeded the proliferation of cancer cells in the ectopic model and prevented the occurrence of lung metastases in the orthotopic model.
Conclusion: Our study reveals a pivotal role for CD63 in regulating macrophage-mediated phagocytosis and tumour proliferation in

osteosarcoma. These findings demonstrate the potential of CD63 as a therapeutic target, which warrants a further investigation.

OFP-11-009

Impact of disruptions in antigen processing and presentation machinery on sarcoma

S. Renne*, L. Sama', S. Kumar, Ö. Mintemur, L. Ruspi, F. Sicoli, A. Bertuzzi, A. Bonometti, P. Colombo, V. D'amato, A. Bressan, L. Terracciano, P. Navarria, F. Grizzi, F. Cananzi
*Humanitas University, Italy

Background & objectives: The antigen processing machinery (APM) plays a critical role in generating tumour-specific antigens that can be recognized and targeted by the immune system. The status of the APM in sarcomas is not well characterized.
Methods: We investigated 126 patients with 8 types of primary bone and soft tissue sarcoma operated between 2001-2021. Tissue microarrays mapped 11 specific areas in each case. The presence/absence of APM proteins (LMP10, MHC-I, TAP2, β2-microglobulin, HLA-I subunit α, and HLA-II) was determined through immunohistochemistry. Bayesian networks were used for analysis; for custom code, see study repository: https://github.com/slrenne/APM_Sarcoma.
Results: All investigated sarcomas had some defects in APM. The least damaged component was HLA Class I subunit β2-microglobulin and HLA Class II. The proteasome LMP10 subunit was defective in leiomyosarcoma (LMS), myxoid liposarcoma (MLPS), and dedifferentiated liposarcoma (DDLPS), while MHC I transporting unit TAP2 was altered in undifferentiated pleomorphic sarcoma (UPS), gastrointestinal stromal tumour (GIST), and chordoma (CH). Among different neoplastic areas, high-grade areas showed different patterns of expression compared to high lymphocytic infiltrate areas. Heterogeneity at the patient level was also observed. Loss of any APM component was prognostic of distant metastasis (DM) for LMS and DDLPS and of overall survival (OS) for LMS.
Conclusion: Sarcomas exhibit a high degree of defects in APM components, with differences among histotypes and tumoural areas. The most commonly altered APM components were HLA Class I subunit β2-microglobulin, HLA Class I subunit α (HC10), and MHC I transporting unit TAP2. The loss of APM components was prognostic of DM and OS and clinically relevant for LMS and DDLPS. This study explores sarcoma molecular mechanisms, enriching personalized therapeutic approaches.

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OFP-11-010

Exploring the potential of optical genome mapping in soft-tissue and bone tumours

E. Mayordomo Aranda*, Á. Díaz González, C. García Ruiz, F. Giner, L. Rubio Martinez, S. Hernández Girón, N. Torres Hernández, C. De la Calva, P. González Rojo, S. Gimenez Ortiz, C. Ramirez Fuentes, J.V. Amaya Valero, E. Such Taboada
*Hospital La Fe, Spain

Background & objectives: Precise diagnosis of soft-tissue and bone tumours is challenging. Optical Genome Mapping (OGM) virtually combines karyotyping, FISH, and NGS-RNA panels in a single workflow. The aim was to assess OGM's performance and compare with conventional techniques.
Methods: Thirty biobanked tumours underwent OGM analysis, prioritizing those with the most biological uncertainties. Sample processing followed manufacturer's guidelines. The analysis was conducted using Bionano Access 1.8.1 software, with the rare variant pipeline, and manufacturer-recommended filters for detecting structural variants (SV) and copy number variations (CNV). A BED file was generated, compiling genes frequently altered in these tumours for focused analysis.
Results: DNA extraction was successful in 20/30 cases with an average sample mapping rate of 74.3%. The histological subtypes in which DNA extraction failed were adipocytic (6) and myxoid (4). OGM detected the pathognomonic alteration in 100% of those cases that meet the quality criteria for analysis, including 1 case with FUS::DDIT3 rearrangement and 6 cases of MDM2 amplification; one of which also showed additional multiple rearrangements involving HMGA2 in a dedifferentiated diagnosis.
The remaining cases where complex karyotypes were expected (undifferentiated pleomorphic sarcoma, myxofibrosarcoma G3 and pleomorphic liposarcoma), OGM confirmed multiple CNVs affecting oncogenes/tumour-suppressor genes like CDKN2A/B (n=2), TP53 (n=1), or RB1 (n=1); as well as chromoplexy and chromothripsis events.
Conclusion: OGM emerges as an appealing tool for delving into the genetic basis of these tumours. Extracting DNA from predominantly adipocytic and mixoid samples poses challenges due to their distinct characteristics and lower nuclear density. Expanding OGM usage across a broader patient cohort has the potential to significantly enhance alteration detection precision, facilitating more accurate diagnoses, predicting evolution, and defining targeted treatments.

Funding: This project is supported by Maria Jordá´s Grand IIS la Fe 2023-1207-1 The samples come from la Fe Biobank.overall survival (OS) for LMS.

OFP-11-011

DVICE - detection of virus-induced cytopathic effect using AI

U. Greber*, A. Petkidis, V. Andriasyan, L. Murer, R. Volle
* Universität Zürich, Switzerland

Background & objectives: Viruses give rise to highly variable outcomes, including lytic, persistent, latent and abortive infections. This largely owes to particular cell states conferring cell susceptibility or resistance to a particular viral agent.
Methods: Here, we present a procedure named 'detection of virus-induced cytopathic effect (DVICE)'. DVICE is based on label-free transmitted light microscopy and artificial intelligence (AI). It robustly quantifies virus infection-specific features in a perturbation-low manner and allows for dynamic assessment of chemically fixed and live specimens.
Results: DVICE interprets cytopathic phenotypes in an ensemble of cells, as induced by a range of human viruses, including coronaviruses, adenoviruses influenza A virus, rhinovirus, herpes simplex virus, and vaccinia virus. Class activation maps and 'leave one out' crossvalidations show that DVICE recognizes infection-specific features with virus class specificity. DVICE also provides a user-friendly graphical interface for readily monitoring live cell infection dynamics in high throughput screening protocols. It is applicable to laboratory and clinical samples, and laboratory diagnostics.
Conclusion: The automated procedure DVICE provides unbiased, robust and accurate scores of viral infectivity. It uses human cell lines in standard multiwell-format tissue culture dishes together with light microscopy imaging. DVICE can be readily adapted to laboratory diagnostics, drug screening, serum neutralization or clinical samples in high-throughput settings.

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OFP-11-012

Invasive fungal disease in chronic liver transplant failure – an underestimated burden

K. Hofmann*, A.V. Puzalkova, T. Pfeffer, I.M. Klein, A. Mehrabi, U. Merle, R. Penzel, A. Stenzinger, C. Flechtenmacher, P. Schirmacher

*German Center for Infection Research (DZIF), Tissue Bank at the partner site Heidelberg, Institute of Pathology, University Hospital Heidelberg, Germany

Background & objectives: Invasive fungal infection (IFI), a severe complication in organ transplants, remains diagnostically challenging. To elucidate its significance in chronic liver transplant failure, comprehensive histo- and molecularpathological analyses were performed at the Institute of Pathology Heidelberg, supported by DZIF biobanking.
Methods: FFPE tissue samples and pathological findings from all explanted liver transplants due to chronic transplant failure from the Heidelberg University Hospital (1991-2021, ≥90-day graft survival) were reexamined. Additional stainings with periodic acid-Schiff and Grocott methenamine silver were used in light-microscopic investigations to uncover occurrence, severity, and associated conditions of IFI. Molecular fungal species identification was performed chip-based by DNA hybridization.
Results: Light-microscopic examination revealed fungal infection in 41 (27.5%) of the 149 analyzed cases with 2/3 being newly specified. Female patients presented a slightly higher risk for IFI. Typically, the large bile ducts were affected, accompanied by acute inflammation with frequent abscess and concrement formation. In 35 cases, molecular identification of the fungal species was achieved. Candida albicans was the most common species, appearing in 61% of cases, including mixed infections with other species in 14% of cases. The cohort included three autopsy cases from patients that died of septic multiorgan failure. For one case, a clear connection to the IFI causing species Candida glabrata could be demonstrated.
Conclusion: These data show the underestimated prevalence and high diagnostic and clinical relevance of IFI in chronic liver transplant failure. Adapted preparation protocols, molecular pathological analyses as well as medication guidelines are urgently needed to identify and prevent chronic transplant organ failure caused by IFIs. The contribution of structured registries and qualified biobanking is evident in such retrospective (but also prospective) studies and improves the diagnostic approach and development of adequate therapeutic strategies.

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SC-17History of EM in pathology

SC-17-003

Exploring the contribution of electron microscopy in pneumoconiosis: case studies of hard metal lung disease

F. Fortarezza*, F.Pezzuto, E. Faccioli, E. Cocconcelli, F. Lunardi, B. Bonvicini, M. Perilli, M. Della Barbera, S. Rizzo, F. Calabrese
University of Padua, Italy

Background & objectives: Hard metal lung disease (HMLD) typically arises from cobalt or tungsten carbide exposure, histologically marked by giant cell interstitial pneumonia (GIP). We present a case series of HMLD investigated through several electron microscopy methods to highlight any involved elements.
Methods: All GIP diagnosed in our Centre over the past decade have been collected, supplemented with clinic-radiological data, and histologically reviewed. FFPE sections from lung tissue were analysed using Scanning Electron Microscopy and Energy Dispersive X-ray spectroscopy (SEM/EDX). In surgical samples asbestos fibers quantification was performed. Molecular analyses of viruses responsible for giant cell cytopathic injury were also performed.
Results: The case series encompasses five male patients aged 47 to 71, with occupational exposure history. Dyspnoea with dry cough was the predominant symptom. Two patients undergoing lung transplantation due to end-stage fibrosis. Histologically, chronic interstitial pneumonia with fibrosis and multinucleated giant cells were observed, especially in transplanted cases. SEM/EDX analysis revealed tungsten presence in three cases. No cobalt was detected. Conversely, several particles (such as molybdenum, chlorine, aluminium, antimuonium, magnesium, etc.), were identified in all samples in different concentration. Asbestos fibers were present, albeit below diagnostic thresholds. Recurrent GIP occurred in one patient post-transplantation, confirmed in subsequent biopsies. Viruses were not identified in all cases.
Conclusion: We present 5 GIP cases with clear occupational exposure history. Extensive ultrastructural analysis revealed hard metal in most of cases, but also diverse particles, and asbestos fibers. This underscores the need to identify elements in pneumoconiosis for comprehensive etiopathogenesis understanding, especially in obscured occupational exposures. Furthermore, the description of disease recurrence on the transplanted organ supports the hypothesis of an autoimmune etiopathogenic mechanism underlying GIP.

SC-17-008

What and where? The ultrastructure of the "dots" in Merkel cell carcinoma

P. Donizy*, M. Maksymowicz, A. Szumera-Cieckiewicz
*Department of Clinical and Experimental Pathology, Wroclaw Medical University, Wroclaw, Poland

Background & objectives: Merkel cell carcinoma is known to be diagnosed according to typical morphology and immunophenotype. Pathologists are trained that positive neuroendocrine signature together with cytokeratin 20 "dots" are specific for this rare skin malignancy.
Methods: We present four cases of MCC diagnosed in our institutions. Three cases showed typical microscopical and immunohistochemical MCC patterns with strong cytokeratin [CKAE1/AE3; CK20] dot-like, perinuclear expression; one MCC without that pattern was qualified as a control case. The ultrastructure of MCC was evaluated in electron microscopy [Philips CM120 BioTWIN] using the protocol for FFPE.
Results: We obtained two different ultrastructural images of "dots" visualized by cytokeratins: (1) two cases presented so-called fibrillar bodies composed of cytokeratin fibrils coiled into spherical structures; such bodies were single in cells, located near the cell nucleus; (2) one case showed nuclear pockets composed of a narrow band of nuclear material, including chromatin that encloses cytoplasmic material. The control case was devoid of the ultrastructural features described above but exhibited characteristic cytoplasmic inclusions corresponding to the MCPy virus.
Conclusion: According to the literature review, the MCC ultrastructure is not well described, and the role and biology of "dots" are not fully understood. The FFPE-based electron microscopy techniques enable better characterization of neuroendocrine tumours and can be an important complement to translational and omics research.

CP-01 The promise of computational pathology

CP-01-004

Pros and cons of digital pathology in nephropathology based on the experience of 220 cases

Fadime Gül Salman*, S. M. Ünlü
* Memorial Hospitals Group, Turkey

Background & objectives: Unfortunately, nephropathology is not a popular field among pathologists, so the number of pathologists experienced in this field is not high. Digital pathology may be very valuable to reach a pathologist experienced in nephropathology. We summarised our objective experience.
Methods: Standard 2-3 micron sections were prepared from a total of 220 kidney needle biopsies, native or allograft, after automated tissue tracking and paraffin embedding. All automatically stained sections were scanned with Leica Biosystems, Aperio GT450 Dx, Digital

Pathology Slide Scanner at x40 magnification, and viewed via Sectra interface using a high resolution monitor.
Results: PAS, PAMS, Masson's trichrome and Congo red sections were re-scanned in 8 cases, and HE sections were rescanned in 4 cases because they were mistakenly scanned at x20. In particular, endothelitis, glomerulitis, peritubular capillaritis and GBM thickness were difficult to evaluate in cases without x40. 70% of the cases were male. The majority (86%) of the cases were allograft, Histopathological evaluation of the biopsies showed segmental sclerosis in 120 cases, acute tubular damage in 96 cases, vascular hyalinosis in 46 cases, peritubular capillaritis (PTCs) in 29 cases, glomerulitis in 15 cases, endothelitis in 11 cases, vasculitis in 9 cases, TMA in 9 cases and crescent in 3 cases.
Conclusion: The main advantages: a) Access to an expert pathologist, ease of following a single glomerulus in serial sections and counting inflammatory lesions such as tubulitis/PTCs, b) Heatmap with very low risk of section overlook, c) Clear image over x40 magnification without the need for immersion.

The main disadvantages: a) Lack of birefringence for Congo red and crystals, b) Lack of fluorescence compatibility with some scanners, c) Laboratory quality must be very well in every aspect, otherwise our mobility would be limited in the digital assessment.

CP-01-005
The re-stAIn algorithm: development and validation of an artificial-intelligence-based tool for slides synthetic restaining
Alessandro Gambella*, N. Michielli, L. Salamone, A. Mogetta, L. Molinaro, M. Papotti, F. Molinari, M. Salvi
* Pathology Unit, Department of Medical Sciences, University of Turin, Italy; Division of Liver and Transplant Pathology, University of Pittsburgh, Pittsburgh, USA

Background & objectives: Pathology laboratories are required to provide multiple tissue sections for immunohistochemical stains, but this routine is burdened by long turnaround times and risk of tissue exhaustion. To solve these drawbacks, we developed an Artificial-Intelligence-Based tool for slide synthetic restaining (re-stAIn).
Methods: The re-stAIn algorithm combines (1) a multi-stage registration framework for precise stain tissue-tethered alignment, with (2) a deep learning-based generative model for synthetic immunohistochemical stain development. We used the re-stAIn algorithm to develop synthetic immunohistochemical images of phospho-histone H3 (PHH3) from hematoxylin-and-eosin slides. Qualitative (stain quality) and quantitative (mitotic counts) metrics of synthetic images were compared with real PHH3-stained slides.
Results: An expert pathologist blinded to the slides' subgroup (synthetic vs. real) evaluated both stain quality and mitotic count of synthetic and real PHH3 stains from lymph node and bladder tissue samples. Synthetic image quality was equivalent or superior to real images in 98% of cases. Moreover, we observed a strong positive correlation (Pearson's $r = 0.792$) between the mitotic count obtained from synthetic vs. real images. Ultimately, the re-stAIn algorithm demonstrated exceptional computational efficiency, requiring about 1.27 seconds to develop an 1800x1800 tile synthetic image on a dedicated workstation.
Conclusion: Our re-stAIn algorithm produces synthetic images with optimal qualitative and quantitative metrics compared to real PHH3 slides. Thanks to its computational efficiency, re-stAIn additionally allows for shortening the turnaround time for immunohistochemical stains and, contemporarily, preserving tissue samples. Pending further validation with different tissue types and additional immunohistochemical stains, the re-stAIn algorithm may pave the road for enhanced digital pathology workflows starting from a single hematoxylin-and-eosin slide.

CP-01-006
From AI development to clinical implementation: prospective deep learning-assisted lymph node screening for colorectal cancer patients
Abdul Latif Khan*, S. Reinhard, A. Perren, B. Dislich, I. Zlobec
* Institute of Tissue Medicine and Pathology, University of Bern, Switzerland

Background & objectives: To assist pathologists, we have developed MetAssist, a deep-learning-based model for detecting lymph node metastases in colorectal cancer (CRC). We have integrated it into our diagnostic routine workflow to conduct prospective clinical quality control and evaluate its accuracy and feasibility.
Methods: The integration uses a remote high-performance cluster (HPC) at the university with an automated workflow between the institute (digital slide scanner) and the HPC (storage and computing resources); results visualization via a simplified web interface. Resected specimens were digitized and analyzed by MetAssist. Meanwhile, the same glass slides were diagnosed by pathologists, who compared the findings and reviewed discrepant cases.
Results: A total of 35 CRC prospective resection specimens (comprising 427 slides with locoregional lymph nodes) were analyzed by MetAssist and independently diagnosed by 14 pathologists for result comparison. MetAssist's sensitivity and specificity, relative to pathologists, were 0.98 and 0.77, respectively. Discrepancies in negative cases were mainly attributed to tissue artifacts, particularly tissue folds and fragments of primary cancer misidentified as positive. However, the tissue within the lymph nodes was found to be negative in most false positives. Pathologists commented on each false positive result. The MetAssist indications prompted a review of the slides. As a result, the diagnostic sensitivity improved to 1.0.
Conclusion: MetAssist is an established quality control tool during the sign-out of CRC cases in our institute. It improves diagnostic accuracy and saves time when screening lymph nodes for CRC metastases. By providing comments to each individual slide (regarding slide quality, or the reason for false negative or false positive result), both the MetAssist model and the integration can be improved for future optimization.

CP-01-007
ODYN: an artificial intelligence-based pipeline for the prediction of malignant transformation in oral epithelial dysplasia
Adam Shephard*, H. Mahmood, S. Raza, A. Khurram, N. Rajpoot
* University of Warwick, United Kingdom

Background & objectives: Oral epithelial dysplasia (OED) is a potentially malignant histopathological diagnosis given to lesions of the oral cavity with an increased risk of malignancy transformation. OED grading encounters substantial rater variability with limited prognostic reliability, potentially leading to suboptimal treatment decisions.
Methods: We developed an artificial intelligence (AI) pipeline named ODYN (Oral DYsplasia Network), to classify OED and assign an ODYN-score for quantifying malignancy risk, using Haematoxylin and Eosin-stained whole slide images (WSIs). ODYN was trained on a large dataset (Sheffield, 358 OED WSIs, 105 control WSIs), and employs a shallow neural network to analyse patch-level nuclear features and determine slide-level ODYN-scores.
Results: The model was externally validated across three independent centres (Birmingham and Belfast, UK, and São Paulo, Brazil; 108 OED WSIs), and gained an F1-score of 0.71 for OED segmentation, and 0.96 for dysplastic vs non-dysplastic tissue classification. Our AI pipeline achieved an AUROC of 0.73 for malignancy prediction, surpassing other state-of-the-art methods. Survival analyses showed the prognostic utility of the ODYN-score (Hazard Ratio HR = 2.95, C-index = 0.63, $p = 0.003$), demonstrating comparable results to

clinical grading systems such as the WHO (HR = 2.43, C-index = 0.61, p = 0.025) and Binary grades (HR = 2.84, C-index = 0.62, p = 0.005).
Conclusion: We present a new AI-based model for both the classification of OED, and the prediction of malignant transformation, which we have made publicly available. Our study uses the largest multi-centric OED dataset, with international data, to date; whilst displaying promising results to aid in OED diagnosis and prognostication. By addressing challenges and refining the model, we envision ODYN playing an important role in improving the diagnosis and management of OED and potentially other precancerous lesions in the future.

CP-02 Recent developments and validation

CP-02-003
Molecular classification of endometrial cancer from H&E stained slide images using supervised deep learning: a proof of concept
Fabiana Inés Aguirre Neira*, V. E. Rodriguez, Á. A. Legoburu, A. R. Llanos, R. Carrera Salas, O. Jiménez Bolancé, J. C. Ferreres Piñas, I. Costa Trachsel
Universidad Autónoma de Barcelona, Spain

Background & objectives: Molecular classification of Endometrial Carcinoma (EC) includes POLEmut, mismatch-repair-deficient (MSI), high-copy number (HCN) and non-specific (NSMP) types, with management and prognostic implications. We present a proof of concept of a deep learning model predicting these groups from digitized slide images.
Methods: We performed a supervised training of a deep learning convolutional neural network (using the Teachable Machine platform) with H&E stained images from formalin-fixed paraffin-embedded ECs biopsies diagnosed at our hospital, previously classified into the four molecular groups by the surrogate WHO algorithm, with a balanced distribution (8 POLEmut, 10 MSI, 12 HCN, 12 NSMP).
Results: Using a data set of 21500 images (240 x 240 pixels, 20x magnification, in jpg format) from 42 digitized surgical specimens (approximately 5000 images per molecular class, divided in 85% learning images and 15% test images), we achieved an overall accuracy of 0.95. Accuracy per class was as follows: POLEmut 0.86, HCN 0.82, MSI 0.67, NSMP 0.85. Misclassifications were observed, including POLEmut as MSI (6%); HCN as POLEmut (9%); MSI as NSMP (15%) and NSMP as POLEmut (6%). The observed limitations were dependence on the selected and labeled data set, high-dimensional input, computational resources, deep learning self-interpretability, domain specificity and out-of-distribution error.
Conclusion: Our study suggests a potential usefulness and viability of deep learning models in the molecular classification of ECs, understanding training nuances and model limitations, as well as integrating histological data. Moreover, this approach could be exported into a in-house designed self-supervised deep-learning piperline for whole-slide-image-based prediction.

CP-02-004
Deep learning-aided molecular subtyping of pulmonary large cell neuroendocrine carcinoma in small hematoxylin and eosin-stained tissues
Teodora-Elena Trandafir*, F. Heijboer, F. Akram, J. Derks, Y. Li, E.-J. Speel, A. Stubbs, A.-M. Dingemans, J. von der Thüsen
* Department of Pathology and Clinical Bioinformatics, Erasmus University Medical Centre, Rotterdam, The Netherlands

Background & objectives: The molecular subtyping of pulmonary large cell neuroendocrine carcinoma (LCNEC) by retention or loss of retinoblastoma1 (RB1) has systemic treatment implications. Histomorphology alone cannot yet differentiate these subtypes in hematoxylin and eosin-stained (H&E) tissues. Alternatively, deep learning (DL) may help.
Methods: We developed a DL pipeline, using a custom-made convolutional neural network, to classify the binary expression of pRb in H&E-stained tissue samples of LCNEC, revised by multiple pathologists. Resections from 149 patients, sampled in maximally three tissue micro-array cores, and biopsies from 29 other patients, together with their immunohistochemically-evaluated pRb statuses, were used to train, validate and test our pipeline.
Results: The pipeline was trained and validated using stratified three-fold cross-validation on a balanced set of 100 resections, with subsequent testing on remaining data. In the best fold, validation results showed a tile-wise balanced accuracy (BA) of 0.73 and area under the receiver operating characteristic curve (ROC-AUC) of 0.77, and a patient-wise BA of 0.76 and ROC-AUC of 0.80. Testing, including biopsies, revealed a tile-wise BA of 0.67 and ROC-AUC of 0.74, and a patient-wise BA of 0.70 and ROC-AUC of 0.75. Using explainable artificial intelligence, qualitative evaluations identified coarse chromatin patterns and nucleoli presence as potential distinguishing features for positive pRb status, and limited cytoplasm for negative pRb status.
Conclusion: Our results indicate the existence of cytomorphological features associated with the molecular subtypes of LCNEC. This analysis, which uses small histopathology samples, may ultimately guide the choice of chemotherapy in the metastatic setting, as pRb expression is predictive of response to chemotherapy favouring a non-small cell lung cancer (NSCLC) treatment regime.

CP-02-005
Anti-tumour activity of eosinophils and intraepithelial lymphocytes in colorectal cancer: a two-pronged approach
Elias Baumann*, P. Krebs, A. Perren, R. Kirsch, M. D. Berger, I. Nagtegaal, I. Zlobec
*Institute of Tissue Medicine and Pathology, University of Bern, Switzerland

Background & objectives: The immune infiltrate composition strongly affects colorectal cancer (CRC) prognosis, with lymphocytes representing a positive prognostic factor. Using deep learning, we explore the immune composition beyond lymphocytes, investigate their possible interactions, correlation with clinical variables, and transcriptomic differences.
Methods: Using haematoxylin and eosin (H&E)-stained CRC cohorts scanned at 0.24mpp from Switzerland, Netherlands, Canada and TCGA (combined n=1654, stage I-IV), we apply in-house developed deep learning models for nuclei and tissue-type segmentation to quantify eosinophils, lymphocytes, neutrophils, and plasma cells in various regions (front, centre and intraepithelial) within 200μm of tumour cells. Transcriptomic analysis utilizes TCGA bulk RNA-Seq data.
Results: Eosinophils in the tumour front (Eos-F) (Time to recurrence (TTR): HR=0.72, p=0.007) and intraepithelial lymphocytes (IELs) (TTR: HR=0.59, p=0.047) are independent prognostic factors individually, and in a combined model (TTR: HR=0.72, p=0.007, HR=0.60, p=0.05). Eos-F remain prognostic in mismatch repair deficient (dMMR) cases (p=0.004). Eos-F do not correlate with IELs (Spearman: 0.09, p<0.001) but with lymphocytes (Spearman: 0.72, p<0.001). Both decrease with stage (p<0.001). IELs correlate with dMMR (p<0.001) and inversely with tumour budding (p<0.001). Differential expression analysis shows upregulation of mast cell activation genes with high Eos-F and interferon-gamma driven cytotoxic immune response with high IELs. IEL-low but lymphocyte-high cases show extracellular matrix modulation and basement membrane pathway upregulation.

Conclusion: We provide evidence for the prognostic value of eosinophils and for a potential mast cell interaction. IELs are ubiquitous in dMMR cases but are prognostic across cases and a combined presence with eosinophils further improves prognosis. Conversely, extracellular matrix driven IEL exclusion may be a reason for a worse prognosis. The two potentially distinct anti-tumour immune response programmes are prognostic markers translatable to routine diagnostics with automatic quantification via open-source deep learning models directly on H&E images.

CP-02-006

Deep learning predicts the effect of neo-adjuvant chemotherapy for patients with triple negative breast cancer

Bart Sturm*, P. Lock, D. Kumar, J. Westerga, W. Blokx, J. van der Laak
* Pathan B.V., The Netherlands

Background & objectives: A subset of triple negative breast cancer patients responds well to NAC. This study aims to predict the outcome of NAC with deep learning technology based on whole slide images of H&E slides from the tumour biopsy prior to therapy.
Methods: A convolutional neural network was trained on 221 H&E biopsies of carcinoma of no special type. Cases were divided in three cohorts, with a good, moderate or bad response to NAC (<10%, 10-50% and >50% residual tumour respectively) based on the EUSOMA scoring. Manual segmentation of the tumour area was performed. The model was tested on 52 new biopsies.
Results: Due to the relative low number of moderate and bad responder cases, and in order to achieve a better discrimination for potential visual biomarkers, the moderate and bad response cohorts were merged. The predictive performance of the model was calculated by means of the area under the receiver operator curve (AUC ROC). 95% Confidence intervals (CI) were calculated for better understanding of the range of values. In the test set the AUC ROC performance score was 0.696 with a CI of 0.532 – 0.861.
Conclusion: This proof-of-concept study shows that H&E pre-operative biopsies from triple negative breast cancer, by means of deep learning technology, contain valuable information having predictive value for the outcome of NAC resulting in an AUC value of 0.696 outperforming a predictive AUC value of 0.63 based on structured clinical data of histological tumour grade, TILs and ki-67 known from the literature.

Poster Sessions

PS-01 Poster Session Autopsy Pathology

PS-01-001

Anatomical spectrum of VACTERLS association: a multi-case pathological analysis

M.A. Abad Vintimilla*, S. Quinones, P.I. Voinescu, R.M. Regojo
*La Paz University Hospital, Spain

Background & objectives: The VACTERL association involves a diverse range of anatomical abnormalities as vertebral abnormalities, anal atresia, heart defects, tracheoesophageal fistula, kidney, limb abnormalities and single umbilical artery, with significant variability among affected individuals. Our aim is to analyse these anatomical defects.
Methods: We reviewed our autopsy records from 1967 to 2023 and found 20 cases of VACTERLS association. All of them had complete autopsy with postmortem radiographs and placental examination (according to the Amsterdam Consensus classification). Our results were compared with previously published studies.
Results: We observed a huge range of anatomical abnormalities, notably, vertebral anomalies were prevalent in 75% of cases, followed by 70% kidney alterations, 55% with cardiac malformations and same percentage for limb defects. Oesophageal defects were identified in 45% including atresia and stenosis. Additionally, tracheoesophageal fistula was observed in 35%. Anal defects and single umbilical artery were found in 25% each of them.
Remarkably a notable majority (75%) exhibited central nervous system alterations. Gender specific difference was found, with 44% of XY presenting cryptorchidism and 45% of XX showing alterations in internal genitalia. Genetic analysis using array and PCR techniques showed normal results in all cases.
Conclusion: VACTERLS association is sporadic, and several organs are affected. Owing to its broad range of alterations and absence of distinct genetic anomaly, it is identified as a diagnosis of exclusion, which also leads to an extensive array of differential diagnoses. This revision enhances our understanding of this syndrome, in terms of the complexity and diversity. This study affords the opportunity to explore the frequency of these anatomical defects. Multidisciplinary approach is indispensable for diagnosis and treatment, rehabilitation and surgical correction.

PS-01-002

Attitude towards autopsy in Oman

S. Al Harthi*, J. Al Habsi
*OMSB, Oman

Background & objectives: The aim of this study is to identify the willingness of the Omani population to provide consent to perform an autopsy and the barriers to obtaining consent. This can help guide future policies regarding medical autopsies.
Methods: This is a survey-based, cross-sectional study. The sample group consists of randomly selected members of the general public over the age of 15. The data will be collected from a diverse demographic background to understand the public's attitude and perception towards post-mortem examination. The estimated minimum sample size required for 95% confidence interval with 5% margin of error is 385.
Results: Out of 839 survey responses, 425 (50.6%) believe post-mortem examinations are necessary, while 301 (35.8%) expressed uncertainty. 173 (20.6%) stated that they would refuse to consent to an autopsy being performed on a relative, with 75 (8.9%) maintaining this stance even if the cause of death is unclear. The majority (71.7%) expressed support for performing medical autopsies if they can provide valuable information to prevent future sudden deaths in the family, and even more so (83%) in cases of suspicious deaths. The majority who oppose postmortem examinations are reluctant due to religious beliefs, concerns about disrespecting the dead, or doubts regarding the usefulness of autopsies.
Conclusion: The aim of this study is to explore the perception and attitude of our population towards postmortem examinations in general, and medical autopsies specifically. This is to gain insight into the barriers to providing consent to an autopsy to help guide future policies. While the majority believe it's unnecessary or are uncertain, most of them responded more positively when provided with a specific purpose for the autopsy. Religious beliefs are the most commonly cited reason for opposing postmortem examinations.

PS-01-003

Exploring tumour evolution in advanced colorectal cancer: comprehensive genomic profiling integrating tissue and liquid biopsy insights in a research autopsy case

L. Siebenhüter, R. Ihringer, E. Sipos, S. Eser, A. Probst, T. Kröncke, B. Märkl, S. Dintner*
*Pathology, Medical Faculty Augsburg, University Augsburg, Germany

Background & objectives: CRC's tumour heterogeneity challenges personalized medicine. Tissue sampling often misses advanced

tumours' complexity. Liquid biopsy (LBx) shows promise in monitoring heterogeneity. Postmortem autopsies complement insights, aiding understanding of intertumoural heterogeneity and guiding therapeutic strategies.
Methods: To analyze autopsy tissue specimens comprehensively, DNA was extracted and a whole exome library was generated using HyperExomeV2 (Roche), sequenced on a NextSeq2000. Simultaneously, ccfDNA from blood plasma was isolated and enriched with the AVENIO ctDNA Surveillance Kit V2 (Roche), then sequenced on a NextSeq550Dx. Genetic data from primary tumours, progression samples, and metastatic lesions were integrated for comprehensive analysis.
Results: Examining an advanced CRC case's response to chemotherapy and anti-EGFR therapy, molecular analysis covered various DNA alterations. Postmortem samples from 8 tumour sites and 16 LBx specimens were analysed longitudinally. Results highlighted therapy's impact, notably in mutation signatures and clonal expansion. Initially described as RAS/BRAF wild-type, autopsy samples showed classic CRC changes like TP53 and APC mutations. Samples exhibited TMBlow, HRDlow, and MSS status. Progression revealed distinct differences in oesophageal metastases, particularly reflecting in mutation signatures. The longitudinal analysis correlated with treatment response and progression behavior, with TP53, APC, FBXL7 indicating clonal expansion and subsequent changes in RAS/BRAF.
Conclusion: In conclusion, tumour heterogeneity significantly influences colorectal cancer (CRC) prognosis, impacting treatment resistance and overall survival. Understanding and managing this heterogeneity are crucial for personalized medicine advancement. The autopsy and LBx analysis in this report offer insights for collective understanding of tumour evolution under therapy, guiding future research and therapeutic innovations tailored to CRC dynamics.

PS-01-004
Spleen inflammatory response to lethal respiratory viral infection - a comparison between AH1N1 and COVID-19
G.A. Dumbravă*, S. Zurac, A. Vilaia, C. Dumitru, C. Popp
*Colentina University Hospital, Department of Pathology, Romania

Background & objectives: Lymphocyte apoptosis, cytokine-mediated immune pathogenesis and microvascular dysfunction are mechanisms involved in spleen impairment described as complication in lethal viral infections.
Methods: The autopsy reports of our department have been reviewed, and 15 cases of lethal AH1N1, respectively 5 cases of COVID-19 have been selected. We compared the protein expression status of ADAM17, ACE2, caspase 1 and caspase 9 by immunohistochemistry in postmortem spleen samples of patients who died of severe infection.
Results: The histopathological assessment revealed white pulp atrophy, and reduction or absence of lymphoid follicles; in one case of AH1N1 spleen infarction is present. Of the 15 samples from patients with AH1N1 infection, 46.66% express ADAM17 and in 13.33% of cases, sinusoidal endothelium shows weak positivity for ACE2. The ADAM17-ACE2 regulation is better highlighted in COVID-19 infection, where 80% (4 of 5 cases) express both markers. While all cases with severe lymphocytic depletion of COVID-19 show strong immunoexpression for caspase 1 and caspase 9, only 26.64%, respectively 33.33% of AH1N1 samples are positive for these markers, including the one with large spleen infarction.
Conclusion: Our results demonstrate a correlation between inflammation, apoptosis and spleen injury in lethal cases of AH1N1 and COVID-19, these pathological pathways being underlined by positive immunoexpression of studied markers. Despite of the limited size of the cohort, the association is much stronger in COVID-19 cases and these results are the base for further studies exploring spleen involvement in severe respiratory viral infection.

PS-01-005
Skeletal dysplasia: ultrasound, macroscopic, radiological, and genetic findings
K. Gonçalves Villarreal*, E. Oliva Domínguez, I. García Miranda, I. Orbegozo Arizabalaga, M.L. Ramírez Feliz, J.I. Iparraguire Santiago, A. del Campo Real, I. Llano Rivas, L. Zaldumbide Dueñas, L. Mosteiro González
*Hospital Universitario Cruces. Basque Country. Spain

Background & objectives: Skeletal dysplasias affect bone and cartilage development, with some types being fatal. Ultrasound is vital in prenatal screening, as it measures specific parameters to determine if the suspected condition is likely lethal. Confirmation often requires autopsy and genetic testing.
Methods: Retrospective, descriptive study, including (n=7) cases with prenatal ultrasound suspicion of skeletal dysplasia in which autopsy, radiography and genetic study were performed. The data were obtained from clinical records at the Pathological Anatomy Service of Cruces University Hospital between 2012 and 2024.
Results: In all instances, there was macroscopic alignment with the observations made during ultrasound examinations, confirming the presence of skeletal dysplasia. The genetic analysis guided by the multidisciplinary approach, incorporated pathological and radiological assessments and could confirm all seven cases initially suspected of harboring severe anomalies with poor prognosis. Within our cohort, three cases of (n=3) thanatophoric dysplasia, and singular cases of chondrodysplasia (n=1), collagenopathy (n=1) (specifically, hypochondrogenesis or acondrogenesis type II), Ellis-van Creveld syndrome (n=1), osteogenesis imperfecta (n=1) were identified. Four cases manifested de novo mutations, while one involved healthy heterozygous carrier parents.
Conclusion: The profound impact of foetal demise on parents cannot be overstated. Autopsy serves as a cornerstone for corroborating ultrasound anomalies and directing genetic diagnosis, ensuring meticulous management, particularly in scenarios considering termination of pregnancy and could also help parents through their grief journey. A multifaceted approach is imperative for the diagnosis of these conditions. Drawing from our experience and recommendation, the establishment of foetal medicine committees stands as an indispensable resource, fostering invaluable insights for addressing these complex pathologies.

PS-01-006
Causes of death among patients who died within 24 hours of hospital admission: an autopsy study
R. Jankovic*, M. Jovanović, J. Jevtić, M. Đuknić, D. Gujaničić, S. Glumac
*University of Belgrade, Faculty of Medicine, Institute of Pathology, Serbia

Background & objectives: Autopsies are crucial for evaluating healthcare quality and important for enhancing patient care. This study aims to analyze causes of death in autopsies of patients who died within 24 hours of hospitalization, correlating clinical data with fatal outcomes.
Methods: Autopsy reports and protocols, as well as clinical data from discharge summaries and autopsy referrals of patients autopsied over a five-year period (2018-2023) at the Institute of Pathology, Faculty of Medicine, University of Belgrade, were analysed. Goldman's criteria were applied to assess the correlation between clinical and autopsy diagnoses.
Results: Slightly more than half of the patients were male (76/133; 57%). Women were statistically significantly older than men (p=0.009). The most common clinical diagnosis of autopsied patients was cardiovascular disease (25.5%). The majority of patients experienced initial

symptoms up to 24 h before seeking medical attention (54.1%). Most patients were being treated for chronic diseases (90.7%). The immediate cause of death in autopsies was most often associated with cardiac insufficiency (73/133, 54.9%). The most common clinically unrecognized causes of death were: bronchopneumonia (16), followed by intestinal infarction (6) and acute ischemic lesion/myocardial infarction (5).

Conclusion: The correlation between clinical findings and pathology is highly significant, as it helps uncover treatment mistakes, thereby aiding in the acquisition of valuable insights essential for the advancement of medical science. The identification of clinically unrecognized causes of death, such as bronchopneumonia, intestinal infarction, and acute ischemic lesions/myocardial infarction, underscores the importance of autopsy examinations in revealing hidden or overlooked conditions. These findings highlight the limitations of clinical diagnosis and the potential consequences of missed or misdiagnosed ailments.

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PS-01-007

Non-traumatic haemorrhages in the brain and its membranes in infants

B. Magrupov*, V. Kochetov
*Center for Professional Development of Medical Workers, Republican Research Center of Emergency Medicine, Uzbekistan

Background & objectives: Non-traumatic intracranial hemorrhage (NICH) belongs to the category of severe cerebrovascular accidents due to morphological immaturity of the walls, vascular malformations, aneurysms, vasculitis, disorders of the blood coagulation system, as well as various diseases accompanied by hypoxia and intoxication.
Methods: During the period from 2012 to 2023, the results of autopsies of 494 children who were treated in the children's building of the Republican Research Center for Emergency Medicine were studied. Macroscopic and microscopic research methods and statistical analysis of the data obtained were used.
Results: Haemorrhages were detected in 86 (17.4%) autopsies (46 -53.5% in boys and 40 (46.5%) girls), with a maximum at the age of 1.5 months - 32 (37%), 2 months - 19 (22%) and 1 year – 18 (21%). Isolated intracerebral haemorrhages occurred in 9 (10.5%) cases. meningeal with intracerebral - in 20 (23.3%), with intraventricular - 8 (9.3%), subarachnoid and subdural - 14 (16.3%), intracerebral, intraventricular and meningeal - 6 (6.9%). In 41 (47.7%) cases, haemorrhages occurred due to pneumonia (in 23 - with congenital immunodeficiency syndrome), in 10 (11.6%) - due to rupture of arteriovenous malformations. The immediate cause of death was encephalomalacia (37-43%) and brainstem dislocation.
Conclusion: The analysis showed that intracerebral haemorrhages were 1.15 times more common in boys than in girls. Among isolated haemorrhages, subdural haemorrhages were most common, and subarachnoid hemorrhages were somewhat less common. In case of combined haemorrhages, simultaneous intracerebral and meningeal haemorrhages prevailed, and subdural and subarachnoid haemorrhages were less common. Of the causes causing the development of intracranial haemorrhages, diseases of the respiratory system - pneumonia - were in first place, and arteriovenous malformations were in second place.

PS-01-008

Autopsies performed in the period 2020-2022 in a secondary care hospital: impact of the pandemic over clinical-pathological discordances

Y. Rey Fanjul*, A. Licetti Bermúdez, E. Mateo Álvarez, C.J. Grau Polo, D. Rodriguez Villar, P. Gonzalvo Rodríguez, J. Cuevas Fernández, E. Asensi Miranda, R. Rodríguez Aguilar
*Sespa, Spain

Background & objectives: The pandemic represented an impact at all levels of assistance, including the number of autopsies performed and associated clinical-pathological discordance. We reviewed necropsies to determine the variation on global discordance degree and highlight their importance in clinical assistance's improvement.
Methods: We applied the modified Goldman classification to evaluate clinical-pathological concordance, divided into five categories based on the degree of discrepancy, with classes I and II considered major discrepancies, classes III and IV minor discrepancies and class V equaling to absence of discrepancy. We reviewed a total of 45 adult autopsies performed through 2020-2022 in a second level hospital.
Results: Out of all 45 autopsies, 25 were requested by clinical services, 10 for Intensive Care Unit, 6 for surgical services and 4 for Emergency Service. Most frequent clinical suspicion was infectious process (16 cases, mainly septic shock), vascular (11), oncologic disease (8), respiratory (5), hemorrhage (3) and abdominal pathology (2). The autopsy's most frequent diagnosis was infectious (18), hemorrhage (7), oncologic disease (6), respiratory (5), vascular (5) and abdominal pathology (4). Applying Goldman's classification, we identified 5 major discrepancies of type I and 6 of type II; 3 minor discrepancies of type III and 6 of type IV, and 25 cases showed no discrepancy (type V). Major discordance reached 24.4%.
Conclusion: We identified a 24.4% of major discrepancies within our sample, higher than the 18.3% described in similar series. The number or autopsies requested fell through the SARS-CoV2 pandemic and restricted the requests to cases with the highest rate of diagnostic doubts, therefore leading to increase the overall clinical-pathological discrepancy degree. The clinical autopsy is another tool to improve the quality of care and routine practice, and the analysis of these discrepancies allows to identify areas for improvement and prevention.

PS-01-009

Postmortem ultrasound cerebellar measurements in the evaluation of gestational age. Innovative use of postmortem ultrasound cerebellar measurements for estimating gestational age in perinatal deaths: an observational cross-sectional study

L.A. Rojo Muchacho*, N. Peñuelas, L. Marimon, N. Carreras, G. Arca, J. Ordi, N. Rakislova
*Hospital Clinic, Spain

Background & objectives: Perinatal mortality rates in low-middle income countries continues highly-rated nowdays. Identifying accurate foetal gestational age assessments in prematurity and intrauterine growth restriction persist critical in perinatal mortality. While transcerebellar diameter/cerebellar vermis (TCD) ultrasound methods show potential, postmortem evaluation remains lacking.
Methods: We studied 137 perinatal deaths, including 132 stillbirths (104 legal pregnancy interruptions, 28 natural deaths), and 5 neonates, alongside ultrasound controls. Gestational ages spanned 15.2 to 40.6 weeks. Extrauterine postmortem ultrasound measured TCD, cerebellar vermis height, and length. Spearman correlation compared these measurements with intrauterine and autopsy data. Linear regression assessed cerebellar measurements, growth restriction and CNS abnormalities usefulness.
Results: Strong correlations were observed between extrauterine TCD, intrauterine TCD, and autopsy TCD. Linear regression analysis showed a strong association between all extrauterine cerebellar measurements and gestational age ($p<0.001$), with TCD (GA= 9.75+0.49[TCD], R2=0.88) and cerebellar vermis height (GA= 10.52+0.97[VermisHeight], R2=0.87) exhibiting the strongest predictive power,

compared to cerebellar vermis length (GA= 13.12+1.62[VermisLength], R2=0.63). Multivariate analysis revealed an interaction between trimester of gestation with vermis measurements and an effect of intrauterine growth restriction on vermis height, while no interaction was found between covariates and TCD measurements.
Conclusion: This study provides initial evidence demonstrating feasibility and validity in gestational age stimation through postmortem extrauterine ultrasound measurements of the cerebellum, especially TCD. Adoption of these methods could enhance postmortem foetal dating data accuracy, especially in resource-constrained settings, where complete autopsies are difficult to perform, thereby improving pathology-based mortality surveillance. Further research is required to validate these findings and assess their broader applicability.

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PS-01-010
Clinical and morphological aspects of SARS-CoV-2 induced endotheliopathy in "gas" and haemorrhagic complications
V. Zinserling*, N. Semenova, D. Gusev, K. Medvedev, N. Kokhanenko, K. Borta
*VA Almazov Research Center, Saint-Petersburg, Russia

Background & objectives: Among the aspects of the pathogenesis of a new coronavirus infection, endothelial damage plays an essential role. And as a result, vascular disorders can lead to the development of air leakage syndrome and/or haemorrhagic events.
Methods: Clinical and morphological comparisons in 34 deceased patients with a new coronavirus infection complicated by bleeding (3) and pneumothorax (31).Standard clinical and morphological comparisons were carried out: an immunohistochemical study of the state of the endothelial lining of vessels of different calibers was carried out using CD31, CD34, von Willibrand factor, as well as SD68 and Mallory staining.
Results: In all observations, a characteristic morphological picture of viral pneumonia typical of a new coronavirus infection was revealed. In particular, alterative changes on the part of the endothelium were naturally determined, which in many vessels exfoliated with the formation of endothelial thrombi (vWF+). Activation of CD34+ cells was observed perivascularly, probably related to the proliferation of myocyte progenitor cells. Perivascular and interstitial fibrosis with an abundance of CD68+ cells was noted in all observations. mbi in the lumen of small vessels of the lungs, which in turn was a predictor of destruction of the pulmonary parenchyma with the development of air leakage syndrome
Conclusion: 1) In the case of the development of "gas" complications of COVID-19, an immunohistochemical study observed multiple endothelial thrombi in the lumen of small vessels of the lungs, which in turn was a predictor of destruction of the pulmonary parenchyma with the development of air leak syndrome. 2) In haemorrhagic events, desquamation of the endothelium was detected, followed by a violation of the integrity of the vascular wall and the development of bleeding.

PS-02 Poster Session Breast Pathology

PS-02-001
Multidisciplinary approach in stratifying risk of upgrade and tailoring management in ADH patients
C. Albarracin*, I. Bedrosian, H. Chen, Y. Wu
*UT MD Anderson Cancer C, USA

Background & objectives: At our institution, a multidisciplinary approach with correlation of histologic and radiographic findings stratified ADH patients with low (<3%) and high risk of upgrade to carcinoma. Surgical excision is recommended only for patients deemed high risk based on these variables.
Methods: A prospectively maintained registry of 1097 ADH patients presented at CMC from 2004 to 2022 was reviewed to identify patients with ADH on CNB who met histopathologic (>2 TDLUs; significant cytologic atypia and necrosis) and/or radiologic criteria (<50% sampling of the lesion) and underwent surgical excision. We reviewed clinical, mammographic and histologic features to identify factors associated with upgrade.
Results: Three hundred and forty-five patients met criteria for the study. The cases included 134 with extensive ADH (>2 TDLUs) and 211 with focal ADH (2 or < TDLUs). The overall upgrade rate to carcinoma on excision was 26.37% (91/345). The extent of ADH did not affect the upgrade rate (42.85% extensive vs 57.1% focal). Mammographic extent of lesion removed/sampled was available in 278 with 35.8% upgrade with <50% removed, 19.1% with >50% removed and 15.4% with >90% removed. The extent of lesion removed (>90%) significantly correlated with the rate of upgrade to carcinoma. Age, biopsy type, type of radiographic abnormality did not affect upgrade rate.
Conclusion: In this cohort of patients diagnosed with ADH by CNB who met criteria for surgical excision based on our institution's histologic and radiographic thresholds, the extent of sampling, as measured by the proportion of mammographic lesion removed by CNB, was a better predictor of risk of upgrade than the histologic variables.

PS-02-002
Her2-low breast cancer: prevalence rate and scoring concordance among pathologists
G. Al-Jussani*, A. Salem, Y. Mullahuwash, F. Alsamarat, D. Abuquteish, M. A. Sughayer
*Hashemite University, Jordan

Background & objectives: Recently, Human Epidermal Growth Factor Receptor-2 (HER2) negative breast cancer patients (score 1+ or 2+ non-amplified) were shown to benefit from anti-HER2 –drug conjugates therapy. We aimed to assess the prevalence rate and concordance of reporting HER2-low expression among pathologists.
Methods: 116 cases with HER2 IHC stains were randomly selected from King Hussein Cancer Center (KHCC). HER2 was scored by 3 pathologists according to CAP-ASCO guidelines. The prevalence rate of HER2-low group (score 1+ and ISH-negative 2+) was calculated along with the overall agreement level using Fleiss' multiple-rater kappa statistics and Cohen's Kappa.
Results: Absolute agreement (3/3) occurred in 80 cases (69.0%), high agreement (2/3) occurred in 36 cases (31.0%) while no agreement (0/3) was not observed. Score 0 was observed in 11/116 (9.5%), HER2-Low in 79 cases (69%) and HER2 positive in (20/116) cases. The highest level of agreement (69 %) was achieved when cases were divided into 4 categories (0, 1+, 2+, 3+). Kappa for overall score, 0, 1+, 2+ and 3+ were 0.656, 0.575, 0.603 and 0.915 respectively (all p-values <0.000). The kappa of overall agreement and individual agreement was improved for combined categories (0.748). Cohen`s weighted kappa for pairwise agreement among pathologists: ranged from 0.649-0.865 (substantial to almost perfect agreement)
Conclusion: This is the first study in Jordan on the concordance of HER2 scoring of breast cancer. Most cases (69%) were concordantly classified by all 3 pathologists while 31% were concordant by 2 of 3 pathologists. Substantial but not perfect agreement among pathologists in assessing HER2 is observed. HER2-low accounted for a significant majority (69%) of cases examined in our study, highlighting the potential benefit for a large portion of breast cancer patients in Jordan from emerging anti-HER2 therapies.

PS-02-003
PD-L1 expression and presence of ICs in HER2-positive breast carcinoma before and after neoadjuvant treatment
M. Bogosavljevic*, T. Ivkovic Kapic, T. Vasiljevic, N. Stanulovic
*Oncology Institute of Vojvodina, Serbia

Background & objectives: HER2-positive breast carcinoma (BC) expresses PD-L1 and presents a potential target for immunotherapy. We examined the association of neoadjuvant anti-HER2 treatment (NAT), tumour-infiltrating immune cell (IC) count and PD-L1 levels with pathologic complete response (pCR) in HER2-positive BC.
Methods: Data collected from the database of Oncology Institute of Vojvodina, from 58 patients who received NAT and undergone surgery, were retrospectively analysed. ICs were scored in three categories (low, intermediate, high). PD-L1 (SP142) was classified as positive (≥1% ICs stained) or negative (<1%). Complete pathological regression (pCR) was defined as absence of invasive carcinoma in breast samples and lymph nodes.
Results: Low IC count was present in 55.2% BC, intermediate in 34.5% and high count in 10.3%. PD-L1 expression was found in 43.1% of BC pre-NAT samples. PD-L1 positivity was in correlation with high IC count (p=0.003). PD-L1 expression and IC score were not associated with pCR (p=0.456; p=0.521). PD-L1 positivity and high IC count showed a correlation with high histological tumour grade (p=0.006; p=0.007). Lymphovascular invasion was in positive correlation with PD-L1 expression (p=0.048). Clinically positive axillary lymph nodes were detected in 64% of PD-L1 positive patients, with positive correlation (p=0.037).
Conclusion: We conclude that certain parameters of poor prognosis such as high histologic grade of the tumour, presence of lymphovascular invasion, clinically positive axillary lymph nodes and high IC count correlate with PD-L1 expression in HER2-positive BC, but we did not find the potential of PD-L1 to predict response to anti-HER2 neoadjuvant treatment.

PS-02-004
Tumour-stroma ratio in breast carcinoma is an easily applicable feature and it is associated with prognosis
A.T. Bol*, J. Noury Rad Davaji, B. Dursun, S. Dizbay Sak
*Ankara University, Medical School, Pathology Department, Turkey

Background & objectives: Tumour-stroma interactions play a crucial role in the development and progression of cancers. Here, we aimed to evaluate the effect of the tumour-stroma ratio (TSR) in breast carcinoma and to compare eyeballing and semi-automated quantification in the estimation of TSR.
Methods: An H&E stained slide representing the highest TSR was selected from 226 invasive carcinoma, NST cases diagnosed between 2009-2018, with a 5-year follow-up. After digitizing, TSRs were evaluated on the whole slide image (WSI), as well as in 3 and 30 mm² areas by eyeballing. In addition, for comparison, semi-automatic QuPath Pixel Classifier was used for 70 cases.
Results: The mean age was 53 years; 9.7%, 46.5%, 43.8% of the tumours were grade 1, 2 and 3 respectively. 86.2% was ER; 19% was HER2 positive. During the follow-up, 39 patients died of disease. The correlation between eyeballing and QuPath was good (ICC=0.86, 0.85, 0.80 for 3, 30 mm2, WSI respectively). Thresholds of 60% and 70% were determined based on mean-median statistics for WSI and 30 mm2. There was a significant correlation between tumour size and TSR (r=0.45, p=0.03) in grade 1 tumours. In terms of overall survival (OS), TSR-30 mm2 revealed a significant difference in whole group (Kaplan-Meier, p=0.02-HR=2.09); OS time decreased as TSR increased in grade 2 tumours (r=-0.23, p=0.02).
Conclusion: The findings indicate that TSR holds significant importance in determining the survival outcomes of breast cancer patients. TSR is a histopathological feature that can be easily evaluated in H&E sections without the need for additional staining. The TSR values obtained through eyeballing show good correlation with QuPath, which provides a more objective evaluation. Including this parameter in pathology reports can contribute to treatment decisions in some breast carcinoma cases.

PS-02-005
Understanding metastatic breast cancer: a 10-year retrospective study
A. Chelu, R.A. Barna*, B. Nataras, M. Iacob, D. Anderco, C. Suciu, C. Lazureanu, A. Muresan, M. Cornianu, S. Taban, A. Dema
*Victor Babes University of Medicine and Pharmacy, Romania

Background & objectives: Breast cancer (BC), prevalent both globally and in Romania, remains a significant health concern. Despite advances in diagnosis and treatment options, metastasis remains the leading cause of death. This study investigates the clinico-pathological characteristics of BC patients with distant metastasis.
Methods: This retrospective observational study analysed histopathological reports of patients with primary BC (PBC) and distant metastases at Timisoara County Hospital between January 2013 and December 2023. Among the examined data were histological subtype, age at primary tumour diagnosis, time to metastasis, metastatic location, whether metastasis was synchronous or metachronous, and the molecular subtypes when accessible.
Results: In 10-year period were identified 11 patients with PBC and distant metastases. Average age at diagnosis was 62 years. Eight cases were invasive carcinoma NST, two invasive lobular carcinoma (IBC), and one undifferentiated carcinoma. The molecular subtypes included one Luminal A, six Luminal B HER2-, one Luminal B HER2+, and one triple-negative. Six cases had 100% correlation between molecular subtype of PBC and metastases. Four cases were synchronous metastases and seven were metachronous. Three cases had metachronous contralateral breast metastases. Another patient had two PBC, one Luminal B HER2- and the other TNBC, with bone metastasis showing Luminal B HER2-. Additionally, two IBC cases had both gastrointestinal and peritoneal metastases.
Conclusion: In conclusion, BC metastases can arise irrespective of age, with Luminal B HER2- cases predominating in this study. Molecular subtypes often remain consistent between PBC and metastases. Metachronous cases predominate, suggesting the need for better identification of high-risk patients and improved treatment options. For instance, Luminal B HER2- BC with recurrences may have a higher risk of metastasis. Moreover, this study reaffirms the occurrence of gastrointestinal metastases in lobular carcinoma, stressing the necessity for better understanding of the underlying mechanisms.

PS-02-006
The significance of the androgen receptor in triple-negative breast cancer: to be or not to be
M.B. Chifu*, I. CARUNTU, S.E. Giuşcă, B. Gafton, C. Terinte, A.D. Timofte, C. Amalinei, I. Prutianu
*"Grigore T. Popa" University of Medicine and Pharmacy, Iasi, Romania

Background & objectives: Triple-negative breast cancer (TNBC) associates positive or negative immunoexpression for androgen receptor (AR), with contradictory prognostic value. We aimed to analyze AR variability across TNBC and its relationships with tumour traits, extending the knowledge on its involvement in breast carcinogenesis.
Methods: The study group encompassed 124 TNBC cases for which clinico-pathological characteristics were extracted from medical sheets. Immunohistochemistry was performed to assess AR immunoexpression. Relationships between AR (positive versus negative) and histological type, tumour grade, stage, residual cancer burden (RCB), tumour infiltrating lymphocytes (TILs), lymphovascular and perineural invasion, Ki-67, treatment, progression-free survival (PFS) and overall survival (OS), respectively, were statistically analysed.
Results: The median age at diagnosis was 61 years. The predominant histologic type was invasive ductal carcinoma, not otherwise specified (NOS), comprising 87.9% of cases. AR immunoexpression was positive in 63% of cases and negative in 37%. No statistically

significant differences were found between AR immunoexpression and all clinico-patological characteristics. Univariate analysis indicated associations between DSF and TILs, tumour stage, and first-line treatment, respectively. Poor OS was statistically significant correlated with histological type, tumour stage, RCB, lymphovascular and perineural invasion, metastatic lesions and first-line treatment, respectively. No significant difference in survival parameters in relation to AR status was found, suggesting no association between AR immunoexpression and the biological course of disease.
Conclusion: Although AR expression was positive in a significant proportion of cases, it did not show a significant association with none of the classical clinico-pathological characteristics, including treatment and survival parameters. Thus, our results are in line with already published reports suggesting that AR does not affect TNBC behaviour. Nevertheless, our findings reveal the predominance of invasive ductal carcinoma NOS within TNBC cases and confirm significant correlations between several clinico-pathological parameters, PFS and OS, underscoring their potential prognostic value.

PS-02-010
Amplicon 8p11.2-p12-based prediction of survival in breast cancer patients – is FGFR1 the driver gene?
R. Erber*, M.G. Carta, P.A. Fasching, M.F. Press, M.W. Beckmann, C.C. Hack, A. Hartmann, F. Ferrazzi, P. Gass, M. Rübner
*Institute of Pathology, University Hospital Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg (FAU), Comprehensive Cancer Center Erlangen-EMN, Comprehensive Cancer Center Alliance WERA (CCC WERA) and Bavarian Cancer Research Center (BZKF), Erlangen, Germany

Background & objectives: Fibroblast growth factor receptor (FGFR) aberrations can be addressed therapeutically. In breast cancer, FGFR1 amplifications are the leading FGFR aberration (6-10%). To confirm FGFR1 as driver gene or to identify a different one, we investigated the 8p11.2-p12 amplicon in detail.
Methods: We analysed mRNA expressions of the 8p11.2-p12 amplicon using a NanoString custom panel (nCounter® technology) in a breast cancer cohort (n=626 patients). Association between expression of the genes of interest (GOIs; FGFR1, ZNF703, ERLIN2, EIF4EBP1, LSM1, BAG4, and TC.1) and clinico-pathological variables including molecular-like subtype, FGFR1 amplification status assessed by fluorescence in situ hybridization, PAM50 subtype, and survival was evaluated.
Results: In our Bavarian Breast Cancer Case-Control Study cohort, median expression of FGFR1 in patients with FGFR1 amplification was significantly different from the one without FGFR1-amplified breast cancer. Moreover, significant differences in median expression levels of FGFR1, ZNF703, ERLIN2, and TC.1 were found, with higher expression in G1+G2 vs. G3 tumours and hormone receptor (HR)-positive vs. HR-negative tumours, while EIF4EBP1 had higher expression in G3 and HR- compared to G1+G2 and HR+ tumours. Furthermore, GOI expression profiles were significantly associated with molecular (-like) subtypes and patients with high vs. low expression exhibited different survival rates. Interestingly, we identified a minimal amplicon (7 genes; from PPAPDC1B to LSM1) associated with long-term survival.
Conclusion: In breast cancer, the 8p11.2-p12 amplicon shows clinically relevant gene expression profiles which could serve as potential targets for precision medicine in breast cancer patients. Moreover, the identified 7-gene minimal amplicon could be used as prognostic predictor for long-term survival.

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PS-02-011
Changes in breast cancer grade from biopsy to excision following surgery or primary chemotherapy
A. Ferenczi*, G. Cserni
*University of Szeged, Hungary

Background & objectives: To compare histological grade of breast cancer and the scores of its components in core needle biopsies (CNBs) and surgical excision specimens (EXC) in patients treated by primary surgery (CHIR) or primary chemotherapy (PST).
Methods: Grade (G) of matched pairs of carcinomas in CNB and EXC was assessed according to the Nottingham grading system. Scores for tubule formation (T), nuclear pleomorphism (P) and mitotic counts (M) evaluated in CNBs and EXC were compared between the patient groups.
Results: PST cases tended to have higher pretreatment G. Concordance rates in the CHIR (n=760) and PST (n=148) groups for T, P, M and G were 79%, 70%, 75%, 71% and 77%, 70%, 50%, 62%, respectively; differences in concordance rates were significant in M ($p<0.0001$) and G ($p=0.024$). For discordant cases in the CHIR group, CNBs tended to overestimate T and underestimate P, M and G, whereas in the PST group, the same trends were identified for T and P, but there was a significant tendency for M and G to be lower in EXC specimens.
Conclusion: The reversal of M and G underestimation in CNB to "overestimation" in the PST group can only be explained with the effect of mitosis reduction following chemotherapy. Whether the posttreatment decrease in G reflects any prognostic value remains to be elucidated.

PS-02-012
Impact of COVID-19 restrictions in breast cancer staging and prognosis at diagnosis
L. Gallego*, N. Shah
*University Hospital Waterford, Ireland

Background & objectives: After COVID-19 restrictions, there is a worldwide tendency to find cancers in more advanced stages. In our centre, breast clinics for symptomatic patients remained opened. We aim to assess the impact of the lockdown on breast cancer diagnosis.
Methods: This is a retrospective cohort study. We identified three cohorts: pre COVID-19, during COVID-19, and post COVID-19, including all first diagnosis patients who underwent surgical treatment (mastectomy or wide local excision) and analysed the data in the reports. We excluded all completion mastectomies and margin resections. For completion, we extracted all metastatic de novo patients from the Oncology database.
Results: The number of patients showed a 13% increase from the first cohort to the last. When it comes to prognostic features, tumour size from Histopathology reports, and from radiology reports in post neoadjuvant therapy specimens, showed a minor increase close to 5%. However, we noted a 17% increase in lymph node involvement, with a larger number of affected lymph nodes and larger size of deposits. In addition, there was a general increase on pT1c, pT2, pT4 and N1 staging, as well as an increase of 33% of the vascular invasion. From the oncology database we discovered a 10% increase on patients with De Novo Metastatic disease.
Conclusion: Our study sees the data from a centre that did not stop the rapid clinic access, and patients were encouraged to attend if symptomatic. Therefore, the higher number of advanced cases and more aggressive tumours shows there is a group of patients who individually delayed consult. This information can empower patients to be proactive and take control of their own health, by not forgetting the importance of self-physical examination and health check-ups, even throughout a pandemic or lockdown.

PS-02-013
Assessment of RNA quality following extraction from FFPE using various protocols compatible with the APIS Breast Cancer Subtyping Kit

A. Gasior*, J. Gorniak, K. Howard, M. Harrison, L. Gough, S. Rollinson, Z. Pounce, A. Wegscheider, A. Niendorf
*APIS Assay Technologies Ltd., United Kingdom

Background & objectives: Formalin-fixed, paraffin-embedded (FFPE) samples, crucial for long-term tissue preservation, undergo fixation, which can affect RNA quality, posing difficulties for molecular techniques. This study evaluated RNA quality obtained from various FFPE extraction kits compatible with the APIS breast cancer subtyping kit.
Methods: Promega's ReliaPrep™ FFPE Total RNA Miniprep System, Thermo Fisher's PureLink™ FFPE RNA Isolation Kit and BioEcho's EchoLUTION™ FFPE RNA Kit was assessed against the QIAGEN RNeasy® DSP FFPE Kit. RNA extracted from FFPE samples (n=21) was quantified and normalized to 2.5ng/μL for RT-qPCR analysis with the APIS Breast Cancer Subtyping Kit, to confirm the detection of biomarker mRNA expression.
Results: All kits extracted RNA with satisfactory yields. BioEcho and Thermo Fisher kits yielded lower RNA concentrations, likely due to the higher elution volumes used (50/30μl). Target call agreement was assessed following removal of samples within 2x ΔCt intermediate precision either side of assay cut-offs, to reduce miscalling. Promega and BioEcho kits showed high agreement (100% for all targets). Lower agreement was observed with Thermo Fisher's kit with 78% agreement for ERBB2 and 91% for MKI67, potentially due to tumour heterogeneity. 100% agreement was observed for ESR1 and PGR across all kits. High agreement confirms highly fragmented, FFPE-derived RNA is of sufficient quality for accurate biomarker detection by the APIS kit.
Conclusion: All kits yielded suitable RNA for APIS Breast Cancer Subtyping Kit. High target agreement was observed in specimens extracted using Promega and BioEcho kits, making them viable alternatives to QIAGEN. Thermo Fisher's kit could also be considered for use, accounting for possible tumour heterogeneity. This study concludes that these alternative kits are suitable for the APIS Breast Cancer Subtyping Kit workflow and reaffirms the accurate detection of highly fragmented, FFPE-derived RNA by the APIS kit.

PS-02-014

Assessment of the dynamic range and quantitative potential of ER, PR, HER2 and Ki67 gene expression by RT-qPCR

A. Gasior*, J. Gorniak, K. Howard, M. Harrison, L. Gough, S. Rollinson, Z. Pounce, A. Wegscheider, A. Niendorf
*APIS Assay Technologies Ltd., United Kingdom

Background & objectives: Accurate determination of breast cancer biomarker (ER/PR/HER2/Ki67) expression is important. With technologies such as RT-qPCR providing a more precise measure we sought to also assess the dynamic range and quantitative measure of these biomarkers on an RNA level.
Methods: Formalin-fixed, paraffin-embedded breast cancer specimens (N=368) from core needle biopsy or resection were used. RNA expression of ER/PR/HER2/KI67 was determined using the APIS Breast Cancer Subtyping Kit and RNA copy number using dPCR. IHC scores were also available. RT-qPCR ΔCt levels were correlated with RNA copy number, IHC % staining and immunoreactivity scores. Expression was binned into 3-4 semi-quantitative ranges.
Results: Normalised RNA copy numbers showed a wide dynamic range for ER (0 to 767 copies), PR (0 to 307 copies) and HER2 (0 to 422 copies) and a smaller range for MKI67 (0 to 1.8 copies). The semi-quantitative method effectively categorized RNA expression levels into High Positive, Moderate, Low Positive and Negative for ER, PR and Ki67. High Positive, Low Positive (HER-low) and Negative ranges were generated for HER2 expression.
Conclusion: We have utilised the dynamic range of RNA expression to provide a ΔCt semi-quantitative scale for assessing targets with the APIS Breast Cancer Subtyping Kit in comparison to IHC % staining and immunoreactivity. This being particularly significant for HER2 low classification, emerging as a crucial marker to identify patients who could benefit from novel anti-HER2 therapies. Similarly, ER-low tumours are now being explored as a clinically and biologically unique subgroup.

PS-02-015

Measuring ESR1 mutations in liquid biopsy and FFPE breast tissue using qPCR

A. Gasior*, J. Gorniak, R. Nana, A. Read, L. Astley, K. Howard, C. Hoy, C. Whitfield
*APIS Assay Technologies Ltd., United Kingdom

Background & objectives: ESR1 mutations are vital markers of ER+ endocrine-resistant breast cancer. Guidelines recommend detection using liquid biopsy, but many labs test formalin-fixed, paraffin-embedded (FFPE) tissue. There is a need for a highly sensitive test to detect mutations in both tissue types.
Methods: The APIS ESR1 Mutations Kit is a qPCR-based method for detecting ESR1 mutations, designed to detect highly fragmented DNA, therefore suitable for cfDNA and FFPE-derived DNA. To demonstrate the kit's detection capability, FFPE breast tissue resections were tested along with the SensID ESR1 Reference Set 1% AF cfDNA, representing liquid biopsy samples. All samples were tested following the kit handbook.
Results: ESR1 wildtype and all ESR1 mutations were successfully detected by the APIS ESR1 Mutations Kit. Expected target calls were observed for the nine SensID mutations at 1% mutant allele frequency (MAF). No false positive results for any of the mutations or wildtype sample were seen, reaffirming the kit's specificity in discerning between mutant and wildtype samples. Wildtype ESR1 from highly fragmented FFPE-derived DNA was detected by the kit, no false positive results were observed showing the kit has good specificity even in high wildtype background. The limit of detection (LoD) determined for the tests with cfDNA is ≤1% MAF and estimated to be ≤0.1% MAF in high background FFPE tissue.
Conclusion: The APIS ESR1 Mutations Kit showcased highly specific and sensitive detection of both the mutations present in the SensID ESR1 Reference Set 1% AF cfDNA and wildtype ESR1 from highly fragmented FFPE-derived DNA. Here, the kit's LoD was affirmed at ≤1% MAF for cfDNA-based sample types and compatibility for detecting ESR1 mutations was demonstrated with both cfDNA and FFPE-derived DNA samples.

PS-02-016

DDR2 expression in breast cancer is associated with blood vessel invasion, basal-like tumours, tumour associated macrophages, regulatory T cells, detection mode and prognosis

T.A. Klingen*, Y. Chen, H. Aas, L.A. Akslen
*Centre of Cancer Biomarkers CCBIO, Department of Clinical Medicine, University of Bergen, Norway. Department of Pathology, Vestfold Hospital Trust, Tønsberg, Norway

Background & objectives: Discoidin Domain Receptor 2 (DDR2) is a receptor tyrosine kinase for collagen, stimulating both epithelial mesenchymal transition and increased stiffness in breast cancer. Here, we examined the level of DDR2 in tumour cells in relation to different microenvironment factors.
Methods: We performed a retrospective study of invasive breast cancers from the Norwegian Breast Screening Program including 200 screen-detected and 82 interval cancers. DDR2 staining examined on core needle biopsies was semi-quantitatively graded based on immunohistochemistry and dichotomized as low or high DDR2 expression. TIL subsets and macrophages were counted, whereas lymphatic and blood vessel invasion were recorded by immunohistochemistry.

Results: High DDR2 tumour cell expression was significantly associated with high counts of CD163 macrophages (p<0.001) and FOXP3 TILs (p= 0.011), presence of BVI (p=0.028), high tumour cell Ki67 (p=0.033), ER negativity (p= 0.001), interval detected tumours (p<0.001), and basal-like (p<0.001) as well as triple negative tumours (p=0.038). High DDR2 expression was related to a shorter recurrence-free survival by multivariate analysis (HR, 2.3, p=0.017), adjusting for tumour diameter, histologic grade, lymph node status, BVI, and molecular subtype.
Conclusion: In conclusion, our study indicates that high DDR2 expression in tumour cells is significantly related to tumour associated macrophages (CD163) and regulatory T cells (FOXP3), possibly stimulating epithelial mesenchymal transition and tumour cell motility with increased blood vessel invasion in breast cancer. Furthermore, high DDR2 expression relates to aggressive tumour features like a basal-like phenotype and interval detection. Our findings may support that DDR2 is an important actor in the microenvironment and a possible independent marker for reduced survival.

PS-02-017
Ring trial of evaluation of HER2 in breast cancer in Greece with emphasis on HER2-low status
E. H. Kourea*, S. Logotheti, O. Tzaida, T. Koletsa, P. Xirou, E. Eleftheriadis, V. Nikolopoulos, A. Nonni
*University of Patras, School of Medicine, Greece

Background & objectives: In the era of HER2-low breast cancer (BC), the concordance of HER2 scoring among pathologists is critical. The aim of this study is to investigate the consensus agreement among five pathologists, for three HER2 clones (0485, CB11, 4B5).
Methods: Three Pathology Laboratories, employing different HER2 clones, provided, each, 30 retrospectively collected, BC-HER2-stained slides. The 90 slides were assessed by 5 breast pathologists, according to the ASCO/CAP 2023 guidelines. Ultralow and borderline 0/1+ cases were also recorded. Fleiss' kappa was calculated for each clone and for each score category (0-3+) to explore the level of agreement among raters.
Results: We first evaluated the consensus agreement among all pathologists. We then sought to determine what level of agreement was observed for each HER2 clone. Statistical analysis revealed moderate agreement (Feiss' kappa=0.56) among the five pathologists for the entire study cases (n=90). The agreement was higher for the Ventana 4B5 clone (Fleiss' kappa=0.64, substantial agreement) and for scores 0 (Fleiss' kappa=0.64, substantial agreement) and 3+ (Feiss' kappa=0.7, substantial agreement). At least 4 pathologists agreed on 25/30 (83.3%), 20/30 (66.7%) and 17/30 (56.7%) 4B5-, CB11 Novocastra/Leica- and 0485 Agilent/Dako-stained cases, respectively. The predominant score for 4B5, CB11 and 0485-stained cases was 0 (17/30, 56.7%), 2+ (13/30, 43.3%) and 1+ (10/30, 33.3%), respectively.
Conclusion: The real-world data on HER2 assessment concordance, in the spectrum of HER2-low BC, although substantial, are not perfect even among experienced breast pathologists. Concordance was significantly better with the Ventana 4B5 clone, which provided a majority of score 0 cases. On the contrary, with the Novacastra/Leica CB11 clone the 2+ score prevailed. These data highlight the inter-assay and inter-observer variability on HER2 immunohistochemical testing and scoring, and the need for laboratories' and pathologists' participation on EQA and national HER2-evaluation schemes.

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PS-02-018
A threefold evaluation of HER2low status of advanced breast carcinomas in core biopsies, matching surgical specimens and their distant metastases. A retrospective study of 47 patients using conventional microscopy, digital pathology and artificial intelligence (AI)
A. Kovács*, L. Klint, S. Janeva, K. Helou, P. Karlsson, R. Pedrosa, D. Kumar, T.Z. Parris
*Dept of Clinical Pathology, Sahlgrenska University Hospital, Institute of Biomedicine, Sahlgrenska Academy, University of Gothenburg, Sweden

Background & objectives: Patients with advanced breast carcinoma with the biomarker HER2-low status (score 1+ or 2+/non-amplified) may benefit from antibody drug conjugate Enhertu®. However, evaluation of immunohistochemistry (IHC) is challenging and further confirmation with molecular assays is not currently available.
Methods: IHC data (either examined in the microscope until 2019 and/or with the digital image from 2019) for 47 breast carcinomas showing HER2-low status in the core needle biopsies, matching surgical specimens, and distant metastases were compared with scores provided by Artificial Intelligence (AI, Aifora®). AI analysis was preceded by deep learning performed by the pathologist.
Results: Digital pathology using AI confirmed the HER2-low status in the majority of cases. Moreover, AI evaluated HER2-ultralow status (1-10% tumour cells with weak membranous staining: > 0 < 1+) with confidence giving an exact number in % of tumour cells showing score 1+. Similarly, when HER2-null status (score 0 or 1+ in <1% of tumour cells) was identified or by evaluating the presence of tumour cells with score 3+ in <10% within an obvious HER2low tumour. HER2 status changed in the same patients' core biopsies, surgical specimens, and distant metastases, mainly from score 0 to 1+, but also vice versa.
Conclusion: The HER2-low concept causes diagnostic challenges for pathologists. Score 1+ and 2+ are mostly heterogeneously distributed within invasive breast carcinomas, which poses difficulty especially when the number of tumour cells is near to the 10% cut-off point. AI evaluation helped to determine a more accurate HER2 status, providing an exact percentage of each HER2 score within seconds with very high accuracy. The Aiforia® solution provided pinpointed individual findings with visual feedback for pixel level validation of the outcome prediction.

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PS-02-019
Assessment of human epididymis protein 4 expression in ductal carcinoma in situ of the breast
J.S. Lee*, N. Kim, M.H. Park
*Department of Pathology, Chonnam National University Hwasun Hospital, Republic of Korea

Background & objectives: Human epididymis protein 4 (HE4) has shown elevated expression in various cancers, notably gynaecologic and pulmonary cancers. This study aimed to assess HE4 levels in both serum and tissues of DCIS patients, exploring potential correlations with clinicopathological features.
Methods: Serum samples from 59 DCIS patients were analysed using the ARCHITECT assay. Tissue microarrays, comprising DCIS and normal tissues, were subjected to RNAscope ISH and immunohistochemistry to evaluate HE4 mRNA and protein levels, respectively. Additional analyses were performed on DCIS tissues from 41 patients. The BreastMark database was utilized to validate HE4's prognostic potential in breast cancer patients.
Results: Serum HE4 levels in DCIS patients ranged from 23.5 to 86.3 pmol/L, with no abnormal cases detected. While serum levels did not significantly vary with clinicopathological parameters, tissue analyses demonstrated increased HE4 expression in DCIS tissues compared to normal counterparts. Notably, there was no significant

correlation between serum and tissue HE4 levels. High mRNA and protein expression of HE4 were observed in 25 of 99 (25.3%) and 34 of 99 (34.3%) cases, respectively. High HE4 expression in DCIS tissues was associated with favourable clinicopathological characteristics. In breast cancer patients, high HE4 expression was significantly associated with good survival in the overall group.
Conclusion: Contrary to expectations, serum HE4 levels were not elevated in DCIS patients. However, increased HE4 expression in DCIS tissues was associated with good clinicopathological characteristics. Further investigations are warranted to elucidate HE4's role in DCIS and its potential implications for prognosis and therapeutic strategies in breast cancer.

PS-02-020
Lymph node micrometastases and ITCs accurate detection after neoadjuvant therapy of breast cancer based on deep learning artificial intelligence
Y. Liu*, Y. Ding, J. Yu, J. Shang, J. Li, S. Wu, X. Liu, J. Li
*The Fourth Hospital of Hebei Medical University, China

Background & objectives: The evaluation of lymph nodes metastasis after breast cancer NAT is a key factor affecting pCR and prognosis. However, Micro-metastasis and ITC recognition were difficulty. Our research aims to substantiate an AI algorithm to assess lymph node status following NAT.
Methods: A ResNet-50 is used to extract the patch features from each slide, resulting in a N × 1024 matrix.1719 number of WSIs from our hospital were retrospectively recruited, the accuracy of this model was verified in Camelyon-17 (C17) as external verification. Model performances were evaluated using area under the curve (AUC), sensitivity, specificity, et al.
Results: The results showed that the model performed well in identifying positive tumours, with a sensitivity of 0.75 and specificity of 0.76 in the internal cohort (376 WSIs), a sensitivity of 0.67 and specificity of 0.92 in C17(500 WSIs). Specifically in recognizing ITC and micro-metastatic tumour cells, the ROC curve achieved an AUC of approximately 0.64 and 0.67 in the internal (8 ITC WSIs;15 Micrometastasis WSIs). We verified in C17 which achieved an AUC close to 0.53 and 0.66. It was significantly improved than visual evaluation. Particularly in recognizing macro-metastatic tumour cells, AUC can reach 0.87 and 0.91 in the internal and external cohorts respectively.
Conclusion: This model was accurate in predicting pathological complete response with satisfactory AUC, and high sensitivity, specificity in C17 external validation cohorts, and had superior performance in identify positive lymph nodes status. Despite promising findings, our study still needs to improve the recognition of ITC. The performance and universality of this study indicated great potential in the application of accurate lymph node metastases detection after neoadjuvant therapy of breast cancer.

PS-02-021
Comparative analysis of hormone receptor and Ki76 expression changesin luminal breast carcinoma following perioperative hormonal treatment
L. Martínez Gauffin*, Y.G. Montoyo Pujol, S. Delgado García, H. Ballester, T. Martin Bayona, J. Ponce Lorenzo, V. Menor Vila, S. Shalygina, L. Gracia Sáenz, E. Castellón Mollà, G. Peiró Cabrera
*Spain

Background & objectives: Perioperative hormonal treatment is a therapeutic option in patients with Luminal breast cancer (BC). We analyse the influence of endocrine treatment on the change in expression of hormone receptors (estrogens -ER- and progesterone -PR-) and Ki67 in a clinical series.
Methods: We performed a retrospective study (January 2020- March 2024) in 201 Luminal BC. Expression and intensity (Allred Method) of ER (clone SP1), PR (clone 1E2), and Ki67 (clone 30-9) were evaluated and compared in pretreatment core needle biopsy (CNB) and post-treatment surgical specimens. Results were correlated with treatment duration, and significant differences were calculated with $\chi 2$ or Fisher tests.
Results: The median patient's age was 61 years, and the treatment time pre-surgery was six weeks. Tumours were predominantly NOS ductal (73,6%), luminal A (76,6%), and grade II (68.7%). The mean ER, PR, and Ki67 expression in CNB were 98%, 62%, and 14%, respectively. Regarding surgical specimens, they were 93%, 25% and 6%. No significant changes were observed in ER expression (p=ns). Among 120 tumours with PR expression >66% in CNB, 52 showed a <10% reduction post-treatment (43.3%; p<0.001). Similarly, high Ki67 levels (>20%) in the pretreatment CNB became low levels (<15%) in 68.1% of surgical specimens (p<0.001). The later results were significant after four weeks of treatment (p<0.001).
Conclusion: Our data support that perioperative endocrine treatment significantly reduces the proliferative index of tumour cells and PR expression and that these changes are time-dependent. However, we did not observe any effect regarding the ER levels. Therefore, further investigation is needed to elucidate the underlying mechanisms leading to this differential response to endocrine therapy.

PS-02-022
HHLA2 and TMIGD2 gene expression in breast carcinoma: correlation with clinicopathological factors and prognostic value
Y.G. Montoyo Pujol*, A. Llopis-Gómez, D.A. Manresa-Corbalán, A. Garzón-Arana, T. Martin Bayona, S. Delgado García, H. Ballester, J. Ponce Lorenzo, E. Castellón Mollà, G. Peiró Cabrera
*Spain

Background & objectives: HHLA2 is a B7 protein that regulates T cell functions via TMIGD2. However, limited data exists on its role in breast carcinoma (BC). We analysed HHLA2 and TMIGD2 expression in BC patients, exploring their association with clinicopathological factors and prognosis.
Methods: We included 151 non-consecutive BC (13.2% Luminal A, 23.2% Luminal B/HER2-, 21.2% Luminal B/HER2+, 21.9% HER2-enriched and 20.5% TN/BL). Relative gene expression was analysed by qRT-PCR using the 2-ΔΔCT method. Results were correlated with clinicopathological factors (age, tumour size grade, vascular invasion, necrosis, immunophenotype, tumour-infiltrating lymphocytes, lymph node status, and Ki67) and prognosis using $\chi 2$ and log-rank tests, respectively.
Results: HHLA2 and TMIGD2 were overexpressed in 4.6% and 57.6% of tumours. No correlation was found between both genes (p=ns). The mRNA expression of HHLA2 increased in Luminal A, whereas TMIGD2 was more frequently found in Luminal B/HER2+, but only as a trend (p≤0.162). Statistical differences were found in tumours ≤20 mm and HHLA2 overexpression (p=0.023). In addition, increased TIMGD2 was associated with the absence of necrosis as a trend (p=0.060). Regarding prognosis value, TMIGD2 overexpression correlated with better disease-free survival (DFS) in BC patients (p=0.036) but not among intrinsic BC subtypes (all cases p>0.05). However, no statistical differences were observed between HHLA2 levels and survival (p=ns).
Conclusion: In the current clinical series, our data support that both genes are associated with favourable clinicopathological characteristics, such as smaller tumour size and absence of necrosis. In addition, TMIGD2 is a biomarker of good prognosis for DFS. Considering these findings and given that HHLA2-TMIGD2 interactions are capable of co-stimulating T cells, there is a need for more research to understand the role of these proteins in BC.

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PS-02-023

A higher CD4/CD8 ratio in stromal tumour-infiltrating lymphocytes (TILs) of locally advanced breast cancer is associated with triple-negative biology and a higher-risk ER+HER2- disease

M. Murkovic*, A. Car Peterko, A. Savić Vuković, K. Rajković-Molek, E. Babarović, M. Avirović
*Clinical Hospital Centre Rijeka, Clinical Department of Pathology and Cytology, Rijeka, Croatia

Background & objectives: The proportion of stromal TILs is a surrogate marker for tumour immunogenicity. The composition of TILs may vary as a consequence of different tumour biology or within the same tumour subtype due to differences in the stages of the disease.
Methods: Clinical data and archived paraffin core-needle biopsy blocks from 89 patients with triple negative (TN)(36) and luminal B (LB)(53) invasive breast cancer were included in present analysis. Quantitative and qualitative evaluation of TILs was performed. The proportion of stromal TILs, CD8, CD4 and PDL-1 positive immune cells (IC), as well as the number of FOXP3 and CTLA-4 positive IC, was determined.
Results: There was no statistically significant difference detected in the proportion of stromal TILs between locally advanced TNBC and LBBC cohorts (P=0.344). However, a higher CD4/CD8 ratio was associated with the TNBC cohort (P=0.018). Within the LBBC cohort, a higher CD4/CD8 ratio was associated with high proliferation index (Ki67>30%) and metastatic nodal involvement (cN+) (P=0.045, P=0.015). Different positive correlations were noticed within the TNBC and LBBC cohorts. In TNBC, higher proportion of CD4+ T cells correlates with the proportion of PDL-1+ IC (rho=0.57, P=0.020) and with the number of FOXP3+ Tregs (rho=0.53, P=0.035). In the LBBC cohort, proportion of CD4+ T cells correlates with the number of CTLA-4+ IC (rho=0.69, P=0.0001).
Conclusion: In locally advanced breast cancer, a higher CD4/CD8 ratio in stromal TILs is associated with triple-negative biology and suggests a higher risk disease within the ER+HER2- cohort. Subtype-specific distribution of regulatory molecules in relation to CD4+ is noticed as well, with PDL-1 and Tregs predominance in TNBC and CTLA-4 in ER+HER2- disease. Further trials are needed to confirm whether the different nature of regulatory mechanisms in locally advanced stages of LBBC and TNBC may explain the difference in CD4/CD8 ratio.

Funding: Funding from research project: Prediktivna i prognostička uloga stanica imunološkog sustava, PD-1, PDL-1 i heat shock proteina u bolesnica s trostruko negativnim, HER-2 pozitivnim i neoadjuvantno liječenim karcinomom dojke. Uniri-biomed - 18-259 1428 Head of research: doc. dr. sc. Manuela Avirović

PS-02-024

Post-neoadjuvant changes in immunohistochemical biomarkers in breast cancer

V.S. Recalde*, M.C. Saez Perrotta, M.B. Iriarte, C. Allemand, P.X. De la Iglesia Niveyro, A. Wernicke
*Argentina

Background & objectives: Changes in immunohistochemical biomarker expression have been identified after neoadjuvant therapy (NAT) in breast cancer. Objectives were to assess such biomarker changes, and to determine the pathological complete response (pCR) rate according to molecular subtype.
Methods: A retrospective, observational, cross-sectional study included 154 breast cancer patients from the Hospital Italiano de Buenos Aires treated with NAT between January 2018 and June 2023. Expression of estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2) was evaluated in pre- and post-treated samples of patients without pCR according to ASCO/CAP guidelines.
Results: Among 154 patients who underwent NAT, 66 (43%) achieved pCR. Pure HER2 positive had the highest pCR rate (81%), followed by triple negative (TN) (47%), triple positive (TP) (37%) and luminal (10%) subtypes. Eighty-eight (57%) patients didn't achieve pCR. Among 63 cases where immunohistochemistry was evaluable, 18 (29%) showed changes in immunohistochemical expression: ER changed in 2 cases (11%), both became negative; PR changed in 9 cases (50%), in 7 it became negative and in 2 it became positive; HER2 changed in 7 cases (39%), 4 cases became negative by immunohistochemistry (IHC) and 3 cases became positive, 1 by IHC and 2 by fluorescence in situ hybridization (FISH).
Conclusion: We observed a change in biomarker status between the biopsy and the surgical specimen in 29% of cases. It is therefore important to evaluate the tumour immunophenotype after neoadjuvant treatment, as it can modify therapeutic decisions.

Pure HER2 positive and triple-negative subtypes had the highest pCR rate.

PS-02-025

FOXC1 immunohistochemistry accurately predicts basal/non-basal molecular subtype status and differential efficacy of adjuvant capecitabine in early triple-negative breast cancer: results from the GEICAM/2003-11_CIBOMA/2004-01 trial

F. Rojo*, C.R. Taylor, C. Barrios, L. Torrecillas, S. Perez-Buira, M. Ruiz-Borrego, J. Bines, J. GM Segalla, A. Guerrero-Zotano, J. Herranz, R. Rincon, R. Caballero, B. Bermejo, P. S Ray, M. Martin
*IIS-Fundación Jimenez Diaz-CIBERONC. GEICAM, Spanish Breast Cancer Group, Spain

Background & objectives: Extended adjuvant capecitabine benefit in triple-negative breast cancer (TNBC) is restricted to PAM50-defined non-basal BC (non-BLBC) subtype. We evaluated Veresca® FOXC1 Immunohistochemistry (IHC) test's ability to predict such benefit in phase III CIBOMA trial (NCT00130533) based on delineation of BLBC/non-BLBC.
Methods: FOXC1 IHC expression was assessed using B2E3 monoclonal anti-FOXC1 (Veresca®, Onconostic Technologies) in 744 TNBC patient samples. Restrictive FOXC1 evaluations were conducted by controlling tissue preanalytical characteristics and staining quality. FOXC1 Score (VFOXC1) was calculated as FOXC1 nuclear staining Proportion Score (PS) + Intensity Score (IS). ROC and Kappa index analysis were performed including prior IHC markers and PAM50 data.
Results: Of 713 (95.8%) TNBC tumours available for IHC analysis, 705 (98.9%), 620 (87.0%) and 525 (73.6%) cases with similar clinicopathological features met criteria for FOXC1 low, intermediate, and high designation, respectively. Low restrictive cohort was mostly VFOXC1=0 (186, 26.4%) PS=4 (150, 21.3%) and IS=2 (184, 26.1%), with 460 VFOXC1 cutoff ≥4 (65.3%) and 519 cutoff ≥1 (73.6%) tumours. VFOXC1 displayed strong association with PAM50 (AUC 0.874, CI95% 0.837-0.911) but weak association with a surrogate IHC-based BLBC definition (EGFR and CK5/6 staining) (AUC 0.548, CI95% 0.500-0.597). VFOXC1 cutoff ≥4 had high concordance with PAM50 BLBC (Kappa 0.425) and identified non-BLBC patients with significant capecitabine benefit (VFOXC1<4, DRFS HR=0.53; 95%CI 0.31-0.90; p=0.019).

Conclusion: The Veresca® FOXC1 test is a superior predictor of BLBC/non-BLBC subtype status and associated differential therapeutic efficacy to extended adjuvant capecitabine in early TNBC patients from the CIBOMA trial. VFOXC1 was better associated with PAM50 intrinsic subtyping than surrogate IHC-based BLBC phenotype. Veresca® test robustly defined BLBC subtype on clinical samples independently of uncertain tissue preservation conditions.

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PS-02-026

Training and evaluation of an AI-assisted HER2 scoring in breast carcinoma-stained whole-slide images

B. Cormier, C. Bossard, Y. Salhi*, F. Thomas, B. Poulet, E. Guinaudeau, L. Lambros, C. Ilham, F. Jossic, I. de Pinieux, S. Thanguturi, S. Salhi, J. Chetritt
*DiaDeep, France

Background & objectives: To improve the accuracy of HER2 scoring, we have developed an artificial intelligence (AI) algorithm designed for precise and consistent quantification of HER2 protein overexpression, supporting pathologists in the assessment of HER2 immunohistochemistry scores.
Methods: The algorithm detects invasive tumour regions and quantifies and characterizes tumour cells, trained on over 5000 labelled images. It segments invasive areas and cells, analysing cell membranes. Its performance was validated against ground-truth scores established by three senior pathologists through majority voting. Post a two-month washout, slides were rescored with AI assistance to compare inter-observer agreement.
Results: The test dataset was built using 68 routine cases of HER2 immunostained slides of Breast Cancer, without any further selection criteria, in order to reflect the routine practice. The model exhibited an overall balanced accuracy of 90.2% on this dataset, thus demonstrating its capability to assist pathologists in their routine practice while providing an interpretable HER2 Score. Notably, 100% of the HER2 3+ scores and 93.3% of the HER2-Low cases were identified by the model, yielding promising results to identify patients eligible to targeted therapy. Moreover, the inter-observer agreement rose from 57% to 75% with the assistance of AI.
Conclusion: This study demonstrates the efficacy of the proposed fully-automated AI system in accurately assessing HER2-immunostained WSI, in accordance with the 2018 ASCO/CAP Guidelines. By providing pathologists with easily interpretable scores, such an AI tool could be used as a regular aid in clinical decision-making, improving reproducibility and aiding in the assessment of challenging cases due to the detailed information it provides for each cases.

PS-02-027

Artificial intelligence predicts survival outcome of breast carcinomas on whole-slide histopathology images

J. Rynkiewicz, J. Paul, Y. Salhi*, C. Bossard, S. Salhi, J. Chetritt
*DiaDeep, France

Background & objectives: We introduce a deep neural network (DNN) specifically designed to assign a survival risk score for breast carcinomas patients directly from whole slide images (WSI) of HE-stained sections of tumour, without any annotations.
Methods: The model integrates two distinct morphological information: one encapsulates cellular-level information, while the other encompasses tissue-level ones, using the Cox proportional hazard loss function. It has been trained and evaluated on the publicly available TCGA-BRCA dataset and tested in an external data of 254 HR+/HER2- patients. Cox multivariate analysis was carried out to assess the AI-based prognostic factor.
Results: The AI model demonstrated an average concordance index of 0.682 when assessed on the testing set. The Cox model, incorporating clinical features (age and TNM stage), produced an average c-index of 0.767. Notably, this value rose to 0.786 upon the inclusion of our AI-based risk score. The proposed model outperforms existing models when it comes to predicting survival. The Cox model indicates that our AI-based risk score can be used as an independent prognostic factor for predicting overall survival ($p<0.005$). Furthermore, we were able to significantly discriminate 2 groups of patients in terms of survival outcome, depending on a AI-based high or low risk.
Conclusion: In this study, we showcased that the algorithm was able to instantly extract prognostic morphological features from H&E whole slide images (WSI) and could be included in the pathology report. This could potentially enhance clinical decision-making, elevating the standard of care. Compared to commonly used molecular signatures, the AI algorithm enables a reduction in response time and cost savings.

PS-02-028

Comparison of lower limit of detection of HER2 epitope with two commercially available HER2 IHC assays using an Immunohistochemistry staining calibrator tool

G. Noumsi*, F. Aidt, K. Salomon, K. Hjort, D. Varma
*Agilent Technologies Spain

Background & objectives: Recent advances in therapeutic molecules prompt a reevaluation of testing protocols, focusing on the lower HER2 expression range. Here, we used standardized HER-2 Boston Cell Standards IHCalibrators® reference microbeads to assess sensitivity in two commercially available HER2 IHC assays.
Methods: Glass microbead slides were stained with either Ventana PATHWAY® anti-HER-2/NEU or Agilent HercepTestTM mAb PharmDx in triplicates using their respective immunohistochemical stainers. The ratio of average staining intensity to the colour control beads was calculated, and results were fitted using a 3-parameter sigmoid dose-response curve for comparing the sensitivity of the two assays.
Results: The detection limits of the two assays shows noticeable differences. The response curve of PATHWAY® anti-HER-2/NEU is shifted to the right with respect to the response curve of HercepTest mAb PharmDx. While the lower limit of detection for PATHWAY® anti-HER-2/NEU was at level 5 of HER2 epitopes per bead detection, it was at level 3 for HercepTestTM mAb PharmDx. The dynamic range of HercepTestTM mAb PharmDx is broader at the low range of the IHCalibrators levels, whereas PATHWAY® anti-HER-2/NEU has a broader dynamic range at the high end of IHCalibrators levels.
Conclusion: With the advent of novel ADCs where the amount of HER2 receptors required for a clinical response is lower, the significance of HER2 epitope detection levels at the low end of the expression range is increasingly relevant. This study demonstrates a significant difference in the lower limit of HER2 detection between the two tested assays, which holds potential relevance when considering low levels of HER2. D0113716.

PS-02-029

Evaluation of diagnostic performance and clinical utility of cleo breast in breast pathology diagnosis

M. Sockeel*, B. Pommier, S. Sockeel, R. Peyret, C. Simmat, N. Pozin, S. Prevot, A. Maran-Gonzalez, G. Mac Grogan, A. Vincent-Salomon
*Primaa, France

Background & objectives: Cleo Breast, a CE-marked medical device, revolutionizes breast pathology diagnosis, detecting various pathologies like carcinoma, calcifications, and lymph node metastases. It offers a first-read solution and conducts detailed mitotic count analysis on H&E stained pathology slides

Methods: The study assesses pathologists' diagnostic accuracy with Cleo Breast, with and without AI, and compares its performance as standalone software versus integrated into LIMS like Sectra. Ten pathologists from four French surgical pathology departments evaluated 200 breast pathology slides, focusing on detecting different breast pathologies, including invasive carcinoma and lymph node metastases, with or without Cleo Breast's assistance.
Results: Cleo Breast demonstrates non-inferiority in diagnostic performance, showcasing high sensitivity in detecting invasive carcinoma (99.1% without AI, 99.8% with AI), carcinoma in situ, calcifications, lymph node metastases (97.6% without AI, 100% with AI), and mitotic scores. Notably, it significantly cuts the analysis time for mitotic scoring in half (107 sec to 51 sec). Furthermore, there are negligible differences observed between using Cleo Breast as a standalone tool versus integrated into Sectra LIMS.
Conclusion: This study marks a significant step in evaluating Cleo Breast's clinical effectiveness in breast pathology diagnosis. It confirms its ability to enhance diagnostic accuracy, especially by streamlining mitotic scoring, thus improving physicians' efficiency. Integration with a LIMS signifies a notable advancement in diagnostic workflow. Cleo Breast emerges as a transformative diagnostic tool, promising to expedite and refine diagnostic processes, leading to better patient care outcomes. This research paves the way for further Cleo Breast adoption in clinical settings.

PS-02-030
Comprehensive characterization of invasive mammary carcinoma with lobular features: integrating morphology and E-cadherin immunochemistry pattern
Y. Sung*, T. Jeon, W. Oh, J. Oh, J. Ahn, A. Kim
*Anam Hospital, Republic of Korea

Background & objectives: Invasive lobular carcinoma (ILC) exhibits unique biological behaviours, necessitating accurate diagnosis. In this study, we reviewed breast cancer, with a particular focus on investigating the E-cadherin staining patterns and lobular morphology of cases that were misclassified in the original reports.
Methods: A comprehensive review was conducted on 481 cases diagnosed with invasive breast carcinoma of no special type (IBC - NST) or ILC through biopsy, in which E-cadherin staining was also performed. Subsequently, these cases were categorized into six groups based on a combination of tumour morphology (ductal / lobular) and E-cadherin expression pattern (membranous / loss / aberrant).
Results: In 211 cases (43.8%), E-cadherin pattern indicating ILC (loss & aberrant) was observed alongside lobular morphology, representing 5.52% of all breast cancer biopsies during the relevant period. 181 cases (37.6%) showed membranous pattern with ductal morphology, 4 (0.8%) were mixed IBC-NST and ILC, and 85 (17.7%) exhibited discordance between morphology and E-cadherin. Notably, of 58 cases reviewed as ILC due to aberrant pattern, only 15 (25.9%) had initial ILC diagnosis. Among 58 cases showing membranous pattern with lobular morphology, only 2 were diagnosed as ILC in the original reports. Similarly, despite the presence of ductal morphology, 17 cases (63%) exhibiting either loss or aberrant pattern were initially diagnosed as ILC.
Conclusion: Despite the E-cadherin expression pattern being recognized as a 'desirable' diagnostic criterion for ILC in the WHO blue book, real-world practice tends to depend on E-cadherin results, even in the presence of evident lobular morphology. Especially, aberrant pattern was often interpreted as membranous pattern, leading to misdiagnoses of IBC-NST. Additionally, cases showing discordance between morphology and E-cadherin patterns were observed in 85 cases (17.7%), highlighting the need for molecular clarification of these discrepancies.

PS-02-031
TRPS1 in breast cancer: a comparative study of five different IHC assays
B. Truumees*, M. Korsdal Stensballe, R. Røge, S. Nielsen
*NordiQC, Denmark

Background & objectives: Immunohistochemistry (IHC) for TRPS1 (Trichorhinophalangeal syndrome 1) is a novel biomarker for breast cancer (BC), especially triple negative breast cancer (TNBC). The aim of the study was to compare the staining patterns of five different TRPS1 IHC assays.
Methods: Five commercially available antibodies for TRPS1 were optimized on TMAs with a range of normal tissues and BCs. Subsequently each IHC assay was validated on TMAs comprising of 135 breast carcinomas (BC), including 64 TNBCs, and 74 various neoplasias. A positive cut-off at ≥10% of neoplastic cells with nuclear TRPS1 expression was applied to determine the diagnostic sensitivity and specificity.
Results: The five different and individually optimized IHC assays provided a fully comparable level of diagnostic sensitivity and specificity. All assays reached an overall diagnostic sensitivity of 97% in BCs. 100% of luminal BCs and 94% of TNBCs were scored as TRPS1 positive. The general diagnostic specificity was in the range of 91-93%. Positive TRPS1 staining in ≥10% of neoplastic cells was seen in a subset of lung, gynaecological and urothelial carcinomas with all assays. In addition, two assays also labelled melanomas (20%). If the positive cut-off was changed to ≥1%, TRPS1 was observed in more neoplasias and the diagnostic specificity was reduced to 82-87%.
Conclusion: All five tested TRPS1 assays exhibited comparable staining patterns in both normal and neoplastic tissues. However, implementing TRPS1 IHC as diagnostic tool for BCs requires rigorous optimization and validation to ensure appropriate diagnostic sensitivity and specificity of the assay, as some antibodies might require special technical assay conditions. This study reveals potential diagnostic pitfalls as other neoplasias that are relevant differential diagnoses of BC also express TRPS1. This underlines the need for further studies on larger cohorts of these neoplasias.

PS-02-032
Multicentre study on distribution of HER2 scores using HercepTest™ mAb pharmDx (Dako Omnis)
L. Rudbeck, D. Varma*, K. Knudsen
*Agilent Technologies Denmark

Background & objectives: A comprehensive multicentre study was conducted across Europe (six laboratories) to evaluate the impact of the new HER2 assay, Agilent HercepTest™ mAb pharmDx (Dako Omnis) on HER2 scoring frequencies. A particular focus was given to ISH-positivity of equivocal 2+ cases.
Methods: HER2 scores from a retrospective evaluation of results obtained for 300 breast tissue samples using the labs' previous commercial HER2 assay were compared with 300 HER2 scores obtained with the newly introduced HercepTest™ mAb pharmDx assay in six labs (3600 cases total). Change in distribution of IHC scores across the different HER2 categories according to ASCO/CAP was investigated.
Results: There was a slight (4% and 5%, respectively) increase in IHC 1+ and IHC 2+ cases identified by the HercepTest™ mAb pharmDx assay compared to the previous assay. The overall IHC 2+ percentage (24%) for the 1800 cases across the six laboratories aligns closely with the range (18–21%) for HER2 IHC 2+ scores previously published. For all sites combined, there was no change (0.19%, CI [-0.09%, 1.3%]) in the number of patients being detected ISH-positive. A survey showed that the labs perceived HercepTest™ mAb pharmDx to provide enhanced staining quality with improved intensity, clear linear staining, and less granularity.

Conclusion: Across the six European labs, there was a minor increase in the percentage of 2+ cases identified in the 1800 cases after implementation of HercepTest™ mAb pharmDx compared to 1800 cases tested with the labs' previous HER2 assay. However, the overall percentage of IHC 2+ cases remain closely aligned with published data for IHC 2+ positivity range. Overall, there is no change (0.19%) in the number of patients being detected ISH-positive, i.e., no change in patients eligible for targeted treatment.

PS-02-033

Hormone receptor-positive early-stage breast carcinomas are enriched in HER2-low phenotype and low levels of tumour-infiltrating lymphocytes

S. Vranic*, F. Skenderi, I. Rose, Z. Gatalica
*College of Medicine, QU Health, Qatar

Background & objectives: In the present study, we explored the status of tumour-infiltrating lymphocytes (TIL) and the prevalence of HER2-low phenotype in a cohort of MammaPrint® (MP) and BluePrint® (BP)-profiled early-stage hormone receptor (HR)-positive breast carcinomas.
Methods: Eighty-eight (56 low-risk and 32 high-risk) early-stage HR-positive breast carcinomas were profiled by the MP/BP assays. The TIL distribution was assessed following the International TILs Working Group recommendations. HER2-low breast cancers were defined by IHC scores 1+ and 2+ without HER2 amplification.
Results: All cases were luminal A (n = 56) or luminal B (n = 32). The tumour grade was strongly associated with the recurrence risk (p = 0.012). The prevalence of HER2-low expression was 65% without differences between the molecular subtypes (p = 0.82) or correlation with the recurrence risk (p = 0.74). Levels of TIL were low (≤10%) in 75% of the cohort (median: 8%, range 0–70%), with only three high-risk cases having TIL ≥50%. The TIL levels did not differ significantly between the risk groups and molecular subtypes (p > 0.05). HER2 status did not impact the TIL distribution (p = 0.62).
Conclusion: Early-stage HR-positive breast carcinomas have low TIL levels regardless of the recurrence risk, molecular subtype, and HER2-low status. These cancers are markedly enriched by HER2-low phenotype, which might have therapeutic implications due to the recently approved anti-HER2 antibody-drug conjugate.

PS-02-034

Risk of upgrade of ADH detected by core needle biopsy of the breast

Y. Wu*, C. Albarracin, H. Le-Petross, N. Sneige, I. Bedrosian
*UT MD Anderson Cancer Center, USA

Background & objectives: Atypical ductal hyperplasia (ADH) of the breast is generally considered an indication for surgical excision to rule out occult carcinoma. We investigated the utility of MRI for stratification of upgrade risk of ADH detected by core needle biopsy.
Methods: Retrospective review of a prospectively maintained institutional database was used to identify women diagnosed with ADH by core needle biopsy between 2004 and 2022. All cases had been presented for multidisciplinary review and recommendation for management was based on standardized imaging and pathology criteria. Clinical variables, imaging and pathology data were collected for each ADH diagnosis.
Results: 362 cases met study inclusion criteria. 312 (86%) were diagnosed by mammography. The overall upgrade rate was 25.7% (93/362); Most of upgrades were in-situ carcinoma (71/93, 76%). 55 patients with mammography detected ADH also underwent MRI, with a correlate for the ADH identified on the MRI in 33/55 patients. There was no difference in overall upgrade rates among cases with no MRI correlation vs. those with an MRI correlation (36% vs 36%). Additionally, the distribution of DCIS vs IDC upgrade was not associated with type of MR abnormality (mass vs non-mass enhancement).
Conclusion: In women with ADH detected by core needle biopsy and referred to surgical excision based on histologic criteria and radiologic criteria, the overall upgrade rate was 25.7%. However, MRI did not further distinguish those at risk of upgrade.

PS-03Poster Session Dermatopathology

PS-03-001

Predictive factors of lymph node involvement in cutaneous squamous cell carcinoma

W. Ben Makhlouf*, N. Boujelbene, I. Zemni, A. Khemir, R. Aissa, I. Abbes, G. Sahraoui, R. Doghri, L. Charfi, K. Mrad
*Tunisia

Background & objectives: Cutaneous squamous cell carcinoma (cSCC) is the second most common form of skin cancer. Advanced disease includes the presence of locoregional metastasis. Herein, we aimed to evaluate the predictive role of primary tumour histopathological features in predicting lymph nodes involvement.
Methods: We retrospectively analysed pathological records from 71 consecutive patients who underwent cutaneous resection for invasive cSCC between January 2015 and December 2017. We considered the following histological parameters: tumour size, histological subtypes, grade of histologic differentiation, lymphovascular invasion, perineural invasion, thickness, desmoplasia, Clark's level, tumour budding and pathological stage.
Results: Eighty-Nine cCSC were identified. The mean age of patients was 64 years with a sex ratio (M/F) of 4.46. The mean duration of follow-up was 27 months. Lymph node invasion was observed in 27% of cases. It was associated with a tumour size > 40 mm (p=0.05), a poorly or moderately differentiated appearance (p=0.04), tumour budding (p=0.03) and lymphovascular invasion (p=0.001). In multivariate analysis, poorly and moderately differentiated appearance (p=0.01), and tumour budding (p=0.03) were independent factors of lymph node involvement. The Clark's level V, the pT3 stage and the high-risk histological subtype appear to be risk factors for lymph node invasion, although with a borderline difference (p=0.09).
Conclusion: The histological grading and tumour budding have to be considered as important parameters to select patients with cSCC to undergo an aystematic lymphadenectomy.

PS-03-002

Acral melanoma: a Singapore story

I. Busmanis*
*Singapore General Hospital, Singapore

Background & objectives: Acral melanoma (AM) occurs on glabrous skin of the extremities and is unrelated to ultraviolet light exposure. Countries in Asia have a proportionally higher incidence of AM compared to Caucasian populations.
Methods: We examined 38 AM cases in Asian patients, 20 male, and 18 female, extracted from files of Singapore General Hospital, over a 45 month period. All cases underwent Somatic Solid Tumour Panel mutation screen assay. The commonest location of melanoma was foot, (32), big toe (10) and heel/sole region (15), versus hand (6).
Results: Histologically, 30 of the cases were classified as acral lentiginous melanoma (ALM) and 8 were nodular melanoma (NM) in an acral location. We also examined for differences in genetic aberrations within the 2 largest groups of AM, the big toe, and heel/sole areas. Numbers are small, but the main difference was in the rate of KIT mutation, more common in big toe cases (4), contrasting with heel/sole cases (1). With respect to molecular findings according to gender, the incidence

of wild type BRAF, KIT and NRAS was the same for both males and females. Notable differences were seen between the incidence of KIT and BRAF in males compared with females.
Conclusion: The commonest molecular finding was wild type BRAF, KIT, and NRAS (16 cases, ~42%), followed by KIT variant (11 cases, ~29%), BRAF variant (7 cases, ~17%), and NRAS variant (4 cases, 9%). In addition, KRAS was identified in a single case, and NRAS together with APC in one other patient. Our overall incidence of BRAF mutation was 17%, lower than described for cutaneous melanoma, and consistent with acral location.

PS-03-003
Clinicopathological evaluation of granuloma annulare: study of a tertiary centre
E. Çeşmecioğlu Karavin*, İ. Hotmanoğlu Şahin, M.E. Oğraş, A.D. Yücelten, L. Cinel
*Turkey

Background & objectives: Granuloma annulare (GA) is an uncommon inflammatory granulomatous skin disease that can have classical and atypical manifestations. GA is diagnosed based on clinicopathologic correlation. This study aimed to discover the clinicopathological features of GA in our centre.
Methods: Thirty-three skin biopsies from 30 cases diagnosed as GA based on clinicopathologic correlation between 2015 and 2024 were evaluated and assessed for the pattern of infiltrate (interstitial/palisading/granulomatous/mixed), depth of infiltrate, presence of collagen degeneration, multinucleated giant cells, vascular changes, presence of dermal mucin, additional features. Clinical variants (localized-generalized), age groups, and lesion type (plaque-papule-nodule) were noted. Statistical analysis was performed.
Results: Most cases (75%) were between the ages of 20 and 60 and female (75%). Annular plaques were the most frequent presentation (45.5%), followed by papules (%39.4). The palisaded pattern was most common (51.5%), whereas granulomatous and interstitial were seen in 5 (15.2%) cases each and mixed pattern in 6 (18.2%) cases. Collagen degeneration was noted in most cases (90.9%), and dermal mucin in 25 cases (75.8%). Giant cells were detected in 27 cases (%81.8). The infiltrate occupied the upper and mid dermis in %54 of the cases. The degree of inflammation, eosinophils, plasma cells, and giant cells was not different between subtypes of GA ($p > 0.05$).
Conclusion: The diagnosis of GA may be challenging due to its morphological diversity. In our study, the most consistent features among the cases were degenerated collagen, dermal mucin, and giant cells. There was no significant relation between pathological features and age, sex, or clinical presentation.

PS-03-004
Cutaneous involvement in multiple myeloma: clinicopathologic findings in a series of 16 cases
A.S. de Oliveira Gomes*, A. Pasco Peña, L.M. Ruíz Estigarribia, M. García Martos, Á. Panizo Santos
*Hospital Universitario de Navarra, Spain

Background & objectives: Cutaneous dissemination as an extramedullary secondary event is uncommon (less than 2%) displaying a diverse cytomorphological spectrum with features according to the degree of maturity and/or differentiation of plasma cells. We analyse 16 cases comparing clinical and pathological features.
Methods: Retrospective review of cases of patients with diagnosed multiple myeloma and skin involvement and/or metastasis from three university hospitals in Spain, over the past 32 years (1992-2024), of which 16 cases were accepted, as they met most of the variables to be studied.
Results: The mean age of the patients was 67 years, and there was no gender predominance. 75% of the patients had extracutaneous metastases. Most of the skin lesions appeared after the diagnosis of multiple myeloma (mean of 21 months), with a more frequent location in the lower extremities. The lesions were mainly nodular, with dermal involvement and diffuse infiltration of plasma cells. The most common immunophenotype was CD138+, CD56+, CD45+, CD79a+, and CD20-. Short-term survival was worse in patients with skin involvement.
Conclusion: In multiple myeloma, skin involvement is generally associated with advanced stages of the disease. Clinically, the process is characterized by the appearance of lesions, which can be macules, papules, nodules, and even violaceous bultons. Microscopically, the lesions showed a dense nodular to diffuse dermal/subcutaneous infiltrate of plasma cells with plasmablastic cytology and preserved CD138 expression. Cutaneous involvement in multiple myeloma is an infrequent event, but with a significant impact on prognosis.

PS-03-005
PRAME (Preferentially Expressed Antigen In Melanoma) immune expression In malign, borderline and benign melanocytic lesions
E. Ekren*, F. Aker
*University of Health Sciences, Haydarpasa Numune Research and Training Hospital, Turkey

Background & objectives: Our study aims to demonstrate PRAME protein expression in malignant, borderline and benign melanocytic lesions and to measure the diagnostic utility of PRAME expression scores in distinguishing malignant lesions from benign lesions.
Methods: PRAME immunohistochemistry was performed on 181 malignant, 18 borderline and 221 benign melanocytic lesions. Prevalence of positive staining cell nuclei compared to all lesions (1:<25%, 2:25-50%, 3:51-75%, 4:>75%) and staining intensity (1: weak staining, 2: moderate staining, 3: strong staining) are evaluated. The combined score was created by the mathematical sum of the prevalence and severity score.
Results: Diffuse positive staining was observed in 93% of in-situ melanomas, 78.6% of invasive melanomas and 80% of melanoma metastases, while 77% of benign melanocytic lesions were completely negative with PRAME. Among melanomas, age, mitosis and ulceration were statistically higher in the diffusely positive group. Among benign lesions, age was statistically higher in the group showing PRAME expression. In the ROC analysis, AUC of the PRAME prevalence score (0.980) was higher than the severity score (0.908) and the combined score (0.976). At the +4 cut-off point, the sensitivity of the PRAME prevalence score in differentiating malignant and benign lesions was 83.67%, its specificity was 100%, and its accuracy was 93,75%.
Conclusion: PRAME immunohistochemistry frequently showed diffuse positivity in in-situ, invasive and metastatic melanomas, whereas sparse and focal staining was observed in benign lesions. While +2 (%>25) prevalence score distinguished melanoma from nevi with 96.6% sensitivity and 96.38% specificity, the optimal cut-off point for evaluating "borderline" lesions was +3 (>50%) prevalence score.

PS-03-006
Sebaceous carcinoma of the skin: gap maps of research evidence cited in the WHO Classification of Tumours 5th edition and of available relevant published evidence: an exploratory comparative study
G. Goldman*, N. Myles, C. Giesen, R. Cierco Jimenez, A. Machado, R. Colling, F. Campbell, T. Lee, I. Cree, D. Lokuhetty, W. EVI MAP group
*IARC/WHO, France

Background & objectives: The WHO Classification of Tumours Evidence-Gap-Map Project aims to advance tumour classification based on best available research evidence. We compared citations on sebaceous carcinoma of the skin in 5th edition, WHO Classification of Tumours (WCT Skin5) to relevant published evidence.
Methods: References on sebaceous carcinoma cited in WCT Skin5 tumours and those available in PubMed were extracted according to structured criteria-based search strings, relevant to tumour characteristics. The references were classified according to study design using EPPI-Reviewer tool, categorised based on Hierarchical levels of Evidence for Tumour Pathology (HETP), plotted, and compared by Chi-squared test. Differences were considered significant at $p<0.05$.
Results: A significant difference was observed in the relative frequencies of citations, depending on evidence levels. In WCT Skin5, non-primary sources (narratives) and low-level evidence studies (case series and case reports) were more frequent than among the PubMed-extracted references ($p<0.05$). Both reference sets showed an overall rarity of high-level evidence, such as systematic reviews. The PubMed evidence contained a higher frequency of moderate level studies, particularly on prognostication of sebaceous carcinoma.
Conclusion: This exploratory study highlights the necessity for enhanced evidence synthesis and assessment to inform classification of uncommon tumours, such as sebaceous carcinoma of the skin, and to bridge evidence gaps for future WCT. The need for higher quality primary studies is also demonstrated. Future tumour classifications should prioritise evidence quality to better serve clinical decision-making and research advancement. WCT EVI MAP is funded by the European Union Horizon grant 101057127.

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PS-03-007
Merkel cell carcinoma of the skin: an exploratory comparative study of gap maps of research evidence cited in the WHO Classification of Tumours 5th edition, and of available relevant published evidence
G. Goldman*, N. Myles, C. Giesen, R. Cierco Jimenez, A. Machado, R. Colling, F. Campbell, T. Lee, I. Cree, D. Lokuhetty, W. EVI MAP group
*IARC/WHO, France

Background & objectives: WHO Classification of Tumours (WCT) Evidence-Map Project (WCT EVI MAP) aims to advance tumour classification based on best available research evidence. We compared citations on Merkel cell carcinoma (MC) in WCT 5th edition of skin (WCT Skin5) to published evidence.
Methods: We extracted 28 references on MC from WCT Skin5, and 607 references from PubMed, using structured criteria-based search strings relevant to tumour characteristics. With the EPPI-Reviewer tool, references were categorised based on study designs, according to the Hierarchical Levels of Evidence for Tumour Pathology (HETP). The results were plotted and compared using a Chi-squared test. A p-value <0.05 indicated significance.
Results: There were no significant differences between the evidence cited in the WCT Skin5 and the evidence available in Pubmed. Both evidence sets showed an overall scarcity of high-level evidence, such as systematic reviews that accounted for 2% and 5% of PubMed and WCT evidence, respectively. The most common were cohort studies, representing 31% and 30% of PubMed and WCT evidence, respectively. The relevant PubMed evidence showed a relative abundance of moderate-level studies, particularly of those related to MC prognostication.
Conclusion: Evidence gap maps may be developed even for uncommon tumours with scarce evidence available. The evidence on MC cited in the WCT Skin5 represented that available on MC in PubMed. The study visualized the available evidence and showed a need for higher-quality primary studies. The identified gaps need to be filled to better inform future WCT editions. WCT EVI MAP is funded by the European Union Horizon grant 101057127.

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PS-03-009
Cutaneous adverse drug reactions
D. Petrovic*, I. Petrovic, K. Kundovic, J. Stojković Filipović, E. Manojlović Gačić, M. Bosić, D. Škiljević, N. Delić, M. Mijuskovic, B. Lekić, S. Minić, M. Gajic Veljic, V. Reljić, D. Zivanovic, J. Perić
*Faculty of Medicine, University of Belgrade, Belgrade, Serbia, Institute for Oncology and Radiology of Serbia, Belgrade, Serbia

Background & objectives: Cutaneous adverse drug reactions (CADR) mimic dermatological or systemic diseases and present in several forms on histology. Our aim was to analyse clinical and histopathological features in patients with CADR and to describe most frequent histological patterns of CADR.
Methods: Retrospective analysis of patient records at the Institute of Pathology, Faculty of Medicine in Belgrade encompassed 8-year period (2016-2023). We analysed demographic, clinical, and histopathological features from 51 patients with clinical suspicion of CADR. Additional information on causative drug was obtained from anamnestic data retrieved from the Clinic for Dermatology and Venereology, University Clinical Centre of Serbia, Belgrade.
Results: CADR was frequent in women (59%) and older patients (>60 years old) (65%), and it was usually referred as lichenoid drug reaction (53%) and toxic allergic exanthema (33%). It often presented with erythematous papules (47%) and plaques (39%), usually with wide distribution, frequently affecting trunk (59%) and extremities (57%). Frequent histological pattern was dermatitis without epidermal involvement (39%), often with eosinophils, followed by interface dermatitis (33%) with seldom presence of eosinophils. Spongiotic pattern was less frequent (14%), even with eosinophils. Granulomatous dermatitis and vasculitis were rare (two cases each). Causative drug was identified in 21 patients, in eight as part of targeted antineoplastic treatment but with no common histological pattern.
Conclusion: Biopsies of CADR were not frequently performed by dermatologists. CADR presented with very heterogeneous histological patterns, often without eosinophils. As such, they could pose a difficult diagnostic dilemma if detailed clinical information is not provided. Cutaneous effects of antineoplastic treatments could be a result of both immune and non-immune-mediated mechanisms. The biopsy should be considered in oncology patients in case of skin eruptions to evaluate it in detail and help in modification of the treatment.

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PS-03-010
Annular lichenoid dermatitis of youth: a series of seven cases
D. Sakız*, G. Öztürk, Z. Topkarcı
*Bakırköy Dr. Sadi Konuk Training and Reserch Hospital, Turkey

Background & objectives: Annular Lichenoid Dermatitis of Youth (ALDY) is recognized as a lichenoid dermatosis, specific clinical and peculiar histologic features and occurs mostly in children and adolescents. The differential diagnosis includes morphea, inflammatory vitiligo, annular erythema, and hypopigmented mycosis fungoides (MF).
Methods: Cases in the archives of our Institute over a period of 8 years, from 2015 to 2022, were included in the study. Clinical,

histopathological findings and treatment responses of all patients were evaluated. The clinical diagnosis included eczema, morphea, mycosis fungoides, pityriasis rosea, and vitiligo. Immunohistochemical examinations were performed on four patients.
Results: Six patients were male, one patient was female. The patients ages ranged between 6-32 years (mean 15,5 years). All cases showed mild basket-woven orthokeratosis, normal granular layer and elongation of rete ridges with a characteristic squared shape at the base of the dermal-epidermal junction, mild to dense basal keratinocyte necrosis was observed, mostly at the tip of rete ridges. A moderate to marked inflammatory infiltrate in a lichenoid pattern of distribution were present in the papillary dermis. Epidermotropism and Pautrier microabscesses were absent. Immunohistochemical analysis showed T cell infiltrate consisting of CD4+ T cells in the dermis, whereas many of intraepidermal T cells were CD8+, CD2+, CD5+ and CD7+.
Conclusion: ALYD is a poorly known distinctive entity, clinical and histological correlation is essential to diagnosis. Annular morphology, absence of desquamation and atrophy, distribution in cutaneous folds and sparing the distal portion of the extremities are typical findings. Histopathological findings are quadrangular epidermal ridges with necrotic/apoptotic keratinocytes at the tips, absence of epidermotropism and eosinophils or plasma cells. The clinical and histological features that help differentiate ALDY from MF and other mimickers are particularly crucial for their proper management and treatment.

PS-03-011
Is it always lupus? A clinicopathological correlation.
E.P. Sánchez López*, M.A. Abad, G. Escuer-Albero, S. Quinones, E. Ruiz-Bravo, M.J. Beato
*La Paz University Hospital, Spain

Background & objectives: Lupus erythematosus is an autoimmune inflammatory disease that presents a wide range of clinical and histological manifestations, which can make diagnosis challenging. The objective of this study is to establish a correlation between clinical suspicion and histological confirmation of lupus.
Methods: We searched for dermatology patients between 2021 and 2022 who had clinical suspicion of lupus/connectivopathy, as well as patients with a histological diagnosis suggestive of lupus. Exclusion criteria involved patients with pre-existing lupus diagnoses. Histological patterns, direct immunofluorescence (DIF) findings, and clinical histories were reviewed, with subsequent acquisition of laboratory data and follow-up information.
Results: We analysed 195 patients, of which 188 had clinical suspicion of lupus. Among them, 70 showed compatible biopsies. Seven patients lacked clinical suspicion but had lupus-compatible biopsies. Of the total cases, 67 underwent DIF, revealing immunoglobulin or complement deposition in 10 cases. However, only two cases correlated with lupus-compatible biopsies. Complement levels and autoantibodies were examined in 159 cases, identifying hypocomplementemia and/or autoantibodies with a lupus-compatible biopsy in 42 cases (21% of total). Vacuolar interface dermatitis was the most common histological pattern found in biopsies consistent with lupus. Lupus was conclusively diagnosed in 47 patients (24% of total), of whom four exhibited histological discordance, and two displayed non-specific findings.
Conclusion: Biopsy assists in diagnosing lupus, necessitating clinical correlation. Our study demonstrates the infrequency of histological lupus diagnosis without clinical suspicion. Lupus clinical and histological features overlap with conditions such as toxicodermia. This was identified as the main histological differential diagnosis, particularly challenging in medicated patients. In lupus-compatible biopsies, the primary clinical differential diagnosis was dermatomyositis, where microscopic findings are indistinguishable from lupus, rendering biopsy unhelpful in distinguishing them. DIF often lacks utility, yielding most negative results despite lupus diagnosis.

PS-03-012
Acral lentiginous melanoma: a clinicopathologic and genetic study of BRAF status among Tunisian patients
Y. Sarra*, H. El Mabrouk, A. Ben Abdelkader, N. Ghariani, I. Bahri, W. Mokni, T. Tlili, B. Sriha, M. Denguezli, D. Hmida
*Department of Pathology, University hospital of Farhat Hached, Souuse, Tunisia

Background & objectives: BRAF mutations have been mainly described in Caucasians patients that mainly carry other subtypes of cutaneous melanoma (CM) than acral lentiginous melanoma (ALM). Aim: to investigate the clinicopathologic features and BRAF status of ALM among Tunisian patients.
Methods: This is a cross-sectional and descriptive study including all ALMs diagnosed in the dermatology department of Farhat Hached University Hospital of Sousse over a period of 13 years. A genetic study of BRAF status (mutated, non-mutated, amplified or deleted) was carried out using the MLPA technique and Sanger-type sequencing
Results: A total of 20 patients were included in this study: 12 man and 8 women. The mean age at diagnosis was 62 yrs. Tumours were all acral mainly located in foot (90%). Breslow thickness varied from 1 to 12 mm with 50% of cases exceeding 4mm. Vascular invasion were seen in 17 cases (80%). The overall survival and disease-free survival rates at 5-years were 18% and 14%, respectively. Genetic study was made possible in only 15 cases: BRAF V600E mutation was detected in 2 patients (13%) simultaneously with a BRAF deletion; Copy number amplification and deletion of BRAF were respectively detected in 2 (13%) and 7 patients (47%).
Conclusion: ALMs is an aggressive disease with higher loco regional recurrence rates and worse survival than non-acral CM of similar T stage. It shows different molecular pathways compared to CM arising in sun exposed area, with a much lower tumour burden mutation and more frequent structures rearrangements as seen in our study from the frequency of BRAF deletion. BRAF mutation occurs in ALM but at lower rates accounting for 13-15% of all ALM.

PS-03-013
Real-life experience with Next Generation Sequencing (NGS) in cutaneous melanocytic lesions
V. Colinet, A. Pouliakis, L. Marot, A. Dekairelle, A. De Roo, E. Harkemanne, L. Secco, V. Siozopoulou*
*Belgium

Background & objectives: A DNA-NGS panel of 117 genes involved in oncology is routinely used to detect mutations that occur in cutaneous melanocytic lesions. Our aim is to determine the most frequent mutations detected by this panel and to correlate with clinicopathological parameters.
Methods: We retrospectively collected NGS molecular data from a panel of 117 genes in 87 cutaneous melanomas and 28 benign melanocytic lesions. We investigated the frequency of mutations and searched for genes in this panel that may be involved in melanoma progression. We collected all demographic and clinicopathologic data of the patients and correlated them with the NGS results.
Results: In the melanoma samples, the most common mutations were in the *TERTp* (54%), *BRAF* (35.6%), *NRAS* (26.4%), *CDKN2A* (14.9%), *TP53* (13.8%), and *NF1* (11.5%) genes. The remaining genes had very low detection levels. The coexistence of *BRAF* and *TERTp*-mutations was significantly associated with metastatic disease (p=0.004) compared to *BRAF* without *TERTp*. *TERTp* as a single marker also correlated with metastatic disease (p=0.007) compared to no-*TERTp* cases. Furthermore, *BRAF* mutation showed higher lymph node metastasis rates (p=0.023) compared to no-*BRAF*. Detection of *TERTp* mutations was higher when NGS was performed on metastatic samples compared to the primary lesions

(p=0.021). *TERTp*, *CDKN2A TP53* and *NF1* mutations were not observed in benign cases.
Conclusion: With our extensive DNA-NGS analysis of 117 genes, the main mutations found in our melanoma set were *BRAF*, *NRAS, NF1*, as well as *TERTp*, *CDKN2A* and *TP53*. The last four were not found in the benign lesions. The rest of the genes examined in this panel did not show a statistically significant correlation, especially in the melanoma samples. *BRAF* mutations, especially when correlated with *TERTp*, have a more aggressive course in our samples.

PS-03-014
Microscopic width of invasion is an independent prognostic factor in cutaneous melanomas
D. Tapoi*, A. Ciongariu, A. Dumitru, M. Costache
*Department of Pathology, University Emergency Hospital Bucharest, Romania

Background & objectives: Cutaneous melanomas rely on the measurement of the Breslow depth for both staging and prognostic estimation. Despite its well-established significance, little is known about the value of other tumour dimensions: the maximum macroscopic diameter and the microscopic width of invasion.
Methods: We analysed 49 pT3 cutaneous melanoma to establish how the macroscopic tumour width, microscopic invasive width, and Breslow depth can predict disease-free and overall survival using Cox proportional hazards regression. Macroscopic width was measured on the surgical specimen. Microscopic width was measured as the distance between the two outermost invasive melanoma cells. Breslow depth was measured according to standard protocols.
Results: Breslow depth was an important prognostic factor for both disease-free survival (HR=6.8; 95%CI:2.4-24.8; p=0.0011) and overall survival (HR=8.81; 95%CI:2.48-48.92; p=0.0034) on univariate analysis, but not on multivariate analysis when other factors such as ulceration, mitotic counts and lympho-vascular invasion were also considered. The maximum macroscopic width was significantly correlated with the microscopic width of invasion (Pearson correlation coefficient=0.6422, p<0.0001). Nevertheless, the macroscopic width was not associated with any outcome. On the contrary, the microscopic width of invasion was a strong independent negative prognostic factor for both disease-free survival (HR=1.3; 95%CI:1.09-1.6; p=0.0057) and overall survival (HR=2.08; 95%CI:1.28-10.96; p<0.028).
Conclusion: Analysing the macroscopic width of invasion does not provide additional prognostic information but the invasive width is a significant predictive factor, even superior to Breslow depth. Therefore, if further studies confirm these findings, the microscopic width of invasion could become a valuable integrated parameter for predicting aggressive behaviour in cutaneous melanomas and could be used to better stratify high-risk patients in order to provide them with the most appropriate therapy.

PS-03-015
Evaluation of histopathological findings of hidradenitis suppurativa lesions and their relationship with the disease course: one centre study
M. Urgancı*, Y.C. Edek, S. Şahin, B. Öğüt, Ö. Erdem, E. Adışen
*Gazi University, Department of Pathology, Turkey

Background & objectives: Hidradenitis suppurativa (HS) is an inflammatory skin disease characterized by painful nodules, abscesses, fistula tracts, and scars. In our study, we assessed the biopsy specimens from patients diagnosed with HS, defined histopathological features and examined their correlation with clinical findings.
Methods: In our single-centre and retrospectively designed study, patients who were followed up with a diagnosis of HS and underwent surgical treatment between 2006 and 2023, and those who had histopathological evaluation of the excision material, were included. The relationship between the histopathological evaluations of these patients and their clinical findings was examined.
Results: In our study, 134 biopsy specimens from 64 patients were evaluated. The most common localization was the axilla; biopsy specimens from the gluteal area, inguinal region, and face were also evaluated. Among the patients, 11 were classified as Hurley stage 1, 35 as Hurley stage 2, and 18 as Hurley stage 3. When the biopsy specimens were examined, the most frequently observed findings were lymphoplasmacytic inflammation (32.8%), abscess formation (31.3%), mixed type inflammation (26.1%), fibrosis (14.1%), foreign body giant cells (14.1%), and acute inflammation (11.8%). Fistula tract appearance, ulceration, and vascular proliferation were among the other observed findings.
Conclusion: Although clinical examination and imaging methods are at the forefront of diagnosis rather than histopathological examination in HS, histopathological evaluation can help in the diagnosis in suspicious cases, understanding the pathogenesis of the disease, determining the inflammatory cell type, and inflammation pattern that predominate in the disease. This study covers a broad spectrum of histopathological findings associated with HS, which can be confounded with different diseases and may present challenges in making a differential diagnosis.

PS-04 Poster Session Digestive Diseases Pathology - Liver/Pancreas
PS-04-001
Standardization of terminology, definition, pathologic evaluation and reporting of ampullary cancers: recommendations of "Peri-Pan" multidisciplinary international group
M. Abu Hilal, B. Uijterwijk, C. Verbeke, V. Adsay*
*Onalti Dokuz Sitesi, Abay Caddesi C Blok 57, Turkey

Background & objectives: Terminology and definition of ampullary cancers (ACs)are fraught with challenges. The PERIPAN international multidisciplinary consensus group was established with the aim to standardize the multidisciplinary diagnostic workflow and achieve consensus on definitions and classifications to improve patient care and future research.
Methods: An international team of 43 experts from 12 countries identified knowledge gaps, reviewed 37.061 articles on these topics, and proposed recommendations using the Scottish Intercollegiate Guidelines Network methodology (SIGN), including the Delphi methodology, 38 consensus questions and 51 recommendations were developed. The most salient of these pertinent to pathologists were presented here.
Results: I. A neoplasm is qualified as ampullary if its (epi)centre is in the intra-Oddi segments of Wirsung/CBD, or papilla of Vater, or the duodenum-facing surface of the ampulla II. Proper grossing is crucial. III. Historical literature and archival databases should be evaluated cautiously due to highly variable definitions. IV. The non-specific term "periampullary" should be avoided in final diagnosis. V. Histologic type should be documented based on the invasive component only along with its size. VI. For cases not classifiable as intestinal/pancreatobiliary, "tubular,NOS" is recommended, preferably with predominant lineage recorded, supported by IHC composed of MUC1/MUC2/CDX2(with the acknowledgement that they are not specific). VII. Synoptic reporting documented in guidelines should be used. VII. IHC for MSI is recommended.
Conclusion: These recommendations are expected to allow more standardized classification and reporting of ACs, towards a more uniform and refined diagnosis, prognostication, and management.

PS-04-002
Hepatic small vessels neoplasms: a heterogeneous morphological entity
A. Beaufrère*, A. Laurent-Bellue, A. Lemoine, A. Bourillon, V. Vilgrain, M. Lewin, C. Guettier, V. Paradis

*Department of Pathology, Hôpital Beaujon, AP-HP.Nord, Clichy, France

Background & objectives: Hepatic small vessel neoplasm (HSVN) is a recently described liver vascular neoplasm, considered as a low-grade entity with few described cases. Our objective was to review a set of HSVN in order to refine their classification based on patho-molecular features.
Methods: We conducted a bicentric retrospective study including 20 HSVN cases (12 surgical specimens and 8 biopsies) reviewed by 4 liver pathologists. Immunostainings by ERG, CD31, CD34, D2-40, Glut1, p53, c-Myc and Mib1 were performed for all cases. Targeted DNA NGS was performed in 16 cases.
Results: Two HSVN morphological patterns were identified: (1) a classic pattern (n=13, 65%) composed of small thin-walled vessels and (2) a hepatocellular-reactive pattern (n=6, 35%) characterized by small vessels outlined by regenerative hepatocellular trabeculae. No atypia nor mitosis were noted. Tumour cells were immunostained by ERG, CD31 and CD34. No expression of D2-40, Glut1 or c-Myc was noted. A wild-type p53 profile was always observed. Mib1 was inferior to 10% in all cases. Twelve cases (75%) presented GNA14 mutations (9 and 3 in patterns 1 and 2, respectively, p=1.00) and three (15%) GNAQ mutations (2 and 1 in patterns 1 and 2, respectively, p=1.00).
Conclusion: HSNV is a heterogenous morphological entity including two different patterns (classic and hepatocellular-reactive), harbouring GNA14 or GNAQ mutations in 90% of cases. Noticeably, HSVN hepatocellular-reactive pattern may mimic hepatocellular adenoma, especially on biopsy specimen.

PS-04-003

Dysregulated TGF/BMP signalling and tumour budding in pancreatic ductal adenocarcinoma

K. Bräutigam*, P. Zens, J.L. Rohrbach, S.L. April-Monn, J. Galván, A.S. Wenning, B. Gloor, V.H. Koelzer, M. Wartenberg
*Institute of Cancer Research, Centre for Evolution and Cancer, London, United Kingdom

Background & objectives: Transforming-growth-factor (TGF) signalling in Pancreatic Ductal Adenocarcinoma (PDAC) is paradoxical (tumour-promoting and/or -suppressive). Disrupted signalling, e.g. through bone-morphogenetic-proteins (BMPs), can lead to epithelial-mesenchymal-transition, and more aggressive PDAC. This study quantifies key signalling-molecules with particular regard to tumour budding.
Methods: We stained a tissue-microarray (TMA) cohort of 117 curatively-resected PDAC for Inhibitor-of-DNA-binding-1 (ID1) and phospho-smad2 (psmad2) and investigated mRNA-expression of TGFA, TGFB1, TGFB2, GREM1 and BMP4 by in-situ-hybridisation. Digital image analysis and spatially-resolved analysis of marker expression were carried out using HALO (Indica Labs, USA) in the PDAC parenchyma, lymphocyte-rich and -poor stroma. Quantitative scores were correlated with clinicopathologic features.
Results: GREM1 and TGFB2 mRNA-expression was significantly lower ($p<0.05$) in malignant glands than in associated stroma. Interestingly, tumours with elevated GREM1 or TGFB2 expression mostly demonstrated high-grade tumour budding. ID1 expression was universally higher in malignant glands than in associated stroma ($p<0.001$). ID1-high tumours showed more frequent perineural and blood vessel invasion. Higher tumoural psmad2 expression correlated significantly with the presence of perineural invasion ($p<0.05$). Trends (non-significant) towards worse survival were observed for high stromal ID1 and psmad2, low tumoural TGFB2, and low stromal TGFB1. No significant differences were found between tumour centre and tumour front, tumour size or lymph node status, for any of the molecules investigated.
Conclusion: We observed that dysregulated TGF/BMP signalling, i.e., upregulation of ID1 in PDAC and lower levels of TGFB2 and -B1 in the tumour and associated stroma respectively, tended to go along with worse survival in PDAC. GREM1, TGFB2 and psmad2 were associated with a more aggressive PDAC phenotype with high tumour budding and perineural invasion.

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PS-04-004

The application of standardized sampling protocols enhances assessment of clinicopathological features in pancreatoduodenectomy specimens

M.S. Brito*, S. Silva, E. Campos, J. Lopes, M. de Almeida, H. Cristino, L. Graça, F. Carneiro, V. Adsay, I. Gullo
*Pathology Department, Centro Hospitalar Universitário de São João, Porto, Portugal

Background & objectives: The correct handling of pancreato-duodenectomy specimens (PDS) is the cornerstone for accurate histopathological assessment, including tumour origin, histological classification, margin/surface involvement and lymph-node status. Aim: to compare clinico-pathological features of PDS in which non-standardized and standardized grossing techniques were applied.
Methods: A series of 169 PDS was selected retrospectively, including 92 PDS (2017-2020) sampled by non-standardized grossing techniques (nsPDS) and 77 PDS (2021-2023) in which a standardized grossing technique was applied (sPDS), namely application of "bi-valving" and "orange-peeling" methods. Clinicopathological variables were collected, including prognostic outcomes, i.e. overall-survival (OS) and relapse-free-survival (RFS). IBM SPSS was used for statistical analysis.
Results: General tumour location (pancreas/biliary-duct/duodenum/ampullary-region) did not differ significantly between nsPDS and sPDS, but ampullary-carcinomas in sPDS were categorized into specific subtypes almost invariably (9/10;90.0%), compared to nsPDS, mainly classified as not-otherwise-specified (10/15;66.7%; p=0.007). The mean number of total/peri-pancreatic lymph-nodes identified in sPDS was 30.3/16.1 compared to 16.8/9.4 in nsPDS ($p<0.001$). Microscopic involvement of surgical margins (R1) was more frequently detected in sPDS (24/70;34.3%) than nsPDS (13/71;18.3%; p=0.031). However, relapse occurred more frequently in nsPDS (29/90;32.2%) compared to sPDS (9/77;11.7%; p=0.002). RFS correlated to vascular involvement of vessel structures referred separately (4 months (CI95% 0.0-12.8) versus 15 months (CI95% 12.1-17.0); p=0.034) and R status (R0 –19 months (CI95% 14.0-21.0) versus R1 –8 months (CI95% 4.6-11.4); $p<0.001$).
Conclusion: Evidence from the literature has stressed the importance of standardized grossing protocols for accurate histopathological evaluation in PDS. This study confirms the benefit of "orange-peeling" method and total-embedding of uncinate/retroperitoneal margin to optimize lymph-node yield and evaluation of R status. Particularly, in this case series, inaccurate R status evaluation in the nsPDS subgroup resulted in underestimation of disease relapse/progression, compared to sPDS. Moreover, the systematic introduction of the "bi-valving" method was able to provide more accurate classification of ampullary-region carcinomas.

PS-04-005

Analysis of tissue PSMA expression in hepatocellular carcinoma – compared to prostate adenocarcinoma – and correlation with PET with 68Ga-PSMA uptake

M. Carroli*, F. Giunchi, L. Vetrone, L. Cardisciani, M. Renzulli, A. D'Errico, A. Farolfi, F. Vasuri
*Pathology Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy

Background & objectives: The aim of this study is to analyse the relationship between tissue prostate-specific membrane antigen (PSMA) expression and PET with 68Ga-PSMA in hepatocellular carcinoma (HCC), compared to prostatic cancer (PCa), to be applied for theragnostic (i.e., both diagnostic and therapeutic) purposes.
Methods: Twenty-one patients, surgically resected for HCC, were prospectically enrolled, together with 19 patients with PCa enrolled for comparison. Clinical and pathological data were collected, including the Standardized Uptake Value (SUV) at 68Ga-PSMA-PET, performed shortly before surgery. PSMA immunohistochemistry(IHC) and immunofluorescence(IF) were performed on paraffin-embedded material: in PCa, PSMA was expressed as intensity of positivity, in HCC an immunoreactive score(IRS) was applied.
Results: As expected, in PCa PSMA positivity was observed in tumour cells, on cell membranes (15.8%), cytoplasms (47,4%) or both (36.8%); in 13 (68.3%) cases, positivity was strong. In PCa, PSMA expression correlated significantly with cribriform pattern (p=0.017, Fisher's test) and with SUV at 68Ga-PSMA-PET (p=0.024).
PSMA expression in HCC was never seen at tumour cell level, but in neoarteries and sinusoidal endothelia, with a mean IRS 5.8 (range 0-12) and 6 (28.6%) negative cases. Conversely to PCa, IF showed some usefulness in HCC, highlighting more positive sinusoids in doubtful cases. IRS correlated with high Edmondson grade (p=0.054, Mann-Whitney test) and with SUV at 68Ga-PSMA-PET (p=0.020, Spearman's test).
Conclusion: PSMA expression was very different between our two models of human cancers, being positive in tumour PCa cells and in the vascular component of HCC. Anyway, similar results were observed: PSMA increases with Edmondson grade in HCC and in cribriform PCa, suggesting an utmost usefulness of 68Ga-PSMA-PET for the treatment and follow-up of high-grade cancers. Further studies are required to understand better the correlations between PSMA expression and SUV –together with the real routine usefulness of IF– in HCC.

PS-04-006
Histological grading of the extent of residual tumour following neoadjuvant therapy in intrahepatic cholangiocarcinoma
G. Wu, X.F. Chen*, R. Luo, Y.X. Koh, T.K.H. Lim, J. Zhou, J. Fan, K. Zhu, Q. Gao, R. Shi
*Department of Anatomical Pathology, Singapore General Hospital, Singapore

Background & objectives: There are emerging roles of neoadjuvant therapy in intrahepatic cholangiocarcinoma (iCCA). However, a histological grading scheme of residual tumour correlated with prognosis is lacking in the literature.
Methods: Histological slides of 151 cases of post-neoadjuvant iCCA resection were reviewed. Intrahepatic cholangiocarcinoma regression score (iCCR) was developed by using a stepwise 5% increment of the residual tumour. The best cut-off was determined by correlating with overall survival (OS) and recurrence free survival (RFS). College of American Pathologists (CAP) and MD Anderson systems (MDA) tumour regression grades were also scored.
Results: The grading of iCCR was as follows: iCCR 0, tumour with complete response; iCCR 1, 1% to 10% of residual tumour; iCCR 2, more than 10% of residual tumour. Patients with minimal residual tumour (iCCR 0 or 1) had longer OS (p=0.027) and RFS (p=0.001) than those with iCCR 2. CAP (p=0.025) and MDA (p=0.016) scores correlated significantly with RFS, but no statistical difference in OS. By univariate analysis, only iCCR correlated significantly with OS (p=0.043, HR: 4.389, 95% CI:1.048-18.383), while all systems iCCR (p=0.002, HR: 3.123, 95% CI: 1.500-6.501), MDA (p=0.01, HR: 2.589, 95% CI: 1.262-5.352) and CAP (p=0.003, HR: 1.675, 95% CI: 1.199-2.342) correlated significantly with RFS.
Conclusion: Our iCCR showed minimal residual tumour of 10% or less (iCCR 0 or 1) correlated significantly with longer OS and RFS. We proposed iCCR, a novel scoring system which is easily applicable with specific cut-off, to be incorporated into the routine pathology reporting of post-neoadjuvant iCCA.

PS-04-008
Utility of metallothionein 1 (MT-1) as a histological biomarker of Wilson's disease
C. Fuster Anglada*, G. Caballero, C. Garcia-Solà, A. Soria, O. Bassegoda, A. Pocurull, X. Forns, I. Graupera, Z. Mariño, A. Díaz
*Pathology Department. Hospital Clinic. University of Barcelona. Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Spain

Background & objectives: Histopathology of Wilson's disease (WD) is nonspecific. Recently metallothionein-1 (MT-1) immunostaining has been proposed as a diagnostic marker of WD. The aim of this study was to evaluate the usefulness of MT-1 to distinguish WD from other liver diseases.
Methods: Retrospective study including 95 liver biopsies from a referral centre. Histopathological evaluation as well as assessment of MT-1 immunohistochemistry (according to Rowan et al) was blindly done by two pathologists. Variables are expressed as medians/IQR25-75 or percentages. Statistical analysis was done with Chi2/U-Mann-Whitney, and the Kappa index was used for inter-observer agreement.
Results: The study includes 24 WD and 66 non-WD biopsies (including 33 MASLD, 10 biliary diseases, 5 cirrhosis, 6 ALD, 5 minimal changes, 4 acute hepatitis and 3 other pathologies) and 5 normal controls. When comparing WD and MASLD, glycogenated nuclei were more present in WD (p=0.033) and steatohepatitis was only observed in MASLD (41%, p<0.01). MT-1 was positive in 63% of WD biopsies and negative in non-WD biopsies (p<0.01), with an H-score of 205 (IQR25-75 117.5 - 272.5) in WD vs H-score of 0 (IQR25-75 0 - 3) (p<0.01) in non-WD. Control cases were negative. Inter-observer agreement was excellent (kappa=0.896). The sensibility of MT-1 is 63% and specificity 96%.
Conclusion: The use of MT-1 is a valid strategy to histologically differentiate between WD and other hepatopathies, with high specificity. This immunohistochemical marker could be useful in clinical practice because of its low economic cost, easy applicability and quick results in a pathology service, compared to intrahepatic copper quantification, which could be reserved only for MT-1 negative but with high clinical suspicion of WD.

PS-04-009
Next-generation pathology insights on cholangioblastic cholangiocarcinoma cell of origin
A. Gambella*, L. Lesniak, A. Lesniak, M. El-Hag, J. Carpenter, A.J. Demetris
*Pathology Unit, Department of Medical Sciences, University of Turin, Turin, Italy - Division of Liver and Transplant Pathology, University of Pittsburgh, Pittsburgh, USA

Background & objectives: A rare cholangiocarcinoma variant with distinctive histopathological features has been variously denominated, including cholangioblastic cholangiocarcinoma (CbCC), owing to its putative oncogenesis from blast-like biliary cells. This study evaluated CbCC cells of origin starting from a case exhibiting hepatocellular differentiation.
Methods: Representative tumour tissue sections of a CbCC case were subjected to next-generation pathology (NGP) assay (i.e., tissue-tethered cytometry and multiplex immunohistochemistry) to assess CbCC tumour cell nuclear area (NA) and protein expression of Hepatocellular-Nuclear-Factor-4-alfa (HNF4α), Hepatocellular-Nuclear-Factor-1-beta

(HNF1β), Arginase-1 (Arg1), and cytokeratin-19 (CK19). CbCC tumour cell profiles were compared with 118252 endogenous liver cells from a normal adult human tissue control.
Results: A CbCC case with otherwise typical histopathological features presented focal hepatocellular differentiation (Arg1 expression). NGP granular analysis of 179322 CbCC tumour cells confirmed two different subpopulations: a prevalent subgroup (142953/179322 tumour cells, 79.7%) showing biliary-only differentiation (HNF4α-/HNF1β+/Arg1-/CK19+) and small nuclei (median-NA: 39.1 μm2), and a minor subgroup (36369/179322 tumour cells, 20.3%) presenting hybrid biliary-hepatocellular differentiation (HNF4α+/HNF1β+/Arg1any/CK19+) and larger nuclei (median-NA: 58.0 μm2; p<0.001). These features resembled those of endogenous liver cells, specifically HNF4α-/HNF1β+/Arg1-/CK19+ biliary epithelial cells (BEC; 3301/118252, 2.8%) with small nuclei (median-NA: 31.5 μm2), and HNF4α+/HNF1β+/Arg1any/CK19+ hybrid transitional cells (HTC; 768/118252, 0.6%) with larger nuclei (median-NA: 36.7 μm2; p<0.001). Accordingly, CbCC tumour cells were classified as BEC-like and HTC-like.
Conclusion: We report the first case of CbCC with focal yet definite hepatocellular differentiation, confirmed by NGP-driven identification of an HTC-like tumour cell subpopulation expressing both biliary (HNF1β) and hepatocellular (HNF4α) nuclear transcription factors. The expansion of this bipotential subpopulation in CbCC compared to healthy liver control supports its role as the cell of origin of CbCC and endorses the hypothesis of CbCC oncogenesis from a progenitor cell with hybrid blast-like differentiation.

PS-04-010
MTAP deficiency is highly homogenous in pancreatic cancer: a heterogeneity tissue microarray study
N. Gorbokon*, K. Teljuk, N. Schraps, K. Möller, S. Büyücek, M. Lennartz, F. Viehweger, S. Steurer, R. Simon, G. Sauter, F. Lutz, T.S. Clauditz, M. Kluth
*Institute of Pathology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

Background & objectives: S-methyl-5′-thioadenosine phosphorylase (MTAP) deficiency can render cancer cells sensitive to drugs targeting MTAP-dependent pathways. We earlier reported MTAP expression loss in 33.0% of pancreatic adenocarcinomas, but little is known about the intratumoural homo-/heterogeneity of the alteration.
Methods: A heterogeneity tissue microarray containing 708 tissue spots from multiple blocks (6 remote areas) from each of 118 adenocarcinomas of the pancreas was analysed by MTAP immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH). A loss of MTAP was considered when tumour cells showed lack of detectable immunostaining while surrounding non-neoplastic tissues showed nuclear staining.
Results: MTAP IHC of the 6 arrayed spots per tumour was interpretable in 1 spot in one tumour, in 2 spots in 13 tumours, 3 spots in 20 tumours, 4 spots in 31 tumours, 5 spots in 28 tumours, and in all 6 spots in 17 tumours. Eight tumours lacked any MTAP results. Of the 96 tumours with at least 3 interpretable spots per tumour, 35 (36.5%) had a complete MTAP loss in all spots, and 61 (63.5%) had only MTAP-positive spots. There was also no heterogeneity in the 13 tumours with 2 interpretable spots: 6 had MTAP loss in both spots, and 7 were MTAP positive in both spots.
Conclusion: Pancreatic adenocarcinoma belongs to tumour entities with highest rates of MTAP deficiency. Our data suggest that MTAP expression loss is largely homogenous in pancreatic adenocarcinomas. If therapies targeting MTAP deficiency should be effective, patients with MTAP deficient pancreatic cancer might benefit from such drugs.

PS-04-011
Differential expression of EpCAM in the spectrum of cholangiocarcinoma: correlation with pathological parameters, peritumoural immune cells and overall survival
I. Grypari*, B. Goeppert, P. Schirmacher, S. Roessler
*Pathology Institute University Hospital of Heidelberg, Germany & Aretaieion Hospital, NKUA Greece

Background & objectives: Cholangiocarcinoma (CCA) is the second most common primary hepatic malignancy with an unfavourable prognosis [1]. Epithelial-cell-adhesion-molecule (EpCAM) is a transmembrane glycoprotein, mediating cell adhesion in normal cells and various malignancies [2] including CCA and is associated with diminished survival [1].
Methods: We examined the immunohistochemical expression of EpCAM in 220 patients, including N=41 intrahepatic CCA-iCCA, N=49 perihilar CCA-pCCA, N=70 distal CCA-dCCA, N=60 gallbladder carcinomas-GBC and N=16 patients without invasive carcinoma. Additionally, non-neoplastic normal tissue (N=117), dysplastic biliary epithelium (N=82) and lymph node metastasis (LN metastasis, N=66) were analysed. EpCAM expression was correlated with CD4-/CD8-/CD20-/CD68-/CD117-/CD25- and FoxP3-positive immune cells and overall survival.
Results: EpCAM expression in tumour differentiated among CCA histology subtypes (p=0.009) and T stage (Chi-square: 18.359, p=0.031). EpCAM manifestation in CCA was related with normal bile epithelium expression levels (Chi-square:21.744, p= 0.01). Strong associations were revealed between primary tumour and secondary infiltrated tissues (R=0.61, p <0.001) and vascular invasion (R=1, p<0.001). EpCAM positivity in LN metastasis was linked with total numbers of CD20- (R=0.387, p=0.005), CD25- (R=0.343, p =0.016), CD68- (R=0.434, p=0.001), CD8- (R=0.279, p=0.005) and FOXP3-positive cells (R=0.364, p=0.009). EpCAM expression in metastatic foci altered in subtypes of CCA based on anatomic location (p=0.028). Overall survival was associated with EpCAM levels in patients with GBC (p=0.047) and dCCA (p=0.006).
Conclusion: EpCAM is variably expressed in different histology subtypes of CCA and different tumour stages, while it is associated with EpCAM expression in normal bile ducts. Furthermore, patients' overall survival is connected with the degree of tumoural EpCAM expression which is consistent with literature [1]. Interestingly, a weak positive interplay between total and specific intraepithelial immune-cells and EpCAM in LN metastasis is highlighted, implying that the microenvironment of lymph nodes possibly modifies the ability of malignant cells to adhere and migrate.

PS-04-012
Clinicopathological characteristics of pancreatic polypeptide-producing neuroendocrine tumour
K. Hirabayashi*, T. Minamisaka, Y. Fukumura, Y. Naito, Y. Okubo, B. Miichi, T. Tajiri, N. Nakamura
*University of Toyama, Japan

Background & objectives: The aim was to elucidate the clinicopathological features of pancreatic polypeptide-producing neuroendocrine tumours (PP-NETs, known as PPomas) through collaborative efforts in Japan.
Methods: This analysis included 286 pancreatic NET cases from six institutions. PP-NETs were defined using immunohistochemistry as tumours with more than 50% PP-positive cells, and various clinicopathological factors were evaluated. In addition, immunohistochemistry for PDX1 and ARX was performed on the PP-NETs.
Results: Thirteen (4.5%) patients, five men and eight women, were identified as having PP-NETs, with a mean age of 60.6 years. The

tumours were mainly located in the pancreatic head (n = 6) and body/tail (n = 7), having a mean diameter of 29.1 mm. Nine and four cases were G1 and G2, respectively. Lymph node metastasis occurred in three patients, and liver metastasis in one person at surgery. Two postoperative recurrences occurred in both liver metastases: one at 50 months and the other at 103 months after surgery, and the patient died 113 months after surgery. Immunohistochemical analysis showed that all PP-NETs were ARX-positive, and six cases were PDX1-positive.
Conclusion: This multicentre study revealed the clinicopathological features and immunohistochemical characteristics of PP-NETs in Japan. ARX is associated with α and PP cell differentiation, whereas PDX1 is associated with β-cell differentiation. The immunohistochemistry results of this study suggest the existence of two subtypes of PP-NETs: α/PP-like and α/PP+β-like. Furthermore, the incidences of postoperative recurrence and death emphasize the need for long-term follow-up strategies for patients with PP-NETs.

PS-04-013
Risk factors of lymph node metastasis and prognosis in 977 Chinese patients with submucosal early gastric carcinoma, emphasizing differences between gastric cardiac and non-cardiac origins
Q. Huang*, Y. Cheng, M. Du, Y. Wang, T. Li, C. He, X. Zhou, M. Lin
*Beth Israel Deaconess Medical CTR, USA

Background & objectives: Differences in risk factors of lymph node metastasis (LNM) and prognosis between submucosal early gastric cardiac (SEGCC) and non-cardiac (SEGNCC) carcinoma remain unclear
Methods: In this retrospective multicentre study, we investigated and compared risk factors (RF) of LNM and prognosis in consecutive 977 patients with radical gastrectomy for SEGCC (n=242) or SEGNCC (n=735). Submucosal early gastric carcinoma was defined microscopically as tumour invasion into superficial (SM1, < 500 μm) or deep (SM2, >500 μm) submucosa layer.
Results: In the cohort, significant RF for LNM included female sex (FS), poor tumour differentiation, tumour size, histology type, SM2, lymphovascular invasion (LVI), and intermediate/high tumour budding grade (IHTBG), whereas the macroscopic type (TMT), and perineural invasion were RF for LNM in SEGNCC only. Independent RF for LNM comprised FS, LVI, and IHTBG in SEGCC, but were FS, TMT, high-grade papillary/mixed adenocarcinoma, LVI, and IHTBG in SEGNCC. The 5-year overall survival (OS) was significantly worse in SEGCC than in SEGNCC patients with LNM. Independent RF for OS included LNM in SEGCC, but also comprised age ≥70 years, tumour size >3 cm, and micropapillary adenocarcinoma in SEGNCC.
Conclusion: Independent RF for LNM included FS, LVI, and IHTBG in SEGCC, but contained FS, TMT, high-grade papillary adenocarcinoma, mixed adenocarcinoma, LVI, and IHTBG in SEGNCC. Similarly, the independent RF for worse prognosis was only LNM in SEGCC, but included age >70 years, tumour size >3.0 cm, micropapillary adenocarcinoma, and LNM in SEGNCC. The evidence presented in our study argues for individualized clinical management strategy for those two groups of submucosal early gastric carcinoma patients.

PS-04-014
Single-cell atlas of pancreatic cancer reveals tumour heterogeneity and microenvironmental interactions
M. Jang*, E.K. Kim, J.H. Lee
*Department of Pathology, National Health Insurance Service Ilsan Hospital, Republic of Korea

Background & objectives: Pancreatic cancer exhibits extensive heterogeneity and an immunosuppressive microenvironment, hindering effective treatment. Single-cell transcriptomics enables high-resolution profiling of cellular diversity within tumours. This study aimed to comprehensively characterize cellular heterogeneity and microenvironmental interactions in pancreatic cancer using single-cell RNA sequencing.
Methods: Single-cell RNA sequencing analysed 65,350 cells from 6 pancreatic cancer samples, enabling characterization of cellular heterogeneity, subpopulations, tumour microenvironment, and cell-to-cell interactions. This high-throughput technique simultaneously measured expression of thousands of genes per cell, providing insights into communication between different cell types.
Results: Single-cell sequencing identified 4 epithelial cell clusters (classical, basal, secretory, and proliferating type), along with 2 cancer-associated fibroblast clusters displaying inflammatory (iCAF) and myofibroblast (myCAF) characteristics. Cell-cell interaction analysis revealed that iCAFs and myCAFs are involved in distinct pathways modulating the tumour microenvironment. Comparison between microsatellite instability-high (MSI-H) and microsatellite stable (MSS) cases revealed a lower proportion of MDSCs in MSI-H tumours. The iCAF subset was more abundant in MSI-H cases, while myCAFs were less prevalent compared to MSS tumours. These findings highlight the distinct tumour microenvironment compositions associated with different molecular subtypes of pancreatic cancer.
Conclusion: This single-cell study unveiled cellular heterogeneity within pancreatic tumours. Distinct subpopulations of epithelial tumour cells and CAFs were identified. Notably, MSI-H tumours displayed reduced MDSC but higher iCAF proportions with distinct pathway activation, implying potential differences in immune evasion strategies and stromal dynamics between subtypes. These findings provide a valuable resource for further dissecting cell interactions, signalling networks, and functional states, enabling precise patient stratification, novel therapeutic target discovery, and development of tailored treatments.

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PS-04-015
Comprehensive immunohistochemical profiling of combined hepatocellular carcinoma and cholangiocarcinoma reveals distinct Notch signalling subgroups with prognostic significance
S. Kim*, C.M. Yang, Y. Kim
*Department of Pathology, Ajou University School of Medicine, Republic of Korea

Background & objectives: Combined hepatocellular carcinoma and cholangiocarcinoma (cHCC-CCC) is a distinct neoplasm other than HCC and CCC. Notch signaling pathway has been reported to play an important role in its carcinogenesis, but its significance in clinical samples has not been fully investigated.
Methods: We evaluated surgically resected specimens of 38 HCCs, 32 CCCs and 42 cHCC-CCCs, collected from 2017 to 2023 in Ajou University Hospital. Expression levels of HCC, CCC, and cHCC-CCC markers, as well as Notch signalling components were investigated through immunohistochemistry.
Results: cHCC-CCC reveals lower expression of Glypican-3 ($p<0.0001$) and higher expression of CK7 ($p<0.0001$), CK19 ($p<0.0001$), and EpCAM ($p<0.0001$) than HCC. cHCC-CCC reveals higher expression of NOTCH1 compared to HCC (mean H-score 43.9 vs. 24.0, $p<0.01$) and CCC (mean H-score 43.9 vs. 29.4, $p<0.05$). Also, higher expression of Hes5 was identified in cHCC-CCC compared to HCC (mean H-score 52.7 vs. 8.6, $p<0.0001$) and CCC (mean H-score 52.7 vs. 27.0, $p<0.01$). Interestingly, the cHCC-CCCs could be classified into Notch1-high/Hes1-low (n=19), Notch1-intermediate/Hes1-intermediate (n=15), and Notch1-low/Hes1-high (n=6) subgroups. The Notch1-high/Hes1-low subgroup includes the highest number of patient deaths (36.8%) compared to the other two groups (20.0% and 16.7%).

Conclusion: The Notch signalling components are significantly expressed in cHCC-CCC compared to HCC and CCC. Among the cHCC-CCCs, tumours with Notch1-high/Hes1-low expression reveal a worse prognosis.

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PS-04-016

The usefulness of liver biopsy in immune checkpoint inhibitor-induced liver injury diagnosis and management

M. Komuta*, R. Izai, S. Ogasawara, M. Sawada, S. Yumita, M. Nakagawa, R. Kojima, K. Koroki, H. Kanzaki, M. Inoue, M. Nakamura, N. Kanogawa, T. Kondo, S. Nakamoto, N. Kato
*Department of Pathology, International University of Health and Welfare, School of Medicine, Narita Hospital, Japan

Background & objectives: Immune checkpoint inhibitor (ICI)-induced liver injury has become a significant concern due to the increasing number of cases secondary to the widespread use of ICIs, and the diagnostic challenges posed by complex clinical situations and lack of specific histological features.
Methods: We investigated the clinicopathological features of 22 ICI-induced liver injury patients by analysing liver biopsy specimens to clarify the histological patterns and their clinical significance, including treatment options. This study included 22 patients, with hepatocellular carcinoma (n=12) being the most common malignancy. Ten patients underwent biopsies prior to ICI treatments, allowing for successful comparison to ICI-induced liver injury.
Results: The median time from the start of ICI treatment to the development of liver dysfunction (LDF) was 52 days. Sixteen patients had grade 3 or higher LDF, with 14 requiring steroid treatment. Pathologically, 19 (86.4%) patients demonstrated a hepatitis pattern, 2 exhibited a cholangitic pattern, and one had a mixed pattern. Among the 19 with a hepatitis pattern, 7 patients had solely lobular hepatitis, often associated with chronic liver diseases, presenting portal inflammation. By comparing these with the previous biopsies, ICI-induced liver injury was able to be diagnosed. Twelve patients exhibited centrilobular necrosis with/without lobular hepatitis, often requiring steroid treatment due to significant LDF. Underline liver disease was not identified.
Conclusion: Our study was able to characterize ICI-induced liver injury patterns and their clinicopathological significances, including treatment options. This emphasizes the crucial role of liver biopsy in ICI-induced liver injury diagnosis. Moreover, pre-treatment biopsy was useful in determining injury patterns and severity, especially in patients with chronic liver diseases.

PS-04-017

Different cancer-associated stroma in biliary tract tumour compared to pancreas cancer

K. Lee*, B. Yu
*Department of Pathology, College of Medicine, Seoul National University, Republic of Korea

Background & objectives: Squamous molecular subtype of pancreas cancer has quasi-mesenchymal or activated stroma with squamoid tumour. This study aimed to classify the tumour stroma of biliary tract tumours based on the approach of pancreatic cancer and to compare the two organ systems.
Methods: 725 resected pancreato-biliary tract carcinomas (212 pancreases, 91 ampullae of Vater (AOV), 104 gallbladder (GB), 72 extrahepatic bile duct cancer (EHBD), 129 large duct type intrahepatic cholangiocarcinoma (LIHD), 117 small duct type intrahepatic cholangiocarcinoma (SIHD) were enrolled, and formalin-fixed paraffin-embedded tissues were immunohistochemically stained for six proteins (AGR2, FAP, MYH9, ITG2, FZD1, PCNA).
Results: Profiling of six markers of pancreas cancers classified biliary tract tumours into four subtypes activated cancer-associated fibroblasts (TS2, high FAP), activated WNT /rho pathway (TS3, high MYH9/ITG2), increased proliferative activity (TS4, high PCNA low all markers), and progenitor subtype (TS1, high AGR2). TS1 subtype was the highest in AOV cancer (51%) and the lowest in SIHD (10%). TS4 was the largest subtype in all organs except AOV tumour and highest in EHBD (79%). Common findings in all organs are high tumour cellularity in TS1, poor differentiation in TS3, and a high portion of squamoid or oncocytic cell type in TS3. TS1 has a better prognosis in all organs except LIHD.
Conclusion: Pancreatobiliary tract cancers commonly have desmoplastic or fibroblastic cancer-associated stroma, but the heterogenous proportion of three activated stroma subtypes and one inactivated stroma. Tumour cells in the same subtype have the same tumour features and similar survival features, suggesting the interaction of tumour cells with stroma and the effect of tumour-associated stroma on tumour cells. Different portions of subtypes may mean different carcinogenesis or risk factors in each organ. Survival differences of subtypes in LIHD should be further analysed.

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PS-04-018

Homozygous V444A c.521T>C polymorphism of the ABCB11 gene implies architectural changes and bile duct loss in patients with adult–onset cryptogenic cholestasis

D. Malvi*, E. Albertini, G. Vitale, A. Conti, S. Ferrari, M.C. Morelli, A. D'Errico, F. Vasuri
*IRCCS Azienda Ospedaliero-Universitaria di Bologna, Italy

Background & objectives: Progressive familial intrahepatic cholestasis (PFIC) is a broad group of genetically-determined liver diseases with specific clinical and morphological alterations, relatively well studied in the child/newborn. Here we studied adult-onset cryptogenic cholestasis (ACC) histopathological patterns in patients tested for a cholestasis gene panel.
Methods: Thirty-two patients were retrospectively re-evaluated so far, mean age 43±15years, with a clinical diagnosis of ACC at adult age; in all cases, genetic analysis was performed, with multiplex PCR-NGS (15-gene panel). Liver biopsy was performed due to a raise in cholestasis serum markers. Sixteen histological variables were reviewed with Haematoxylin-Eosin and Reticulin stains, together with Keratin-7, BSEP and MDR-3immunohistochemistry (IHC).
Results: Some gene mutations correlated with specific histopathological variables: FIC1mutations (PFIC1; n=6) correlated with lobular necrosis(p=0.006). ABCB4mutations (PFIC3; n=7) correlated with biliary regression with or without neoduttulogenesis(p=0.014) and loss of MDR-3 at IHC(p=0.040).
Interestingly, the homozygous single-nucleotide polymorphism (SNP) OMO-V444Ac.521T>C in the ABCB11 gene (coding for BSEP), found in 19(59%) cases, correlated with the presence of biliary regression (14 out of 19 cases, p=0.009), and architectural distortion(12 out of 19 cases, p=0.074), in the absence of a significant portal inflammation, lobular necrosis or cholangitis. Only 2 patients had NOTCH2 mutation; no cases with mutations of pathogenic/likely pathogenic ABCB11(BSEP gene) were observed so far in our adult series (but revision is ongoing).
Conclusion: ACC represents a heterogeneous group of cholestatic diseases with different pathological alterations potentially due to the different mutation penetrance in cholestatic-related genes (including PFIC). The finding of morphological alterations, such as bile duct

regression and architectural distortion, in patients biopsied for ACC, should suggest the search of the OMO-V444Ac.521T>C variant in ABCB11 gene since this SNP –very incident in the population and not considered pathogenic– is linked to other cholestatic disorders such as pregnancy cholestasis, hepato-biliary cancers and drug-induced cholestasis.

PS-04-019

Single cell-level dissection of the tumour microenvironment of hepatocellular carcinoma

A. Benjak, M. Coto-Llerena, O. Kollmar, D. Schnidrig, B. Durante, L. Di Tommaso, L. Terracciano, S. Piscuoglio*, C.K. Ng
*IRCCS Humanitas Research Hospital, Italy

Background & objectives: Tumour behaviour is governed by the complex interplay of tumour cells and immune, stromal, endothelial and other cell types in the tumour microenvironment (TME). We aimed to dissect the cellular composition of hepatocellular carcinoma (HCC) to the single-cell resolution.
Methods: We obtained single-cell RNA-sequencing data (10x Genomics) on ~55,000 cells from 15 HCC samples and 2 normal liver samples. We used Seurat3 to cluster and integrate the cells, annotated the cell types with SingleR, consensusTME, sctype and CellTypist and determined copy number using Numbat.
Results: Genes related to proliferation, PI3K/AKT/mTOR and WNT/beta-catenin signalling were up-regulated in nearly all HCC cells, and most HCCs demonstrated intra-tumour genetic heterogeneity on the copy number level. Clustering of the pathway activities of HCC hepatocytes revealed two clusters, distinguished by their activities related to angiogenesis, epithelial-to-mesenchymal transition, interferon alpha/gamma response, complement cascade and glycolysis. We identified 13 clusters of T/NK cells, 10 of macrophages, 9 of fibroblasts and 12 of endothelial cells. Specific cell subsets were enriched among HCCs, including lipid-associated macrophages, angiogenic endothelial cells, and those that were depleted in HCCs included regulatory T-cells, CD16- NK cells, liver sinusoidal and antigen-presenting endothelial cells.
Conclusion: Our analysis revealed not only the complexity of the diversity and phenotype of the five most common cell types in HCC, namely hepatocytes, T/NK cells, macrophages, fibroblasts and endothelial cells, but also the heterogeneity between the single-cell landscapes between HCCs. A comprehensive profiling of the co-operating tumour and non-tumour cells will not only help us further our understanding of HCC biology but will reveal novel therapeutic approaches in HCC.

PS-04-020

Hepatocellular carcinoma immune microenvironment analysis: a comprehensive assessment with computational and classical pathology

C. Ercan, S. Renne, L. Di Tommaso, C.K. Ng, S. Piscuoglio*, L. Terracciano
*IRCCS Humanitas Research Hospital, Italy

Background & objectives: The spatial variability and clinical relevance of the tumour immune microenvironment (TIME) are still poorly understood in hepatocellular carcinoma (HCC). We aim to develop a deep learning (DL)-model for the spatial analysis and distribution of immune infiltration.
Methods: A cohort of 92 HCC surgical liver resections and 51 matched needle biopsies were histologically classified according to their immunophenotypes: inflamed, immune-excluded, and immune-desert. To characterise the TIME on immunohistochemistry (IHC)-stained slides, we designed a new multi-stage DL algorithm, IHC-TIME, which can automatically detect immune cells and their localisation in TIME in tumour-stromal, centre-border segments.
Results: The pathologist-level TIME classification provides prognostic value for HCC patients. Two models were trained to detect and localise the immune cells on IHC-stained slides. The framework models, i.e. immune cell detection models and tumour-stroma segmentation, reached 98% and 91% accuracy, respectively. Patients with inflamed tumours showed better recurrence-free survival than those with immune-excluded or immune desert tumours. Needle biopsies were found to be 75% accurate in representing the immunophenotypes of the main tumour. Finally, we developed an algorithm that defines immunophenotypes automatically based on the IHC-TIME analysis, achieving an accuracy of 80%.
Conclusion: The deep learning-based tool developed can accurately analyse and quantify immune cells on IHC-stained slides of HCC. The microscopical classification of the TIME can stratify HCCs according to the patient prognosis. The computational pathology tool provides a new way to study the HCC TIME.

PS-04-021

Spatial proteomic profiling of intraductal papillary mucinous neoplasms and associated carcinoma

C. Rift*, R. Daucke, N.S. Bager, V. Petrosius, B. Kovacevic, S. Engelhardt, A. Toxværd, P. Vilmann, J.P. Hasselby, C.P. Hansen, E. Schoof, P. Klausen
*Department of Pathology Rigshospitalet, Denmark

Background & objectives: No biomarker can predict the risk of malignant transformation of intraductal papillary mucinous neoplasms (IPMNs). The aim is to demonstrate feasibility of proteomic mapping of IPMN and associated pancreatic ductal adenocarcinoma (PDAC) to understand tumour trajectories and identify novel biomarkers.
Methods: Formalin fixed, and paraffin embedded surgical specimens with concomitant IPMN and PDAC were included. Laser capture microdissection (LCM) of EPCAM stained slides were performed. Areas of low- and high-grade dysplasia, PDAC, and, if possible, normal duct tissue were identified. Both epithelial and adjacent stromal cells were dissected and stored separately. The samples were analysed by in-depth Liquid Chromatography-Mass Spectrometry (LC-MS).
Results: We included surgical specimens from 12 patients, 5 males and 7 females, mean age 71.4 years. Mean size of the lesions was 50.8 mm (range 20-190 mm). The IPMN was classified according to the WHO classification of pancreatic neoplasms. Upon LCM, an area of 50,000 µm2 was selected by a pathologist for each morphological component. Each component was sampled in triplicates, distributed in spatially separate sites on the slide. In total, 172 samples were microdissected and analysed by LC-MS. Between 3,500 – 4,000 protein groups were retrieved for each component. We observed distinct proteomes for each tumour component, including significant differences between the epithelium and stroma in key signalling pathways.
Conclusion: We demonstrate feasibility of extraction of an unprecedented high number of unique protein groups by LC-MS from relatively small amounts of laser micro dissected archival material, overcoming artefacts induced by formalin fixation. Distinct clustering of epithelium and stromal tumour-components was observed in principal component analysis. Further data-driven analysis of the large dataset will spawn potential biomarkers for accurate diagnosis, prognosis, and treatment selection for patients with IPMN and PDAC.

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PS-04-022

Histologic predictors of response to atezolizumab and bevacizumab in hepatocellular carcinoma biopsies

A. Sayadi*, M. Bouattour, M. Dioguardi Burgio, M. Albuquerque, V. Paradis, A. Beaufrère

*Department of Pathology, Hôpital Beaujon, AP-HP.Nord, Clichy, France

Background & objectives: Atezolizumab-bevacizumab is the first line therapy in unresectable hepatocellular carcinoma (HCC). Whereas few molecular factors have been associated to response, no routinely histological factors have been described. Our objective was to identify histologic features associated with response to atezolizumab-bevacizumab.
Methods: We conducted a retrospective study (2019-2023) including 108 pre-treatment biopsies of patients with unresectable HCC treated by atezolizumab-bevacizumab. CT scans at 3 months were used to define responders as partial or complete response according to mRECIST. Histologic criteria were reviewed by two liver pathologists, including subtype according to the World Health Organization classification based on predominant pattern.
Results: HCC was mainly observed in male patients (n=96, 89%) and in cirrhotic liver (n=67, 62%). HCCs were mainly classified as "not other specified" (NOS, 48%). The most frequent observed subtypes were macrotrabecular massive (MTM, 26%), squirrhous (SQ, 10%) and steatohepatitic (SH, 9%). 40% of patients (n=43) were classified as responders, distributed as follow: 70% in NOS group (n=30), 16% in MTM group (n=7), 5% in SQ group (n=2) and 5% in SH group (n=2) (p=0.015). In univariate and multivariate analyses, factors negatively impacting response were MTM subtype (Odds ratio (OR): 0.3 [0.10;0.83], p=0.025) and SH subtype (OR: 0.16 [0.02;0.71], p=0.029). No clinical variables were significantly associated with response.
Conclusion: Histological factors including MTM and SH subtypes impact the response to atezolizumab-bevacizumab in unresectable HCC. These criteria, easily assessable on biopsy, could be used to stratify patients on response to atezolizumab-bevacizumab.

PS-04-023
Proposal of a histologic grading system for hepatoblastoma to predict patients' prognosis
I.H. Song*, S. Gang, B. Ahn, J. Namgoong, J. Kim
*Department of Pathology, Asan Medical Center, University of Ulsan College of Medicine, Republic of Korea

Background & objectives: Hepatoblastoma is the most common paediatric liver malignancy. Although histopathologic patterns of hepatoblastoma have been established, their clinical significance is not fully understood. We aimed to investigate histologic patterns of hepatoblastoma and their prognostic significance.
Methods: A total of 112 patients with hepatoblastoma who received surgical resection were retrieved from the institutional database between 1991 and 2023. We classified them into 3 groups based on histologic findings: grade 3, presence of embryonal, pleomorphic, macrotrabecular, or small cell undifferentiated patterns; grade 2, ≥2 mitoses/2mm^2 without any of those patterns; and grade 1, the remaining.
Results: Median age of the patients was 1.3 years (range, 0.1–11.7). The proportion of cases exhibiting each histologic pattern were as follows: foetal, 98.2%; embryonal, 37.5%; pleomorphic, 7.1%; macrotrabecular, 0.9%; small cell undifferentiated, 6.2%; and cholangioblastic, 22.3%. Epithelial type (42.0%) and mixed epithelial and mesenchymal type (58.0%) had no impact on the patients' survival. However, higher histologic grade based on our new system was significantly correlated with shorter patients' disease-free and overall survivals (p = 0.005 and 0.044, respectively). Multivariable analysis revealed older patient age than 8 years, presence of metastasis, and histologic grade 3 as independent bad prognostic factors for disease-free survival (p = 0.004, 0.034, and 0.017, respectively).
Conclusion: We suggest that our new histologic grading system can predict survival outcome in patients with hepatoblastoma as well as patient age, PRETEXT grouping and metastasis.

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PS-04-024
"The Third Pathway" to whipple grossing: duct-centric (sagittal) sectioning of the pancreas allows finer appreciation of origin and spatial distribution of tumours and anatomic variations
N. Tezcan*, D. Cengiz, R. Esmer, B.K. Aktas, A. Armutlu, B. Saka, O.C. Taskin, H.G. Kayim, E. Bozkurt, G. Tellioglu, O. Bilge, E. Alper, O. Basturk, B. Gurses, V. Adsay
*Koç University, School of Medicine, Department of Pathology, Turkey

Background & objectives: The pancreas/periampullary region's complex anatomy makes it challenging to distinguish cancers originating from various organs removed with the Whipple operation. Two common approaches to handling Whipple specimens are bivalving and axial techniques. Recent studies have highlighted their advantages and disadvantages.
Methods: A third approach that fundamentally keeps the Wirsung and common bile duct (CBD) intact at the centre of the sections by using sagittal dissection of the ampulla/pancreas-head along with axial sectioning of the proximal CBD was employed in 127 cases with radiologic correlation.
Results: This approach revealed previously undocumented aspects of anatomy, cancer links, and orientation; 1) The pancreas has two distinct heads. In the retro-ampulla, the embryologic counterparts of ventral and dorsal pancreas are distinct and separated by a fascia. 2) Pancreatic head cancers occurring in three orientations: Ventral-retroampullary, Ventral-uncinate, Dorsal/corpus. 3) Preoperatively diagnosed "pancreatic cancers" often orient toward the CBD, frequently associated with low cystic duct insertion to CBD and arising in the insertion area. 4) Anatomic anomalies like common channel, divisum, santorinicele, and duodenal diverticulum are relatively common and spatially associated with cancers, raising questions about a causal association. 5) Illustrating that cystic dilatations accompanying tumours—often diagnosed as IPMNs microscopically—are frequently upstream obstructive (secondary) dilatations (i.e., Pseudo-IPMNs).
Conclusion: The duct-centric(sagittal) dissection of the pancreas, reveals previously overlooked anatomical phenomena and their differential association with neoplasms. Notably, PDACs exhibit a preference for the ventral or dorsal pancreas and are often found at the low-insertion area. Moreover, neoplasms show spatial associations with anomalies like diverticula and santorinocele, suggesting potential causal relationships. Since this method follows the main ducts through their route, intraductal neoplasias and the preferential distribution of preinvasive and invasive neoplasms in/around these ducts can be accurately documented.

PS-04-025
Innovative integrated morpho-molecular approach (next-generation sequencing plus digital PCR) greatly enhances the diagnostic accuracy in malignant biliary strictures
F. Vasuri*, E. Albertini, L. Miranda, T. Maloberti, S. Chillotti, D. Malvi, D. de Biase, A. D'Errico
*IRCCS Azienda Ospedaliero-Universitaria di Bologna, Italy

Background & objectives: The ERCP-guided cytological/histological diagnosis of biliary strictures is strongly recommended, but the scarcity of sampled material makes the diagnosis challenging. Our aim was to analyse the diagnostic accuracy of combined morphology, Next-generation sequencing (NGS) and *digital*-PCR (dPCR) in biliary strictures.
Methods: Twenty prospective patients were included so far, 12(60%) males and 8(40%) females. Clinical and laboratory data were collected. NGS was performed on paraffin-embedded tissue by a

laboratory-developed panel allowing the analysis of hot-spot regions in 28 genes. dPCR was performed (replacing FISH) by QuantStudio™ AbsoluteQ™ solid dPCR: the copy-number variation (CNV) of the chromosomes 3, 7, and 17 was analysed.
Results: At histopathology, 10 (50%) cases were negative, 5 (25%) positive (infiltrative biliary carcinoma) and 5 (25%) were morphologically doubtful. Two cases were not assessable by NGS; another case was not assessable by either method. At NGS, 6/17(35.3%) cases showed at least one mutation (among CDKN2A, SMAD4, TP53, ARID1A, BRAF, KRAS, FGFR1). Variants were present in 4 out of 5 positive cases, and in 1 doubtful case. NGS showed 80% sensibility and 87.5% specificity, with a significant correlation with pathological diagnosis (p=0.008, chi-square). By dPCR, 3(15.8%) cases showed CNV at chromosome 3; 2(10.5%) at chromosome 7 (60% sensibility, 100% specificity): all of them were positive cases (p=0.007), including the positive case wild-type at NGS.
Conclusion: The combination of NGS and dPCR reached 100% sensibility in our series and allowed us to confirm the doubtful cases (one as malignant, the others as benign). NGS proved to be more sensible for the diagnosis of malignancy, but in 15% the specimens were not suitable: in these cases, dPCR was helpful, contributing in specificity and showing that this method can replace FISH in the diagnostics of biliary strictures, keeping its reliability even in scarcely cellular specimens. Enrolment is ongoing.

PS-04-026
Diagnosis of patients with fibrolamellar carcinoma: a Dutch nationwide study
J. Verheij*, A. Furumaya, A. Gumede, J. de Vos-Geelen, J. Erdmann, B. Takkenberg, M. Doukas, V. Weeda
*Amsterdam UMC, The Netherlands

Background & objectives: Fibrolamellar carcinoma (FLC) is a rare primary liver cancer characterized by abundant eosinophilic cytoplasm and lamellar fibrotic bands. Adequate diagnosis is important for prognosis and treatment. The current study describes the diagnosis of fibrolamellar carcinoma in a Dutch historical cohort.
Methods: Adult patients diagnosed with FLC between 1990 and 2020, with pathology slides and clinical data available, were included through the Netherlands Cancer Registry and Automated National Pathological Anatomy Archive. Two expert hepatopathologists revised histopathology and immunohistochemistry (CD68 and CK7).
Results: In total, 48 adult patients, 25 (52%) male, diagnosed with FLC were included. Biopsies were available for 27 patients (56%) and resection specimens in 21 patients (44%). Upon expert review, in nine patients (19%) diagnosis FLC was unequivocally confirmed. Patients diagnosed with unequivocal FLC had a mean age of 27 years. Four additional lesions harbored characteristics of both FLC and conventional hepatocellular carcinoma (HCC). Three patients exhibited morphological features suggestive of FLC, yet with negative CD68 staining. In the remaining 32 patients diagnosis was revised in cholangiocarcinoma (n=6, 13%) and conventional HCC (n=22, 46%). The lesions identified as conventional HCC were of steatohepatitic (n=11), scirrhous (n=7), and conventional (n=4) subtypes.
Conclusion: The presence of fibrotic bands in steatohepatitic and scirrhous HCC can lead to misdiagnosis of FLC as conventional HCC. This could have important treatment consequences as there is a tendency towards surgical treatment of FLC if feasible. Contrarily, evidence supporting the efficacy of systemic treatments for FLC remains limited. All in all, our Dutch historical cohort underlines the challenging diagnosis of FLC and emphasizes the critical role of expert review in accurate diagnosis.

PS-04-027
RNF43-mutations are associated with stronger antitumour immune responses and improved outcomes in pancreatic cancer
A.S. Wenning*, P. Aeschbacher, B. Gloor, A. Perren, E. Karamitopoulou-Damantis
*Institute of Tissue Medicine and Pathology, University of Bern, Switzerland

Background & objectives: Dysfunction of the tumour suppressor gene RNF43 is considered to drive carcinogenesis in various cancers. In our previous study, RNF43-mutations were correlated with fewer and later recurrences in pancreatic cancer. We undertook a detailed assessment of the impact of RNF43-mutations.
Methods: We evaluated the role of RNF43 by next generation sequencing (Oncomine Tumour Mutation Load Assay, ThermoFisher) in a well-characterized cohort of 283 microsatellite stable (MSS) and 5 microsatellite instable (MSI) pancreatic ductal adenocarcinomas (PDACs). Each 10 patients with (RNF43mut) and without (RNF43wt) RNF43-mutations were additionally assessed by multiplex immunofluorescence to evaluate their immune features.
Results: The RNF43-mutation rate in the MSS-PDAC cohort was consistent with the rate reported in the Cancer Genome Atlas (TCGA) cohort (19/283, 6.7% resp. 9/150, 6%), whereas it was significantly higher among MSI-PDACs (2/5, 40%). In MSS-PDACS, RNF43mut cases had higher TMB values (5.5 mut/mb versus 1.67 mut/mb, p<0.01) and significantly longer overall survival (OS; 47 months versus 18 months, p<0.0001) than RNF43wt cases. Moreover, RNF43mut cases exhibited higher T cell infiltrates (CD3+, CD3+CD4+ and CD3+CD8+ cells) and lower counts of CD68+ total macrophages, as well as CD68+CD163+ macrophages than RNF43wt cases (p<0.001 respectively).
Conclusion: RNF43mut cases show improved clinical outcomes and stronger antitumour immune responses than RNF43wt cases in MSS-PDACs. Moreover, RNF43-mutations were significantly more frequent in MSI-PDACs. Our results underscore the need for deeper understanding of molecular factors modulating the biological behaviour and treatment response of PDACs that can help refining the stratification and optimizing the clinical management of patients.

PS-04-028
Clinicopathological and molecular characteristics of malignant hepatic angiomyolipoma
Y. Yoo*, H.J. Kang, I.H. Song
*Ewha University Medical Center, Republic of Korea

Background & objectives: Hepatic angiomyolipomas were considered benign, but reports of malignant cases have increased. To more accurately predict their clinical behaviour, we evaluated the malignant score based on histological variables and investigated the correlation between the score and prognosis.
Methods: An electronic data search of our database identified a total of 135 patients histologically diagnosed with hepatic angiomyolipoma from 2000 to 2022. Hematoxylin and eosin-stained slides were reviewed to measure the malignant score based on histologic findings. P53 and Ki-67 immunohistochemical stains were performed in all cases. Targeted next-generation sequencing was performed in three cases with the highest malignant scores.
Results: The median age of the patients was 46 years (range, 23-79). The male-to female ratio was 1:3.2. Fifty-nine patients (44%) were observed without treatment, and 6 (4%) received local ablation, with none showing recurrence or metastasis. Seventy patients (51.9%) underwent surgery. Of those, only one showed clearly malignant behaviour with spontaneous rupture and peritoneal metastases. In this case, the tumour was 13 cm and grossly infiltrative. High-grade nuclear atypia, increased mitoses, extensive necrosis, and vascular invasion were observed, resulting in a malignant score of 6, the highest among all cases. The Ki-67 proliferation index was 49%. Abnormal p53 immunostaining and a pathogenic TP53 mutation, E286K, was also detected.
Conclusion: Hepatic angiomyolipoma rarely exhibit malignant behaviour. We suggest that our malignant score, based on tumour size,

infiltrative border, high-grade nuclear atypia, increased mitotic activity, necrosis, and vascular invasion, can predict malignant behaviour of hepatic angiomyolipoma. A high Ki-67 proliferation index, abnormal p53 immunohistochemical staining and/or presence of a pathogenic TP53 mutation can also be helpful in diagnosing malignant hepatic angiomyolipoma.

PS-05Poster Session Endocrine Pathology

PS-05-001

Hyalinizing trabecular tumour of the thyroid: interest of GLIS3 immunohistochemical study to detect PAX8::GLIS3 rearrangement

Z. Alsugair*, F. Descotes, J. Lopez, m. Decaussin-Petrucci
*France

Background & objectives: Hyalinizing trabecular tumour of the thyroid (HTT) is a rare, low-risk neoplasm that poses diagnostic challenges. PAX8::GLIS3 rearrangements characterize HTT. We aimed to explore HTT's genetic profile, focusing on PAX8::GLIS3 rearrangements and GLIS3 immunohistochemical staining.
Methods: We conducted a retrospective study involving 8 cases histologically diagnosed as HTT. RNA-sequencing and immunohistochemical staining for GLIS3 were performed on all cases.
Results: The study included five females and three males, with a tumour size ranging from 3 to 45 mm. RNA sequencing analysis showed PAX8::GLIS3 rearrangement in 6 cases (75%). No other molecular alterations were found. However, one case failed due to the tissue quality, and one case did not show any gene fusion. Immunohistochemical staining for GLIS3 revealed nuclear positive expression in tumour cells for all cases where gene fusion was detected (100%). However, there was no GLIS expression in the case where no gene fusion was found.
Conclusion: Our study confirms the consistent presence of PAX8::GLIS3 rearrangement in hyalinizing trabecular tumour (HTT) of the thyroid. Additionally, our novel finding of GLIS3 expression via immunohistochemistry enhances diagnostic precision for these tumours. Notably, our series demonstrates the correlation between positive GLIS3 expression and detection of PAX8::GLIS3 fusion by RNA sequencing, potentially expediting HTT diagnosis.

PS-05-002

Tall cell papillary carcinoma as the most common histological subtype of the radioiodine refractory thyroid cancer

F. Pani, M.A. Bani*, C. López Jiménez, L. Lamartina, J. Hadoux, D. Hartl, S. Moog, E. Baudin, A. Al Ghuzlan
*Department of Medical Biology and Pathology, Morphological Pathology Laboratory, Gustave Roussy Cancer Campus, Villejuif, France Paris-Saclay University, Gustave Roussy Cancer Centre, Inserm US23, CNRS UMS3655, AMMICa, Villejuif, France

Background & objectives: Pathological features (PF) in radioiodine refractory thyroid cancer (RAIR-TC) are scanty explored. We aim at describing the PF to predict RAIR-TC status in a cohort of DTC patients with intermediate/high risk of recurrence based on the ATA risk classification.
Methods: Retrospective study between 2016 and 2021. PF were examined including: pathological subtype, size, tumour focality, extra-thyroidal extension, presence of capsular invasion, presence of vascular invasion, number of mitosis, presence of necrosis, lymphocytic infiltration (LI) peri and/or intra-tumoural. Based on the clinical data we defined the status of RAIR.
Results: 79 patients (median age 63 years, range 19-83) became RAIR after a median of 3.5 years (range 2-4.2 years). Tall cell papillary thyroid cancer (PTC) subtype was the most common histological type (79/56, 70.1 %) followed by the poorly differentiated TC (79/18, 22.7 %) and the oncocytic carcinoma (79/5, 6%). Interestingly, in the tall cell PTC subtype multifocality and high grade features were associated negatively with the RAIR status. Moreover, among the tall cell PTC subtype, high LI was associated with the refractory time (median 4.2 years) compared to the tall cell PTC without LI (median 2.8 years, $p<0.05$).
Conclusion: These preliminary data showed the need to clearly distinguish the aggressive forms of differentiated carcinoma and the high grade features to predict RAIR status. The presence of LI might delay the refractory time but these data need to be confirmed in a larger cohort of patients.

PS-05-003

PD-L1 expression and BRAF-TERTp signature in a continental cohort of anaplastic thyroid carcinoma

A. Bychkov*, P. Gaddam, C.K. Jung, M. Hirokawa, T. Higashiyama, J. Hang, W. Lai, S. Keelawat, Z. Liu, H.Y. Na, S. Satoh, Z. Mussazhanova, M. Nakashima, K. Kakudo, S. Agarwal
*Kameda Medical Center, Japan

Background & objectives: Immunotherapy using checkpoint inhibitors shows promise for advanced cancers. While PD-L1 expression in papillary thyroid carcinoma is well-studied, data on the highly aggressive anaplastic thyroid carcinoma (ATC) is limited. We aimed to comprehensively assess PD-L1 status in large ATC cohort.
Methods: In this retrospective study across 9 Asian institutions, 179 ATCs were centrally scored for PD-L1 expression using the SP263 (Ventana) clone. A tumour proportion score (TPS) $\geq$1% was required to consider a case positive. PD-L1 expression was compared with histology, specimen type (small vs. large), molecular profile (BRAF V600E and TERT promoter), and patient outcomes.
Results: Most ATCs (73.2%) exhibited PD-L1 positivity, with a median TPS of 18%, and TPS $\geq$50% observed in 30.7% of cases. PD-L1 negativity was more common in small-sized specimens ($p = 0.01$). Epithelioid and pleomorphic patterned ATCs showed higher PD-L1 positivity compared to sarcomatoid types. The presence of a coexistent differentiated component was associated with more frequent negativity and lower TPS than pure ATC ($p < 0.01$). Such PD-L1 conversion was noted in 71% of cases with a coexistent differentiated tumour. BRAF V600E, but not TERTp mutations, correlated with PD-L1 positivity ($p = 0.034$). However, PD-L1 expression did not influence patient outcomes.
Conclusion: The majority of ATC are PD-L1-positive, making them candidates for anti-PD therapy. Histopathological pattern in ATC may be indicative of PD-L1 expression status. A negative PD-L1 result on needle biopsies may not preclude PD-L1 expression in other tumour foci. Positive correlation between PD-L1 and BRAF V600E reinforces the potential for combining immunotherapy with multikinase inhibitors in ATC.

PS-05-004

Ki67 proliferation index (PI) is not able to further stratify digestive grade 2 neuroendocrine tumours (NET G2)

M. D'Arezzo*, S. Fraticelli, A. Laffi, A. Bertuzzi, A.G. Lania, P. Spaggiari, S. Uccella
*Italy

Background & objectives: NET G2 are well differentiated NEN with Ki67 3%-20%. This is a clinically and pathologically heterogeneous disease and some authors have suggested, for therapeutic purposes, that they are subdivided in "low G2" and "high G2" according to undefined cut-offs.

Methods: We retrospectively reviewed all cases of surgically treated NET G2 from the digestive tract (2011-2023), analysing the following histological features: growth pattern, mitotic count, necrosis, angioinvasion, cell type (morphology, hormone secretion), and Ki67 PI (manual count in hotspot). We then compared our results with clinical data (overall survival, body-mass-index, and smoking habits).
Results: A total of 93 cases were included; after re-evaluation of Ki67 PI, 15 cases were reclassified: 4/93 as G1 and 11/93 as G3, thus being excluded from the study. Median age at diagnosis was 59 and 43,6% (34/78) of cases were females. Median follow up was 59 months. Angioinvasion was present in 59% of cases (46/78); necrosis in only 2. We subdivided our NET G2 pool based on different ki67 threshold (<5; <10; <15; <18) to see possible significant differences comparing overall survival, body-mass-index, smoking habits and angioinvasion. However, using Students t-test and Kaplan Meyer estimator we couldn't observe significant differences amongst the analysed subgroups.
Conclusion: NET G2 is still a wide and heterogeneous category from both a clinical and histopathological point of view. Our preliminary results did not find statistically significant differences by subdividing this category only based on the Ki67. Thus, the practical subdivision in "low G2" and "high G2" groups empirically used in clinical practice is not supported by evidence. Further studies are needed to identify biomarkers related to prognosis in digestive NET G2.

PS-05-005
Subcentimetric papillary thyroid carcinomas: unravelling the role of location within the thyroid gland
E.A. Szasz*, R. Catana, A. Nechifor-Boila, A. Borda
*Pathology Department of Mures County Clinical Hospital, Romania

Background & objectives: Subcentimetric papillary thyroid carcinoma (SPTC) usually have an excellent prognosis, but few aggressive cases were reported. We aimed to analyse clinicopathological features of SPTCs based on their location (subcapsular versus nonsubcapsular) in order to detect high-risk factors.
Methods: In this retrospective study, we reviewed all consecutive SPTC cases registered at the Department of Pathology, Târgu-Mureş Emergency County Hospital between 2003-2014. The following have been assessed: tumour size, subcapsular versus nonsubcapsular location, extrathyroidal extension/invasion into the perithyroidal adipose tissue, multifocality, resection margins, lymph node involvement, histological subtype, tumour border and stromal reaction (fibrosis/desmoplasia/sclerosis).
Results: Our study included 164 SPTCs, of which 89 were subcapsular and 75 were nonsubcapsular. High-grade morphological features, such as tumour desmoplasia (p=0.022) and sclerosis (p=0.001), infiltrative tumour borders (p=0.005), positive resection margins (p=0.005), invasion into the perithyroid adipose tissue (p=0.001), were significantly more prevalent among subcapsular SPTCs. Out of the four patients with SPTC who had documented lymph node metastasis, three had subcapsular SPTCs. Nonsubcapsular SPTCs were characterized by a paucity of the above-mentioned morphological features.
Conclusion: SPTCs present unique challenges in diagnosis and management due to their small size and potential aggressive behaviour. Our findings indicate that there is justification for a more vigilant and thorough follow-up and management approach for small subcapsular tumours, given their apparent association with high-grade morphological characteristics. Alternatively, nonsubcapsular SPTCs could be deemed suitable candidates for inclusion in active surveillance programs.

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PS-05-007
Can clinicopathological features predict poor prognosis in papillary thyroid carcinoma? Rethinking the importance of size.
E. Joy*, T. Somanathan, A. Mathews, S. A, N. Abraham George, A. Mathew
*Regional Cancer Centre, Thiruvananthapuram, India

Background & objectives: Papillary thyroid carcinoma (PTC), usually with an excellent prognosis, sometimes has an aggressive metastatic pattern.
Objective: To compare the clinicopathological features in metastatic and non-metastatic PTCs thus finding predictors of poor outcome in this era of rising trend in PTCs.
Methods: This is a retrospective study conducted in our Department of Pathology which included 149 consecutive cases of PTCs reported in 2016. Details regarding the demographics, disease, and treatment were collected in a structured format from hospital records. Slides and paraffin blocks were retrieved from the archives and assessed for various histopathological features.
Results: A Subset of 15 cases with ≤1 cm was studied; 7 (46%) exhibited lymph node metastasis, and one displayed lung metastasis. These findings support the 2022 WHO update, which no longer categorizes microcarcinoma separately but considers morphological features due to potential aggressiveness.
Conclusion: PTCs measuring ≤1 cm usually follows an indolent course and carry an excellent prognosis. but a subset might exhibit aggressive behaviour, warranting similar treatment as larger tumours. The rising global occurrence of PTCs underscores the critical need to identify distinct clinicopathological features in aggressive cases.

PS-05-008
Association of Pan-TRK immunohistochemistry expression with NTRK and other gene fusions in thyroid cancer
C.K. Jung*, J.M. Park, S. Jung, S.Y. Kim, S. Jeon, Y. Chung
*Department of Hospital Pathology, College of Medicine, The Catholic University of Korea, Republic of Korea

Background & objectives: Pan-TRK immunohistochemistry (IHC) is a screening method for identifying NTRK fusion-positive tumour. Although it is becoming increasingly popular in various tumours, its diagnostic accuracy in detecting NTRK fusions in papillary thyroid carcinoma (PTC) is still not fully understood.
Methods: We analysed the expression levels of pan-TRK IHC in a group of PTC samples that did not carry the BRAF p. V600E variant. We selected 44 PTC samples that showed varying levels of pan-TRK expression for further analysis using targeted next-generation RNA sequencing to identify gene fusions. The H-score method via QuPath software was used to evaluate pan-TRK expression.
Results: Among the 44 cases successfully analysed for gene fusions, 27 cases showed the presence of seven distinct gene fusion variants. The most common fusion detected was CCDC6::RET, found in 11 cases, followed by ETV6::NTRK3 in 8 cases. Less common gene fusions were TPM3::NTRK1 (n=3), QSTM1::NTRK3 (n=2), TPR::NTRK1 (n=1), NCOA4::RET (n=1), and SND1::BRAF (n=1). The highest median H-score (181) was recorded for TPM3-NTRK1 fusions, while cases without any detectable gene fusions showed a median H-score of 74, representing a baseline level of pan-TRK expression. TPR::NTRK1, CCDC6::RET, and SND1::BRAF fusions had relatively lower median H-scores of 73, 69, and 67, respectively. The minimum score observed for NCOA4::RET was 54.
Conclusion: We suggest that pan-TRK IHC is a valuable diagnostic tool in thyroid pathology, particularly in detecting the presence of TPM3::NTRK1 fusions through heightened immunostaining. However, the method has limited ability to differentiate between different NTRK gene fusions and unrelated genetic changes, such as BRAF and RET fusions. This highlights the need for further research to determine its diagnostic specificity and effectiveness in developing PTC treatment strategies.

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PS-05-009

Immunohistochemical expression of ER, PR and AR in papillary thyroid carcinoma

M. Kochoska*, T. Angelovska, V. Risteski, M. Bogdanovska-Todorovska, R. Jovanovic, S. Kostadinova-Kunovska
*Institute of Pathology, Faculty of Medicine, University Ss. Cyril and Methodius, Skopje, Republic of North Macedonia

Background & objectives: From all types of thyroid carcinomas, papillary thyroid carcinoma (PTC) is the most common type. The present study aimed at evaluating the immunohistochemical expression of estrogen receptors (ERs), progesterone receptors (PRs) and androgen receptors (ARs) in PTC compared to goiter.
Methods: The retrospective study included 12 cases of PTC and 6 cases of goiter. The cases were diagnosed in the period between December 2020 and March 2021. All of them were retrieved from our database and immunohistochemical staining of formalin fixed paraffin embedded tissues was performed, for ERs, PRs and ARs.
Results: From twelve cases of PTC, three were male and nine were female with age range from 19 to 72. All of the goiter cases were female patients, with age range from 34 to 64. Six out of twelve PTC cases were positive for ER in comparison to two out of six goiter cases with a statistically significant difference ($p < 0,05$). Regarding PR, eight out of twelve PTC cases were focaly positive, and all of the goiter cases were negative. Ten out of twelve cases of PTC were positive for AR, in comparison to one out of six goiter cases with a statistically significant difference ($p < 0,05$).
Conclusion: The results of the present study indicate that malignant cells in PTC express ER, PR and especially AR, in comparison to goiter. That is suggesting that these hormonal receptors may play a role in thyroid cancer tumorigenesis, and that these patients may benefit from hormonal therapy, which should be verified in further studies.

PS-05-010

Subcentimeter papillary thyroid carcinoma: high-risk features and patient age

B. Kovacevic*, B. Jovanović, D. Mikic, J. Karajovic, S. Cerović
*Institute of Pathology and Forensic Medicine, Military Medical Academy, Belgrade, Serbia

Background & objectives: Subcentimeter/small papillary thyroid carcinoma (SPTC) has an excellent prognosis. Lymph node metastasis (LNM), vascular invasion, gross extrathyroidal extension (ETE), and tumour subtype may influence clinical outcomes. We analysed the correlation between patients' age and potentially high-risk features in SPTC.
Methods: The study included 561 consecutively diagnosed SPTC in our Institute from 2013 to 2024. According to the patient's age, SPTCs were classified into three groups. Group 1 (Gr1): ≤40 years; Group 2 (Gr2): 41-60 years; Group 3 (Gr3): ≥61 years. For each group, the following features were analysed: tumour size, LNM, ETE, vascular invasion and tumour subtype.
Results: From a total of 561 SPTCs, Gr1, Gr2 and Gr3 included 96, 269, and 196 cases respectively. The size of Gr1 SPTC (2.45±5.43mm) was significantly larger (p=0.043) than the size of Gr2 (2.20±4.00mm) and Gr3 (2.0±3.22mm). Twenty-four (25%) of Gr1 patients had LNM which was a significantly higher ($p<0.001$) comparing 23(8.6%) and 9(4.6%) of Gr2 and Gr3 patients. ETE was present in 2(2.1%) of Gr1 tumours, absent in the Gr2, and present in 1(0.5%) case of Gr3 SPTCs (p=0.049). Vascular invasion was significantly more common (p=0.016) in Gr1(7.3%), comparing Gr2(4.1%) and Gr3(1%) tumours. The most common subtype in Gr1(36.5%) was classic while in Gr3(72.47%) was follicular (p=0.011).
Conclusion: The presence of high-risk features in SPTC is related to the patient's age and is significantly more common in younger than 40. It indicates that SPTCs in younger patients have a potential for growth, invasiveness, and regional LNM. The potential of SPTC progression in patients older than 40 years is much lower, specifically in older than 61 years. Younger patients may require more radical treatment or at least a more intensive follow-up contrary to older patients.

PS-05-011

International medullary thyroid cancer grading system: have you integrated it into your daily practice yet?

L.D. Micoogullari*, D. Etit, A. Subasioglu, M. Haciyanli, B.O. Pamuk
*Izmir Katip Celebi University Ataturk Training and Research Hospital, Medical Pathology, Turkey

Background & objectives: International Medullary Thyroid Cancer Grading System (IMTCGS) was developed to improve prognostication. IMTCGS is not a WHO-grading scheme yet thus, limiting its' application in daily practice. In this study, we aimed to compare the histopathological and clinical parameters with IMTCGS.
Methods: A retrospective review of 72 patients with histopathologic diagnoses of medullary thyroid cancer (MTC) between the years 2006 and 2021 was made. The histopathological characteristics were evaluated by 2 pathologists on hematoxylin&eosin stained sections including mitotic count and necrosis incorporated in IMTCGS. Clinical data were collected from hospital database system. IBM SPPS System 22 was used for statistical analysis.
Results: MTC cases were divided into low- and high-grade groups according to IMTCGS. MTC grade was found high in 17 (23,61%) and low in 55 (76,39%) cases. Twelve cases in the high-grade group showed necrosis, 3 showed high mitotic rates (defined as ≥5 mitoses per 2 mm2), and 2 showed both parameters, respectively. MTC grade groups were found associated with tumour size (p=0,002), angioinvasion (p=0,001), nodal metastasis (p=0,006), solid and small cell carcinoma-like variants of MTC (P=0,042), perineural invasion (p=0,014), biochemical recurrence (defined as postoperative elevated calcitonin levels) (p=0,005), recurrence (diagnosed via imaging techniques or cytopathological correlation) (p=0,018), distant metastasis (p=0,003), tumour stage (p=0,041) and, survival (p=0,002).
Conclusion: This is the first Turkish study evaluating IMTCGS. Our findings support that incorporating IMTCGS into daily pathology practice -even without evaluating Ki67 proliferation index- and WHO scheme may help clinicians to predict prognosis better. Also, it is a simple and applicable grading system in any tertiary health care centre across the globe. Future studies with larger series are needed to demonstrate how MTC grading may impact treatment protocols.

PS-05-012

Desmoplasia: is it an usual accompanier of medullary thyroid carcinoma or a significant prognostic parameter?

L.D. Micoogullari*, D. Etit, A. Subasioglu, M. Haciyanli, B.O. Pamuk
*Izmir Katip Celebi University Ataturk Training and Research Hospital, Medical Pathology, Turkey

Background & objectives: Up to 75% of medullary thyroid carcinoma (MTC) patients show lymph node metastases early in the disease process and in the tumours with desmoplasia. In this study, we aimed to evaluate desmoplasia as a reproducible and applicable morphological parameter.
Methods: A retrospective review of 72 patients with histopathologic diagnoses of MTC between the years 2006 and 2021 was made. Desmoplasia, which was defined as the presence of a newly formed fibrotic

stroma that is not found in the non-neoplastic thyroid, was evaluated by 2 pathologists on hematoxylin&eosin stained sections. IBM SPPS System 22 was used for statistical analysis.
Results: Desmoplasia was found in 48 cases (66,67%). Desmoplasia was grouped into 4 classes as: thin fibrous septae, broad fibrous septae, thin and broad fibrous septae, and only stromal reaction. Broad fibrous septae was defined as a septae with thickness equal to 0,3 mm or greater. Most of the cases (n=33, 45,83%) belonged to broad fibrous septae group. Desmoplasia was found associated with angioinvasion (p=0,001), nodal metastasis (p=0,026), and extrathyroidal extension (p=0,001). Furthermore, broad fibrous septae was found associated with angioinvasion (p=0,003) and nodal metastasis (p=0,016). Thin fibrous septae and only stromal reaction groups had the least effect on nodal metastasis and angioinvasion.
Conclusion: This is the first Turkish study to evaluate desmoplasia in MTC cases. In MTC cases, desmoplasia may be mistaken for amyloid deposition thus, may be easily overlooked. Our results have shown that desmoplasia could have importance in predicting patient prognosis. Moreover, with our definition of desmoplasia groups, it is a highly reproducible and reliable parameter that can be applied all across the globe. Adding a 'desmoplasia' section to pathology reports may be beneficial in patient management.

PS-05-013
Prognostic significance of Lin28A protein expression in papillary thyroid carcinoma
D. Oflas*, E. Tekin, B. Badak, N. Kebapci, A. Akalin, M. Bilgin, E. Dündar
*Erzurum City Hospital, Department of Pathology, Turkey

Background & objectives: Papillary thyroid carcinoma (PTC), the most common endocrine malignancy, while the prognosis is usually favourable, lymph node metastasis (LNM) is an important predictive factor for morbidity. Here we investigated the association between Lin28A immunohistochemical expression and LNM in PTC cases.
Methods: 143 cases diagnosed with PTC who underwent bilateral total thyroidectomy and regional lymph node dissection were included in the study. The slides were re-evaluated according to the latest classification. The demonstrative tumour sections were stained with the Lin28A. Any degree of cytoplasmic staining in more than 50% of tumour cells was considered positive. Lin28A positivity was compared with clinicopathological data.
Results: 72% of the cases were female, with an average age of 45.06 years. The most common tumour subtype was classic (70.6%), followed by the tall cell (11.9%). Lymph node metastasis was present in 51.7% of cases, while extrathyroidal spread was seen in 9.1%. All lymph node metastasis were macrometastasis (>2 mm) in size, and 45.9% (n:34) of the cases were central lymph node metastasis and 54.1% (n:40) were lateral neck metastasis. The Lin28A staining was positive in 17.5% of cases. Statistically significant differences were found between Lin28A positivity and lymph node metastasis, perineural invasion, and extrathyroidal spread (p=0.014, p=0.004, p=0.037). No significant relationship was detected with distant organ metastasis (p=0.629).
Conclusion: In conclusion, although there are very few studies on Lin28A expression in PTC cases, it correlates with poor prognostic features. Especially in groups exhibiting low-risk histopathological features, it holds the potential as an important predictive marker for unforeseen possibilities of lymph node or distant metastasis. It opens the door to future studies for targeted treatment in cases showing recurrence and resistance where standard treatments fall short. These findings need to be supported by studies with larger series.

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PS-05-014
Clinicopathological features of high-grade follicular cell-derived non-anaplastic thyroid carcinomas: a single centre experience
S. Pancetti*, A.A. Salvatore, M. Cieri, G. Mercante, A.G. Lania, S. Uccella
*IRCCS Istituto Clinico Humanitas, Italy

Background & objectives: This study is aimed to assess clinicopathological correlations in high-grade follicular cell-derived non-anaplastic thyroid carcinomas (HGTC) diagnosed in our hospital. According to the latest WHO classification, we considered poorly differentiated thyroid carcinoma (PDTC) and differentiated high-grade thyroid carcinoma (DHGTC).
Methods: We searched the files of our Institution and found 31 cases of HGTC (5 DHGTC and 26 PDTC), diagnosed and treated in our hospital between 2015 and 2023. Histological slides were reviewed and immunohistochemistry for HBME1, Ki67, PHH3, and p53 was performed. The slides were evaluated by an endocrine pathologist blinded to the clinical outcome. Detailed clinicopathological characteristics were collected.
Results: The histopathological review confirmed all 5 DHGTC (original diagnosis after 2022). Of the 26 PDTC: 12 were reclassified as DHGTC, 5 were confirmed as PDTC, and 9 were downgraded as DTC. The 17 HGTC showed a large mean diameter (55.1mm), high rate of vascular invasion (96.3%), positive resection margins (46.15%) and presence of distant metastases (52%). OS was 61% at 3y and DFS 3% at 3y.
There were few significant differences between DHGTC and PDTC: diameter (DHGTC 50.4 vs PDTC 65.6 p=0.069) extrathyroidal extension (DHGTC 83.33% vs PDTC 20%, p=0.03), PET avidity (DHGTC 100% vs PDTC 58,3%, p=0,037). There were no differences on OS and DFS.
Conclusion: HGTC is a completely different entity with a worse prognosis compared to DTC. In our series, despite the different morphological and molecular features of DHGTC and PDTC, patients' prognosis seems not to be different for these two entities. However, considering the adverse prognosis of these entities, their proper recognition and a careful histopathological and molecular characterization, with exclusion of DTC remains important in view of determining predictive biomarkers that can be useful for improving patients' outcome.

PS-05-015
Rapid evaluation of endocrine gland tissue by nonlinear microscopy
T. Weber, B. White, T. St Jacques, J. Fujimoto, S. Rosen, Y. Sun*
*Beth Israel Deaconess Medical Center, USA

Background & objectives: Nonlinear microscopy (NLM) is a fluorescence microscopy technique that can rapidly examine fresh/fixed tissue and provide H&E-like images. NLM has been successfully used to evaluate a variety of tissues, however its ability to characterize endocrine tissue has not been examined.
Methods: Non-processed formalin-fixed tissue was obtained from adrenal gland, pancreas, pituitary gland, testicle specimens under an IRB approved protocol. Tissue slices were stained with acridine orange and sulforhodamine 101 in a 1:1 ethanol:water solution for 2 minutes, followed by a 30-second saline rinse. The tissue slices were then imaged in real-time using NLM and compared with standard paraffin-embedded H&E histology.
Results: We evaluated over 100 tissue samples, including adrenal cortical tissue, pituitary gland, pancreatic tissue, and Leydig cell tumour. NLM images of benign adrenal cortical tissue highlight the zona fasciculata and zone glomerulosa with well-delineated secretory granules, which typically appear as vacuoles in conventional histology. NLM also captured islets of Langerhans in the pancreas with defined endocrine

granules. Images of the pituitary gland showed cellular secretory granules, which are well-recognized by electron microscopy. NLM images of Leydig cell tumour displayed numerous Reinke crystals, structures that are challenging to visualize in processed tissue. Three pathologists confirmed that diagnostically important features observed in the H&E images were also identifiable in the NLM images.
Conclusion: This proof-of-principle study demonstrated that NLM readily replicates traditional H&E staining for endocrine organs, offering significant advantages over conventional histology and frozen section analysis by eliminating the need for fixation, embedding, microtome sectioning, or slide preparation. As a novel optical imaging platform, NLM has the potential to augment rapid pathological evaluation of fresh tissue, aligning with the advancements in digital pathology and precision medicine.

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PS-05-016
Neuroendocrine tumours of the lung: reconsideration of histopathological guidelines and classification
I. Vamvakaris*, G. Evangelou, G. Lolas, M. Anagnostopoyloy, T. Papastergiou, G. Liadakis, L. Jensen, K. Syrigos
*Sotiria Hospital Athens, Greece

Background & objectives: In this study we evaluated the coexistence of tumourlets and DIPNECH and asked whether they always have common characteristics with the primary neuroendocrine tumour. Furthermore, we demonstrate that additional slices are required from the lung parenchyma to evaluate this coexistence
Methods: FFPE tissue blocks from 81 patients undergoing resection for pulmonary neuroendocrine were prospectively collected. All histological slides were reviewed by two independent pathologists. Additionally, all tumours underwent immunohistochemistry (IHC) analysis. The cases were classified according to the WHO classification (5THedition). Additionally, ten more blocks were sampled focusing in normal lung parenchyma. No neoadjuvant therapy had been administered.
Results: Of the 81 cases, 47 were classified as typical carcinoids (TC) and 34 as atypical carcinoids (AC). Tumourlets and DIPNECH were detected in all patients when additional sampling from normal lung parenchyma was done. At least six additional blocks were required to confirm the coexistence, indicating that the presence of both entities would be missed if fewer blocks were sampled. When comparing the proliferation index (Ki67) between the primary tumour and the associated tumourlets, no differences were observed in the group of TC. On the other hand, a lower Ki67 (<5%) was observed in tumourlets from fourteen patients in the AC group when compared to that of their primary tumours.
Conclusion: In summary, our results indicate that the coexistence of tumourlets and DIPNECH is probably often missed in the majority of patients with lung NETs due to a lack of guidelines in evaluating normal lung parenchyma. Therefore, it is recommended to routinely increase the sampling (six more blocks) in suspected carcinoid tumours. Furthermore, the assumption that associated tumourlets and/or DIPNECH share the same characteristics as the primary tumour should be questioned and further sub-classification for this entity should be regarded (DIP-A-NECH,"A" for atypical).

PS-05-017
Immunohistochemical evaluation of somatostatin receptor 2 (SSTR-2) expression in benign and malignant tumours of the thyroid gland
K. Vargas Osorio*, E. Pérez-Béliz, A. Jiménez Pérez, E. Díaz-López, U. Anido-Herranz, J.M. Cabezas-Agrícola, I. Abdulkader Nallib, V. Púbul-Nuñez, J. Cameselle Teijeiro
*Clinical University Hospital, University of Santiago de Compostela, Spain

Background & objectives: The expression of somatostatin receptors (SSTRs) in medullary thyroid carcinoma (MTC) is well known, but there is still limited data about these receptors in thyroid lesions of follicular lineage. We investigated the expression of SSTR-2 in the thyroid gland.
Methods: Immunohistochemical expression of SSTR-2-C-terminal was investigated in paraffin-embedded tissue from 78 thyroid lesions. Two different antibodies were used: the monoclonal antibody (Ab) UMB1, 1/100, pH6, Abcam, Cambridge, UK, and the polyclonal Ab, 1/50, pH9, Gennova, Seville, Spain, with appropriate controls. Only immunostaining with a membrane pattern of any intensity was considered positive.
Results: Positive expression of SSTR-2 (with both Abs) was detected in: 6/6 (100%) cases of MTCs, 7/19 (36.8%) papillary thyroid carcinomas (PTCs), 0/9 follicular thyroid carcinomas (FTC), 5/8 (62.5%) oncocytic carcinomas, 0/4 high-grade FTCs, 2/3 (66.6%) anaplastic carcinomas, 0/5 follicular adenomas, 3/6 (50%) oncocytic adenomas, 1/5 (20%) Graves disease, and 1/5 (20%) follicular nodular disease. Positivity was also found in 3/3 (100%) lymph node metastases of MTC. No reactivity was detected either in lymph node or bone metastases from 1 case of PTC and 1 FTC, respectively. The thyroid tissue adjacent to the tumours examined was also negative for these Abs.
Conclusion: The expression of SSTR-2 is not limited to the MTC but was also found in tumours of follicular lineage, mainly in malignant and benign oncocytic tumours, some PTCs, some anaplastic carcinomas as well as in some non-neoplastic conditions. These findings could justify the use of somatostatin analogues in diagnosis and/or therapy of some follicular derived tumours refractory to conventional treatments.

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PS-06 Poster Session History of Pathology
PS-06-001
A series of aorta aneurysms in a historical pathology museum
R.H. Henriques De Gouveia*, T. Ferreira, G. Nogueira Fontinha, V. Sousa, L. Carvalho
*Universidade da Madeira, Portugal

Background & objectives: Aorta Aneurysms (AA) are a relevant source of morbidity/mortality. In fact, the study of global burden of disease showed 172,427 deaths in 2019 (82.1% increase, when compared with 1990). The authors aim to analyse AA in a Historical Pathology Museum.
Methods: To achieve the aim, a search for Aortic Aneurysm specimens was performed inside the collection of the XIXth century, UNESCO's World Heritage Anatomical Pathology Museum – Medical Faculty, Coimbra University. A museum, that houses thousands of objects of various natures [including books, photographs, scientific equipment, anatomo-pathological specimens (dried or in glass containers with fixative-liquid), to artificial (clay, wax) models].
Results: Fifteen (n=15) biological specimens were found. Fourteen (n=14) are preserved in fixative liquid and one is dry. They were procured during autopsies. These aneurysms affect different segments of the aorta, namely the arch (6), ascending (2), thoracic (1), abdominal (4) or multiple (2). Their form is saccular (8) or fusiform (6). They present atherosclerotic lesions. Some show complications, as mural thrombosis (1), arterial wall dissection (1) or destruction of the surrounding tissues of the chest wall, including bone perforation (1).
Conclusion: Aortic Aneurysms are localized, progressive dilatations of the aorta. Often asymptomatic, they continue to be underdiagnosed. The study of this museological series reinforces the existence of aortic

aneurysms in the XIXth and early XXth centuries, namely in Portugal (Europe). It also shows their atherosclerotic aetiology, and thus the need to invest in risk factors' prevention. Being autopsy specimens and presenting severe complications in some, emphasizes the need of early diagnosis and medico-surgical preventive/therapeutic measures, in order to avoid catastrophic outcomes.

PS-06-002

The contribution of palaeopathology in modern medicine through an interesting ancient case of a possible exogenous ochronosis

D. Moissidou*, E. Labajo, M.B. Sanchez, S. Havaki, P. Selemenakis, G. Kamel, B. Perea Perez
*Queen Mary University of London, Malta

Background & objectives: Palaeopathology holds significant information for the evolution and comprehension of contemporary diseases, coexisting with modern pathology. Ancient mummified tissue serves as crucial material in palaeopathological investigations, as illustrated by this interesting case study of a mummified Egyptian head.
Methods: Histological analysis was conducted on skin tissue samples extracted from an ancient Egyptian mummified head. The aim was to investigate potential skin pathologies and validate initial observations of a possible skin disorder through macroscopic examination. Modified histological procedures were employed alongside a range of histochemical, immunohistochemical, and electron microscopy techniques, as well as Fourier transmission infrared spectroscopy.
Results: Results revealed generally well-preserved skin tissue architecture, including smooth muscle, blood vessels, dermis and skin appendages. Additionally, calcified areas were observed in the dermis and surrounding hair follicles, along with fibrosis suggestive of potential chronic skin inflammation. Immunohistochemical analysis confirmed these findings related to chronic conditions. Transmission electron microscopy revealed collagenous elastolysis and elastorrhexis, as well as amorphous structures in the interstitium. Fourier transmission infrared spectroscopy indicated proteinic assembly, aligning with the immunohistochemistry. However, given the postmortem changes experienced in ancient mummified tissues, including alterations due to embalming techniques, further investigation is necessary for further validations.
Conclusion: The findings exhibited pathological similarities to exogenous ochronosis, a rare skin disorder often associated with the use of cream for skin lightening, typically used by darker skin individuals. Notably, the samples originated from a member of the royalty, and historical evidence suggests that ancient Egyptian royal families utilised skin-lightening agents. This case can serve as a compelling example of how palaeopathology contributes in comprehending modern pathology context and the evolution of diseases.

PS-06-003

Museum of Anatomic Pathology - bringing the past into the future

G. Nogueira Fontinha*, J. Pimentel, V. Almeida, L. Veloso, N. Sousa, J. Rocha, L. Bastião, L. Carvalho, V. Sousa
*1. Institute of Anatomical and Molecular Pathology, Faculty of Medicine of the University of Coimbra, Coimbra, Portugal 3. Pathology Service, University Hospital Anatomical Pathology Coimbra – Portugal

Background & objectives: Museums of Anatomic Pathology are invaluable when it comes to teaching. Their historical nature can lead however to a veiled existence to the communities around it. A project to bring the past into the future has begun.
Methods: The Museum of Anatomic Pathology of the University of Coimbra has partnered with CCG and BMD Software for a two-part project – the creation of a website for laymen and an app for in-site visitors. For the virtual modelling of the museum, 3D scanning of specimens and annexation of information and ancillary images Figma and LIDAR are being used.
Results: The website will allow for a brief online visit of the 3D modelled museum and access to some of its simpler specimens while providing historical contextualization. The app is to be used by in-site visitors - it serves as a mini map of the museum and by scanning the QR codes of specimens one can read about the history of the specimen, its pathological information and value and even see related medical images such as x-ray scans. By scanning our specimens with LIDAR visitors will be also able to use augmented reality to inspect the 3D scanned specimen in any position and to zoom in/out for a more detailed look.
Conclusion: The goals of this project are to let the Museum be known by laymen and to make visits by future health professionals more interactive and interesting. For the former these museums are a sight of wonder and unknowingness and can strengthen the ties between the scientific community and general society. For the latter these are an amazing source of teaching as one can see in real specimens the gross features of pathology and have an epidemiologic perspective of the past.

PS-06-004

Soft tissue and bone tumours of the limbs – Museum of Anatomical Pathology

G. Nogueira Fontinha*, R.H. Henriques De Gouveia, J. Pimentel, V. Almeida, M. Viseu, M. Reis Silva, A. Alarcao, M.A. Santos, T. Ferreira, V. Sousa, L. Carvalho
*1. Institute of Anatomical and Molecular Pathology, Faculty of Medicine of the University of Coimbra, Coimbra, Portugal 2. Pathology Service, University Hospital Anatomical Pathology Coimbra – Portugal

Background & objectives: Until the last two centuries the treatment of tumourous masses of the limbs was solely based in destructive amputation. We delve into the collection of the Anatomical Pathology Museum of the University of Coimbra regarding its 29 amputation specimens
Methods: According to the WHO Classification of Soft Tissue and Bone Tumours soft tissue sarcoma incidence outweighs that of bone sarcoma by ten. The most common soft tissue sarcomas are of lipomatous nature, and these have a low incidence in the limbs while the most prevalent high-grade sarcoma of the bone is by far the osteosarcoma affecting mainly the knee.
Results: The collection includes 6 upper and 23 lower limb specimens. The most common diagnosis is of sarcoma NOS (13) followed by osteosarcoma (10), fibrosarcoma (2), "globo-cellular sarcoma" (2), alveolar sarcoma (1) and carcinoma (1). Osteosarcoma location is mainly in the femur and knee region (60%) in accordance to actual epidemiology but less usual locations are present such as the humerus (10%). Distribution of sarcoma NOS is proportional to the cases in each location. "Globo-cellular sarcoma" is no longer present in the literature, and it occurs in the hand and elbow. "Alveolar sarcoma" is probably not an alveolar soft part sarcoma due to location (thigh) and year of first description (1952).
Conclusion: Looking into the collection diagnosis one can perceive the recent evolution of the classification of soft tissue and bone tumours. It seems that osteosarcoma remains one of the easiest diagnosis to be recognized without ancillary studies and its prevalence and location endures the passage of time. The question of "globo-cellular sarcoma" persists and eludes the international literature of the last 50 years being perhaps nothing more than a globoid cell morphologic feature of an uncertain sarcoma.

PS-07 Poster Session Nephropathology

PS-07-001

C5b9 and other complement proteins are enriched in the glomerular amyloid deposits of patients with monoclonal amyloidosis: a study based on immunohistochemistry, immunofluorescence and mass spectrometry

H. Gakiopoulou*, J. Courraud, K. Palamaris, I. Theochari, A. Stofas, N. Alevizopoulos, E. Theodoropoulou, E. Psimenou, E. Kastritis
*1st Department of Pathology, School of Medicine, National and Kapodistrian University of Athens, Greece

Background & objectives: Although complement is implicated in most types of glomerular diseases, its potential role in renal disorders associated with monoclonal-gammopathies, has not thoroughly explored.
Methods: Based on the observation that C3 and C4d are often found in amyloid deposits, we investigated immunohistochemically the presence of the C5b9 (membrane-attack-complex), the end-product of the classical, lectin and alternative complement pathways, in a series of 38 patients with monoclonal-amyloidosis (AL/AH) and monoclonal-immunoglobulin-deposition-disease (MIDD). The presence of complement proteins in amyloid deposits was further investigated with mass-spectrometry.
Results: C5b9-immunohistochemistry was performed in renal biopsies from 20 patients with monoclonal-amyloidosis (14 λ-AL, 5 κ-AL and 1 AH) and 18 patients with MIDD (11 κ-LightChainDepositionDisease/κ-LCDD and 7 λ-LCDD).In the majority of λ-AL patients, C5b9 staining was observed predominantly in the glomerular-amyloid-deposits (less in vascular-deposits),often exhibiting a strong intensity. Four out of 5 κ-AL cases also showed C5b9 staining, however weak in most of them. When C5b9 was found in MIDD, it was observed along the glomerular-basement-mebranes. It was weak in 5/11 κ-LCDD, moderate in 2/11 and negative in 4/11 κ-LCDD cases. In the 7 λ-LCDD, C5b9 showed traces or weak staining in 4 cases and a moderate staining in 3 cases.
Conclusion: Using mass spectrometry we detected 15 complement proteins within amyloid deposits (fewer in Congo red-negative areas). Preliminary results showed elevated levels of C9, C3, C5, C8 and C4 in amyloid deposits, particularly prominent in positive glomeruli and moderately in positive vessels. In conclusion, C5b9 and complement proteins seem to be enriched in the glomerular amyloid deposits of patients with monoclonal-amyloidosis. These preliminary results suggest a possible role of the complement cascade activation in AL with potential future therapeutic implications.

PS-07-002
Glomerular CD68+ cells in transplant kidneys correlate with glomerulitis and predict poorer renal functions
P. Liang*, H. Chuang, T. Chen
*Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan

Background & objectives: Glomerulitis signals microvascular inflammation (MVI) and links to antibody-mediated rejection in kidney transplants. Since applying the Banff criteria for glomerulitis only has a fair to moderate inter-rater agreement, we intended to evaluate CD68+ cell count reliability as an MVI marker.
Methods: The retrospective, single-centre study used biopsies from patients with renal function changes after kidney transplant. Three renal pathologists from different institutes evaluated each case's Banff glomerulitis g score and glomerular CD68+ cell count. The clinical parameters were collected at the time of biopsy, three months, and six months later.
Results: After excluding biopsies with other diseases (including glomerulonephritis and diabetic nephritis), 121 kidney allograft biopsies were selected for the study. Cases with a Banff g score > 0 are considered Banff-glomerulitis. Cases with a glomerulus CD68+ cell count > cut-off number are regarded as CD68-glomerulitis. The highest concordance between Banff-glomerulitis and CD68-glomerulitis was seen when the cut-off number was set to 6 or 8. Patients with CD68-glomerulitis were associated with Banff ptc score >0 ($p < 0.05$) and Banff gc score >0 ($p < 0.05$). Patients with CD68-glomerulitis have a significantly lower estimated glomerular filtration rate ($p < 0.05$) and higher urine protein creatinine ratio ($p < 0.05$).
Conclusion: The number of glomerular CD68+ cells is associated with MVI, deteriorated renal function, and higher levels of proteinuria in transplant kidneys. The CD68+ cell count (>6) shows stronger inter-rater reproducibility than Banff g score (>0) (Fleiss-kappa 0.7 vs. 0.54). Glomerular CD68+ cell count can be a reliable surrogate marker for MVI and glomerulitis in transplant kidneys.

PS-07-003
The epigenetic enzyme DOT1L histone methyltransferase links oxidative stress, inflammation and fibrosis in diabetic kidney
S. Manea*, M. Vlad, A. Lazar, A. Manea
*IBPC "N. Simionescu", Romania

Background & objectives: Despite the appropriate therapeutic interventions, diabetic patients have a high risk to develop diabetic kidney disease (DKD). We investigated the role of DOT1L epigenetic enzyme in mediating the expression of genes related to oxidative stress, inflammation, and fibrosis in DKD.
Methods: Male non-diabetic and streptozotocin-induced diabetic C57BL/6J mice were treated with 5 mg/kg EPZ004777 (DOT1L inhibitor) or vehicle, for 4 weeks. Human endothelial cells (EC) were exposed to normal or high glucose concentrations in absence/presence of EPZ004777. EC were subjected to transient transfection to overexpress DOT1L. Kidney- and EC-derived samples were examined by histochemistry, immunofluorescence microscopy, real-time PCR or western blot.
Results: The gene and protein expression levels of DOT1L, the pro-oxidant enzyme NADPH oxidase (Nox) catalytic subunits, inflammation-associated cell adhesion molecules (E-selectin, ICAM-1, VCAM-1), and extracellular matrix (ECM) proteins (collagen IV, fibronectin, laminin) were found significantly elevated in the kidney of diabetic mice. EPZ004777 pharmacological intervention significantly attenuated the augmented glomerular hypertrophy and the up-regulated expression of Nox subtypes, pro-inflammatory makers and the accumulation of ECM proteins in diabetic kidney. DOT1L blockade suppressed the high glucose-induced up-regulation of Nox1-5 catalytic subunits, cell adhesion molecules and ECM components in cultured EC. Significantly elevated mRNA levels of Nox1-5, E-selectin, ICAM-1, VCAM-1, collagen IV, fibronectin, and laminin were determined in human EC overexpressing DOT1L.
Conclusion: Alterations in histone methylation-based epigenetic mechanisms contribute to persistent transcriptional changes associated with a pro-oxidant, pro-inflammatory and pro-fibrotic phenotype of diabetic kidney. DOT1L is likely to promote long-lasting transcriptional effects, since no specific histone demethylase exists to counteract DOT1L-induced H3K79 methylation, an epigenetic imprint of active gene expression. The findings of our study suggest that DOT1L pharmacological targeting could become an important supportive therapeutic strategy to attenuate oxidative stress, inflammation and the excess synthesis of ECM proteins in DKD.

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PS-07-004
Exploring the histological diversity of renal lesions in connective tissue disorders beyond lupus: a comprehensive analysis

V. N Gowda*, A. Nalwa, D. Gupta, A. Saxena, V. Vishwajeet, V. Verma, M. Chaturvedy, R. Jhorawat
*Department of Pathology, AIIMS, Jodhpur, India

Background & objectives: Connective tissue disorders (CTDs) are a heterogeneous group of disorders due to dysregulated and disturbed immunoregulation, leading to tissue injury. We aim to explore renal histopathological diversity in CTDs, identifying distinct patterns and comprehensive understanding of non-lupus-related renal involvement.
Methods: Renal biopsy cases were reviewed retrospectively between 2018 to 2023, with patient demographic data, lab investigations, light microscopy and immunofluorescence (IF) findings. Patients with systemic lupus erythematosus were excluded from the study.
Results: Nine cases were included in the study with a mean age of 40 years and female predominance. All cases had raised serum creatinine levels, six cases with ANA and one with anti-U1RNP positivity. Cases included Sjogren's syndrome, systemic sclerosis, rheumatoid arthritis and dermatomyositis. Varied morphological spectrum on light microscopy: membranoproliferative glomerulonephritis, tubulointerstitial nephritis, membranous nephropathy and focal segmental glomerulosclerosis. Interstitial fibrosis and tubular atrophy were severe (n=2), mild (n=6) and moderate (n=1). No full house pattern seen on IF. Codominant expression of IgG and C3 seen in one case (n=1) and IgA and C3 seen in one case (n=1). No extraglomerular deposits in tubules and blood vessels seen, unlike lupus.
Conclusion: Renal manifestations in CTDs are a frequent presentation with varied morphological spectrum and IF findings in renal biopsies. Such lesions aid the clinician in decision-making for therapy options and in predicting prognosis. A renal biopsy is essential to ensure proper diagnosis with an interdisciplinary approach to optimize treatment in patients with CTDs.

PS-07-005
A novel method for enhanced evaluation of lupus nephritis: utilizing Banff 2018 classification criteria
M. Zivotic*, G. Nikolic, M. Pecic, A. Mioljevic, D. Milivojevic, V. Brković, M. Baralić, M. Radović, S. Radojevic Skodric
*Institute of Pathology, Faculty of Medicine University of Belgrade, Serbia

Background & objectives: The ISN/RPS classification is utilized for the routine assessment of kidney biopsies from patients with lupus nephritis (LN), whereas the Banff classification is routinely employed in kidney transplant pathology, providing additional details regarding the activity and chronicity of kidney lesions.
Methods: The retrospective study included 149 kidney biopsies diagnosed as LN: class I (n=1), class II (n=24), class III (n=33), class IV (n=70), class V (n=20), and class VI (n=1). Clinical (age, proteinuria, serum creatinine and urea values) and pathohistological variables (ISN/RPS and Banff parameters) were examined and compared among LN classes, as well as among chronic kidney disease (CKD) stages.
Results: Patients with LN class V frequently exhibited nephrotic range proteinuria (p=0.007). All examined clinical parameters (age, proteinuria, serum creatinine, and urea values) showed significant differences (p<0.050) across CKD stages. Proteinuria decreased with an increase in CKD stage, while the other parameters significantly increased. Most ISN/RPS parameters, as well as Banff parameters determined in the glomeruli (g, cg, mm) varied across LN classes (p<0.050) but did not differ across CKD stages. Banff parameters assessed in the tubulointerstitium (ci, ct, ti, i-IFTA, i) and blood vessels (cv) showed significant differences between both LN classes and CKD stages (p<0.050).
Conclusion: While the ISN/RPS classification is suitable for defining LN classes, supplementing it with Banff parameters could enhance the correlation with CKD stage assessed at the time of biopsy. Further follow-up studies are warranted to explore if the Banff assessed parameters could serve as predictors for CKD progression or predictors for the response to therapy.

PS-08 Poster Session Cardiovascular Pathology
PS-08-001
Myocardial ischemia reperfusion injury and autophagy: role of Galectin-3
S. Al-Salam*, S. Hashmi
*College of Medicine & Health Sciences, United Arab Emirates

Background & objectives: Myocardial ischemia reperfusion (IR) injury is associated with increased autophagy. Galectin-3 (GAL-3) is closely associated with early myocardial infarction, myocardial IR injury and later myocardial fibrosis. We aim to investigate the role of GAL-3 in autophagy during early IR injury.
Methods: Male C57B6/J mice and GAL-3 knockout (KO) mice were used for mouse model of IR injury. Heart samples were processed for immunohistochemical and immunofluorescent labelling, and enzyme linked immunosorbent assay. The interaction of GAL-3 and autophagy proteins were assessed. Data were presented in mean ± S.E. Statistically significant differences (p<0.05) were calculated between experimental groups by one-way analysis of variance.
Results: There was a significant increase in left ventricular (LV) concentrations of GAL-3 in GAL-3 wild-type mice when compared with their sham control at 24-hour following reperfusion. LV autophagy flux is increased at 24-hour following reperfusion. There were significant higher concentrations of LV LC3B, ATG13, Ulk-1, Beclin, ATG5, and p-AMPK in Gal-3 KO mice than GAL-3 wild-type mice at 24-hour following reperfusion. While, there were significant higher concentrations of LV p-mTOR, p- NF kappa-B, and beta-catenin in LV of GAL-3 wild-type mice than GAL-3 KO mice at 24-hour following reperfusion.
Conclusion: Our findings support GAL-3 interaction with autophagy and prosurvival signalling proteins and demonstrate absence of GAL-3 can potentiate autophagy in the LV in IR injury at 24-hour follow reperfusion.

PS-08-002
Cardiac amyloidosis: frequency and characterization in a large Swiss autopsy cohort
A. Baschong*, S. Ersözlü, H. Moch, Z. Varga, F. Ruschitzka, A. Flammer, C.A. Meier, U. Maccio
*Department of Pathology, Universitätsspital Zürich, Switzerland

Background & objectives: Cardiac amyloidosis (CA) is an underdiagnosed disease. With availability of disease modifying drugs, diagnosis of common subtypes, transthyretin (ATTR-CA) and light chain (AL-CA) is of particular interest. We aim to determine the frequency and extent of CA in an autopsy cohort.
Methods: We conducted a retrospective, single-centre study of all adult autopsies (age > 18 years) with findings of CA performed in our institute during a period of ten years (January 2014 - August 2023). A semiquantitative scoring system for the amyloid load in the myocardium and vessels was established. Two pathologists independently scored the slides of the left and right ventricle.
Results: CA was found in 5% of autopsies (103/1932 patients; 59.2% males; 40.8% females); first diagnosed at autopsy in 92%. The median age at death was 86 years (range: 46 – 97y, 6.8% <70y). The most common type was ATTR-CA (n = 97, 94.2%) followed by AL-CA (n = 6, 5.8%). The majority had isolated CA (n = 60, 58.8%)

and in 41.7% systemic amyloid deposits were found (n = 43). The amyloid load was mostly either present in the myocardium alone (n = 41, 39.8%) or combined in vessels and myocardium (n = 40, 38.8%). Amyloid restricted to cardiac vessels was present in a small subset (n = 22, 21.4%).
Conclusion: The present study shows the cardiac amyloid load in a large cohort of autopsies where CA was first diagnosed. Future studies should correlate these findings with clinical and radiological data to enhance the diagnostic sensitivity in antemortem patient populations.

PS-08-003

Capillary density and lymphatic vessels in endomyocardial biopsies from patients with cardiac amyloidosis

A. Pucci*, V. Musetti, A. Aimo, L. Bonino, V. Castiglione, F. Greco, M. Rossetti, A. Celi, A. Barison, M. Coeani, M. Ciardetti, C. Palmieri, C. Passino, M. Emdn, G. Vergaro
*Italy

Background & objectives: Cardiac amyloidosis (CA) is characterized by the extracellular deposition of amyloid fibrils. CA could represent a failure of cardiac drainage, caused by progressive capillary rarefaction. We investigated lymphatic vessels and capillary density on endomyocardial biopsies (EMBs) with CA.
Methods: Lymphatic (Podoplanin+) and capillary (CD31+) vessel densities were evaluated by immunohistochemistry on EMBs from the left ventricle (LV) in 3 patients' groups: a) heart valve donors without cardiac pathology, i.e., controls (n=7); b) patients with septal LV hypertrophy (CH) without CA (n=10); c) CA patients (n=20).
Results: Both ATTR- and AL-CA patients displayed a significantly lower capillary density as compared to controls ($p<0.001$ for both), with no difference between the ATTR- and AL-CA groups (p=0.490). Areas heavily laden with amyloid deposits typically lacked capillary and lymphatic vessels. However, the global density of lymphatic vessels did not differ significantly between CA patients and controls (p=0.594 for AL-CA, p=0.816 for ATTR-CA), nor between AL- and ATTR-CA patients (p=0.138). No significant factors were found to predict lymphatic capillary density, including the extent of amyloid or fibrosis.
Conclusion: Compared to healthy subjects, CA patients showed a significant reduction in capillary density in the LV endomyocardial layers. Although most amyloid deposits showed no blood or lymphatic vessels, the overall lymphatic vessel density was comparable in EMBs of CA vs. healthy subjects. These observations could be relevant for antibody-based therapies targeting AL or ATTR amyloid fibrils. Antibodies might access extracellular spaces via remaining blood capillaries, and intact lymphatic vessels could support the immune response.

PS-08-004

Expression of pro-autophagic Beclin-1 and pro-apoptotic Caspase-3 in post-traumatic period of experimental blunt cardiac injury

M. Stepanchenko*, E. Klyuchnikova, O. Korpacheva, A. Zolotov, S. Mozgovoi
*Omsk State Medical University, Russia

Background & objectives: After blunt cardiac injury, autophagy and apoptosis are activated. We have suggested that different realisations of these phenomena would be possible due to different stress resistance status.
Methods: The study was carried out on 106 white rats. The control group included subgroups with high and low stress resistance, the experimental group included the same subgroups with experiment duration of 6, 12, 24 hours. The experimental group was simulated experimental cardiac injuries and performed immunohistochemical research on the extracted hearts with antibodies to Beclin-1 and Caspase-3.
Results: There was an increase in Beclin-1 expression in the experimental group compared to the control group. In the high-stress-tolerant animal group, the expression index increased in the post-traumatic period, while the low-stress animal group experienced a gradual decline in the expression index.
In the immunohistochemical study of Caspase-3 expression there was no signal in the control group. There was a lack of marker expression in subgroups of rats with high stress tolerance at research points of 6 and 12 h, and a slight increase subgroups with a 24-hour duration. In subgroups of low stress-tolerant animals, the Caspase-3 protein expression index showed a gradual increase over the post-traumatic period
Conclusion: After an experimental blunt cardiac injury, autophagy and apoptosis are activated regardless of animal stress resistance. However, marker expression patterns vary in animals with different stress resistance. The data suggest that autophagy acts as a tissue adaptation reaction and manifests itself in less severe myocardial damage, which is observed in animals with high stress resistance. When the implementation of this phenomenon is inefficient, apoptosis becomes the dominant tissue response in individuals with lower stress resistance and more severe myocardial damage.

PS-08-005

The influence of endurance exercise training intensity on the acute phase of murine coxsackievirus B3 myocarditis

M. Van Hecke*, K. Favere, S. Eens, P. Guns, H. Heidbuchel, T. Roskams
*KU Leuven, Belgium

Background & objectives: Previous murine studies have demonstrated a detrimental effect of exercise on the acute course of viral myocarditis. In this study, we evaluate the impact of both moderate and high-intensity running protocols on the acute course of coxsackievirus B3-induced myocarditis.
Methods: 70 male C57BL/6J mice were randomised to 3 weeks of treadmill running, either of moderate, constant intensity (ModEEX) or of increased intensity until exhaustion during the last week (HiEEX) or remained sedentary (SED). Two weeks into the study, animals were either injected with CVB or vehicle (PBS). All animals were sacrificed 1 week post-inoculation and their hearts were histopathologically evaluated.
Results: Semiquantitative scoring of the myocarditis severity revealed marked inflammation and necrosis in all CVB animals without group differences. Digital quantification of the extent of the inflammatory lesions was highest in hiEEX mice (2.78% of the cardiac cross section) followed by SED mice (1.80%) and ModEEX mice (1.22%). Morphologic evaluation of the inflammatory lesions using HE, performed by experienced pathologists, showed more edema, RBC extravasation and ongoing necrosis in HiEEX mice, whereas ModEEX and SED mice showed higher presence of mononuclear inflammatory cells. The elaborate immunohistochemical assessment confirmed fewer numbers of NK cells, T-helper cells (and their subtypes) and cytotoxic T-cells, and iNOS- and Arg1-reactive macrophages in the HiEEX mice.
Conclusion: Using the male C57BL/6J mice CVB3-model and the reproducible exercise protocols that our group previously established, we have now investigated the impact of training intensity on the early phase of viral myocarditis, since existing evidence seems to support a U-shaped relationship between exercise and adverse cardiovascular events such as ventricular arrythmias. Our findings support that high intensity exercise during acute infection may aggravate the myocardial damage, possibly by delaying the necessary immune reaction.

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PS-08-006

The influence of endurance exercise training on myocardial fibrosis and arrhythmogenesis in a coxsackievirus B3 myocarditis mouse model

M. Van Hecke*, K. Favere, S. Eens, P. Guns, T. Roskams, H. Heidbuchel
*KU Leuven, Belgium

Background & objectives: Athletes presenting with ventricular arrhythmias often have nonischaemic myocardial fibrosis (MF). In this study we investigated the impact of endurance training on long-term outcomes such as fibrosis and arrhythmogenicity in an experimental coxsackievirus B3 (CVB)-induced myocarditis model.
Methods: Male C57BL/6J mice were randomly assigned to 13 (preEEX, n=30) or 2 (EEX, n=72) weeks of moderately intense treadmill running or not (SED). Next, animals were either injected with CVB or vehicle (PBS), after which only EEX animals continued training. Clinical, histopathological and electrophysiological changes were assessed before all animals were sacrificed 7 weeks post-inoculation.
Results: Mice of the CVB-EEX, but not the preEEX-CVB group, showed less weight loss and better-preserved running capacity. Mortality rates were lower in CVB-EEX and preEEX-CVB mice. Histological assessment still demonstrated myocarditis in the CVB groups, with higher numbers of iNOS-reactive macrophages and cytotoxic T-cells in CVB-EEX mice. Interstitial fibrosis and fibrosis with extensive distribution were both increased in CVB-EEX mice (P=0.049 and P=0.048), with a numerical but not significant increase in the number of scars per cross-section. In vivo electrophysiology studies in this group only induced non-sustained runs and increased cumulative beat count and duration (P=0.084). PreEEX mice did not show histopathological or electrophysiological differences compared to SED mice.
Conclusion: The presence of MF in athletes with arrhythmias might be related to adverse myocardial remodelling due to continued training during a (subclinical) viral infection. In contrast to previous studies, the effect of the exercise training during myocarditis was investigated on the long-term in this study. Our data suggest that continued training during viral myocarditis alters the inflammatory response and enhances fibrogenesis. The impact on ventricular arrhythmogenesis requires further exploration. When training was discontinued upon infection, no differences are observed anymore.

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PS-09Poster Session Electron Microscopy
PS-09-001
Morphological and crystallographic features of meningioma psammoma bodies

A. Denysenko*, R. Moskalenko
*Sumy State University, Ukraine

Background & objectives: Meningioma is one of the most common central nervous system tumours. Usually, it is characterized by slow growth, asymptomaticity, and biomineralization. The work aims to study morphological and crystallographic aspects of meningioma biomineralization manifested by forming psammoma bodies (PB).
Methods: The study group included 30 meningiomas with signs of biomineralization (group I) and 30 samples without them (group II). We use histological method, scanning electron microscopy (SEM) with energy-dispersive X-ray spectroscopy (EDX), transmission electron microscopy (TEM) with electron diffraction (ED), and Fourier transform infrared spectroscopy (FTIR). We performed the statistical analysis of the results using GraphPad Prism 8.0.
Results: Histologically, meningioma tissue was represented by medium-sized, relatively uniform cells of the endothelial phenotype. SEM of group I meningioma tissue revealed the presence of many bright white-grey objects (oval and round formations), which correspond to calcium apatite structure. TEM shows that the samples are conglomerates (1-5 μm in size) of crystals in an amorphous matrix. Crystalline particles have sizes from 30 to 200 nm. Electron diffraction from conglomerates presents a halo of intensity corresponding to the amorphous phase and weak rings and point reflexes from crystalline particles. The most intense signal on FTIR is observed in the region, corresponding to phosphate-ion bending in hydroxyapatite.
Conclusion: Meningiomas were morphologically very close to the endothelium of the meninges, except for the formation of PB. They are rounded, layered formations, varying from 30 to 200 nm individually and from 1 to 5 μm in agglomerates. According to the results of SEM, TEM, and FTIR, the structure of the biomineral in PB corresponds to calcium hydroxyapatite.

PS-10Poster Session Gynaecological Pathology
PS-10-001
Compliance with sampling guidelines in borderline ovarian tumours: auditing current practice

M. Alzamora*, P. Rodrigues Veiga, R. Dias, C. Bartosch
*Department of Pathology, Portuguese Oncology Institute of Porto (IPO-Porto), Portugal

Background & objectives: Grossing of borderline ovarian tumours (BOTs) is challenging due to their heterogeneous nature and, frequently, large sizes. Optimal sampling may aid diagnosis and management, but tangible data is scarce. We aim to assess the sampling of tumours diagnosed as BOT.
Methods: We retrospectively identified BOT cases diagnosed on frozen section at our institution (2013-2023), and divided tumours into small (<10cm) and large (≥10cm). We conducted a sampling audit, documenting the number of sections taken per centimetre (SPC) of largest tumour axis. Additionally, we recorded final diagnoses and presence of intraepithelial carcinoma and/or microinvasion.
Results: We identified 72 BOTs on frozen section (serous: 50.0%; mucinous: 43.1%). There were foci of microinvasion and/or intraepithelial carcinoma in 33.3%, mostly mucinous (51.8%). Median tumour size was 16.0cm, with mucinous tumours being significantly larger (p<0.001) than serous. 31.9% of cases were classified as small and 68.1% as large.
A median of 35.1 sections were taken per case, with an overall median sampling of 2.2SPC. Number of sections was significantly higher in small tumours (p<0.001). There was no difference in sampling between large serous and mucinous tumours (p=0.843). In tumours with intraepithelial carcinoma/microinvasion, a median of 2.1SPC were collected. Twelve cases were upgraded to carcinoma in final report.
Conclusion: In summary, our audit confirms compliance with current guidelines recommending taking 2SPC in large BOT or those with intraepithelial carcinoma/microinvasion, yet uncovers an intriguing tendency toward increased sampling in smaller tumours. This work will serve as baseline for further investigation on the potential implications of sampling for accurate diagnosis and patient management.

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PS-10-002
Morphological patterns of high-grade serous tubo-ovarian carcinoma in association with HRD

M.E. Aquino Correa*, L. Valdivieso, A. Castillo, M. Jimeno, L. Hernandez, J. García-Gómez, K. Matute-Molina, A. Feu
*Hospital Universitari Germans Trias i Pujol, Spain

Background & objectives: High grade serous carcinomas (HGSC) exhibit a homologous recombination defect (HRD) in 50% of cases rendering them more sensitive to chemotherapy and PARP-inhibitors.

We aimed to correlate morphology with HR status in HGSC, as certain morphological data have been associated.
Methods: We performed a retrospective study including HGSC cases diagnosed at our centre in 2023. Tumours were categorized into three morphological patterns: classic (>70% papillary/micropapillary), SET (>70% solid/endometrioid/transitional), mixed (<70% classic/SET pattern). Fallopian tubes were evaluated (SEE-FIM protocol) to detect serous tubal intraepithelial carcinoma (STIC). HRD testing was conducted via next generation sequencing (NGS) using the SOPHiA GENETICS platform (Illumina).
Results: A total of 21 HGSC cases were collected, with 4 cases deemed unassessable due to insufficient tumour representation. Among the 17 evaluable cases, 8 were HR-proficient and 9 were HRD. 2 HRD tumours presented mutations in BRCA1 and 1 in BRCA2. HR-proficient tumours exhibited SET pattern in 4 cases, classic pattern in 3, and mixed pattern in 1. HRD tumours exhibited SET pattern in 7 cases, classic pattern in 1, and mixed pattern in 1. Two tumours with mutations in BRCA1 displayed SET pattern. The sole BRCA2 mutated tumour showed a mixed pattern. STIC was observed in 4 HR-proficient cases (4/8) and none of the HRD cases (0/10)
Conclusion: Although the number of cases is limited to reach definitive conclusions, HRD tumours appear to be associated with SET morphological pattern and the absence of STIC, consistent with previous literature. Both findings could be useful as predictive biomarkers for therapy response and improved overall survival in HGSC. Our goal is to strengthen this correlation by expanding the sample size.

PS-10-003
Should all undifferentiated uterine sarcoma be molecularly tested?
D. Arciuolo*, S. Patrizi, S. Vallese, R. Alaggio, L. Pedace, C. Nardini, F. Vinciarelli, P.U. Belen, A. Travaglino, G. Scaglione, A. Santoro, F. Locatelli, E. Miele, G.F. Zannoni
*Pathology Unit, Department of Woman and Child's Health and Public Health Sciences, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Italy

Background & objectives: Undifferentiated uterine sarcoma (UUS) is defined by the absence of specific lines of differentiation. We investigated the morphological, molecular, methylation profile and copy number variation of a series of UUS to better classify this entity and identify possible therapeutic target.
Methods: The study included 19 consecutive UUS diagnosed at Policlinico Agostino Gemelli, Rome, from 01/2020 to 01/2024. All the cases were RNA sequenced and 10 out of 19 underwent DNA methylation profiling and copy number variation analysis.
Results: RNA sequencing identified 4 cases with a newly identified fusion: EVC2::ENPP2, SETD2::SACM1L, ZDHHC9::AFF2 and DENND6::NCOR1 with peculiar morphological features. DNA methylation classified 2 cases with a high calibrated score (CS) as malignant rhabdoid tumour and as undifferentiated sarcoma, all the other cases tested showed low CS. Copy Number Variation were more than 2 in all the cases except in 2 cases. CNV analysis identified alteration of 9p (CDKN2A/B) in 2 cases, amplification of CCND2 in 2 cases and amplification of CDK4 in 1 case. Prognosis. Two out of 3 patients alive had less than 2 CNV.
Conclusion: A deeply molecular analysis helps in identifying new fusion in UUS cases. Sarcoma classifier in cases of UUS is not able to recognize a methylation group that might help in classify these entities and better define its cell of origin. CNV confirmed its prognostic ability and identified a subgroup of UUS with better outcome. Lastly, for the first time in UUS, a possible therapeutic target with CDK4-inhibitor was shown.

PS-10-004
Vulvar and non-vulvar cancer risk in women with biopsy verified vulvar lichen sclerosus – a nationwide cohort study
L. Baandrup*, E.L. Kaderly Rasmussen, C.G. Hannibal, R. Hertzum-Larsen, S.K. Kjær
*Department of Pathology, Zealand University Hospital, Roskilde; Unit of Virus, Lifestyle and Genes, Danish Cancer Institute, Copenhagen; Department of Clinical Medicine, University of Copenhagen, Denmark

Background & objectives: Vulvar lichen sclerosus (VLS) is a chronic inflammatory condition associated with development of human papillomavirus (HPV)-independent vulvar cancer. However, few studies have evaluated the risk of neoplastic transformation prospectively and the association between VLS and non-vulvar cancers is largely unknown.
Methods: In the nationwide Danish Pathology Registry, we identified women with biopsy verified VLS 1978-2019. The cohort was linked to the Danish Cancer Registry with follow-up until 2022 and standardized incidence ratios (SIR) with 95% confidence intervals (CIs) were calculated as relative risk estimates of vulvar and non-vulvar cancers according to HPV-association. HPV-associated cancers included cervical, vaginal, oropharyngeal, and anal cancers.
Results: The cohort included 16,921 women with VLS and no previous cancer. Compared with the general female population, women with biopsy verified VLS had significantly increased rates of vulvar squamous cell carcinoma (SIR=16.2; 95% CI: 14.2-18.4) and the SIRs did not vary substantially according to length of follow-up. Regarding the non-vulvar cancers, the SIR estimate combining all HPV-related cancers was 0.5 (95% CI: 0.3-0.7) and with decreased rates of each of the individual HPV-associated cancer sites. Compared with women in the general population, women with VLS also had decreased rates of lung (SIR=0.6; 95% CI: 0.5-0.7), liver (SIR=0.5; 95% CI: 0.2-0.9), and thyroid (SIR=0.5; 95% CI: 0.3-0.9) cancer.
Conclusion: This study shows a 16 times higher risk of vulvar cancer in women with biopsy verified VLS compared with the general female population. Data suggest that the association is caused by local factors and not a general cancer disposition as women with VLS had decreased risk of non-vulvar cancers particularly HPV-associated and smoking-associated cancers. We hypothesize that women with VLS may have different exposure to HPV and smoking compared with the general female population.

PS-10-005
High-risk HPV E6/E7 mRNA in situ expression in cervical premalignant lesions
I. Benedetti*, L. Barrios, R. Rodriguez
*Universidad de Cartagena, School of Medicine. Histopathology Research Group, Colombia

Background & objectives: There is a high inter-observer variability in Cervical Intraepithelial Neoplasia (CIN) classification. RNAscope HPV-test stains E6/E7-mRNA transcripts in FFPE tissue, detecting high-risk-HPV genotypes. Its expression was determined in normal cervix, CIN- I and CIN-III, to grade these lesions accurately.
Methods: The HR-HPV-E6/E7 mRNA expression was evaluated by chromogenic in-situ hybridization (CISH) using a TMA with conization and hysterectomy tissues from 169 patients, with representative areas from normal cervix and CIN. The CISH staining was visually scored by two pathologists based on the average number of dots per cell according to a semi-quantitative analysis. The CISH staining score values were compared.
Results: HPV-E6/E7-mRNA in-situ expression for 18-HR-HPV genotypes was determined in a cervical TMA including: 78 tissue cores with normal cervix, 81 tissue cores with CIN-I/LSIL, and 153 tissue cores with CIN-III/HSIL. According to the CISH staining evaluation,

the mean HR-HPV E6/E7 mRNA in situ expression scores in normal cervix (0.26, 95%CI=0.07-0.43), CIN-I (0.59, 95%CI=0.32-0.86), and CIN-III (1.94, 95%CI =1.67-2.0) were significantly different (p=<0.0001, ANOVA). The mean HPV E6/E7 mRNA in situ expression score in CIN-III (1.94, SD±1.67) was significantly higher than mean HPV-E6/E7-mRNA in situ expression in normal cervix (0.26, SD ±0.79) (p<0.0001,t-test), and, also it was significantly higher than mean HPV-E6/E7-mRNA in situ expression in CIN-I (0.59, SD ±1.22),(p<0.0001, t-test).
Conclusion: The in situ expression of E6/E7 mRNA for eighteen HR-HPV genotypes shows a significant increased expression from normal cervix and CIN I to CIN III with confirmed transforming HPV-18 infection. These findings suggest that detecting HR-HPV E6/E7 mRNA in situ expression by CISH staining in CIN could help to grade these lesions more accurately. The expression of E6/E7 HPV mRNA in cervical carcinogenesis is an aspect of the progression of this neoplasm that should continue to be studied.

PS-10-006
Differences in gene expression between cervical squamous intraepithelial lesions and normal cervix
I. Benedetti*, R. Rodriguez, L. Barrios
*Universidad de Cartagena, School of Medicine. Histopathology Research Group, Colombia

Background & objectives: A previous cDNA microarray found differential gene expression between high-grade-squamous-intraepithelial lesions (HSIL) and normal cervix. By chromogenic in-situ hybridization (CISH), mRNA expression of TMEM45A, KRT16 and RBP1 were evaluated, to determine their participation in the pathogenesis of premalignant cervical lesions.
Methods: Differential expression was evaluated in a tissue microarray with areas of normal cervix, low-grade (LSIL) and HSIL from 169 patients, mean age=35.4 years. CISH was performed using the RNAscope®2.5HDRed-assay with gene-specific probes and evaluated by two pathologists. Staining scores were calculated on a semi-quantitative scale and their mean values for each cervical tissue type were compared using t-test and ANOVA.
Results: RBP1 mRNA expression was significantly higher in HSIL (1.30, 95% CI=1.09-1.50) compared to LSIL and normal cervix (p<0.001). There was no statistically significant difference (p=0.965) between RBP1 mRNA expression score in normal cervical squamous epithelium (0.42, 95% CI= 0.23-0.61) and LSIL (0.51, 95% CI= 0.28-0.74). TMEM45A mRNA expression showed a higher staining score, significantly higher in HSIL (1.51, 95%CI= 1.26-1.76) than in normal cervix (1.10, 95% CI= 0.80-1.40), (p=0.046). The mean scores of KRT16 mRNA expression in normal cervix (0.95, 95% CI= 0.70-1.20), LSIL (0.88, 95% CI= 0.60-1.15) and HSIL (1.11, 95% CI= 0.89-1.33), were not significantly different (p=0.573).
Conclusion: In situ evaluation of the RBP1 gene mRNA shows differential expression in HSIL compared to LSIL and healthy cervical tissue, confirming the finding found in the previously performed gene profile. The differential expression of TMEM45A between normal cervix and HSIL favours a possible role of this gene in the carcinogenesis of well-differentiated epithelial lesions. Additional studies are being performed to detect the expression of these genes at the protein level and determine if there is a correlation with these findings.

PS-10-007
Targeted molecular testing in endometrial carcinoma and application of the International Federation of Gynaecology and Obstetrics (FIGO) staging system 2023 – impact in clinical management
S. Carralas Antunes*, F. Cunha, S. da Mata, C. Albuquerque, A.L. Silva, P. Silva, A.L. Carvalho, Z. Nunes, A. Félix, J. Ferreira
*Hospital Garcia de Orta, Portugal

Background & objectives: Incorporating molecular data into Endometrial Carcinoma (EC) classification improves risk stratification, yet universal POLE testing poses challenges. We detail our adoption of FIGO2023 classification via selective NGS and IHQ analyses of EC cases diagnosed between November 2022 and March 2024.
Methods: Out of 135 EC cases, we retrieved 96 EC cases who underwent a selective testing algorithm: p53 and MMR IHC on all EC biopsies, with POLE testing restricted to those with high-grade morphology or either abnormal MMR/p53 IHC on biopsy and those with stage >IA. We applied FIGO2009 and FIGO2023 staging criteria and accessed major changes in clinical management (2020ESGO/ESTRO/ESP).
Results: Patients' mean age was 71yrs. Histology: endometrioid (72%), serous (8%), clear cell (CCC) (5%), carcinosarcoma (8%), other high-grade (HG) EC (6%). The most frequent molecular subgroup was MMRd(40%) followed by NSMP(28%), P53abn(25%) and POLEmut (7%). Eight were multiple classifiers (POLEmut=3). All 7 POLEmut cases occurred in younger women (mean:64 yrs;p<0.05). All but one (CCC) were HG endometrioid; 5/6 POLEmut were FIGO2009 stage I. In 85/96 patients with complete staging, FIGO2023 stage distribution was 34%stage I; 42%stage II; 17%stage III and 7%stage IV. Eleven patients changed stage from FIGO2009, due to histological [(high-grade morphology (n=8) or substantial LVI(n=2)] or molecular findings (POLEmut=1). Molecular testing downstaged all POLEmut cases and upstaged one P53abn HG endometrioid EC case using 2020ESGO/ESTRO/ESP guidelines.
Conclusion: Using our protocol, POLE testing was not performed in 39/135 (28%) of EC cases. This number could be reduced further by excluding stage IV disease (7%EC). Only one case changed stage between FIGO2009 and FIGO2023 classifications exclusively due to molecular findings. The addition of molecular testing changed the risk category in 7% EC mostly due to POLEmut cases. Targeted POLE testing restricted to those patients in whom this would alter adjuvant therapy is a viable option.

PS-10-008
Comprehensive immunohistochemical analysis of mesonephric marker expression in low-grade endometrial endometrioid carcinomas
Y.A. Cho*, C.K. Park, Y. Lee, S. Choi, H. Kim
*Samsung Medical Center, Republic of Korea

Background & objectives: Although several markers have proven to be useful for identifying/confirming mesonephric/mesonephric-like differentiation (MLD), only a few studies have been performed in endometrial endometrioid carcinomas (EECs). We aimed to analyse the frequency and pattern of MLD marker expression in low-grade EECs.
Methods: We performed immunostaining for the detection of MLD markers including thyroid transcription factor 1 (TTF1), GATA-binding protein 3 (GATA3), and cluster of differentiation 10 (CD10) expression in 50 low-grade EEC tissue samples and evaluated their staining proportion and intensity.
Results: Nine tumours (18.0%) expressed at least one MLD marker in varying proportions and intensities, and 2 of these tumours were positive for 2 MLD markers (TTF1/GATA3 and GATA3/CD10, respectively). Three (6.0%) tumours showed moderate-to-strong nuclear TTF1 immunoreactivity in ≤5% of the tumour cells. Five tumours (10.0%) had at least moderate nuclear GATA3 staining, and three of them displayed a staining proportion of ≥15%. Three tumours (6.0%) were focal (mean proportion, 15%) but strongly positive for CD10. Our findings indicate that a subset of EEC can express one or more MLD markers with varying staining proportions and intensities.
Conclusion: Given that a diagnosis of uterine mesonephric-like adenocarcinoma should be established based on a combination of characteristic histologic features, unique immunophenotypes, and confirmed molecular findings, pathologists should not exclude EEC based only

on the presence of focal immunoreactivity for MLD markers. Awareness of the atypical expression patterns of MLD markers in EEC helps pathologists avoid misdiagnosing EEC as a uterine mesonephric-like adenocarcinoma.

PS-10-009

Re-thinking peritoneal cytology: exploring its role in endometrial cancer molecular classification

L. Christe*, E. Baumann, W. Solass, F.A.M. Saner, S. Imboden, F. Siegenthaler, M.D. Mueller, T.T. Rau
*Institute of Tissue Medicine and Pathology, University of Bern, Switzerland

Background & objectives: Positive peritoneal cytology (PC) has been excluded of the FIGO 2009 staging system. However, the importance of PC in endometrial cancer is still controversial. In this study we explored the prognostic significance of positive PC among the different molecular subgroups
Methods: This study included 206 patients with endometrial cancer who underwent primary surgical treatment between 2012 and 2020 at the Bern University Hospital Switzerland, with molecular classification of the primary tumours. The PC results were retrospectively added to the characterization of the cohort and analysed
Results: PC was realized in 153/206 patients. 11 patients were excluded because of missing molecular or clinical information or unclear peritoneal cytology results. PC was positive in 4/17 POLE mutated carcinoma, in 8/26 TP53 mutated carcinoma, in 11/38 mismatch repair deficient carcinoma and in 13/65 carcinoma of no specific molecular profile. Regarding the 5-year overall survival, in univariate survival models, we observe a correlation between shorter survival and a positive PC (HR:2.03, P=0.11); high grade (HR 16.61, P=0.007) and high stage are significantly associated with shorter survival (HR 3.25, P=0.02). Considering Time to Recurrence (TTR) in the TP53 mutated group, positive PC is associated with a shorter TTR (HR: 5.70, P=0.155)
Conclusion: The impact of peritoneal cytology on the different molecular subtypes has not yet been thoroughly explored. In this study we observe a correlation between a positive PC and a shorter TTR in the TP53 mutated group although not statistically significant. This association is in line with the findings of a prior study of our group showing a significant association between positive PC and decreased survival in the TP53 mutated group. These investigations need to be repeated in bigger cohorts.

PS-10-010

HER2 status evaluation in endometrial carcinoma p53-abnormal: multiple approaches for a single purpose

S. Coluccelli*, M. Errani, C. Ravaioli, A.G. Corradini, A. Costantino, T. Maloberti, D. de Biase, G. Tallini, A. De Leo
*Solid Tumour Molecular Pathology Laboratory, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy

Background & objectives: Endometrial carcinoma (EC) p53-abnormal (p53abn) represents the subtype with the worst prognosis. Anti-HER2 therapy represents a possibility of new target treatment in ECs p53abn. The aim is to characterize the HER2 status in p53abn EC series by different methods.
Methods: Immunohistochemistry (IHC) and Next-Generation Sequencing (NGS) were used to assign TCGA molecular EC subtypes: POLE mutant (POLE), mismatch repair deficient (MMRd), p53 mutant (p53abn) and no specific molecular profile (NSMP). HER2 status was evaluated through several approaches: IHC, dual-colour dual-hapten in situ hybridization (D-DISH) and RT-qPCR-based kit MammaTyper® to quantify HER2 expression levels.
Results: 220 ECs were divided into the following molecular subgroups: 17 (7.8%) POLE, 69 (31.4%) MMRd, 45 (20.5%) p53abn, 89 (40.5%) NSMP. HER2 overexpression/amplification was identified in 10/45 (22.2%) p53abn ECs. HER2 status was heterogeneous in 50% of the cases. The MammaTyper® test was successfully performed in p53abn ECs with a 100% concordance with D-DISH results in terms of HER2 expression, including challenging cases with heterogeneous amplification. HER2 overexpression/amplification was statistically associated to specific pathologic features such as MELF, infiltrative growth margins, and substantial LVSI. However, HER2 was not found to be statistically correlated with prognosis.
Conclusion: Although p53abn ECs are clinically aggressive, these tumours may present different molecular features as HER2 overexpression/amplification. Anti-HER2 target therapy represents a new therapeutic option. HER2-positive carcinomas represent a subgroup of tumours characterized by distinct histological features, although without significant prognostic impact. The feasibility of using more than one diagnostic test to define HER2 status could have important clinical implications for the better determination of challenging or equivocal cases and thus for the appropriate personalization of therapy.

PS-10-011

Immunohistochemical assesment of PAX2, PTEN and ARID1A in a series of 23 cases of atypical polypoid adenomyoma of the uterus

V. Cristóbal Redondo*, E.B. Troncoso Hernández, V. Pedrero Castillo, R.E. Casco Zuniga, E. Castellón Mollà, M. Sala Ferichola, J.A. López Fernández, G. Peiró Cabrera
*Dr. Balmis General Universitary Hospital of Alicante. Department of Pathology. Institute for Health and Biomedical Research, Alicante., Spain

Background & objectives: Uterine atypical polypoid adenomyoma (APA) is an infrequent benign tumour with high recurrence rate and low malignant potential. We aimed to study PAX2, PTEN and ARID1A expression to determine its usefulness in the detection of atypia or progression to carcinoma.
Methods: We selected 23 patients diagnosed with APA in our Institution between 2000-2024. Medical records were retrospectively reviewed to extract relevant clinical data. Biopsy slides were retrieved to assess histopathological findings, and immunohistochemistry (IHC) for PAX2, PTEN and ARID1A was performed on representative paraffin-blocks. Clinical and IHC results were correlated, and significant differences were calculated with $\chi 2$ or Fisher tests.
Results: In our series, APA was seen in at least one follow-up biopsy. Mean age at diagnosis was 40 years (range 24-68) and median follow-up 29 months (1-144). More than half of the patients recurred (12/23). Loss of PTEN, ARID1A or PAX2 was seen in 39%, 17.4% or 47.8% of cases, with no correlation with hyperplasia or atypia (p=ns). Overall, at least one marker was aberrant in 78.3% (18/23) cases, and loss of two markers were seen in 26.1% (5/6) cases with hyperplasia (p=0.10), but not associated with atypia (4/6; p=ns). Three patients developed endometrioid carcinoma: two had PAX2 loss exclusively, and in one, all markers were preserved.
Conclusion: In our APA series, we found expression loss in one marker in 78.3% cases, and in two markers in 26.1%, the latter without correlation with hyperplasia, but a tendency towards the presence of atypia. PAX2 loss in two cases of endometrioid carcinoma should be interpreted with caution due to the limited number of patients. Thus, further research is needed including more cases to define the value of these markers in APA to predict the risk of developing carcinoma.

PS-10-012

Folate receptor alpha prevalence and association with ovarian cancer patient and disease characteristics

E. Deutschman*, B. Liang, A. Morneault, D. Libert, K. Moore, U. Matulonis, R. Coleman, A. Oaknin, T. Van Gorp, B. Howitt, E. Diver, M. Method, C. Sloss

*ImmunoGen, USA

Background & objectives: Folate receptor alpha (FRα) is overexpressed in ovarian cancer. Mirvetuximab soravtansine (MIRV), an FRα-targeting antibody-drug conjugate, is active in high-grade serous epithelial ovarian cancer (HGSOC). This study correlates FRα, a determinant of MIRV eligibility, with patient and disease characteristics.
Methods: FRα was assessed using the VENTANA FOLR1 (FOLR1-2.1) RxDx Assay. The percentage of viable tumour cells exhibiting 0, 1+, 2+, and 3+ membranous staining was quantified. PS2+ scores were assigned based on the percentage of cells with 2+ staining and compared to stage, BRCA status, platinum-free interval (PFI), tumour FOLR1 mRNA expression, tumour location, and tissue age since diagnosis.
Results: 95% of HGSOC tumours had detectable FRα with 36%, 64%, and 79% displaying PS2+ scores ≥75%, ≥50%, and ≥25%, respectively. Expression was heterogeneous. Increased FRα was observed in Stage IV (76%), III (75%), and II (80%) disease at diagnosis compared to Stage I (60%). FRα trended higher in BRCA-mutated tumours (90% vs. 78%) and exhibited a Spearman correlation of 0.583 with tumour FOLR1 mRNA. Specimen collection date and PFI were not associated with FRα. FRα was consistent across primary and metastatic sites, however variability (7.6% ± 24.1%) was observed across cores from the same specimen. In non-HGSOC, FRα expression was low to negative, with low-grade serous exhibiting the highest levels.
Conclusion: FRα was highest in HGSOC and was associated with advanced stage and BRCA status. Sample age, anatomical site, and PFI did not affect FRα expression, suggesting that any sample is suitable for determining FRα status. Variability was observed in cores from the same specimen, which appeared to be driven by tumour heterogeneity versus biological changes. FRα protein and mRNA correlation was too weak to support using RNA as a surrogate biomarker. Marked expression was observed in the low-grade serous tumours.

PS-10-013
Clinicopathological and molecular profiles of three cases of HPV-independent cervical squamous cell carcinomas: insights and implications
A. Erbagci*, G. Kir, F. Özen, A. Karateke
*Istanbul Medeniyet University, Turkey

Background & objectives: According to the 2020 WHO Classification, 5-7% of cervical SCCs are HPV-independent. This study investigates three such cases, aiming to detail their clinicopathological, immunohistochemical, and genetic characteristics to inform targeted therapies.
Methods: Three HPV-independent cervical SCC cases were studied using the FDA-approved Aptima HPV assay. Evaluations included tumour morphology, PD-L1 scores, and lymphocytic responses, alongside immunohistochemical staining for p53, p16, and c-erbb2. Genetic profiling was conducted with next-generation sequencing (NGS) to identify key mutations and amplifications.
Results: The first patient exhibited a tumour with precancerous lesions, extensive dirty necrosis, high-grade atypia, and pronounced keratinization, alongside multifocal weak PD-L1 expression. Immunohistochemical staining showed mutant p53, patchy p16, and score 3 c-erbb2 expression, with severe lymphocytic response, TP53 mutations, and ERBB2 amplification detected by NGS. She passed away two years post-diagnosis. The second and third patients' tumours, similar in morphology but without precancerous lesions, exhibited strong PD-L1 expression, indicating increased immunogenicity, and harboured PIK3CA mutations with wild-type p53 and negative p16; c-erbb2 was absent. Both remain alive with disease, at 10 and 15 months respectively.
Conclusion: Our study highlights the diverse clinicopathological and molecular profiles of HPV-independent cervical SCCs. The significant findings of TP53 mutations and ERBB2 amplification in one patient and PIK3CA mutations in the other two illustrate the varied molecular pathways that may drive the development and progression of these tumours. These insights underscore the importance of comprehensive tumour profiling in informing personalized treatment strategies for HPV-independent cervical SCCs, emphasizing the potential for targeted therapies based on unique genetic and immunohistochemical characteristics.

PS-10-014
Unravelling the molecular landscape of UTROSCT: insights from a clinicopathological, morphological, immunohistochemical and molecular analyses of 36 cases
M. Flídrová*, N. Hájková, J. Hojný, J. Dvořák, R. Michálková, J. Laco, G. Mccluggage, G. Giordano, E.M. Silini, K. Michalova, M. Bizoń, P. Dundr, M. Kendall Bártů
*Department of Pathology, First Faculty of Medicine, Charles University and General University Hospital in Prague, Prague, Czech Republic

Background & objectives: UTROSCT is a rare uterine mezenchymal tumour with uncertain biological behavior, typically associated with recurrent alterations affecting mostly the NCOA1-3 genes. We investigated the clinicopathological, immunohistochemical (IHC), and molecular characteristics of a large UTROSCT cohort.
Methods: 36 cases of UTROSCT were assembled. The IHC analysis included 25 antibodies. The morphologic characteristics were evaluated independently by 2 pathologists using all available slides. DNA and RNA from FFPE tissue blocks or unstained tissue slides was used for next generation sequencing (NGS) analysis using targeted capture panel (DNA NGS) and whole transcriptome RNA-Seq.
Results: Our cohort showed variable expression of sex cord, smooth muscle, epithelial markers, and hormone receptors. RNA analysis revealed recurrent gene fusions in 22/33 cases with sufficient RNA quality. Cases with either NCOA2 or GREB1 fusion tended to be of higher stage compared to tumours without these fusions, but statistical significance was reached only for cases with NCOA2 fusion. Pseudoglandular tumour architecture was present in 50% of NCOA2-altered tumours and in only 4% of non-NCOA2 altered tumours. The relationship between IHC expression and fusion events was analysed separately for GREB1 and NCOA2 alterations. RNA-Seq unsupervised hierarchical clustering analysis showed differences between expression in GREB1-altered tumours compared to non-GREB1 altered ones.
Conclusion: Our study revealed recurrent gene fusions in most UTROSCT. To our knowledge, this is the first study with a comprehensive RNA expression analysis. Some of these fusions may be associated with aggressive behaviour. Tumours with NCOA2 or GREB1 fusions may exhibit some clinicopathological differences in comparison with non-altered cases. The molecular landscape of UTROSCT and the clinical differences between the fusion-driven groups underscore the importance of genetic profiling for prognostication; demonstration of fusions may also assist in diagnosis.

PS-10-015
A clinicopathologic analysis of 30 cases of molar and nonmolar hydropic conceptions with divergent p57 expression
M. Fukunaga*
*Shinyurigaoka General Hospitial, Japan

Background & objectives: A divergent p57 staining pattern is characterized by two populations of villi; each may have different morphologies and different staining patterns of p57. Conception with divergent p57 expression is very rare and always poses diagnostic challenge.

Methods: Thirty cases of molar and nonmolar hydropic conceptions with divergent p57 expression all of which were in the first trimester, were retrieved from 1055 cases with hydropic placental tissue and were clinicopathologically analysed with immunostaining of p57 (Kip2) (p57), which is a product of paternally imprinted, maternally expressed genes.
Results: p57 divergent expression was detected in 13 cases of twin gestation comprised of a p57-negative complete mole (CM) and p57-positive nonmolar villi and in 7 cases of placental mesenchymal dysplasia (PMD) and in 5 cases of CM with PMD component, in which p57 positive cytotrophoblasts and p57 negative villous stromal cells were observed. PMD showed normal villi and enlarged villi with cellular stroma and no trophoblastic hyperplasia. Remaining 5 cases were nonmolar hydropic conceptions with normal villi and enlarged villi with focal trophoblastic hyperplasia. Two patients with twin with CM and 1 of CM with PMD had persistent trophoblastic disease and 2 of twin with CM developed lung metastasis.
Conclusion: This study showed that most of hydropic placentas with divergent p57 expression were associated with CM or PMD. The presence of distinct two populations of villi is clue that may be dealing with divergent p57 expression. The presence or absence of under-diagnosed early-stage CM or PMD should be kept in mind. Patients with twin with CM and those with CM with PMD carry a risk for persistent trophoblastic disease and requires appropriate treatment and follow-up as conventional CM patients.

PS-10-016
EPM2AIP1 immunohistochemistry as a surrogate of promoter methilation analysis in endometrial carcinoma
S. Gatius*, M. Santacana, M. Vaquero, D. Cuevas, N. Eritja, X. Matias-Guiu
*Hospital Universitari Arnau de Vilanova de Lleida/IRBLleida, Spain

Background & objectives: Mismatch repair (MMR) status in endometrial carcinoma is crucial for diagnosis, prognosis, treatment, and Lynch syndrome pre-screening. MLH1 loss is usually caused by MLH1 promoter hypermethylation. We tried to confirm the role of EPM2AIP1 as surrogate of MLH1 promoter methylation.
Methods: Fifty-five endometrial carcinoma (EC) cases with MLH1 loss expression and 20 EC controls with MLH1 preserved expression by IHC were selected. Promoter methylation analysis was performed in the 55 cases. EPM2AIP1 immunohistochemical analysis (Clone: OTI2A2, OriGene Technologies) was done in 75 EC.
Results: Among 55 cases, 47 displayed hypermethylation (47/55), while 8 did not (8/55). All 47 hypermethylated cases showed negative nuclear expression of EPM2AIP1. Of the eight unmethylated cases, 5 showed positive nuclear expression of EPM2AIP1, while 3 were negative. Discrepant cases were analysed, including two endometrial endometrioid carcinomas (EEC) arising from atypical hyperplasia. EPM2AIP1 was negative in EEC areas but positive in hyperplastic zones. Their methylation scores were 13.8% and 14.4%. The third discrepant case had a low tumour percentage and extensive necrotic areas. Methylation analysis was repeated in the surgical specimen, confirming methylation. EPM2AIP1 nuclear expression was positive in all 20 controls. Following re-evaluation, concordance between both techniques was 100%.
Conclusion: The immunohistochemical analysis of EPM2AIP1 is a good surrogate for MLH1 promoter methylation tests. Our results suggest higher specificity of the immunohistochemical test, as we can evaluate results using histological samples and avoid false negatives due to normal tissue contamination or low tumour percentage, especially in curettage biopsies or surgical specimens when macro-dissection is not possible.

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PS-10-017
A novel semi-quantitative multiplex PCR method for rapid copy number high subtype stratification in endometrial cancer. Pilot study
S. Gatius*, A. Velasco, A. Vilar, S. Villatoro, M. Vaquero, R. Marin, M. Ajenjo-Bauza, S. Walz, A. Henning, M. Varela, X. Matias-Guiu
*Hospital Universitari Arnau de Vilanova de Lleida/IRBLleida, Spain

Background & objectives: Endometrial cancer (EC) copy number high (CNH) molecular subtype is usually identified by abnormal p53 immunostaining. However, p53 immunohistochemistry is not a perfect surrogate of CNH. Here we describe a novel PCR-based method for the rapid CNH stratification.
Methods: DNA from 16 p53 abnormal ECs were assessed by two methods: 1) MODAPLEX platform, by a semi-quantitative multiplex PCR assay interrogating 14 targets distributed over three chromosomal stable- and two CNH-associated instable regions, 2) NextSeq 550 Dx (Illumina®) sequencing with analysis with an in-house pipeline (CliBioNGS), by measuring CNVs according to their length in base pairs and compared among them.
Results: Informative results were obtained in 12 cases. MODAPLEX platform identified CNH status in 10 out of the 12 cases, while two out of the 12 p53 abnormal cases were identified as copy number low (CNL) NextSeq 550 Dx sequencing identified 10 samples with larger copy number regions (CNH) and 2 samples with shorter (CNL), with 100% concordance between the two methods. The two p53 abnormal tumours that resulted CNL by both MODAPLEX and NGS assays were high grade endometrioid carcinomas, one showing p53-abnormal, diffuse p53 strong staining with a NM_000546.6:c.1101-1G>A TP53 splicing mutation (VAF 77.30%), and the second one a p53-abnormal, null-pattern with a NM_000546.6:c.243_252del;p.Pro82Leufs*38 TP53 mutation (VAF 30.80%).
Conclusion: This pilot study confirmed a high level of accuracy of the novel semi-quantitative multiplex PCR MODAPLEX method assay compared with CNH status by NGS sequencing. The results confirm that a subset of p53-abnormal tumours is indeed LCN, demonstrating that p53 immunohistochemistry and TP53 mutation status are good, but not perfect surrogates of CNH status. Compared to IHC, the MODAPLEX assay allows an objective data analysis while including multiple genomic biomarkers in the CNH stratification, with a very short turnaround time

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PS-10-018
Morphometric study of endometrial vessels in patients with abnormal uterine bleeding associated with chronic endometritis
M. Gushchin*, L. Mikhaleva, M. Orazov, R. Mitrelis, S. Mikhalev, R. Vandysheva, D. Masalimova
*A.P. Avtsyn Research Institute of Human Morphology Petrovsky National Research Center of Surgery, Russia

Background & objectives: Chronic endometritis (CE) is the most common cause of abnormal uterine bleeding (AUB) and other menstrual disorders. This is reliably evidenced by the high prevalence of CE among patients with AUB, reaching from 3–10% to 72%.
Methods: We examined material in the middle stage of the proliferation phase after pipel biopsy or hysteroscopy of the endometrium from 95 patients aged 21 to 40 years with AUB. Measurements and analysis of indicators of the architectonics of arterioles were carried

out diameter (Dpr) and area (Spr) of the lumen of the vessel (average value per 10 fields of view).
Results: As a result of the study, endometrial stromal fibrosis was observed in 61% patients with severe CE, 37.5% patients with moderate CE and 55.5% with mild CE. Analysis of the architectonics of arterioles showed that blood vessels with CE become smaller in diameter, Spr and Dpr decrease. Based on the data obtained from a statistical study (Mannu-Whitney method), it was determined that in patients with the presence of already mild CE, the diameter and lumen area of the arterioles is significantly reduced in comparison with arterioles in patients without CE ($p<0.05$). The most pronounced narrowing of the Spr of arterioles is observed in patients with moderate and severe CE ($p<0.05$).
Conclusion: Changes in the architectonics of endometrial arterioles in the proliferation phase in patients with CE may be one of the leading pathogenetic mechanisms for the development of functional failure of the endometrium, leading to the appearance of abnormal uterine bleeding and disruption of the uterine menstrual cycle.

PS-10-019
Extra-pulmonary lymphangioleiomyomatosis: incidental finding detected in staging surgery for gynaecological neoplasia
A. Hidalgo Romero*, Z. Calixto, R.N. Zagrean, L.S. Huayna
*Vall d'Hebron Barcelona Hospital, Spain

Background & objectives: Lymphangioleiomyomatosis (LAM) a rare lung disease (1-2 per million), is linked to tuberous sclerosis (TS), where the prevalence increases to 40%. It mainly affects lungs but can involve other tissues.
Methods: We present four cases of extrapulmonary LAM detected incidentally in staging surgeries for gynaecological neoplasia in asymptomatic patients without pulmonary LAM or TS.
Results: Four women (ages 44-70) underwent total hysterectomy with bilateral adnexectomy and lymphadenectomy/sentinel lymph node biopsy for gynaecological neoplasia. All had additional spindle cell growths (1.8-9mm) in lymph nodes and the uterus. These cells had a polygonal nucleus, discrete nucleolus with pale eosinophilic cytoplasm and were arranged in nests or a storiform pattern. These cells showed muscle markers (smooth muscle actin, desmin, caldesmon), melanocytic markers (HMB45, Melan A), estrogen and progesterone receptors and a network of vascular channels (D2-40 positive). Extra-pulmonary LAM was diagnosed based on histology and immunohistochemistry.
Conclusion: Extrapulmonary LAM represents a clinically significant diagnosis due to its clinical implications for the patient and challenging due to its variability of presentation. Our case series demonstrates LAM's potential as an incidental finding. When faced with this diagnosis, pathologists must note the remote possibility of TS. A multidisciplinary study is recommended to rule out TS and pulmonary disease. One of our cases showed pulmonary LAM. This approach is important because of the possibility of early detection and early timely management.

PS-10-020
Trop-2 expression in cervical carcinoma (CX) - a possible target for the antibody drug conjugate sacituzumab
L. Horn*, B. Wolf, M. Forberger, R. Hiller, A. Freude, S. Droste, A.K. Hoehn
*University Hospital Leipzig, Germany

Background & objectives: The Trophoblast Cell Surface Antigen 2 (TROP-2) is associated with invasiveness and tumour progression in several malignancies. TROP-2 was identified as a target protein for treatment of solid tumours using antibody-drug conjugates (ADC). Expression-data in CX is limited.
Methods: Trop2 expression was evaluated using an H-score. Staining scores of Trop2 correlated with the histological subtype of CX and p16-expression as a surrogate marker for HPV-association. The evaluation of immunohistochemistry for Trop2 blinded to p16-status.
Results: 100 CX were included in the study. 79 represented squamous (SCC) and 21 adenocarcinomatous (AC) histology. Overall, 5% were negative for p16-immunostaining (4 AC, 1 SCC). All cases represented at least moderate diffuse expression of Trop2. There were no differences between histologic subtype ($p>0.05$), nor p16-expression status ($p>0.05$).
Conclusion: The antibody drug conjugate (ADC) topoisomerase-1-inhibitor irinotecal, coupled via a linker to a humanised IgG-1ntibody hRS7 binding to TROP-2 (i.e. sacitumzumab) represents an effective treatment approach to several carcinoma types. Virtually all examined CX showed at least moderate staining for TROP-2 within the tumour cells. So, TROP-2 may represent a potential target for ADC in cervical cancer. There are no differences of TROP-2 expression within the different histological subtype (SCC vs. AC) and p16-expression (positive vs. negative).

PS-10-021
Upregulation of FOXP3+ regulatory T lymphocytes in patients with high-grade cervical squamous intraepithelial lesions
S. Isajevs*, A. Mitildzans, V. Gordjusina, D. Rezeberga
*University of Latvia, Latvia

Background & objectives: Recent studies showed that T regulatory cells might be a potential biomarker for cervical diseases. The aim of our study was to compare the FOXP3, CD4, CD8, Ki-67, p53 expression in patients with cervical squamous intraepithelial lesions (SIL).
Methods: 78 patients aged 18–46 years referred to the Department of Gynaecology at Riga East University Hospital were enrolled in the study. The patients underwent colposcopy guided cervical biopsy. The FOXP3, CD4, CD8, Ki-67, p53 expression was assessed by immunohistochemistry. The Aptima HPV assay was used for HPV testing.
Results: Obtained results showed that 28 patients had CIN 1 (LSIL), 24 patients had CIN 2 (HSIL) and 26 patients had CIN 3 (HSIL). In patients with CIN 2 and CIN 3, FOXP3+ regulatory T lymphocytes were significantly upregulated compared to patients with CIN 1, respectively, 15 (6-32) vs. 6 (1-12) cells/mm2, $P<0.0001$ and 15 (6-32) vs. 3 (2-7) cells/mm2, $P<0.0001$. In addition, patients with CIN 3 had increased numbers of CD8 T lymphocytes compared to patients with CIN 2 and CIN 1. The associations between the numbers of FOXP3+ positive cells and HPV positivity, CD8 T cell infiltration, the numbers of Ki-67 positive cells and p53 expression were demonstrated.
Conclusion: To conclude, FOXP3+ regulatory lymphocytes were upregulated in patients with HSIL, which correlated with HPV status, CD8 T lymphocytes, Ki-67 and p53 expression. The routine assessment of FOXP3+ positive cells in patients with SIL could be beneficial for the diagnosis and degree of SIL and risk stratification of SIL regression/progression.

PS-10-022
Development of a digital method for assessing tumour-stroma ratio and tumour infiltrating lymphocytes in vulvar squamous cell carcinomas
O. Jacobsen*, L. Baandrup, S.K. Kjær, L.G. Larsen, A.K. Fiehn
*Department of Pathology, Zealand University Hospital, Roskilde, Denmark

Background & objectives: Manual evaluation of tumour-stroma ratio (TSR) and tumour-infiltrating lymphocytes (TILs) may be time-consuming and prone to interobserver variation. The study aim was to develop a digital method for evaluating TSR and TILs in vulvar squamous cell carcinomas (VSCC).

Methods: Formalin-fixed, paraffin-embedded tissue slides from 41 VSCC were sectioned and stained with cytokeratin/CD3 and cytokeratin/CD8. An independent training set was used to develop deep learning-based, Application Protocol Packages (APPs). A TSR APP segmented the tissue based on architectural details into background, epithelium, or stroma. A TILs APP quantified CD3+ and CD8+ lymphocytes in the intraepithelial and stromal compartment, respectively.
Results: A pathologist evaluated performance of the APPs which were retrained until satisfying result. TSR was defined as area of tumour epithelium out of total tumour area consisting of tumour epithelium and stroma. TSR was almost identical on CD3 and CD8 stained slides with median of 64% ranging from 33% to 91%. Density of lymphocytes was calculated as number of positive cells per mm2. Median density and range of CD3 lymphocytes in the intraepithelial compartment was 222 (13-2320) and 1978 (397-6683) in stromal compartment. Number of CD8 positive lymphocytes was lower in both compartments with median density of 154 (9-1372) in the intraepithelial and 1000 (176-5052) in the stromal compartment.
Conclusion: Digital image analysis including artificial intelligence is an emerging field and has great potential to support the pathologist in the future. The developed automated method provides precise and objective values of TSR and counts of CD3+ and CD8+ TILs in the intraepithelial and stromal compartment of VSCC, respectively. The algorithms should be validated in a larger sample of VSCC cases and correlated with clinicopathological characteristics and prognosis to determine the relevance of these measures in a clinical setting.

PS-10-023
Polymorphisms and expression of IL-10 gene in ovarian cancer patients from Georgia
P. Balakrishnan, J. Shah, S. Surmava, E. Kvaratskhelia, E. Abzianidze, N. Vardiashvili, K. Kankava*
*Tbilisi State Medical University, Georgia

Background & objectives: Some genetic alterations, determining predisposition to ovarian cancer have already been identified, but most ovarian tumours are still regarded as sporadic. The aim of our research is to identify new predisposing factors that might increase ovarian cancer risk.
Methods: 48 patients with ovarian cancer along with 48 age-matched controls were included in the study. Single Nucleotide Polymorphism (SNP) genotyping and gene expression assays for IL-10 were performed using TaqMan Assay (Thermo Scientific, USA). Histology of tumours was revised in all cases. All statistical analyses were performed by GraphPad Prism 9.3.1 for macOS.
Results: The genotype distributions of IL-10 gene polymorphisms among cancer and control groups were all according to the expected Hardy–Weinberg equilibrium. There was no statistically significant difference in frequency of genotypes and alleles between the two study groups ($p>0.05$). In another analysis, the samples were grouped according to the polymorphic variant IL-10 (− 1082) A/G. Subjects having the homozygous variant (A/A) had lower IL-10 mRNA levels than those with the homozygous wild (G/G) genotype in both, ovarian cancer patients and controls, $p<0.05$. mRNA levels on IL-10 were different among cases and controls ($p<0.05$). Patients with OC had higher level of mRNA for IL-10. No correlations with histologic type were identified.
Conclusion: These results support the theory that IL-10 gene expression levels differ in patients with and without ovarian cancer. Thus, polymorphic variant IL-10 (− 1082) A/G couldn't be confirmed to explain this difference in gene expression levels.

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PS-10-024
Mesonephric-like adenocarcinoma of the uterine corpus: comparison of GATA-binding protein 3 Expression and its diagnostic performance among different antibody clones
H. Kim*, H. Kim
*Seegene Medical Foundation, Republic of Korea

Background & objectives: Mesonephric-like adenocarcinoma (MLA) of the uterus is a distinct suptype of endometrial carcinoma. GATA-binding protein 3 (GATA3) is used as a sensitive and specific marker. We investigated statistical parameters of different GATA3 clones to find the best clone for diagnosis.
Methods: We conducted immunostaining for three GATA3 clones - L50-823, 7B5, and UMAB218 - in 23, 25, and 5 cases of MLA, endometrioid carcinoma, and serous carcinoma. Histoscore was generated. Receiver operator characteristic curves were plotted, and area under ROC was calculated to measure the performance of each clone. Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were calculated.
Results: For L50-823 and UMAB218 clones, mean histoscores of MLA (145.17 ± 115.43 and 86.74 ± 92.51) was significantly higher than other types ($p<0.001$, both). In contrast, 7B5 clone showed no significant differences among the types. Compared to L50-823, UMAB218 had higher specificity but lower sensitivity. The AUCs of L50-823, 7B5, and UMAB218 were 0.921, 0.80, and 0.604, respectively. When the cut-off histoscore of the L50-823 clone was 7.5, sensitivity, specificity, PPV, NPV, and accuracy were 91.30%, 86.67%, 84.00%, 92.86%, and 88.68%, respectively. All clones demonstrated varying proportions of intratumourally heterogeneity.
Conclusion: L50-823 clone had higher AUC than other two clones, indicating better performance of L50-823 in distinguishing uterine MLA from EC and SC. With the cut-off histoscore of 7.5, L50-823 clone showed the highest sensitivity, NPV, and accuracy.

PS-10-025
Diagnostic role of immunostaining for thyroid transcription factor 1 (TTF1) and paired box 8 (PAX8) in distinguishing pulmonary metastases of mesonephric and mesonephric-like adenocarcinomas from primary lung adenocarcinoma
H. Kim*, N. Ji, H. Kim
*Seegene Medical Foundation, Republic of Korea

Background & objectives: Mesonephric/mesonephric-like adenocarcinoma frequently expresses thyroid transcription factor 1, a sensitive and specific marker for primary lung adenocarcinoma. We investigated the expression of TTF1 and paired box 8 (PAX8) to assess diagnostic roles in distinguishing pulmonary metastatic MA/MLA (PMM) from PLA.
Methods: We reviewed electronic medical records and pathology slides of eight patients who underwent surgery and/or chemotherapy for PMM. We conducted immunostaining for TTF1 and PAX8 using tissue samples obtained from six, eight, and 21 patients with primary MA/MLA, PMM, and PLA, respectively.
Results: Five of the eight patients were initially diagnosed as having advanced-stage diseases. Two patients with stage IB uterine MLA developed lung metastases at five and 57 months after hysterectomy. Single isolated pulmonary nodules detected in two patients were suspected to be primary lung cancers. Six patients had two or more pulmonary nodules. All primary MA/MLA tissues reacted with TTF1, and their staining intensities and proportions varied. Compared to primary tumours, all PMMs exhibited reduced TTF1 immunoreactivity. In contrast, the majority of PLAs displayed intense TTF1 expression. Meanwhile, all except one PMM strongly expressed PAX8, while only one PLA showed focal and weak PAX8 expression.

Conclusion: There is a significant difference in TTF1 immunoreactivity between PMM and PLA. Moreover, PMM had significantly higher PAX8 immunoreactivity than PLA. We concluded that immunostaining for TTF1 and PAX8 is helpful for distinguishing PMM from PLA in the differential diagnosis of single or multiple pulmonary nodules. Their staining intensities and proportions are significantly different from each other. Single pulmonary nodules occurring in patients with known malignancies can pose diagnostic challenges.

PS-10-026

Comparison of clinicopathological and prognostic characteristics between minimal deviation adenocarcinoma and gastric-type endocervical adenocarcinoma

S. Lee*, S. Kum, H. Kim
*Republic of Korea

Background & objectives: Minimal deviation adenocarcinoma (MDA) has been known as an extremely well-differentiated variant of gastric-type endocervical adenocarcinoma (GEA). In this study, we compared the clinicopathological and prognostic characteristics of MDA to those of GEA.
Methods: Nine MDAs and 22 GEAs were included in this study. We reviewed electronic medical records and pathology slides to collect their clinicopathological and prognostic information. Statistical analyses were performed to examine whether there are significant differences in clinicopathological characteristics and patient outcomes between MDA and GEA.
Results: GEA exhibited higher initial stage, increased parametrial extension, lymphovascular invasion, and recurrence rates compared to MDA. GEA patients had significantly lower survival rates; all experienced recurrences, unlike MDA patients who had 100.0% five-year recurrence-free survival ($p<0.001$). Seven of 22 GEA patients died during the study, while all MDA patients remained disease-free. GEA's five-year overall survival was 37.0% vs. 100.0% for MDA ($p=0.009$). GEA showed more frequent singly dispersed or clustered tumour cells ($p=0.008$), diffuse stromal desmoplasia ($p<0.001$), nuclear stratification ($p=0.020$) and severe pleomorphism ($p=0.005$), loss of nuclear polarity ($p<0.001$), coarse chromatin ($p=0.002$), and two or more mitotic figures ($p=0.005$). In contrast, none of the MDA cases exhibited these histological features.
Conclusion: We observed significant differences in clinicopathological characteristics and patient outcomes between MDA and GEA. Our observations are not consistent with previous data demonstrating similar clinical behaviour and prognosis of MDA patients to those of GEA patients. Further investigations using a larger cohort are warranted to determine the clinical behaviour and aggressiveness of MDA.

PS-10-027

Quantification of intraepithelial CD8 T lymphocytes by dual immunostaining and digital image analysis as a prognostic biomarker in high-grade serous ovarian carcinoma

J. Machuca Aguado*, A. Muñoz-Álvarez, R. Rendón-García, A.F. Conde-Martín, J.J. Ríos, M.Á. Idoate Gastearena
*Virgen Macarena University Hospital, Spain

Background & objectives: High-grade serous ovarian carcinoma (HGSOC) is an aggressive neoplasm for which immunotherapy could represent an alternative treatment, yet precise characterization and quantification of tumour-infiltrating lymphocytes (TILs) are essential. Novel methodologies, like digital image analysis, are needed to develop useful algorithms.
Methods: We conducted an observational study involving 74 patients diagnosed with HGSOC, with clinical follow-up. Quantification of intraepithelial (ieTILs) and stromal (sTILs) CD8+ T lymphocytes was performed, including tissue segmentation and cell classification using machine learning algorithms. A double immunohistochemical staining of CD8 and pan-cytokeratin was utilized. ieTILs were quantified as the CD8+/tumour cell ratio, and sTILs as the CD8+/mm2.
Results: In multivariate analysis, the quantity of CD8+ ieTILs evaluated as a continuous variable emerged as an independent prognostic factor for overall survival (OS) (HR=0.1; p=0.034) and platinum-free interval (PFI) (HR=0.3; p=0.001). Moreover, the median CD8+ ieTILs allowed stratification of patients into two groups, being an independent prognostic factor for OS (HR=0.446; p=0.04), but not for PFI (HR=0.554; p=0.07). sTILs showed no prognostic correlation.
Conclusion: The quantity of CD8+ ieTILs in HGSOC is a favourable and independent prognostic parameter for OS and PFI, a relationship not observed with sTILs. These findings support the potential clinical application of algorithms based on digital analysis of ieTILs for selecting patients eligible for immunotherapy.

PS-10-028

Clinicopathological characterization of a case series of struma ovarii

J.P. Maldonado*, M. Meruje, V. Almeida, R. Almeida, S. Petronilho
*ULS Coimbra, Portugal

Background & objectives: Struma ovarii is a rare neoplasm, defined as a mature teratoma in which thyroid tissue is the predominant or sole component. Preoperative diagnosis is challenging, as clinical, radiological and laboratory features are not specific, potentially leading to incorrect patient management.
Methods: We aimed to review the clinical and histopathological features of patients diagnosed with struma ovarii. We retrospectively identified sixteen cases diagnosed at our institution between 2014 and 2024. Data were collected from the medical records, including: age at diagnosis, clinical presentation, Ca-125 levels, thyroid function, imaging findings, pre-operative diagnosis, macroscopic and microscopic features. Additionally, histological slides, when available, were reviewed.
Results: Median age was 43yrs(17-78yrs). Patients mostly presented with abdominal pain (75%). Ca-125 was normal (100%). Two patients had hyperthyroidism. Tumours were confined to the ovary (100%) and mostly unilateral (81%). All were cystic (76% multilocular), three including a solid component. Median size was 7,3cm(3-15,5cm). Pre/peri-operative diagnoses were: benign cyst, including mature teratoma (86%) and borderline/malignant tumour (14%). Patients underwent: cystectomy (7/16); unilateral (2/16)/bilateral (7/16) adnexectomy; hysterectomy(1/16); complete surgical staging(1/16). Microscopically, ten were exclusively composed of thyroid tissue; six had representation of other mature tissues. Bilateral tumours included struma ovarii with contralateral mature teratoma (2/3, one with associated Brenner tumour); and bilateral struma ovarii(1/3). The latter consisted almost entirely of cysts lined by nonspecific-appearing epithelium, with scarce septal thyroid follicles (TTF1+).
Conclusion: Although struma ovarii presents a diagnostic challenge in the pre-operative setting, most cases in our series were diagnosed as "benign cysts", leading to correct patient management. Histological diagnostic is usually straightforward, except for predominantly cystic cases with a paucity of thyroid follicles. In this setting, extensive sampling to find typical areas of struma or presence of other mature elements, as well as careful examination to look for thyroid follicles within fibrous septa should be undertaken. Additionally, immunohistochemistry may be helpful.

PS-10-029

Erythropoietin-Producing Hepatocellular (EPH) carcinoma receptors expression in endometrial carcinomas

M. Merheb*, S. Gatius, N. Eritja, A. Martinez, X. Matias-Guiu
*Hospital Universitari Arnau de Vilanova de Lleida/IRBLleida, Spain

Background & objectives: EPH receptors constitute the largest family of receptors with tyrosine kinase activity in mammals. Specific EPH receptors might act as genetic drivers in endometrial carcinoma (EC). We determine the differential immunoexpression of EPH receptors in EC.
Methods: TMAs were constructed with 75 endometrial endometrioid carcinomas (EEC) of different grades (26 grade 1, 13 grade 2, 23 grade 3) and 62 serous carcinomas (SC). Immunohistochemical analysis of EPH receptors was performed, assessing the histoscore for each case. Statistical analysis used GraphPad Prism 6.0. The Mann Whitney test compared two groups, while ANOVA tested differences among groups.
Results: The expression of two EPH receptors is significantly increased in SC compared to EEC ($p<0.001$). Statistical significance is maintained when comparing high-grade EEC versus SC ($p<0.001$). When grouping low-grade EEC (grade 1 + grade 2) and comparing them with SC, statistical significance is maintained with both markers ($p<0.001$).
Conclusion: Specific EPH receptors show increased expression in SC, suggesting a role in the genesis of this type of tumours. Additionally, their expression may constitute a predictive biomarker of response to targeted treatments in these aggressive tumours with few therapeutic strategies currently available.

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PS-10-030
Napsin-A expression in mesonephric and mesonephric-like adenocarcinomas: implications for distinguishing these from clear cell carcinoma
J. Mirkovic*, E. Olkhov-Mitsel, O. Fadare, G. Mccluggage
*Sunnybrook Health Sciences Centre, Canada

Background & objectives: We investigated Napsin-A immunohistochemistry expression in correlation with morphologic features in mesonephric adenocarcinomas and mesonephric-like adenocarcinomas of the female genital tract. This is important since these neoplasms may exhibit morphologic overlap with clear cell carcinoma which commonly express Napsin-A.
Methods: The study cohort comprised 38 mesonephric/mesonephric-like lesions including 27 mesonephric-like adenocarcinomas (MLAs; 17 ovarian, 8 uterine, 1 abdominal wall, 1 sigmoid mesocolon) and 11 cervical mesoneprhic carcinomas (MAs), from 3 institutions. Napsin-A staining (distribution and intensity) was assessed on whole tissue sections.
Results: Napsin-A staining was observed in 13/38 (34.2%) cases. All positive cases exhibited focal (1%-to-40%) staining. Although sometimes positive staining was restricted to areas of particular morphology (papillary or tubular), overall, there was no obvious correlation between Napsin-A positivity and the different morphological patterns within the neoplasms.
Conclusion: Napsin-A staining was observed in 13/38 (34.2%) cases. All positive cases exhibited focal (1%-to-40%) staining. Although sometimes positive staining was restricted to areas of particular morphology (papillary or tubular), overall, there was no obvious correlation between Napsin-A positivity and the different morphological patterns within the neoplasms.

PS-10-031
The retrospective investigation of Silva pattern and tumour budding score in cervical carcinomas; a single-centre study
A. Namal*, Ş. İlvan, A. Yavuz
*Cerrahpasa Medical Faculty, Turkey

Background & objectives: In our study, we investigated the relationship between Silva pattern (SP) and tumour budding score (TBS) in cervical carcinomas with clinical and prognostic parameters to provide better treatment options and prognosis estimation.
Methods: 50 cases diagnosed with endocervical adenocarcinoma and adenosquamous carcinoma from resection materials between 2008 and 2023 who were treated and followed up at our centre, were retrospectively analysed. All cases were histopathologically evaluated for SP and TBS by two pathologists and their relationships with prognostic parameters, recurrence, disease-free survival (DFS), overall survival (OS), disease-related death (DRD) were investigated.
Results: HPV-associated adenocarcinoma was diagnosed in 35 cases, HPV-independent adenocarcinoma in 4 cases, and adenosquamous carcinoma in 11 cases. SP and TBS classifications correlated significantly with tumour size, FIGO stage, grade, invasion depth, and lymphatic invasion. However, no significant differences were found in lymph node and distant organ metastasis, recurrence, disease-free survival (DFS), and overall survival (OS). Notably, SP-A cases had no lymph node metastasis or distant recurrence. Two cases with distant organ metastasis were SP-C and TBS-3. One SP-A case experienced recurrence, contrary to literature. A significant relationship existed between SP and TBS classifications.
Conclusion: Cervical carcinomas are a highly heterogeneous tumour group in terms of both clinical and histological features. Surgical decisions and determining the prognosis rely on traditional prognostic factors, but integrating the Silva invasion pattern into pathology reports is stressed for better surgical planning. The significance of tumour budding score for prognosis in cervical cancers has been shown in few studies; further research is needed to explore its use in treatment and follow-up.

PS-10-032
Adopting molecular classification for endometrial carcinomas: a feasibility study in a DGH setting
R. Nasa*, K.V.C.K. Dharmadasa, J. P Leelamma, H. Shah, Z. Maarouf, F. Young
*NCIC NHS Trust, United Kingdom

Background & objectives: The FIGO-2023 staging for endometrial carcinomas advocates the integration of molecular classification alongside the histological subtype. All endometrial cancers undergo testing for MMR proteins. POLE testing is conducted selectively in specific cases, as per the guidelines by the BAGP.
Methods: The histological diagnosis, along with ER, MMR, p53 IHC, and POLE mutation status of 51 endometrial carcinoma cases diagnosed on endometrial biopsy at Cumberland Infirmary, Carlisle, UK in 2023, were assessed for the feasibility of molecular classification. These cases were reclassified to incorporate the molecular subtype and the distribution of various histological subtypes within these molecular groups was also performed.
Results: In 2023, 51 cases of endometrial carcinoma were diagnosed. Molecular testing could not be conducted in three cases due to insufficient material. Molecular classification was applicable only in 19 (37.2%) cases as POLE testing was not performed in the remaining cases. Among these 19 cases, eight cases had driver mutations in PIK3CA gene, six showed p53 abnormalities, eleven were identified as MMRd, and one case had no significant mutation.
Conclusion: Molecular classification was feasible in only 37% of our cases due to the unavailability of POLE testing. Smaller biopsies offer improved tissue fixation and superior antigen preservation. Without POLE testing, there is a risk of misclassifying patients as MMRd/p53 abnormal since POLE mutations can lead to subsequent secondary abnormalities. We advocate for POLE testing to be performed upfront on all endometrial biopsies.

PS-10-033
Variations in terminology of metastatic mucinous tumours involving the ovary and omentum
L. Ninivirta*, K. Baranova, E. Goebel, J. Walsh
*London Health Sciences Centre, Canada

Background & objectives: The terminology used when metastatic appendiceal mucinous tumours spread to the ovaries varies considerably between pathologists. Our study aimed to investigate the different terms used across Canada with respect to ovarian or omental involvement by an appendiceal primary tumour.
Methods: Retrospective data was obtained from Jan 2010 - Oct 2022 with a single institution search for cases of ovarian or omental involvement by an appendiceal primary tumour – specifically low-grade appendiceal mucinous neoplasm (LAMN) and mucinous adenocarcinoma. Additionally, a survey was sent to Canadian academic centres, asking pathologists about their use of diagnostic terminology in reporting these malignancies.
Results: 50 in-house cases were identified and a further 15 pathologists inputted their preferred diagnostic terminology into the survey, with an additional partial response included in analysis (16 total). A number of different terms for the same process were identified, for example: "mucinous carcinomatosis ovarii", "metastatic mucinous adenocarcinoma", "LAMN involving the ovary", "mucinous neoplasia". In addition, diagnostic terminology was found to vary when the same malignancy involved different sites (ovary and omentum).
Conclusion: There are a wide variety of terms in use to describe metastatic appendiceal mucinous neoplasms. Pathologists vary in their terminology, even within single institutions. Our study has highlighted an area of pathologist variation, with the potential to help understand and standardize diagnostic terminology.

PS-10-034
The role of extracellular traps as indicators of early pregnancy loss
N. Nizyaeva*, T. Gusarova, N. Tikhonova, I. Stepanova, A. Akhmetshina, A. Stepanov, L. Mikhaleva
*Petrovsky National Research Center of Surgery, Russia

Background & objectives: Miscarriages has often an inflammatory cause. Serum levels of neutrophil proteinase 3 (PR3), myeloperoxidase (MPO) and their complex (PR3/MPO) are indicators of neutrophil activation. Content of PR3/MPO-complex in blood can serve as a quantitative characteristic of neutrophil extracellular traps (NETs).
Methods: The aim was to assess the levels of PR3, MPO and PR3/MPO complex and show the role of NETs in genesis of loss pregnancy. The study included 80 pregnant women (18-40 yy, 5-13weeks of gestation): 60 patients had a missed abortion, and 20 women were with uncomplicated pregnancy. Levels of PR3, MPO, PR3/MPO-complex in blood serum were revealed by ELISA.
Results: Patients with missed abortion had higher PR3 (343ng/ml; 109-455) ($p<0.0001$), MPO (707ng/ml; 465-869) ($p<0.0001$) and PR3/MPO-complex (10u/ml; 5.9-15) ($p<0.0001$), than healthy women PR3 (21ng/ml; 18-22), MPO (217ng/ml; 146-236) and PR3/MPO-complex (5.0u/ml; 4.0-5.4). We revealed a strong positive correlation in both groups between PR3 and MPO (healthy: $r=0.717$; abortion: $r=0.796$), and only for abortion between PR3/MPO-complex and PR3($r=0.546$), MPO($r=0.396$). ROC analysis was applied to estimate the sensitivity (SN)and specificity (SP)of PR3 (SN=97%; SP=100%, AUC=0.995), MPO (SN=87%; SP=95%, AUC=0.941) and PR3/MPO complex (SN=77%; SP=95%, AUC=0.888) to differ women with missed abortion from healthy pregnant women.
Conclusion: PR3, MPO and their complex in serum can serve as potential markers of missed abortion and indicate neutrophil activation. PR3 increases more strongly. Significant increase of circulating PR3/MPO-complex indicates a possible role of NETs in the missed pregnancy pathogenesis.

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PS-10-035
Mesenchymal tumours of the ovary and ligament: a comprehensive analysis of fourteen cases
A.L. Nocito*, S. Sarancone
*Spanish Hospital, Argentina

Background & objectives: Mesenchymal tumours of the ovary and ligament are rare. The goal of this presentation is to showcase cases retrieved from our archival data, conduct an analysis of the potential differential diagnoses, and ascertain whether these neoplasms coexist with other pathologies
Methods: Our approach involved an exhaustive search within the ovarian pathology archive. Subsequently, we scrutinized macroscopic data and reviewed slides using hematoxylin-eosin staining, immunohistochemistry, and, notably, one case with molecular study results
Results: Out of 1480 registered tumours, a mere 14 cases were identified as mesenchymal neoplasms. This included 5 leiomyomas (2 in the broad ligament, 3 in the ovary), 5 hemangiomas, 1 Ewing sarcoma (ES), 1 angiosarcoma, 1 osteoma, and 1 metastatic leiomyosarcoma. Noteworthy was a hemangioma, the largest, situated on the right ovary of a 6-month-old girl. Importantly, no other associated injuries were documented in this case
Conclusion: Diagnosing hemangiomas poses minimal challenges due to conclusive macroscopic and microscopic images. Differential diagnosis with fibroma/thecoma were taken into account. Microscopic observation, trichrome technique, and the application of immunohistochemistry techniques facilitate accurate diagnosis.

Ewing's tumour diagnosis proved inherently challenging, given its morphological similarity to other entities. However, employing an appropriate immunohistochemical panel and molecular biology techniques enabled a precise diagnosis. Regarding angiosarcoma, a thorough differential diagnosis with other mesenchymal tumours was undertaken, and the implementation of immunohistochemistry definitively confirmed the diagnosis

PS-10-036
Uterine leiomyomas diagnosed as bizarre nuclei showing fumarate hydratase deficiency, 22 years' experience in our hospital
A. Pasco Peña*, I. Fernandez, R. Guarch, E. Carracedo, A. Córdoba, A. Panizo
*Hospital Universitario de Navarra, Spain

Background & objectives: Histologically, leiomyomas (LM), includes LM with bizarre nuclei and LM with fumarate hydratase (FH) deficiency. This study aims to show that both types share histological characteristics, and the use of FH technique as screening to detect loss of expression.
Methods: Retrospective and descriptive study of patients diagnosed with leiomyomas with bizarre nuclei, during the period 2000-2022 at the University Hospital of Navarra. Medical records were reviewed, as well as histological and immunohistochemical characteristics and evolution. Fumarate hydratase (FH) immunohistochemistry was performed and leiomyomas with loss of expression were selected.
Results: We found 14 patients diagnosed with leiomyomas with bizarre or atypical nuclei, of which 5 (35.7%) lack of FH expression. These patients had a mean age at diagnosis of 51.93 years. Nearly all performed procedure were hysterectomy, 13 (92.9%), compared to myomectomy, 1 (7.1%). The mean tumour size was 5.7 cm, with the largest being 14 cm and the smallest 1.5 cm. The most frequent histological features of all cases were haemangiopericytoid vascular pattern and atypical nuclei, 12 (85.7%). None of the patients had cutaneous leiomyomas or renal tumours during follow-up or previously.

Conclusion: The histological pattern lacks specificity but lead us towards a possible loss of FH expression. The prevalent shared histological features were the haemangiopericytoid vascular pattern and atypical nuclei. The FH immunohistochemical technique allows screening for leiomyomas with some of the histological features described. The loss of FH expression in uterine leiomyomas prevails at the somatic level than at the germinal level yet does not imply the development of leiomyomatosis syndrome and renal cancer, it is necessary a genetic study.

PS-10-037

Identification of biomarkers of relapse in endometrial carcinomas of intermediate clinical risk by proteomics and transcriptomics

A. Peláez-García*, I. Ruz-Caracuel, A. López-Janeiro, L. Yebenes, A. Berjón, A. Redondo, R. Barderas, M. Mendiola, D. Hardisson
*Pathology, Hospital Universitario La Paz. Molecular Pathology and Therapeutic Targets Group, IdiPAZ, Madrid, Spain

Background & objectives: The objective of the project is to identify and validate biomarkers useful in predicting the risk of recurrence in intermediate risk endometrioid endometrial carcinomas based on the molecular characteristics of tumours (hypermutated or without specific molecular profile) through multiomics analysis.
Methods: Thirty-six tumour samples from patients with recurrent and non-relapsed endometrial cancer were analysed by proteomics and transcriptomics. Protein and RNA extraction was performed from paraffin-embedded tissue of the patients. Proteomic analysis was performed by four independent quantitative 10-plex TMT experiments performed separately on an Orbitrap Exploris 480 (ThermoFisher). Whole transcriptome sequencing was conducted from RNA samples on a Novaseq (Illumina).
Results: In total, 4792 proteins were identified and quantified after data analysis and bioinformatics with MaxQuant and the R program. Among them, 137 and 91 proteins showed significant upregulation and downregulation (p-value ≤ 0.05), between both conditions. Cufflinks and FPKM were used to identify 117 differentially expressed genes in relapsing patients.
Conclusion: Relevant pathways affected included proteins associated with planar cell polarity (PCP) and beta-catenin-independent WNT signalling, which are promising pathways for identifying diagnostic biomarkers in intermediate-risk endometrioid endometrial carcinomas.

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PS-10-038

Artefactual immunostaining for MLH1 in endometrial carcinoma – a potential pitfall

J. Pimentel*, J. Gama, J. Madeira, R. Almeida, S. Petronilho
*Centro Hospitalar e Universitário, Portugal

Background & objectives: Immunohistochemical testing for mismatch repair (MMR) proteins is essential in endometrial carcinoma, given its role in molecular classification, treatment selection and Lynch syndrome screening. Artefactual MLH1 staining has been previously reported, potentially leading to erroneous diagnosis of isolated PMS2 loss.
Methods: We aimed to describe patterns of MLH1 (M1 clone, Ventana/Roche) expression that can lead to inaccurate interpretations. We retrospectively identified 38 patients diagnosed with endometrial carcinoma (biopsy: n=8; surgical specimen: n=30) at our institution (2018-2023), with loss of MLH1/PMS2(n=35) or isolated PMS2 loss(n=3), for which MLH1 promoter methylation/genetic results were available in the electronic records. MMR protein expression was re-evaluated.
Results: Regarding cases diagnosed with loss of MLH1/PMS2, MLH1 complete loss was seen in 19/35 (54%) cases. Focal, weak/moderate nuclear expression (mostly staining superficial tumour) occurred in 11/35 (31%), one also presenting focal punctate expression. Diffuse punctate expression was seen in 4/35 (11%), all biopsies. 34 cases were associated with MLH1-promoter methylation. One case had somewhat heterogeneous, moderate staining, deemed equivocal (in a patient with previous diagnosis of Lynch syndrome). All three cases originally diagnosed as isolated PMS2 loss showed weak, focal, mainly superficial staining for MLH1, which on reevaluation was interpreted as MLH1/PMS2 loss. These patients had undergone genetic testing, which revealed no mutations in MLH1 or PMS2.
Conclusion: We found that artefactual immunostaining for MLH1, occurring as diffuse punctate expression (mainly in biopsies) or as weak/moderate, focal, superficial expression was frequent, although most cases were correctly identified as MLH1/PMS2 loss in the initial evaluation. However, as seen in three of our cases, these staining patterns constitute a pitfall that pathologists must be aware of and can result in an incorrect interpretation of isolated PMS2 loss and unnecessary referral to genetics service.

PS-10-039

Practical implementation of TCGA endometrial carcinoma classification

G. Raskin*, A. Chernev, A. Druy, M. Mukhina, E. Kravtcova, M. Filipenko, U. Boyarskikh
*Dr. Berezin Medical Institute, Russia

Background & objectives: Four molecular subtypes of endometrial carcinoma (EC) have been recently recognized by TCGA initiative: POLE-mutated, MMR deficient (dMMR), TP53-aberrant and unspecified. The purpose was implementation of EC TGGA classification into clinical practice.
Methods: 148 samples of EC from patients aged 32-84 y.o. were investigated. Primarily, MSH2, MSH6, PMS2, MLH1 and p53 protein status was evaluated by immunohistochemistry and POLE gene hotspot mutations by allele-specific PCR. Subsequently, FFPE-derived tumour DNA was analysed for somatic mutations by targeted NGS.
Results: dMMR type was revealed in 46 patients (31%), TP53-aberrant in 32 (22%), unspecified in 64 (43%). 6 cases (4%) were classified as POLE-mutated based on PCR's results: POLE variants p.S459F (n=1), p.P286R (n=5). 2 cases with POLE mutations were accompanied by p53 mutant type expression/PMS2 loss. These cases were primarily interpreted as mixed adenocarcinoma, then both considered as POLE-mutated. One sample had p53 mutation and simultaneous loss of PMS2/MLH1, considered as dMMR. NGS didn't reveal additional POLE mutations beyond hotspots. POLE-mutated cases were enriched in somatic variants in numerous genes (PTEN, ARID1A, PIK3CA, ATM, BRCA1, FBXW7, DROSHA), corresponding to the 'ultra-mutated' phenotype. In one case POLD1 c.2959del splice variant was detected together with MLH1/PMS2 loss.
Conclusion: TCGA classification of EC elevates the accuracy of endometrial cancer's diagnosis. Mixed endometrial carcinoma must be considered only after POLE and MMR evaluation.

PS-10-041

CCNE1 amplification in early-stage ovarian carcinomas

A. Rodríguez Villena*, E. Guerra Alia, I. Carretero del Barrio, E. Cristóbal, T. Caniego, J. Palacios, B. Pérez-Mies
*H.U. Ramón y Cajal, Spain

Background & objectives: CCNE1 is pivotal for cell-cycle regulation. CCNE1-amplification is linked to platinum drugs resistance and it's emerging as a potential therapeutic target. However, its prevalence by histological subtypes in early-stage ovarian carcinomas (ESOCs)

remains uncertain. This study investigates CCNE1-amplification in ESOCs.
Methods: Fluorescence in Situ Hybridization (FISH) with Empire genetics CCNE1/CEN19p FISH dual colour Probe was performed on 5 tissue microarrays (TMAs) from the RECLAMO study of previously characterized ESOCs from the Spanish Group of Ovarian Cancer Research (GEICO). Ratio ≥ 2 was considered amplified. Chi-square, t-student and Kaplan-Meier´s tests were employed for statistical analysis.
Results: This series is formed by 298 ESOCs distributed in 95(32%) high grade serous (HGSOC), 23(8%) low grade serous (LGSOC), 28(9%) high grade endometrioid (HGEOC), 68(23%) low grade endometrioid (LGEOC), 30(17%) clear cell, 25(8%) mucinous (MOC), 6(2%) undifferentiated (UOC) and 3(1%) other histological subtypes. FISH of CCNE1 was assessable in 267 cases (89,6%). CCNE1 was amplified in 28 cases (10,5%), but with a different distribution by histological subtypes: HGSOC (16; 17,6%), LGEOC (2; 3,5%), CCOC (6; 12,2%), MOC (2; 9%) and UOC (2; 33%). No cases of HGEOC or LGSOC amplified (p=0,008). 69% showed concurrent p53 mutated pattern (p=0,007). CCNE1-amplification didn't correlate with outcomes across subtypes.
Conclusion: CCNE1-amplication in early stage HGSOC (17,6%) is similar to previously reported in advanced stages. The frequency of CCNE1-amplification varied across different histological subtypes, with higher prevalence in HGSOC, CCOC and UOC, although the majority of cases with CCNE1-amplification also exhibited concurrent p53-abnormal pattern suggesting a potential association between these genetic alterations. In our study, CCNE1-amplification doesn't correlate with outcome across ESOC histological subtypes, but some subtypes are underrepresented. More research is needed to understand CCNE1-amplification's role in ESOCs.

PS-10-042
The MODAPLEX platform as an alternative molecular classification tool for endometrial carcinoma
L. Ruiz*, V. Gonzalez-Diaz, J. Crook, M. Grantham, N. Singh
*Barts Health NHS Trust, United Kingdom

Background & objectives: Establishing the molecular subtype is a key factor in the assessment of endometrial carcinoma (EC). Rapid assessment enables timely staging, prognostication and treatment selection. We compared the MODAPLEX platform with the Proactive Molecular Risk Classifier for Endometrial Carcinoma (ProMisE).
Methods: 160 EC tissues were assessed using the MODAPLEX for POLE mutation status. Next, twenty cases each of confirmed POLE mutated, mismatch repair deficient, no specific molecular profile, and TP53 abnormal EC were assessed with the MODAPLEX. Results were compared with ProMisE, which utilises immunohistochemistry and sequencing technologies to classify EC. Both classification models were assessed for accuracy and cost-effectiveness.
Results: Our results revealed that the MODAPLEX platform is comparable and perhaps a more efficient and sensitive tool for identifying microsatellite instability (MSI), copy number variation (CNV), and POLE mutations compared to the ProMiSe algorithm. The MODAPLEX boasts multiplex sequencing characteristics utilising PCR and capillary electrophoresis, which enabled the simultaneous processing, analysis, and reporting of MSI, CNV, and POLE mutations in less than four hours. The system provides an automated workflow without the need for bioinformatics support and can be easily incorporated into pathology laboratories.
Conclusion: The ProMiSE algorithm has greatly benefitted the prognostication of EC patients. However, due to the limitations of immunohistochemistry and inaccessibility of sequencing technologies in many clinical settings, particularly in under-resourced healthcare systems, finding a cost-effective and reliable method for classifying EC is crucial. Our findings suggest that the MODAPLEX is a clinically applicable single-test alternative to the ProMisE algorithm, providing an accurate, cost-effective, and efficient solution for the molecular classification of EC tumours.

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PS-10-043
Differential clinic-pathological and prognostic features of three main abnormal patterns of p53 staining of HPV-independent vulvar squamous cell carcinoma
A. Saco*, N. Carreras, N. Peñuelas, L. Diez-Ahijado, M. Del Pino, L. Marimón, J. Ordi, N. Rakislova
*Hospital Clínic, Barcelona, S12.pain

Background & objectives: There is no available evidence regarding the differential features of human papillomavirus (HPV)-independent vulvar squamous cell carcinomas (VSCC) with different p53 abnormal immunohistochemical(IHC) patterns. We aimed to explore differential clinic-pathological and prognostic features among VSCC with p53 overexpressed, null and cytoplasmic patterns.
Methods: We retrospectively identified 192 patients of surgically treated VSCC with available HPV testing, p16 and p53 IHC and follow-up data. From them, we selected all tumours HPV-independent and p53 IHC-abnormal, rendering a total of 150 VSCC. Histopathological and clinical features including the recurrence-free and disease-specific survival were analysed.
Results: Among the 150 VSCC, 116 (77.3%) showed p53-overexpression, 22 were (14.7%) p53-null and 12 (8.0%) showed p53-cytoplasmic pattern. Patients with tumours showing p53-cytoplasmic pattern showed deep infiltration (mean of 11.3 ± 8.7 mm vs 7.30 ± 4.76 mm [p53-overexpressed group] vs 7.15 ± 5.09 mm [p53-null group], p=0.037), with no significant differences in other features. The analysis of recurrence-free survival showed a slight trend towards higher recurrence for the p53-cytoplasmic group (p=0.157), especially when compared with p53-null group (p=0.060). Similar tendency was observed for disease-specific survival: worse survival rates for p53-cytoplasmic group (p=0.193), especially when compared with p53-null group (p=0.055).
Conclusion: Our findings indicate that HPV-independent VSCC display clinic-pathological and survival differences when stratified by p53 IHC staining patterns. Patients with cytoplasmic expression might represent a prognostically adverse group. Multi-centre studies with molecular correlation are crucial to further explore the differential features of the three abnormal p53 IHC patterns in HPV-independent VSCC.

PS-10-044
A role of Stathmin expression in the differential diagnosis and prognosis of ovarian sex-cord stromal tumours
A. Šafanda*, P. Dundr, R. Michálková, R. Matěj, M. Švajdler, T. Shatokina, J. Laco, J. Hausnerová, Z. Špůrková, G. Mehés, J. Drozenová, M. Náležinská, K. Němejcová
*Department of Pathology, First Faculty of Medicine, Charles University and General University Hospital in Prague, Prague, Czech Republic

Background & objectives: Stathmin regulates microtubule dynamics and is expressed in various malignancies in association with poor prognostic outcome. We analysed its immunohistochemical expression in a large cohort of ovarian sex cord-stromal tumours to assess its diagnostic and prognostic value.
Methods: We examined stathmin expression in 390 ovarian sex cord-stromal tumours, including adult granulosa cell tumours (AGCT), juvenile granulosa cell tumours (JGCT), Sertoli-Leydig cell tumours

(SLCT), fibroma/thecoma (F/T), Leydig cell tumours/steroid cell tumours (LCT/SterCT), sex cord-stromal tumours NOS (SCST-NOS), Sertoli cell tumours (SCT), and sclerosing stromal tumours (ScST). Immunohistochemistry (H-score, overall) was performed on tissue microarrays, and statistical analyses were conducted.
Results: Expression of stathmin was present in all cases of AGCT (281/281), JGCT (5/5), SLCT (33/33), SCST-NOS (4/4), SCT (3/3) and ScST (2/2) with high extensity and variable intensity. The lowest overall expression was seen in LCT/STerCT (5/12, 42%) and F/T (38/50, 76%). Significant differences were detected among groups, particularly between F/T and AGCT, JGCT, and SLCT. Stathmin expression can be used as an adjunct diagnostic marker, with high discriminatory ability between F/T and AGCT. However, we found no significant prognostic value of expression in selected groups of tumours (AGCT, SLCT).
Conclusion: The results of our study showed that stathmin expression varies among ovarian sex cord-stromal tumours and can be a useful adjunct marker in differential diagnosis of these tumours. According to some studies, stathmin expression can be used as a prognostic and predictive marker, but the data concerning ovarian sex cord-stromal tumours are missing.

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PS-10-045
Exploring molecular features of metastatic carcinoma to gynaecologic tract
O. Saglam*, R.F. Rojas, R. Ali, C. Corless
*Oregon Health Science University, USA

Background & objectives: Ovaries are the most common sites of metastasis in the gynaecological tract. Metastatic carcinomas make up 3-30% of malignant ovarian neoplasms, with the gastrointestinal tract (GIT) being the most common source, characterized by poorly defined molecular features.
Methods: We evaluated 225 cancer-related genes in 33 metastatic carcinoma samples, using the GeneTrail Solid Tumour panel on an Illumina platform. Microsatellite instability (MSI) was assessed by a tailored algorithm, and tumour mutation burden (TMB) was determined by nonsynonymous variants. The genomic variants were classified into 3 categories based on their association with therapies or prognostic significance.
Results: The mean patient's age was 51 years (32-77). Ovaries were the most common metastatic sites (n=26) and followed by vagina (n=6). The primary sites included 18 lower and 1 upper GIT, 5 breast, 3 appendix, and 4 unknown sites. All samples were MSI-negative, with a mean TMB of 6.5 mutations/Mb (0-11). KRAS mutations were the most common tier-1 mutations in metastatic colonic carcinoma (11/18). BRAF mutations were observed in 3 GI samples, while PIK3CA and MTOR mutations in one metastatic breast cancer. TP53 mutations were most common in the second-tier group (n=23), followed by APC mutations (n=10).
Conclusion: Consistent with the literature, ovaries are the most common gynaecologic sites for metastatic carcinomas. With low TMB (<10) and the absence of microsatellite instability, immune checkpoint inhibitors may not be effective in most metastatic GIT cancers. TP53 mutations are common and suggest accelerated colorectal cancer progression through oncogenic and inflammatory pathways. BRAF and KRAS-targeted therapies have the potential to be a primary focus in clinical trials for metastatic GIT cancers.

PS-10-046
Invasive cervical carcinoma in patients under 25 years old: a single-centre series with follow-up
G. Scaglione*, D. Arciuolo, A. Travaglino, A. Santoro, N. D'Alessandris, B. Padial Urtueta, F. Addante, F. Vegni, M. Valente, R. Benvenuto, N. Narducci, L. Mastrantoni, F. Camarda, L. Pedone Anchora, G.F. Zannoni
*Pathology Unit, Department of Woman and Child's Health and Public Health Sciences, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy

Background & objectives: Cervical cancer, driven by human papillomavirus infection, is the fourth most common neoplasm in women. Despite a 1.1% incidence in young patients, limited pathological data exist. We present a single cohort analysis of cervical cancer under 25, emphasizing pathological features.
Methods: We collected 24 cases of invasive cervical neoplasia from the Department of Surgical Pathology of the Fondazione Policlinico Gemelli (Italy, Rome) between 2000 and 2020. Histopathological features were evaluated by two experienced gynaecopathologists according to the WHO 2020 criteria. All cases were reclassified according to FIGO 2018. Survival analysis was performed using the Kaplan-Meier method.
Results: The mean follow-up was 39 months. Among the 24 cases, 19 were squamous carcinoma, 5 adenocarcinoma, with a mean age of 22.5 years (13-25 years). The mean age for the invasive adenocarcinoma group was slightly lower than squamous group (20 vs. 23.57 years). The majority of patients were stage I (60%), while 40% were distributed among higher stages. The mean horizontal dimension was 28.8 mm and wall invasion 3.5 mm. A total of 24% of patients had LVSI. Molecular analysis for HPV was performed in 10 cases, showing predominantly high-risk HPV (types 16, 31,58). Five women died of the disease with a median of 12.8 months (3-22 months).
Conclusion: Invasive cervical cancer is extremely rare in females younger than 25 years of age, but our study shows a worrying trend with a notable presence of advanced stages and unfavourable outcomes. In addition, the impact of aggressive treatment on future fertility underlines the complex considerations in the management of these cases. Thus, while cervical cancer remains rare in younger patients, the presence of advanced disease and unfavourable outcomes highlights the importance of vigilant screening, early detection and tailored management strategies.

PS-10-047
The complex landscape of endometriosis and cancer: a breakthrough with spatial transcriptomics analysis
G. Scaglione*, C. Nero, V. Iacobelli, S. Alivernini, B. Tolusso, A. Piermattei, A. Travaglino, A. Santoro, F. Sillano, R. Trozzi, L. Giacò, G. Mantini, A. Fagotti, G. Scambia, G.F. Zannoni
*Pathology Unit, Department of Woman and Child's Health and Public Health Sciences, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy

Background & objectives: Ovarian endometriosis (OE) has an intrinsic risk to develop cancer. We aim to investigate the pathways of progression to cancer analysing transcriptomics profiles from OE, endometriosis-associated ovarian cancer (EAOC), and ovarian endometriosis cancer-associated (OECA). The immune microenvironment was also considered.
Methods: Formalin-fixed paraffin embedded from 6 OE, 6 EAOC including 3 clear cell and 3 endometrioid carcinoma, were selected for spatial transcriptomic analysis using GeoMX platform (Nanostring). Samples were hybridized by Human Whole Transcriptome Atlas probe-set (>18000 targets). 185 regions of interest were identified using morphology markers, as PanCK, CD68, CD3 antibodies (Nanostring). cDNA libraries were sequenced using Illumina pipeline (Novaseq6000).
Results: Spatial transcriptomic analysis revealed differential expression in biomarkers, indicating the presence of two subtypes of

endometriosis. Clusters of endometriosis cells in OE exhibited alterations in ARID1A and other genes related to Müllerian cancer. Additionally, they showed upregulation of HMOX1, SERPINB6, MUC4, involved in inflammatory recruitment and malignant transition. Differential analysis between OE, OECA and EAOC demonstrated CAPN6 upregulation in OECA and EAOC, which leads to tumour development by promoting cell proliferation, angiogenesis and inhibiting apoptosis. In OE, T-cells showed an increase in several significant signalling pathways linked to oxidative stress and complement activation (CXCL6, S100A9). Furthermore, the immune signature indicated that a part of OE was distinctly clustered with cancer.
Conclusion: The molecular link between endometriosis and ovarian cancer is still undefined. However, we have identified a potential marker (CAPN6) that is expressed differently in OEAC and EAOC compared to OE. Our analysis revealed a shared molecular signature among immune cells in both EO and EAOC. These findings hold promise for further research and clinical applications. Furthermore, spatial transcriptomic analysis has revealed the dimension of heterogeneity in endometriosis, highlighting molecular associations with cancer despite morphological differences.

PS-10-048
Comparative assessment of TP53 mutation status by next-generation sequencing and p53 immunohistochemistry in endometrial carcinoma
L. Szalai*, Z. Melegh, E. Tanács-Bencze, E. Tóth, I. Vereczkey
*National Institute of Oncology, Hungary

Background & objectives: Endometrial carcinomas can be divided into four molecular groups based on POLE and TP53 mutation status and mismatch repair (MMR) deficiency. We routinely perform next-generation sequencing (NGS) on all tumours, which allowed us to compare its performance with p53 immunohistochemistry.
Methods: At our Institute, 375 patients with endometrial carcinomas were investigated between January 2022 and January 2024. In all patients, ER, PR, p53 and MMR (MSH2, MSH6, MLH1, PMS2) immunohistochemistry was performed, followed by NGS analysis (Oncomine Comprehensive Assay v3), which included assessment of the POLE, TP53 and MMR mutation status. The analysis was performed on a Thermo Ion S5 platform.
Results: The distribution of the tumours by histological type and molecular group was similar to that reported in the literature. Regarding the TP53 mutational status, 34 (9.1%) patients had discrepancies between the immunohistochemical and molecular findings. Among these patients, 13 had either MMR-deficient or POLE-mutant tumours. Among the remaining 21 patients, 11 had wild-type TP53 on immunohistochemistry, while TP53 mutations were identified by NGS. Three patients had subclonal abnormal p53 staining, one of whom had a TP53 mutation. In the remaining 7 patients, immunohistochemistry showed an abnormal staining pattern (1 cytoplasmic, 1 null, and 5 overexpressed), with no TP53 mutation detected.
Conclusion: According to the current guidelines, the assignment of endometrial carcinomas into the copy number high molecular group is based on p53 immunohistochemistry. We found discrepancies in p53 status between the two methods in 9.1% of our patients. This could be explained by multiclassifier phenotype in 13 patients. In the additional 21 patients, the observed differences may have molecular, analytical or preanalytical causes. The classification and clinical management of these discrepant cases are not well delineated and may require further clarification.

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PS-10-049
Evaluation of HER2/neu expression in serous endometrial carcinoma: a single institutional study from a tertiary cancer referral centre, India
P. Thakur*, B. Rekhi, S. Menon, K. Deodhar, N. Mittal, J. Ghosh, A. Maheshwari, S. Gupta
*Tata Memorial Hospital, India

Background & objectives: Among four subtypes of endometrial carcinomas, copy number high/p53-abnormal, especially serous carcinoma is the most aggressive. Recent studies indicate the possibility of targeted therapy in HER2/neu overexpressing serous carcinomas. This study aimed at evaluating HER2/neu expression in 125 serous carcinomas.
Methods: Clinicopathological features of 125 serous endometrial carcinomas (p53abnormal+p16INK4 block-like staining) and mixed endometrial carcinomas with a distinct serous component, from Jan 2018 to March 2024, were evaluated. HER2/neu immunoexpression was scored from 0 to 3+. Equivocal tumours (21/24) were subjected to FISH testing. Outcomes, in the form of progression-free survival (PFS), and overall survival (OS) were evaluated in 83 patients.
Results: The age of the patients ranged from 29-82 years(median=63). Among 116 serous endometrial carcinomas and 9 mixed carcinomas, 20 tumours displayed score 3+(intense, complete, or basolateral/lateral membrane staining in >30% tumour cells); 24 displayed 2+(intense complete or basolateral/lateral membrane staining in ≤ 30%, or weak to moderate in ≥10% tumour cells); 27 displayed 1+(faint incomplete membrane staining in any proportion or weak complete in <10% tumour cells) and 54 showed negative immunostaining. FISH for Her2/neu amplification in 21/24 tumours with a 2+score, revealed amplification in 4 tumours. Finally, 24/125(19.2%) tumours were HER2/neu-positive. The median OS was 15 months and PFS was 11 months.
Conclusion: This constitutes the first study on HER2/neu expression in serous carcinomas from our subcontinent. There was no difference between HER2/neu positive and negative tumours in terms of survival. Her2/neu overexpressing tumours were associated with cervical involvement(p=0.04). A notable percentage (19.2%) of HER2/neu-positive serous carcinomas seems to provide further evidence for testing endometrial carcinomas routinely for HER2/neu testing, at least the p53-abnormal, including serous subtype in our settings and triaging some of those patients for targeted therapy, in certain clinical settings.

PS-10-050
Endometrial assessment for fertility-sparing treatment of young women with early-stage endometrial carcinoma: proposal for a standardized synoptic reporting
Z. Zhao*, J.X.H. Ang, R. Nadarajah, S.L. Wong
*Singapore General Hospital, Singapore

Background & objectives: Recent guidelines on fertility-sparing treatment (FST) of patients with endometrial carcinoma emphasize regular endometrial assessment. However, there is no consensus on histological reporting of such cases. This study aims to review local practice and propose standardized reporting in this scenario.
Methods: A retrospective clinicopathological review of patients younger than 40 years old, diagnosed with early-stage, low-grade endometrial endometrioid carcinoma (EEC) and underwent FST at our institution between 2015 and 2021 was performed. The classification scheme for treated EEC proposed by Wheeler et al. in 2007, encompassing resolution, regression, persistence, progression and recurrence, was applied in this study.

Results: A total of 94 endometrial biopsies from 14 patients were identified, with a median age of 32.5 years (range: 28 - 37 years) and a median BMI of 37.4 (range: 22.1 - 47.1). They received oral therapy (4/14, 28.6%) or combined oral therapy with IUCD (10/14, 71.4%), with a median follow-up of 31.5 months (range: 11 - 76 months). Treatment outcome included resolution (7/14, 50%), persistence (2/14, 14.3%), progression (2/14, 14.3%) and recurrence (3/14, 21.4%). The time from initial diagnosis to resolution ranged 4 to 15 months. Successful pregnancies were achieved in 2 patients, including one livebirth. Three patients underwent hysterectomies, including one with progression and distant metastasis during FST.
Conclusion: Young women with endometrial carcinoma may prolong FST beyond recommended durations due to strong fertility desires, increasing the risk of disease progression. Standardized reporting of endometrial biopsies during FST, including disease severity and volume compared to prior biopsies, along with identification of exogeneous progesterone effect and categorized comments on the current treatment response, can facilitate treatment adjustments. Routine reviewing prior endometrial biopsies, obtaining deeper tissue sections and seeking second opinions in challenging cases are recommended for accurate assessment.

PS-11Poster Session Haematopathology

PS-11-001
Characteristics of orbital lymphoma: a clinicopathological study of 21 cases

D. Aniceto Baptista*, A. Pardal, E. Fonseca
*Department of Pathology, Centro Hospitalar e Universitário de São João, Porto, Portugal

Background & objectives: Ocular adnexal lymphomas, derived from B, T/NK cells, primarily affect structures like the lacrimal gland, sac, and orbit, constituting approximately 10% of adult orbital malignancies. Our study aimed to assess clinicopathologic characteristics and prognosis in patients with these lymphomas.
Methods: We conducted a retrospective analysis of 21 patients diagnosed with biopsy-confirmed ocular adnexal lymphoma (OAL) at a Portuguese tertiary care hospital between 2012 and 2022. Lymphomas were categorized according to the 5th edition of the WHO classification. Survival outcomes were evaluated considering age, gender, disease site, disease extent, and lymphoma type to identify potential prognostic factors.
Results: The median age of the patients was 66 years (range: 38-88), with a female-to-male ratio of 1:1.1. The majority of cases were characterized by extranodal marginal zone lymphoma (EZML) (57.1%; n=12), followed by diffuse large B-cell lymphoma (23.8%; n=5), mantle cell lymphoma (9.5%; n=2), and follicular lymphoma (9.5%; n=2). Orbital localization was predominant (n=19), with 46.7% of cases presenting with localized disease. During follow-up, three patients exhibited spread to the contralateral eye, lymph nodes, and facial soft tissues, while two had central nervous system, pleural fluid, bone, and optic nerve involvement. Ultimately, ten patients died, with diffuse large B-cell lymphoma accounting for five deaths.
Conclusion: Our study underscores the predominance of B-cell lymphomas in ocular adnexal lymphoma (OAL), notably EZML emerging as the most prevalent subtype, followed by diffuse large B-cell lymphoma (DLBCL), consistent with existing literature. While OAL primarily affects older adults, as observed in our study, we did not observe a female preponderance, contrary to previous findings. Particularly noteworthy is the poorer prognosis observed in patients with DLBCL, characterized by advanced disease stage, dissemination, and reduced overall survival.

PS-11-002
Transient abnormal myelopoiesis and Down Syndrome. Investigating the features of hepatic hematopoiesis in foetuses affected by trisomy 21

A. Canino*, F. Angotzi, C. Gerosa, R. Murru, E. Noto, M. Vincis, D. Fanni
*Università degli studi di Cagliari, Italy

Background & objectives: Trisomy 21 carriers are prone to develop transient abnormal myelopoiesis (TAM) and acute myeloid leukaemia of Down Syndrome (AML-DS). In this study, we aimed to investigate the features of hepatic hematopoiesis in foetuses affected by trisomy 21.
Methods: We enrolled twenty-one foetal liver samples from foetuses carrying trisomy 21 between the 12th and the 19th week of gestation. In addition, we added to hematoxylin-eosin morphological evaluation the immunohistochemical markers for glycophorin C, MPO, LAT, CD34 and CD117 in 6 of the specimens displaying 12 to 17 weeks of gestational age.
Results: In sections stained with hematoxylin-eosin, the hepatic parenchyma showed areas characterised by both stage II and stage III hematopoiesis, which was irrespective of the gestational age. Staining with glycophorin C revealed a pattern consistent with hyperplastic erythropoiesis, documented by erythroid foci measuring 50 to 100 μm and increased erythroblasts. Megakaryocytopoiesis consistently showed dysplastic features with frequent micro megakaryocytes and cells with spherical or hypolobulated nuclei. Myeloid progenitors identified by MPO staining were primarily located in the subcapsular area and the stroma around large vessels. CD34+ hematopoietic progenitors were rare and scattered throughout the hepatic parenchyma.
Conclusion: Our results hint at hepatic hematopoiesis already dysregulated since foetal life in foetuses carrying trisomy 21 that shows dysplastic features akin to those found in myelodysplastic syndromes in adults. These alterations mainly affected the megakaryocytic lineage and the stepwise progression of hepatic hematopoiesis through its physiological stages. These morphological features compose a specific picture of hepatic hematopoiesis in carriers of trisomy 21, which could represent the precursor to the development of TAM and AML-DS.

PS-11-003
Immunohistochemical profiling of CD94 expression in mature T and NK-Cell cells and neoplasms: correlation with flow cytometry and clinical relevance

O.C. Eren*, I.S. Isgor, K. Lopez, Q. Gao, D. Frosina, E. Hernandez, A. Jungbluth, A. Dogan
*Memorial Sloan Kettering Cancer Center, Turkey

Background & objectives: CD94/NKG2, a C-type lectin receptor present on the surface of NK and a subset of CD8+ T-lymphocytes, can be targeted with monoclonal antibodies. We present the first study profiling CD94 expression in mature T and NK-cell neoplasms using immunohistochemistry (IHC).
Methods: An initial cohort (n=47) including benign/malignant T and NK-cell proliferations was evaluated by CD94 flow cytometry and IHC, to assess correlation and validate IHC. A separate second cohort (n=104) including various mature T and NK-cell neoplasms —HSTCL, EATL, MEITL, T/NK-LGL, ENKTL, and ALCLs (ALK+, ALK-, breast implant-associated)— was then assessed by IHC to benchmark CD94 expression and establish clinical utility.
Results: In the initial cohort (validation), FC yielded 22 positive and 25 negative cases. In normal tissues, expression was restricted to cells of innate immunity (NK-cells, gamma/delta and subset of CD8+ cytotoxic T-cells). IHC identified 22 cases as positive, 17 as negative,

and 8 as partial/equivocal. Both in normal tissues and lymphomas, IHC replicated the pattern predicted by FC. Overall concordance was high (77%). Concerning the second cohort, HSTCLs were consistently CD94+ (90% of cases). In EATL and MEITL, these rates were 75% and 60%, respectively. Among T/NK-LGLs, 65% of cases were at least partially CD94+ by IHC. 87% of ENKTLs were positive, while ALCLs (both ALK+ and ALK-) were negative.
Conclusion: Results validate IHC as an effective alternative to FC for CD94-profiling. For samples with low tumour-cell-percentage (low-level marrow infiltration), evaluation remains suboptimal with difficulty discerning cells-of-interest. HSTCLs and ENKTLs are consistently CD94+. Similarly, a significant portion of EATL, MEITL and T/NK-LGL are positive, but not ALCLs. In conclusion, CD94 IHC has utility in diagnosis of T/NK-cell lymphomas and differential diagnosis from ALCL. Moreover, as targeted therapies via anti-CD94 antibodies become available, the assay may accurately select patients for clinical trials.

PS-11-004
Spectrum of hemoglobinopathy in antenatal females screened for carrier status at a tertiary care centre in Central India
G. Goel*, V. Krishna, D. Garkoti, D. Joshi, V. Walke
*AIIMS Bhopal, India

Background & objectives: Hemoglobinopathies comprise thalassemia and structural variants. Carrier screening is helpful in prevention of major haemoglobinopathy. Aim: To highlight the significance of antenatal screening for haemoglobinopathies Objectives: Determine frequency of carriers among antenatal cases. Study spectrum of haemoglobinopathies among antenatal cases.
Methods: A retrospective, cross-sectional study was conducted on 1949 antenatal females who came for routine checkups during a period of one year from January 2023 to December 2023. A complete blood picture and HPLC were carried out for all the cases. The mutation analysis for all the cases of heterozygous beta thalassemia for five common mutations was also carried out.
Results: Blood samples from a total of 1949 females were collected for complete blood picture and HPLC as part of routine antenatal screening. The patients' age ranged from 20 to 35 years. Out of 1949 females, 211 (10.82%) showed the presence of abnormal haemoglobin. Out of 211 hemoglobinopathies, the majority of the cases had Heterozygous beta-thalassemia (108, 51.1%) followed by heterozygous HbS (80, 37.91%),Hb D Punjab (8, 3.79%), Homozygous HbS (5, 2.36%), heterozygous HbQ India(3, 1.42%), 2 cases (0.94%) each of heterozygous HbE and compound heterozygousfor beta-thalassemia and HbS and one case each of (0.47%) Homozygous HbE, Heterozygous HPFH and Hb J Meerut.
Conclusion: In view of the 10.82% prevalence of hemoglobinopathies in antenatal screening, the effectiveness of antenatal screening in the prevention of hemoglobinopathies is highlighted. Though heterozygous beta-thalassemia and heterozygous HbS are the most common hemoglobinopathies detected, the spectrum also includes other variants.

PS-11-005
Clinicopathological and genetic features of extranodal marginal zone B-cell lymphoma of lower gastrointestinal tract
B. Han*, J. Yim, S. Lim, Y.K. Song, S. Kim, H. Yun, Y.K. Jeon
*Department of Pathology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

Background & objectives: Despite increasing incidence, the clinical and genetic features of extranodal marginal zone B-cell lymphoma of lower gastrointestinal tract (ENMZL-LGI) remain unclear.
Methods: 56 patients with pathologically proven ENMZL-LGI were included. Of them, 38 patients harboured ENMZL localized LGI and presented with single lesion (n=26) or multiple/diffuse segmental lesions (n=12). 18 patients harboured systemic ENMZL involving LGI and other organs, either synchronously (n=8) or metachronously (n=10). MALT1 FISH was performed in 28 patients and target sequencing covering 121 lymphoma-related genes in 30 patients.
Results: The median age of ENMZL-LGI was 61.5 years with female to male ratio of 1.24:1. Most patients (71.4%) were asymptomatic. Systemic ENMZL-LGI showed male predominance (P=0.042), common symptomatic presentation (P=0.012), larger tumour (P=0.004), higher ECOG performance status (P=0.008), higher Lugano stage (P<0.001), and received combination therapy more frequently (P=0.007). MALT1 translocation by FISH was observed in 10 (35.7%) of evaluated cases. KMT2C (46.7%) was most frequently mutated, followed by TBL1XR1 (16.7%), NOTCH1, BRAF, and ATM (10% each), and NOTCH2 and TNFIP3 (6.6% each). t (11;18) (q21; q21) BIR3::MALT1 fusion was observed in 4 patients. BRAF mutations were restricted to systemic ENMZL-LGI. Systeic ENMZL-LGI showed worse progression-free survival compared to localized ENMZL-LGI (P<0.001).
Conclusion: Genetic features of ENMZL-LGI were comparable to ENMZL of other organs. Systemic ENMZL- LGI was associated with poor prognosis of patients.

PS-11-006
The features of chronic myelotoxic effects of heavy metal salts in rats
Y. Lyndina*, N. Hyriavenko, K. Sikora, Y. Sikora, M. Lyndin, A. Romaniuk
*Sumy State University, Ukraine

Background & objectives: Various endogenous and exogenous factors negatively affect the quality of hematopoiesis. One of the most potent pollutants is heavy metal salts (HMS). Their negative effect is manifested through the induction of lipid peroxidation, deactivation of enzyme systems, DNA damage, other.
Methods: The structure of the bone marrow was studied on femurs of rats. The animals were divided into two groups: animals that consumed regular drinking water; rats that received a water with mixture of HMS. To study their chronic effects, the animals were euthanized on the 90th day of the experiment. Tissue sections were stained with hematoxylin and eosin.
Results: Under conditions of chronic exposure to HMS, there was a gradual decrease in the area occupied by erythrocyte and leukocyte precursors, although the number of megakaryocytes significantly increased (control group indicators were 5.25±1.42%, 14.75±1.42%, 0.16±0.05% in the epiphyses and 17.83±0.75%, 51.17±3.27%, 0.16±0.05% in the diaphyses, respectively). Thus, after three months of the experiment, the area occupied by erythropoiesis was 3.33±0.51% in the epiphyses and 14.3±1.63% in the diaphyses, leukopoiesis – 12.8±0.98% and 43.8±1.9 respectively, and thrombopoiesis – 0.25±0.05%. These changes are associated with the direct and indirect hematotoxic effects of heavy metals.
Conclusion: Excessive consumption of heavy metal salts results in pronounced changes in hematopoietic tissue, manifested by a statistically significant increase in the number of megakaryocytes and a decrease in the area occupied by erythro- and leukopoiesis. These changes indicate the myelotoxic properties of heavy metals, which are reflected in quantitative indicators of peripheral blood.

PS-11-007
Differential STAT3 signalling in the tumour microenvironment of EBV-positive versus EBV-negative diffuse large B-cell lymphomas
N. Moulai*, R. Bennoui, M. Guermi, S. Ahmed Allal, W. Ouahioune
*Faculty Of Medecine Of Blida, Algeria

Background & objectives: Our study explores the STAT3 pathway's role in shaping the tumour microenvironment in EBV-positive and EBV-negative diffuse large B-cell lymphoma not otherwise specified (DLBCL NOS), aiming to understand its impact on tumour dynamics and treatment outcomes.
Methods: We performed an immunohistochemical analysis of STAT3 phosphorylation in 162 diagnosed cases of DLBCL NOS, identifying 13 EBV-positive and 149 EBV-negative cases. STAT3 expression levels were correlated with clinical outcomes and immune checkpoint expression, including PD-L1. Statistical significance was assessed using Pearson's correlation and Mann-Whitney U tests to compare between the two groups.
Results: STAT3 was highly expressed in 100% of EBV-positive cases, significantly higher than in EBV-negative cases, which showed 20.5% expression ($p<0.0001$). High STAT3 expression correlated with increased PD-L1 levels and was associated with poorer clinical outcomes in EBV-positive patients. Additionally, EBV-positive DLBCL showed a unique activation pattern of immune responses within the tumour microenvironment, suggesting a pivotal role of STAT3 in modulating tumour immunity. Our results showed a significant difference between the two groups EBV (+)-DLBCL and EBV (-)-DLBCL on the response to R-CHOP treatment ($p=0.01$). The analysis of the survival rate according to the Kaplan Meier method showed a significant difference in the survival rate between the two groups, $p=0.0001$.
Conclusion: Our study highlights a significant variation in STAT3 activation between EBV-positive and EBV-negative DLBCL, contributing to unique tumour microenvironments and impacting prognosis. These findings suggest the STAT3 pathway as a potential therapeutic target for developing tailored treatment strategies in DLBCL, especially in EBV-positive cases. Further research is necessary to elucidate the direct mechanisms of STAT3 in immune modulation and their effects on therapeutic outcomes.

PS-11-008

Clonality and clonotype assessment in T follicular helper cell lymphoma by next-generation sequencing of TRB and TRG rearrangements

R. Nakayama*, L. Kroeze, J. Luijks, J. Rijntjes, A. Amir, P. Groenen, K. Hebeda
*Japanese Red Cross Wakayama Medical Center, Japan

Background & objectives: Because T follicular helper cell lymphoma (TFHL) can be difficult to diagnose due to a limited lymphoma load in the tissue, we performed next-generation sequencing (NGS) of TRBV-TRBJ, TRBD-TRBJ, TRGV-TRGJ rearrangements. We compared the results with the standard EuroClonality/BIOMED-2 assay.
Methods: DNA was extracted from 34 formalin-fixed paraffin-embedded TFHL tissues from 2 pathology archives, dating back 6 years. NGS amplicon-based T-cell clonality analysis was performed using the two-step PCR protocols developed by EuroClonality, followed by sequencing on an Illumina platform. The nucleotide sequences were analysed for abundance, clonotype, the amino acid junctional region and functionality using ARResT/Interrogate software.
Results: TFHL percentage ranged from 20 to 80% of total T-cells (average 40%). All but one (100 bp) showed amplification of $\geq$200 bp genomic fragments. The NGS-based clonality assay revealed clonality (n=25), bi-clonality (n=5), oligoclonality (n=1), polyclonality (n=3) after integration of the individual target results. A high level of concordance was found with only one case showing clonality by the NGS-based approach and not by the standard assay. Clonality was detected in the case with poor DNA-quality (100 bp). One or more productive clonal TRBV-TRBJ rearrangements were identified in 30 of 31 clonal cases. The productive TRB gene rearrangements were further assessed to investigate bias in gene usage and junctional regions.
Conclusion: Both methods resulted in a high detection of clonality ($\sim$90%) in TFHL when combining incomplete and complete TRB, and TRG gene rearrangements. NGS-based clonality detection in addition provided information on relative clone size, and especially on clonotype, which can be valuable to detect small TFHL clones in follow up or staging biopsies.

PS-11-009

PS6 expression is associated to different molecular pathways in diffuse large B-cell lymphoma cell-of-origin subtypes

E. Neves Filho*, C.G. Hirth, L. Gomes Neto, P.G. Silva, S.H. Rabenhorst
*LABGEM, Brazil

Background & objectives: Several biomarkers have been evaluated to address diffuse large B-cell lymphoma (DLBCL) molecular landscape. Ribosomal protein S6 (PS6), a downstream effect media of the AKT/mTOR pathway, has been implicated in carcinogenesis, but its role in DLBCL still needs elucidation.
Methods: In a series of 113 DLBCL cases considering germinal centre (GC) versus nonGC subtypes according to Hans algorithm, we investigated PS6 expression by immunohistochemistry and its associations with some immunophenotypic presentations, including EZH2, BCL2, MYC and TP53 expression and miR-155b and miR-125b detection by in situ hibridization.
Results: PS6 was expressed in 63.7% (72/113) of the studied cases. In the GC patients, PS6 was associated to miR-155b detection ($p=0.014$), while, in the nonGC subtype, an association between PS6 and TP53 overexpression was observed ($p=0.048$). Interestingly, PS6 seems to be related to EZH2 expression regardless of DLBCL subtypes ($p=0.000$ for GC and $p=0.004$ for nonGC cases).
Conclusion: In conclusion, PS6 is commonly expressed in DLBCL and associated to EZH2 independently on cell-of-origin subtypes. Moreover, molecular pathways involving PS6 and miR-155b and PS6 and TP53 seems to be a GC and non GC characteristics, respectively.

PS-11-010

ALK-positive anaplastic large cell lymphoma (ALK+ ALCL): comprehensive diagnosis

Z. Prouzová*, M. Mrhalová, E. Kabíčková, R. Kodet, M. Kalinová
*Department of Pathology, 3rd Faculty of Medicine, Charles University and University Hospital Královské Vinohrady, Department of Pathology, 1st Faculty of Medicine, Charles University and General University Hospital in Prague, Czech Republic

Background & objectives: ALK+ ALCL is T-NHL, where the ALK oncogene located at 2p23 is pathologically activated. The activation is caused by translocations that produce fusion genes with different translocation partners. The most frequent translocation is t (2;5) (p23; q35), which fuses with the NPM1 gene.
Methods: Histology: morphological evaluation of tissue. Immunohistochemistry: type of ALK protein expression including localization, T-marker expression. RT-PCR: detection of the most common fusion gene NPM1::ALK. RQ-PCR: detection of expression of the translocated part of the ALK gene. NGS: search for translocation partner in patients without NPM1::ALK fusion. I-FISH: detection of a break in the 2p23 region.
Results: We examined 96 ALK+ ALCL patients (2-80 years; median 16 years). In 89 patients, we examined the chromosome 2 break (region 2p23) and in all cases the break was detected. We detected the NPM1::ALK fusion gene in 71 cases, ATIC::ALK in 9 cases, TPM3::ALK fusion in 3 patients, CLTC::ALK in 2 cases, MYH9::ALK in 2 cases, RNF213::ALK fusion in 2 cases, and TPM4::ALK and SQSTM1::ALK, SATB1::ALK and CAPRIN1::ALK fusions in 1 case each. We detected high levels of expression of the translocated

portion of the ALK gene in all patients examined (92), with a median of 183029 copies.
Conclusion: Comprehensive molecular typing of ALK+ ALCL patients provides information about the biology of the disease and helps to estimate the prognosis of the disease. NGS allows the detection of translocation partners of the ALK gene in ALK+ ALCL. The SQSTM1::ALK and CAPRIN1::ALK fusion genes have not been described in ALCL yet. Quantitative detection of the expression of the translocated part of the ALK gene is used both for the diagnosis of ALK-positive ALCL and for monitoring minimal residual disease.

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PS-11-011
Automated detection and classification of hematopoietic cells in bone marrow aspirate smears for routine screening using a deep-learning algorithm (Aiforia)
L. Saft*, E. Vaaara, E. Ljung, A. Kwiecinska, D. Kumar, B. Timar
*Karolinska University Hospital and Institute, Sweden

Background & objectives: The cytomorphological assessment of bone marrow aspirate smears plays an important role in the workup of hematological disease. A convolutional neural network-based algorithm was developed for the detection of hematopoietic cells as a quick screening tool in routine diagnostics.
Methods: May-Grünwald Giemsa-stained bone marrow aspirate smears from patients with normal or reactive findings were digitized (3DHISTECH slide scanner) and uploaded to the AIFORIA Create Platform Version 5.7.1 (Aiforia Technologies Plc). A deep learning algorithm based on nine major hematopoietic cell classes was developed, externally validated and correlated to a random manual differential cell count on routine clinical samples.
Results: A total of 1950 single cell annotations allocated to nine cell classes were used for the training and verification of the model with a final total class error of 0,15% and a mean of 99,2% for precision and sensitivity. External validation by three hematopathologists achieved 87,65% precision and 86,65% sensitivity using 2048 single cell annotations in 515 validation regions performed at two occasions. The mean total error in comparison to the AI model was 25,41%, lowest for granulocytes (8,56%) and plasmacells (6,9%) and highest for blasts (60,18%). The output of the AI model in randomly selected regions of interest in routine clinical samples showed high correlation with manual microscopy (r=0,98).
Conclusion: AI applications in digital pathology represent a rapidly emerging technology and can improve the diagnostic workflow and accuracy. Automated detection and quantification of hematopoietic cells in bone marrow aspirate smears is useful as a quick screening tool, particularly in normal and reactive conditions and in routine staging examinations. Such approaches could potentially provide a basis for standardization and the development of additional algorithms in neoplastic haematology.

Funding: Analytic Imaging Diagnostic Arena (AIDA), Strategic Innovation Program Medtech4Health, Sweden

PS-11-012
CD23 expression in lymphoplasmacytic lymphoma: diagnostic utility and biological correlations
F. Scarmozzino*, M. Pizzi, N. Danesin, M. Pinto, G. Scapinello, L. Trentin, F. Piazza, A.P. Dei Tos
*University of Padua, Italy

Background & objectives: Lymphoplasmacytic lymphoma (LPL) is a mimicker of marginal zone lymphoma (MZL) in the bone marrow. This study assessed the immunophenotype of LPL with focus on its differential diagnosis with MZL and on the frequency of aberrant phenotypes, highlighting phenotypic-biological correlations.
Methods: This retrospective study considered 81 clinically annotated LPL, diagnosed at Padua University Hospital between 2017 and 2023. Bone marrow biopsies at diagnosis were reviewed to assess morphological and phenotypic features (e.g. CD10, Bcl6, CD23, CD5, MNDA, MUM1 expression). MYD88/CXCR4 mutational status was also considered. The findings were confronted with 73 MZL diagnosed in the bone marrow over the same time period.
Results: The study population included 52 males and 29 females (median age: 69.3 years). The neoplastic infiltrate ranged from <1% to 95% of bone marrow cellularity. Immunohistochemically, all cases were positive for pan-B-cell markers and MUM1, with variable expression of CD10 (4%), CD5 (18%) and MNDA (61%). CD23 was expressed in 73% of cases, usually with only focal/partial positivity. CD23 expression was associated with higher rates of MYD88L265P (96% vs 81%; p= 0.05) and with lower frequency of CXCR4 mutations (11% vs 30%; p= 0.16). Comparison with MZL highlighted more frequent CD23 expression in LPL (73% vs 34%, p< 0.01). No other markers significantly differed between the two entities.
Conclusion: Focal/partial CD23 expression is an underrecognized feature of LPL, which may support the differential diagnosis with MZL. CD23 positivity correlates with the disease mutational status, possibly indicating phenotypic-molecular correlations.

PS-11-013
Interpretation of B cell malignancies using an ultrasensitive dual mRNA in situ hybridization (ISH) for kappa and lambda light chain restriction demonstrates high level of reproducibility between three sites
B. Su*, A. Baker, A. Ehsan, A. Evans, S. Gladden, B. Mosteller, J. Su, A. Babic
*Roche Diagnostics Solutions, USA

Background & objectives: Determining clonality in B cell lymphomas with ultrasensitive dual ISH for light chain restriction holds great promise. In this study we determined inter-laboratory reproducibility of a newly developed device across three sites.
Methods: Each site stained five sections from 28 FFPE biopsies of bone marrow or lymphoid tissue of B cell malignancies or reactive mimics with ISH probes targeting kappa and lambda mRNA over five days. There were similar numbers of kappa restricted, lambda restricted, and non-restricted specimens. Two pathologists from each site determined a kappa:lambda ratio with corresponding restriction status.
Results: All six pathologists determined that 140/140 (100%) of the slides were evaluable. The overall percent agreement (OPA) was 98.5%. Kappa restricted percent agreement (KRPA) was 98.8%, lambda restricted percent agreement (LRPA) was 99.6%, and non-restricted percent agreement (NRPA) was 97.5%. Reproducibility of Kappa/Lambda status was assessed using Average Kappa Restricted Agreement (AKRA), Average Lambda Restricted Agreement (ALRA) and Average Non-restricted Agreement (ANRA rates). The overall AKRA, ALRA and ANRA rates were 95.6 %, 98.8% and 96.6 % for the between-sites, 95.5 %, 98.8% and 96.6 % for the between-reader, and 95.5 %, 98.8% and 96.6 % for between-day comparisons, respectively.
Conclusion: All slides stained with the ultrasensitive mRNA dual ISH assay were evaluated by pathologists and deemed acceptable for interpretation. Interpretation of the assay was highly reproducible across all observations as well as between sites, readers, and days. Pathologists may benefit from this emerging method of determining clonality for potential B cell malignancies in FFPE tissue.

PS-11-015
PPM1D mutations are associated with high frequency of fibrotic progression or accelerated phase in myeloproliferative neoplasms

X. Zhang*, R. He
*USA

Background & objectives: PPM1D encodes a protein phosphatase which is a negative regulator of TP53 activity. PPM1D mutations are reported in clonal hematopoiesis and different myeloid neoplasms, especially therapy-related myeloid neoplasms. We aimed to investigate the significance of PPM1D mutations in Myeloproliferative Neoplasms.
Methods: Myeloproliferative neoplasms (MPNs) with PPM1D mutations were identified by querying the genomics database of our institution from 2022 to 2024. Myeloid next-generation sequencing (NGS) analysis was performed on bone marrow or peripheral blood. A total of 10 cases with pathogenic/likely pathogenic PPM1D mutations were identified. The clinical findings, marrow blast count, fibrosis stage, NGS and cytogenetic findings were collected.
Results: Of the 10 cases, the average age was 74, with a male to female ratio of 1:1. The different clinical subtypes of MPN were essential thrombocythemia (ET, 7), polycythemia vera (PV, 2) and primary myelofibrosis (PMF, 1). The driver mutation was JAK2 V617F in 7 cases, with an average Variant Allele Frequency (VAF) of 42% (3-61%), and CALR frameshift mutation in 2 cases (VAFs of 41% and 66%), and MPL p.Trp515Lys mutation in 1 case (VAF of 55%). Two cases had bone marrow blast count of 10-19%, consistent with accelerated phase of disease. Six cases had at least MF-2 (of 3) myelofibrosis, consistent with fibrotic progression.
Conclusion: Previous studies have suggested that PPM1D mutations in MPN are likely acquired later in disease and may not necessarily represent clonal hematopoiesis. Consistent with previous studies, PPM1D mutations in MPN are mostly C-terminal truncating mutations with an average VAF of 17%. PPM1D mutations are associated with high frequency of fibrotic progression (60%) and accelerated phase (20%), as well as relatively high VAF of the MPN driver mutation, suggesting that it could be a potential biomarker for disease progression in MPN.

PS-12Poster Session Molecular Diagnostics Pathology Symposium

PS-12-001
Comprehensive genomic profiling of tumour spatial heterogeneity for clinically-actionable genomic alterations

J.K. Killian*, D. Lin, R.S. Huang, L. Ritterhouse, S. Lakis, P. Pokharel, D. Pavlick, D. Jin, N. Ferguson, L. Dennis, D. Fabrizio, C. Malboeuf, M. Montesion, G. Frampton, K. Murugesan
*FOUNDATION MEDICINE, USA

Background & objectives: Tumour spatial profiling of real-world cancer specimens for heterogeneity of actionable genomic alterations (AGA) is relevant to the diagnosis and treatment of cancer patients. Small biopsy procedures and laboratory tumour microdissection practices could impact detection of AGA of various categories.
Methods: We utilized precision needle punch enrichment (NPE) technology for multi-focal comprehensive genomic profiling (CGP) of 25 real-world pan-cancer FFPE blocks from different patients. Companion-diagnostic (CDx) therapy-associated short variants and indels (SV), unequivocal copy number amplifications and losses (CNA), and gene rearrangements/fusions (RE), as determined by FoundationOne®CDx, were compared between 4 spatial targets per tumour (3 NPE, 1 whole-specimen curl).
Results: NPE and unmicrodissected tumour curls had surface areas of 1.3mm2 and 325.5mm2, respectively, with median inter-NPE distance of 11mm. 10 of 25 tumours harboured reportable CDx-associated AGA, including RAS-wildtype status (SV allele frequency's quartile coefficient of dispersion per block = 0.15 for BRAF V600E) in colorectal carcinoma (CRC), ALK fusion in lung adenocarcinoma (LUAD), ERBB2 amplification in CRC (QCD of log2 CN ratio= 0.06), PTEN mutation in breast carcinoma (0.05 for splice site 1026+1G>A), MET Ex14 in LUAD (0.06 for D1010H), and EGFR mutation in LUAD (0.05 for L858R). Intra-tumoural spatial derivatives, including the 3 NPE and 1 curl per block, demonstrated 100% concordance for CDx-associated SV, CNA, and RE.
Conclusion: CDx-associated SV, CNA, and RE were concordant across intra-tumoural space, consistent with early emergence (a.k.a. truncal mutation) and stability during tumorigenesis. Overall, these results have important implications for diagnostic testing, including patient biopsy/surgical sampling and laboratory microdissection practices, which we find to be sound for the detection of therapy-related AGA in this study. Further specimen accrual and data analysis is ongoing to evaluate the tumour spatial and liquid biopsy concordance of additional AGA and biomarkers.

PS-12-002
Investigating the use of fresh cytological specimens as an alternative to FFPE tissue for biomarker detection in non-small cell lung cancer

B. Mills*
*United Kingdom

Background & objectives: Tissue biopsy remains the gold standard source of tumour DNA, however it is invasive, time consuming and susceptible to artefact and intratumoural heterogeneity. Cytology samples, already routinely obtained, offer an alternative source of tumour DNA for biomarker testing in NSCLC.
Methods: This study aimed to assess the concordance of mutation testing between tumour DNA obtained from tissue biopsy and cytology samples. The Genexus Oncomine Precision Assay was utilised, covering all current diagnostic gene targets that influence the provision of targeted therapy in NSCLC. Additionally, a literature review was conducted to determine the current landscape of liquid biopsies in NSCLC.
Results: Sufficient DNA from the cytology samples of sixteen patients with a predetermined hotspot tissue mutation was successfully extracted and sequenced. High quality sequencing was achieved with both sample types producing results within the accepted quality metrics for clinical reporting. A concordance rate of 56% between detection of hotspot mutations in tissue and cytology DNA was achieved, with preanalytical factors including time of sampling and previous delivery of targeted therapy the likely cause of disparity. The use of cytology samples achieved a rapid average turnaround time of 5 days in comparison to a turnaround of 21 days for tissue biopsy NGS results.
Conclusion: These results demonstrate the feasibility of using cytology samples as an alternative source of tumour DNA for mutation profiling in NSCLC across a genetically diverse patient cohort. Implementation of this into the clinical pathway has potential to significantly reduce the turnaround time of vital results to aid treatment decisions and improve therapy outcomes in NSCLC. Further validation studies are warranted to corroborate these findings in a larger patient cohort and assist in overcoming the current limitations of tissue biopsy.

PS-12-003
Lessons from external quality assessment (EQA) for BRCA1 and BRCA2 testing in hereditary breast, ovarian, pancreatic and prostate cancer – are large genomic rearrangements (LGR) being missed?

V. Williams*, J. Fairley, A.R. Maqsood, M.H. Cheetham, N.L. Wolstenholme, S. Deans, S.J. Patton
*EMQN CIC, United Kingdom

Background & objectives: Pathogenic *BRCA1/BRCA2* variants are associated with response to PARP inhibitors, up to 15% of hereditary breast and ovarian cancer variants are LGRs. Interrogation of data from global EQA has provided insight into germline *BRCA1/BRCA2* LGR testing by clinical laboratories.

Methods: Four DNA samples (extracted from lymphoblastoid cell lines) containing LGRs were sent to laboratories for *BRCA1/BRCA2* testing during EQA between 2017 and 2023. The percentage of laboratories that tested for LGRs was determined. Additionally, the percentage of these laboratories that made genotyping errors, including false negative results, was calculated for each sample over the specified time period.
Results: In 2023, 29% (83/284) of laboratories participating in the EQA for BRCA testing in germline DNA did not correctly report a large *BRCA1* deletion present in the sample provided for testing; 10% reported incorrect results and 19% did not test for LGR. Results from EQA show the percentage of laboratories reporting LGRs has not increased over the six-year period. However, for laboratories that do test LGRs, the quality of testing and reporting has improved over this period. The percentage of laboratories reporting genotyping errors for LGRs has reduced from 22% in 2017 to 10% in 2023. We have summarised recurrent errors and challenges for laboratories reporting LGRs observed during EQA.
Conclusion: This data reveals approximately 19% of clinical laboratories are not performing copy number analysis and there are recurrent errors in reporting BRCA LGRs. There is a risk patient with BRCA LGRs may not receive an accurate genetic diagnosis or PARP inhibitor therapy. If LGR testing is not performed, a limitation should be clearly stated within the report with a referral for further analysis. The quality of BRCA LGR reporting has improved for laboratories participating in EQA over a 6-year period.

PS-13Poster Session Neuropathology

PS-13-001
Anaplastic meningiomas - CDKN2A/B and p16 in diagnosis and progression

L. Carvalho*, M. Reis Silva, G. Malva, S. Simões, A. Alarcao, A.F. Ladeirinha, T. Ferreira, M. Viseu, M.A. Santos, A. Novo, O. Rebelo
*1. Institute of Anatomical and Molecular Pathology, Faculty of Medicine of the University of Coimbra, Coimbra, Portugal 2. CIMAGO – Research Center for Environment, Genetics and Oncobiology, Faculty of Medicine, University of Coimbra, Coimbra, Portugal 3. Pathology Service, University Hospital Anatomical Pathology Coimbra – Portugal

Background & objectives: Cyclin-dependent kinase inhibitor (CDKN2A/B) in chromosome 9, codifies tumour suppressor protein p16 and is prone to homozygous deletion. This deletion has been observed in anaplastic meningiomas. We evaluated p16 protein immunohistochemistry as a screening tool for homozygous CDKN2A/B deletions.
Methods: Fourteen anaplastic meningiomas, diagnosed according to the 2021 WHO classification of tumours of the CNS, were evaluated by Immunohistochemistry for p16 expression in selected and represented FFPE tissue - Ventana autostainer (mouse monoclonal, E6H4, Roche-Diagnostics). We used 5% positive-stained cells, cutoff level for positive p16 cases. CDKN2A/B deletion (hetero-homomozygous) was determined by FISH: ZytoLight ® SPEC CDKN2A/CEN 9, positivity >30%.
Results: We explored 14 cases (4 female and 10 male; mean age 71 years) of anaplastic meningiomas, CNS WHO grade 3, according to the 2021 brain tumours classification. Five of these cases represented recurrency from anaplastic meningioma, 3 from atypical meningioma and 2 from meningioma grade I. p16 was expressed in 7 cases (50%), CDKN2A/B homozygous deletion in one case (7%); CDKN2A/B heterozygous deletion - 5 cases (35%). CDKN2A homozygous deletion case displayed p16 expression loss. Four cases with hemizygous deletion presented detectable p16 protein expression. Intratumoural heterogeneity of the p16 immunoreaction was frequently observed.
Conclusion: Search of Homozygous CDKN2A/B gene deletions has been studied and validated recently for pathology routine application in meningioma progression of grade 3 cases as recommended by WHO classification of CNS of 2021. Progression-free survival of meningioma with heterozygous CDKN2A/B deletions is not entirely clear. Our data suggests that absence of p16 protein might be an indicator for deletions homozygous CDKN2A/B gene. Heterozygous CDKN2A/B might parallel with p16 expression, representing a sub-cellular population occurring late in tumoural progression with heterogenous distribution.

PS-13-002
Molecular subgroups of paediatric medulloblastomas and potential biomarkers

P. Eguía Aguilar*, F. Chico, L. Cabrera, G. Baay, S. Juárez, M. Pérezpeña, J. García, S. Sadowinski, S. Torres, V. González, A. Escobar, C. Barrera, A. Vicenteño, D. Anaya
*Hospital Infantil de México

Background & objectives: Medulloblastoma is classified into four molecular subgroups WNT, SHH, and non-WNT/non-SHH. The latter is the most heterogeneous. Our objective was to identify the molecular subgroups of paediatric medulloblastomas and propose potential biomarkers.
Methods: One hundred twenty-one medulloblastomas were analysed using a panel of biomarkers by IHC, FISH, and RT-qPCR. In parallel, the expression of 6 genes proposed as biomarkers to differentiate the G3 and G4 subgroups (BLACAT1, SUZ12, YY1, DISC1, ANO2 and ARHGAP18) was evaluated. Unsupervised hierarchical clustering, Kruskall Wallis, and U-Mann Whitney were used for data analysis.
Results: The Medulloblastomas group was classified: WNT 11%, SHH 27%, G3 23%, and G4 37%. Regarding the molecular markers that were evaluated in the four subgroups, BLACAT1 and DISC1 stood out, both showing significant differences between G3 and G4 ($p=0.0005$, $p= 0.0331$, respectively). The YY1 and SUZ12 genes showed higher expression in G3, showing a positive correlation with BLACAT1 ($p=0.0001$, $r=0.7822$; $p=0.0116$, $r=0.58$, respectively). Finally, the ANO2 marker showed lower expression in the SHH subgroup compared to G3 ($p<0.0001$), G4 ($p<0.0001$), and WNT ($p=0.0028$).
Conclusion: BLACAT and ANO2 have been reported in several types of tumours, including gliomas, while DISC1 has been less explored, but is known to participate in neurogenesis and has abundant expression in glioblastoma. The differential expression of the proposed genes in the molecular subgroups suggests their participation in tumour development and can be considered as potential markers for diagnosis and treatment.

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PS-13-003
Neuropathological findings in methadone-related deaths

D. Gorelova*, O. Reshetnikova, E. Romanova, A. Ermakov
*Immanuel Kant Baltic Federal University, Russia

Background & objectives: Illicit opioids consumption is a public health challenge worldwide. A prescription of methadone used in a treatment of addiction problem. Violation of the substitution therapy protocol can lead to neurological consequences. Present study evaluates brain tissue features in methadone-related deaths.
Methods: Post-mortem investigations of one hundred and sixteen dead bodies with registered supra-therapeutical consumption of methadone were conducted. The gross study was followed by microscopy of brain tissues and internal organs. The results of histopathological examination were carried out with an emphasis on the brain tissues, meninges and then were analysed in correlation with the neurological symptoms and toxicology data.

Results: Histological examination of the brain tissues revealed acute and chronic circulatory disorders combined with a brain parenchyma's damage. Acute capillaries' hyperemia, accompanied with a stasis, multiple perivascular petechial haemorrhages and stromal edema was a common pattern in leptomeninges. Eighty percent of a dead bodies brains had a chronic meningeal changes including fibrosis with a progression features, focal sclerotic changes in blood vessels' walls, post-haemorrhagic hemosiderosis within thickened leptomeningeal tissues. Histopathology of the brain's parenchyma presented with perivascular and pericellular edema, vascular walls' edema, haemorrhages, blood congestion and acute swelling of neurons. Chronic changes, including glial proliferations, hemosiderosis, round-cell infiltrates, neuronal chronic ischemic injuries were found in majority of studied cases.
Conclusion: Case histories study indicated the presence of a variety of neurological symptoms in patients on methadone substitution therapy. Post-mortem investigation has shown a common presence of acute leptomeninges and brain parenchyma pathologies on the background of their chronic structural damage. Clinical encephalopathies symptoms caused by intoxication should be considered in the addiction treatment protocol. The role of the central nervous system injuries in the thanatogenesis of the methadone-mediated deaths has been discussed.

PS-13-004
Arrangements of alpha-synuclein proteoforms in Lewy bodies according to specific antibody clones – pilot study
D. Hrabos*, S. Hasegawa
*Dept. of Clinical and Molecular Pathology, Palacky University Olomouc, Czech Republic

Background & objectives: Lewy bodies, round-shaped inclusions containing 140 amino-acids long protein alpha-synuclein, are the main hallmark of Lewy body diseases. We aimed to analyse arrangement of alpha-synuclein proteoforms in the Lewy body structure with variety of commercially available antibodies.
Methods: Formalin-fixed paraffin-embedded tissue from 5 Parkinson's disease patients was used to analyse Lewy bodies by multiplex immunofluorescence. We analysed 35 classical Lewy bodies (substantia nigra, pons) and 20 cortical Lewy bodies (temporal and cingulate cortex). We used antibody clones with affinity to different epitopes - 42 (aa 91-99), 4D6 (aa 124-134) and Syn303 (aa 1-5).
Results: Interestingly, classical Lewy bodies showed specific arrangement of alpha-synuclein proteoforms. Peak intensity for fluorescent signal using 4D6 antibody clone (FITC) against C-terminus was observed as symmetrical ring at the periphery of the classical Lewy bodies. Thus, periphery of the classical Lewy body contains predominantly synuclein without C-terminal truncation. On the other hand, antibody clone 42 (Cy5) showed diffuse and strong fluorescence in the classical Lewy body, suggesting evenly distributed alpha-synuclein within the body morphology. Peak intensity for clone Syn303 (Cy3) was observed in the form of more centrally located symmetrical ring. Florescent signal for all three antibody clones was diffuse and evenly distributed in the cortical Lewy bodies.
Conclusion: Detailed morphology of Lewy bodies is still unknown. In our study, we showed a difference in alpha-synuclein proteoforms arrangement in classical Lewy bodies. Specifically, we have showed different localisation of C-terminally truncated alpha-synuclein in comparison to full-length protein. Further, we have showed difference between arrangement of the proteoforms between classical and cortical Lewy bodies.

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PS-13-005
Unfolded protein response is activated in the brain of Parkinson's disease patients and in human iPSC-derived cerebral organoid models of the disease
D. Hrabos*, S. Hasegawa, G. Gonzalez
*Dept. of Clinical and Molecular Pathology, Palacky University Olomouc, Czech Republic

Background & objectives: Endoplasmic reticulum stress followed by unfolded protein response contributes to the progression of alpha-synuclein pathology in Parkinson's disease. We compared the activation of the endoplasmic reticulum stress in Parkinson's disease patients and cerebral organoid models of the parkinsonism.
Methods: Formalin-fixed paraffin-embedded tissue from substantia nigra and hippocampus of 8 Parkinson's disease patients and 4 healthy controls was analysed (tissue microarray) for expression of endoplasmic reticulum stress-associated proteins by multiplex immunofluorescence. Proximity ligation assay was performed to analyse alpha-synuclein and Grp78 interaction. Similarly, human iPSC-derived cerebral organoid models of amyotrophic lateral sclerosis/Parkinson–dementia complex (L-BMAA) and Parkinson's disease (MPP+) were analysed.
Results: We observed a marked increase of Grp78, ATF4 and ATF6 in situ in substantia nigra and hippocampus of Parkinson's disease patients, with significant increase of ATF6 positive nuclei in patients' tissue. Moreover, a significant increase was observed in proximity ligation assay positive signals in Parkinson's disease patients ($p=0.002$). Our cerebral organoids models of neurodegeneration, induced by toxins MPP+ and L-BMAA, showed decrease cell viability (MPP+ demonstrated higher toxic effect). Importantly, both toxins also caused a marked increase in the expression of Grp78, ATF4 and ATF6 in situ, with significant ATF6 nuclear translocation. Additionally, both MPP+ and L-BMAA treatment caused changes in cerebral organoids' cell populations, e.g. loss of matures neurones.
Conclusion: In our study, we proved the activation of unfolded protein response in Parkinson's disease patients' brains. Importantly, we showed in situ protein-protein interactions of alpha-synuclein and Grp78 in Parkinson's disease-affected brain. These results suggest a connection between pathologically activated unfolded protein response and the accumulation of alpha-synuclein in endoplasmic reticulum. Lastly, we have developed human cerebral organoids models of parkinsonism with significant activation of endoplasmic reticulum stress. These will help with further research and development of endoplasmic reticulum stress-modifying drugs.

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PS-13-006
Hydroxytyrosol, a powerful polyphenol of olive oil, prevents neuroinflammation induced by oxysterols, cholesterol oxidation products, in Alzheimer's disease
L. Jones*, R. Cecci, M. Grosso, P. Gamba, G. Leonarduzzi, G. Testa
*University of Turin, Italy

Background & objectives: Oxysterols link to Alzheimer's Disease (AD) by inducing neuroinflammation. Hydroxytyrosol (HXT) has recently emerged effective in AD prevention but, to date, little data is available regarding its anti-inflammatory effects. Our study focuses on SIRT1-dependent anti-inflammatory pathways through which HXT acts.
Methods: SK-N-BE cells underwent treatment with either oxysterols (20μM) only or pre-treatment with HXT (20μM) followed by oxysterols additionally. Inflammatory mediator levels were analysed by real-time RT-PCR and Bio-Plex multiplex immunoassay method. SIRT1 and TLR4 expression and synthesis were analysed by real-time RT-PCR and Western blotting or immunofluorescence, respectively; NFκB p65 translocation was detected by immunofluorescence.
Results: Our data shows, in SK-N-BE cells, an increase in expression and synthesis of IL-1β, IL-6, IL-8, TNFα, IFNγ, and MCP-1 inflammatory mediators induced by an oxysterol mixture, which includes the main oxysterols found in severe AD brain samples. This increase was

markedly prevented by HXT cell pre-treatment. It was also demonstrated that oxysterols trigger an induction of neuroinflammation via TLR4-mediated NFκB activation. Moreover, mRNA overexpression and protein up-regulation of SIRT1 induced by HXT was observed. Through SIRT1 activation, HXT was able to inhibit the oxysterol-induced TLR4 up-regulation and the consequent NFκB p65 translocation. Notably, with use of sirtinol, a specific SIRT1 inhibitor, the anti-inflammatory effects of HXT were not observed.
Conclusion: AD, the predominant type of dementia, lacks current effective treatments, prompting exploration of alternative therapies. Growing experimental evidence suggests that the Mediterranean diet reduces risk of dementia and cognitive decline. Of note, olive oil contains the potent polyphenol HXT, currently considered to be a new natural therapeutic agent. HXT's ability to mitigate oxysterol-induced neuroinflammation via SIRT1/TLR4/NFκB pathway is demonstrated in our findings. This research suggests HXT as a potential nutraceutical, offering promise in preventing neuroinflammation and, consequently, neurodegeneration in AD.

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PS-13-007
Morphological and molecular study of FGFR2 rearranged low-grade glial and glioneuronal tumours
M. Koblížek*, M. Stanek, L. Krskova, A. Vicha, M. Strnadova, M. Zapotocky, V. Benes, J. Zamecnik
*Department of Pathology and Molecular Medicine, Second Faculty of Medicine, Charles University and Motol University Hospital, Prague, Czech Republic

Background & objectives: Low-grade glial and glioneuronal tumours (LGG/GNTs) are brain tumours commonly associated with epilepsy, predominantly affecting young individuals. While previous studies have identified a small subset of LGG/GNTs harbouring FGFR2 gene fusion, they remain relatively understudied.
Methods: We searched our archive of 385 molecular genetically tested LGG/GNTs to identify tumours with FGFR2 gene fusion and these were enrolled into study. Fusion partners of FGFR2 gene were identified in all cases. Morphology and immunohistochemical profile of studied tumours was reassessed and tumours were reclassified according to 5th WHO classification. Furthermore, methylation profiling of all tumours was performed.
Results: We identified 12 cases of LGG/GNTs with FGFR2 gene fusion. Common fusion genes including FGFR2::INA and FGFR2::KIAA1598 were identified, as well as rare and novel genes FGFR2::ZCCHC24 and FGFR2::BAIAP2L1. Studied tumours were diagnosed as polymorphous low-grade neuroepithelial tumour of the young in 7 cases, dysembryoplastic neuroepithelial tumour in 2 cases, ganglioglioma in 2 cases and multinodular and vacuolating tumour in 1 case. Methylation classifier v12.5 performed well on dysembryoplastic neuroepithelial tumour and ganglioglioma cases, but other tumours were assigned to different methylation classes.
Conclusion: We confirmed that FGFR2-altered tumours form a heterogeneous group of neoplasms with different morphological and immunohistochemical characteristics and they can be classified as four different WHO tumour entities. We identified fusion genes described frequently in literature, but also rare and novel fusion genes.

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PS-13-008
Non-functional pituitary neuroendocrine tumours (NF-PitNETs): an algerian series of 84 cases
K. Lounis*, N. Bouzid, S. Ait Younes
*Nafissa Hamoud Hospital, Algeria

Background & objectives: NF-PitNETs represent a heterogeneous group of tumours characterized by the lack of hormonal hypersecretion resulting in significant diagnostic delay.
The aim of this study is to evaluate by immunohistochemistry their hormonal profile, and their cell line by studying transcription factors.
Methods: It is a descriptive and observational study conducted between 2013-2020 at the Department of Pathology, Nefissa Hamoud University Hospital, Algiers. The diagnosis was established by histopathological examination, and the IHC study has evaluated the hormonal profile and the detection of the cell line, using 3 markers; tumours were classified according to the WHO classification of pituitary tumours.
Results: 209 PitNETs of which 84 NF–PitNETs were collected. NF-PitNETs represent 40.2% with an average age of 50.7 years and a sex-ratio =2.1. These tumours are macroadenomas and or giant adenomas (16.7%), and invasive in 51.2%. The NF-Pit NET were divided into: Gonadotroph NF- PitNETs: 72% - Silent corticotroph: 7.1% - Somatotroph: 6%. New entities were also found: 03 cases of Plurihormonal Pit1 + NF- Pit NETs and a single case of Null cells NF-PitNETs. The comparison between the 2 tumour groups (NF-Pit NETs vs F-Pit NETs), shows that NF-PIT NETs are characterized by a later age of occurrence, male predominance, grade 2b, and lack of microadenomas.
Conclusion: This study using immunohistochemistry allowed to identify the NF-PIT NETs , stratify them, and to distinguish variants with high risk of recurrence such as corticotropic adenomas. The study has also confirmed the more aggressive character than their functional counterparts; these tumours are most often diagnosed at the stage of macroadenoma and accomplishment of total or near-total resection can be challenging.

PS-13-009
A comparative study on the clinicopathologic and molecular characteristics of primary and secondary diffuse large B-cell lymphoma in the central nervous system
K. Na*, J. Do, L. Yenwongfai, S. Do

*Department of Pathology, Kyung Hee University College of Medicine, Republic of Korea
Background & objectives: Diffuse large B-cell lymphoma of the central nervous system (CNS-DLBCL) is an aggressive B cell lymphoma with clinical and molecular heterogeneity. This study analysed molecular alteration in primary and secondary CNS-DLBCL and compared their differences.
Methods: We utilized next-generation sequencing (NGS) to identify genomic alterations in PCNSL and SCNSL patients. We compared single nucleotide variants (SNV) and copy number variations (CNV) in association with Gene expression profiling (GEP) and survival data, proposing risk predictive values to aid in diagnostic differentiation between the two types of lymphomas.
Results: The MCD genotype, a mutation in MYD88 and CD79B, was the most common alteration in primary CNS-DLBCL cases and was associated with lower survival rates. MYD88 mutation was significantly higher in PCNSL compared to SCNSL (75.0% vs. 33.3%, p=0.042). Recurrent copy number loss of 6p21 occurred in 56.1% of cases, more often in PCNSL (65.6%) than in SCNSL (22.2%) (p=0.028). Activated B-cell-like (ABC) subtype PCNSL harboured higher frequency of 6p21 loss compared to GCB subtype (76% vs. 28.6%, p=0.032).
Conclusion: Based on the presence of the MYD88 mutation and/or the 6p21 loss, our results showed that the positive predictive value of either marker was 88% and the PPV of both markers together was 93% for the diagnosis of PCNSL.

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PS-13-010

Can molecular markers stratify IDH-mutant astrocytomas beyond homozygous CDKN2A/B deletion?

Z. Reisz*, K. Eggleton, R. Ellmers, P. Hirani, C. Limbachia, L. Bhaw, R. Laxton, B. Clark, A. King, I. Bodi, S. Al-Sarraj
*Clinical Neuropathology, King's College Hospital NHS Foundation Trust, London, United Kingdom

Background & objectives: The prognostic stratification of IDH-mutant astrocytomas currently relies on their histological grade (e.g., degree of cellular atypia, mitotic count, necrosis/microvascular proliferation) and the CDKN2A/B status that may not explain the aggressive behaviour of some of the cases missing these features.
Methods: A retrospective cohort study of 198 patients diagnosed with "Astrocytoma, IDH-mutant" was conducted using a departmental CNS tumour database (2016-2023). Genomic and epigenetic data obtained from multimodal (DNA/RNA) NGS panel, whole genome sequencing (WGS) and DNA methylation array were correlated with the histological grade (following the 2021 CNS WHO criteria) and the biological behaviour of the tumour (PFS/OS).
Results: High-grade histological features were seen in 69.7% of the cases (84 cases gr. 3, 54 cases gr. 4). CKDN2A/B deletion was present in one third of the high-grade tumours and was associated with early disease progression regardless of the zygosity status (70.6% of followed cases). Seventeen cases were profiled as subclass "high-grade astrocytoma" often with instable genome on CNV plot, which was an independent adverse prognostic factor. "MC Astrocytoma, lower-grade" alone was not found to be prognostic. Three histologically low-grade tumours (3/60) had either heterozygous CDKN2A/B loss, high-risk methylome profile or gene amplifications that were associated with early tumour progression. 70% of the low-grade astrocytomas showed stable appearances on follow-up.
Conclusion: In conclusion, high-risk methylome profile and CDKN2A/B deletion were adverse prognostic factors in IDH-mutant astrocytomas regardless of the histological grade. In the term of tumour progression, no significant difference was seen between heterozygous and homozygous CDKN2A/B loss. The methylation class "Astrocytoma, IDH-mutant; lower-grade" was not prognostic alone, unless it was associated with flat copy number variation profile and lack of histological worrisome features.

PS-13-011

Neurochemical, neurotrophic and redox-related changes in the hippocampus of the BTBR mouse model of autism spectrum disorders

V. Sikora*, M. Bove, L. Trabace
*University of Foggia, Italy; Sumy State University, Ukraine

Background & objectives: Autism Spectrum Disorders (ASD) are neurodevelopmental conditions characterized by a wide range behavioural symptoms and different severities. ASD pathophysiology is still controversial, linked to oxidative stress, excitation-inhibition unbalance, neurotransmitter dysfunctions, immune activation, neuroinflammation, genetic and environmental factors.
Methods: In this study, we used 10-week-old male BTBR T+tf/J (BTBR) mice (as a preclinical model of ASD) and C57BL/6J control mice. The quantification of dopamine (DA), glutamate (Glu), 3,4-dihydroxyphenylacetic acid (DOPAC), gamma-aminobutyric-acid (GABA), reactive oxygen species (ROS), NADPH-oxidase 2 (NOX2), brain-derived neurotrophic factor (BDNF) and nerve growth factor (NGF) levels were performed in the hippocampus (HIPP) tissues.
Results: Our neurochemical results demonstrated a significant increase in DOPAC content in the hippocampus of BTBR animals compared to controls ($P<0.05$), whereas we observed a significant decrease in GABA levels in BTBR mice ($P<0.05$). Interestingly, no difference was observed in DA and Glu levels between BTBR and control mice. Furthermore, the autistic model mice also showed a significant reduction in the hippocampal BDNF ($P<0.05$) and NGF ($P<0.05$) levels compared to the control animals. Moreover, ROS amount in the hippocampus was significantly enhanced in BTBR mice ($P<0.05$), together with NOX2 levels, which also showed an increase in BTBR related to C57BL/6J animals ($P<0.05$).
Conclusion: The alterations observed in the hippocampus of the BTBR mice might suggest complex interactions of underlying mechanisms of neuronal dysfunction, shifts in neurotransmitters metabolism, and the development of oxidative stress. Based on our findings, BTBR mice demonstrated an overproduction of ROS, together with signs of neuronal (neurotrophic factors reduction) and neurotransmitter systems (increase of dopamine degradation and neuronal excitation) damage.

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PS-13-012

High-grade astrocytoma with piloid features: a novel CNS tumour type with a proposed intermediate prognosis

A. Vamanu*, R. Laxton, A. Swampillai, O. Al-Salihi, L. Brazil, M. Durve, J. Glendenning, L. Bhaw, K. Eggleton, C. Limbachia, B. Clark, A. King, I. Bodi, S. Al-Sarraj, Z. Reisz
*London Neurodegenerative Diseases Brain Bank, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, United Kingdom

Background & objectives: High-grade astrocytoma with piloid features (HGAP) is a novel CNS tumour type, characterised by a distinct methylation profile and simultaneous disruption of the MAPK, RB and telomere maintenance pathways. Further information regarding the behaviour of these tumours would be desired.
Methods: Retrospective analysis of a departmental CNS tumour database identified 13 cases (25-82 years) with HGAP methylation profile (DKFZ, brain tumour classifier v12.5) or combination of piloid tumour morphology with MAPK-pathway alteration and concomitant CDKN2A/B loss or ATRX mutation. The cases were reviewed for clinical presentation, molecular data and therapeutic management.
Results: Most common locations were the posterior fossa and the optic pathway/thalamus (10 cases). Ten cases showed a diagnostic methylation profile, while 3 cases were not classifiable by methylation array. Eight cases harboured NF1 variants (four in context of neurofibromatosis type 1), while 2 cases had an FGFR1 mutation and an FGFR1::TACC1 fusion, respectively. There was CDKN2A/B deletion in 10 samples and CDKN2B mutation in one case. Concomitant ATRX alteration was seen in 11 samples. Gross resection was feasible only in 2 cases. Despite all patients receiving adjuvant chemoradiotherapy, 7 cases showed radiological progression during short follow-up (6-48 months) and 2 patients died of the disease (OS: 20 and 34 months).
Conclusion: Our results suggest that these tumours frequently progress with an overall intermediate prognosis for HGAP. Although DNA methylation array is essential to confirm the diagnosis, additional next generation sequencing for screening germline and/or actionable variants may be beneficial for patient management.

PS-13-013

Examine the possibility of adding molecular pathological criteria for the re-classification of grade I meningiomas – modelled on the examples of diffuse astrocytic tumours

C.Y. Yoo*, S.H. Yang
*The Catholic University of Korea, St. Vincent Hospital, Republic of Korea

Background & objectives: Meningiomas are the most common intracranial tumour, and most are benign with grade I. Imitating a new classification system of diffuse astrocytic tumours, we investigated the possibility of a new classification based on molecular pathological knowledge of these meningiomas.
Methods: 277 cases of meningiomas diagnosed in this institution were studied. Most are grade I meningioma, and a total of 14 cases of atypical or anaplastic meningiomas were included for comparison. TERT mutation tests were performed only in 115 cases where consent was obtained, and immunohistochemical tests using AKT1, CDKN2A, PIK3CA, POLR2A, and SMO antibodies were performed in all cases.
Results: Clinically, recurrence was observed in 16 grade I meningiomas and 7 atypical meningiomas. TERT mutation was found only in atypical or anaplastic meningiomas. CDKN2A was not expressed in most cases. Although there was no statistical significance, the following interesting results were observed. There were examples of AKT1 and POLR2a showing exceptionally strong nuclear staining, especially in fibrous meningiomas. SMO showed strong nuclear staining in most cases but disappeared in some fibrous meningiomas. PIK3CA generally showed low staining properties, but meningothelial meningiomas showed slightly higher staining properties than fibrous meningiomas. In both grade I and atypical, there was no difference in the degree of staining between recurrence cases and non-reoccurrence cases.
Conclusion: The experiments we tried are extremely limited. In the case of grade I meningioma, it is expected that there will be different molecular pathological mechanisms depending on the histological type, but more detailed and expensive experiments are needed in order to be verified. But it remains to be seen whether these tasks will have a significant impact on the diagnosis and prognosis of grade I meningioma patients. In meningiomas, histological classification is still considered valid.

PS-14Poster Session Other Topics

PS-14-001

Improving diagnostic skills with spaced repetition: the SpacedPath project, a randomized controlled trial

S. Barhdaoui*, T. Kervarrec, P. Sohier
*France

Background & objectives: Effective learning is critical to knowledge acquisition in histopathology. We report here the efficacy of spaced repetition (SR), a technique for efficient memorization which uses repeated review of content determined by a SR algorithm to improve long-term retention.
Methods: We created 135 flashcards using the Anki spaced repetition software and a serie of short videos on epidermal tumours and cutaneous adnexal tumours. Volonteer pathologists were randomly assigned to one of two different sets of spaced repetition material. Participants were evaluated three months after inclusion using an online evaluation testing their diagnostic performance on 20 previously unseen cases.
Results: The study included 337 pathology residents and certified pathologists. The online evaluation was completed by 23% of the participants (79/337). Among them, 58% (46/79) used the SR learning material. Learning by SR improved diagnostic performance in terms of accuracy and speed. Participants had a significantly higher mean score for the diagnoses they had reviewed using SR than for the diagnoses they had not reviewed with SR (7.3/10 vs. 5.4/10, $p<0.0001$), and achieved these diagnoses in a shorter mean time (11.1 min vs. 13.6 min, $p = 0.018$). Participants were very satisfied with this learning technique. In addition, 92% of participants shared their intent to reuse SR for their own learning.
Conclusion: Our findings suggest that SR can be used to improve the diagnostic accuracy and speed of pathologists. SR has a strong effect on the acquisition of diagnostic skills and its use should be promoted in initial pathology training as well as continuing medical education. Future studies should investigate the long-term effects of SR to determine whether the benefits of SR persist over time and to determine the optimal way to implement spaced repetition in pathology medical education.

PS-14-002

The mystery of peripancreatic pacinian corpuscles: report of 3 cases

A. Kolaki*, E. Stoupi, I. Vlachos, I. Grypari, K. Bramis, M. Kostandoulakis, D. Tiniakos
*Greece

Background & objectives: Pacinian corpuscles (PC) are mechanoreceptors for sensing vibration and pressure occurring in the deep dermis of hands and feet and rarely elsewhere in the body. They are exceptionally rare in the pancreas. We report three cases of peripancreatic PC.
Methods: Case 1: A 70-year-old man underwent distal pancreatectomy for a pancreatic ductal adenocarcinoma (PDAC), pT3N0. Case 2: A 77-year-old female underwent Whipple procedure after neoadjuvant chemotherapy for PDAC ypT2N1. Case 3: A 67-year-old female underwent Whipple procedure for and intra-ampullary adenocarcinoma, pT3aN0. Histochemical and immunohistochemical stains were performed.
Results: Only 5 cases of pancreatic/peripancreatic PC have been reported to date. In our 3 cases, one or two PC measuring 1.5-2 mm in greatest diameter were noticed within the adipose tissue of the posterior pancreatic surface, remotely from cancer. Perineural invasion was reported in all cases but not within the PC. The central neural axon was surrounded by onion skin-like loose concentric lamellae (n=7-18) forming the inner core or bulb surrounded by a thin fibrous capsule. The several lamellae of the Pacinian corpuscles stained with Masson trichrome and vimentin. The thin inner core, stained positively for S100. Cutaneous PC express EMA in the outer core in contrast to pancreatic PC.
Conclusion: It is speculated that PC in or around the pancreas may serve sensory functions related to pressure, vibration, regulation of blood pressure, and lymphatic flow, as well as neuronal regulation of exocrine and endocrine pancreatic secretion. In PDAC, PC may also mediate the perception of abdominal pain. Their differences from cutaneous PC and their significance for PDAC prognosis have not been elucidated to date and will be the focus of further study.

PS-14-003

Erythroderma: a clinicopathological study of 110 cases from 2016 to 2023

K. Kundovic*, D. Petrovic, I. Petrovic, M. Bosić, E. Manojlović Gačić, J. Stojković Filipović, D. Škiljević, J. Perić, D. Miličić, S. Tanasilović, S. Popadić, V. Reljić, N. Delić, B. Lekić, S. Minić
*Faculty of Medicine, University of Belgrade, Belgrade, Serbia, Department of Pathology, General Hospital, Kraljevo, Serbia

Background & objectives: Erythroderma is potentially life-threatening erythema affecting at least 90% of the skin surface. The diagnosis of underlying cause can be challenging, and skin biopsy is necessary. We aim to analyse clinic-pathological findings in erythrodermic patients diagnosed in a university setting.
Methods: We retrieved histopathology records of patients with referral diagnosis of erythroderma at the Institute of Pathology Faculty of Medicine in Belgrade in an 8–year period (2016 – 2023). The study included 110 patients; patients with congenital erythroderma

were excluded. Demographic, clinical, and histopathological features were analysed.
Results: Erythroderma mostly affected patients over 60 years old (79%) and men (71%); it was rare in children (4%). Beside erythema, the most prominent findings were plaques (68%) and scaling (63%); 45% of patients complained of itching. None of the patients was previously diagnosed with skin diseases. In histopathology, dermatoses were the most frequent causative factor (63%). Skin lymphomas (mycosis fungoides and Sezary syndrome) and infections were rare (4% and 1%, respectively), Among dermatoses, spongiotic dermatitis was the most frequent (64%) with two thirds having eosinophils, suggestive of atopic dermatitis and eczema. Psoriasiform and interface dermatitis were less common (24% and 11% respectively). Pemphigus was an underlying cause in one patient.
Conclusion: Our study showed that spongiotic dermatitis with eosinophils was the main pattern in biopsies of erythrodermic patients. Atopic dermatitis, eczema and cutaneous allergic reactions could be the leading cause of erythroderma. Psoriasis was not as frequent as reported in literature. Although lymphomas were often clinically suspected, they were rarely found, and diagnosis of dermatitis was established. Our findings confirm the essential role of biopsies and histopathological analysis in erythrodermic patients.

PS-14-004
High mobility group protein AT-hook 2 (HMGA2) is highly expressed in a broad range of human tumours
V. Chirico, F.B. Ergüven, K. Möller*, N. Schraps, F. Lutz, F. Viehweger, M. Kluth, G. Sauter, R. Simon, T. Krech, S. Steurer, S. Minner, N. Gorbokon, M. Lennartz, A. Menz
*Institute of Pathology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

Background & objectives: High mobility group AT-hook 2 (HMGA2) is an essential component of theenhanceosome that governs the transcription of numerous genes during organogenesis. HMGA2 in adult tissues is commonly associated with tumour formation and cancer aggressiveness.
Methods: To better comprehend the role of HMGA2 expression in cancer, a tissue microarray containing 18,582 samples from 144 different tumour entities and 608 samples of 76 different normal tissue types was analysed by immunohistochemistry (IHC).
Results: HMGA2 expression was generally markedly higher in cancer than in corresponding normal tissues. HMGA2 staining was found in 5,963 (37.5%) of the 15,915 interpretable tumour samples, involving 118 of 144 tumour categories. The frequency of HMGA2 positivity was highest in cancers of the ovary and the endometrium (14.0-100%), thyroidal neoplasms (28.6-97.4%), and pancreaticobiliary cancers (18.8-73.3%). High level of HMGA2 staining was associated with invasive and high-grade tumours of urinary bladder carcinomas ($p<0.0001$ each), poor overall survival ($p<0.0001$) in clear cell renal cell carcinoma (RCC), nodal metastasis in papillary thyroid cancer ($p=0.0063$), absence of microsatellite instability in colorectal cancer ($p=0.0002$) and absence of HPV infection in squamous cell carcinomas ($p<0.0001$).
Conclusion: HMGA2 is highly expressed in a very broad range of tumour entities. These findings emphasize a potential role of HMGA2 as a drug target and demonstrate utility for HMGA2 IHC to differentiate between neoplastic and non-neoplastic tissues in various organs.

PS-14-005
Infectious biobanking and biodata management of the German Center for Infection Research – a key infrastructure for multiple research approaches
T. Pfeffer*, K. Hofmann, I.M. Klein, P. Schirmacher
*German Center for Infection Research (DZIF), Tissue Bank at the partner site Heidelberg, Institute of Pathology, University Hospital Heidelberg, Germany

Background & objectives: The DZIF Tissue Bank, as part of the German Center for Infection Research (DZIF) Translational Infrastructure Bioresources, Biodata and Digital Health (TI BBD), supports multiple infectious disease-related research projects and various interdisciplinary studies with biosamples, biodata, latest technologies, and know-how.
Methods: As the first biobank being accredited for the biobanking standard DIN EN ISO 20387, the DZIF Tissue Bank at the Heidelberg-site is the central national infectious disease tissue biobank, coordinating the infectious diseases biobanking of DZIF consisting of the DZIF Tissue Bank Heidelberg and the Liquid Biobank Munich. It supports numerous projects for infectious research leading to high-ranked publications.
Results: One of its significant achievements was the contribution and coordination of the unique COVID-19 autopsy registry and biobanking in Baden-Württemberg, Germany. All offered services (e.g. biosample-storage, IHC, IF, chemical stainings, Tissue-Micro-Array assembly, nucleotide extraction) follow Standard Operating Procedures, guaranteeing a maximum of quality, safety, and reproducibility. Located at the Institute of Pathology Heidelberg, the DZIF Tissue Bank has access to >800.000 biosamples including a broad range of infectious diseases. Due to the support of >100 research projects, it contributed to >40 high-ranked publications. As part of the TI BBD it has access to e.g. the pathogen repository, biosample collections DZIF-wide and provides ethical consulting, OMICs analyses, and bioinformatics.
Conclusion: Quality assured tissue biobanking as provided by the national DZIF Tissue Bank in Germany is an important and efficient research infrastructure and contributes to infectious diseases research. Services and derivates provided by the DZIF Tissue Bank enhance the efficiency of biobanking for infectious diseases and as part of the TI BBD, its biosamples and metadata management is at highest level.

PS-14-006
Implementation of a continuous evaluation method in pathology teaching
María José Gálvez-Medina*, Fernando Leiva-Cepas, Dr Julio Osuna Soto, Alicia Sanz Zorrilla, Inmaculada Sánchez Ramírez
*Hospital Universitario Reina Sofía, Spain

Background & objectives: Pathology is a discipline that provides the basis for understanding disease in medicine through morphology. The objective was to analyze the evaluation of students' grades with constant monitoring of the knowledge acquired.
Methods: A survey was carried out on 148 Medicine Degree students at a Faculty in Andalusia about their preferences in pathology teaching modalities and their satisfaction with face-to-face courses, as well as a continuous evaluation of the knowledge acquired in the theoretical classes. A qualitative analysis was carried out comparing the responses obtained and the differences between practice and theory.
Results: Student satisfaction with the lecture-based curriculum was positively correlated with student grades (Spearman correlation coefficient 0.21). Furthermore, students with lower grades supported the continuous model prevailing (Spearman correlation coefficient 0.41). The majority supported virtual microscopy, autopsies, seminars, and podcasts as preferred teaching methods.
Conclusion: The data supports the implementation of a Pathology curriculum where tutoring, post-mortems, and supplemental learning tools play an important role. As well as a true approach of the subject to the reality of the specialty.

PS-15Poster Session Paediatric and Perinatal Pathology
PS-15-001
Foetal and neonatal hydraencephaly: a study of 7 cases
F. Loued*, R. Ayadi, I. Mallek, A. Lahmer, D. Bacha, S. Ben Slama
*Department of Pathology, Monji Slim Hospital, Tunis, Tunisia

Background & objectives: Hydranencephalia is a rare and fatal disorder of the central nervous system with total or partial absence of the bilateral cerebral hemispheres. The aim of our work is to study the various positive diagnostic criteria of hydranencephalia on feto-pathological examination.
Methods: A retrospective feto-pathological study was conducted, concerning cases of hydranencepahlia diagnosed in our department of pathology. Our Study carried out over a period of 6 years from January 2018 to December 2023.
Results: Seven cases of Hydraencephalia were collected. Five were of male gender. Five were foetus and two were new-born of 48 hours of life. The mean foetal age was 26.6 weeks of gestation. Two were the result age of a medical abortion. Maternal age ranged from 23 to 34 years, with a mean of 28 years and one month. Two mothers were primiparous. All our cases presented with facial dysmorphia, dominated by micrognatsim (5 cases). On neuro-pathological examination, the brain was completely autolyzed in all our cases.
Conclusion: There are many etiologies of hydrancephalia such as chromosomal (trisomy 13) and infectious (rubella, toxoplasmosis, herpes, Cytomegalovirus). It can also be syndromic. In most cases, death occurs in utero or during the first few weeks of life. Genetic counseling is essential in syndromic forms. In these cases, the risk of recurrence is specific to the type of syndrome.

PS-15-002
Lethal osteochondrodysplasias: study of 32 cases
I. Mallek*, R. Ayadi, F. Loued, A. Lahmer, D. Bacha, S. Ben Slama
*Department of Pathology, Abderrahmen Mami Hospital, 2083, Ariana, Tunisia

Background & objectives: Lethal osteochondrodysplasias are rare genetic conditions. Their incidence is estimated at 1 per 10,000 births. Objective: Our aim was to outline the malformative and dysmorphic features of lethal osteochondrodysplasias, foetal pathological management, and subsequent pregnancy management.
Methods: Our study involved 32 cases of lethal foetal osteochondrodysplasias. Our Study carried out over a period from January 2018 to December 2023.
Results: Three disease recurrences in three families were noted. Among 32 cases, 26 foetuses (14 to 36 weeks) and 6 newborns were analysed, 59.5% male and 40.5% female. Predominant conditions: achondrogenesis (34.5%) and lethal osteogenesis imperfecta (28%), followed by thanatophoric dysplasia (15.5%) and Schneckenbecken dysplasia (12.5%). Extra-skeletal anomalies observed. Achondrogenesis type I: 75% facial dysmorphia, 75% pulmonary hypoplasia, 50% genital malformations. Achondrogenesis type II: 66% facial dysmorphia, 66% lung hypoplasia. Lethal osteogenesis imperfecta: 100% facial dysmorphia, 22% lung hypoplasia. Thanatophoric dysplasia: 60% facial dysmorphia, 40% brain malformations. Schneckenbecken dysplasia: 75% facial dysmorphia, pulmonary hypoplasia, 50% genital malformations. Majewski syndrome: facial dysmorphia, pulmonary malformations. Asphyxiating thoracic dysplasia: bile duct malformation.
Conclusion: Our study demonstrates the importance of a detailed analysis of the foetal skeleton, both through ultrasound and foetal pathological examination, to establish the diagnosis of lethal osteochondrodysplasia. Appropriate genetic counselling must be considered.

PS-15-003
New approaches to morphological diagnosis of placenta percreta
N. Nizyaeva*, I. Kulikov, E. Milyutina, V. Mkhitarov, K. Artemyeva, A. Akhmetshina, A. Milovanov
*Petrovsky National Research Center of Surgery, Russia

Background & objectives: Placenta accreta spectrum (PAS) is a dangerous complication of pregnancy leading to maternal morbidity and mortality. The aim of the study was to establish correlations between clinical and visual research data (MRI, Ultrasound) and histological changes in case of PAS.
Methods: In all cases, all women were after cesarean section, diagnostic curettage, and abortion. The study included 240 pregnant women (34-37 weeks), (pl. accreta (n=101), pl.increta (n=119), pl.percreta (n=42). Histological examination with hematoxylin and eosin staining and an immunohistochemical study with primary antibodies to cytokeratin7 were performed.
Results: As in the FIGO system the proposed subcategories of PAS are designated as grades based on the degree of invasion and local tissue destruction (pl.accreta/ pl.increta/ pl.percreta). Uterine aneurysm (thinning of the wall) was identified intraoperatively in 215 cases (89.6%) and did not depend on the depth of invasion. Surgical separation of the uterine wall with invaded villi and bladder wall were performed (n=20). Significant fibrosis of the bladder and uterine wall was observed in 2 women, only. Immunohistochemical study (to cytokeratin 7) revealed invasive cytotrophoblast cells in the uterine wall located up to adventitia of subserosal vessels only. But no villi outside the uterine wall.
Conclusion: In this way, using histological examination we revealed thinning of the uterine wall up to serosal layer. Hereby, placental villi and trophoblast extended beyond the uterus is not histology equivalent to placenta percreta. To identification pl.percreta an integrated approach should be used, taking into account data from visual diagnostic methods (ultrasound, MRI) and intraoperative view. Thus, placenta percreta may be one of the variants of adhesive disease.

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PS-15-004
Clinicopathological characteristics of hepatoblastoma: a 13-year retrospective study with analysis of imagiological/pathological treatment response and histological types
R. Rolim*, J. Lopes, H. Barroca
*Instituto Português de Oncologia Lisboa, Francisco Gentil, Portugal

Background & objectives: Hepatoblastoma is a rare malignant paediatric neoplasm, with several established pre-operative prognostic factors. The current guidelines advocate for histological type classification, with discrimination of neoplastic patterns/elements and quantification of treatment response, a distinction not always clear.
Methods: Two pathologists reviewed all cases of hepatoblastoma between 2011 and 2024, both core-biopsy and surgical specimen. Clinical data was collected from the patient's files. The evaluated elements were: diagnosis, histological type, percentage of patterns, areas of mesenchymal elements and treatment response (necrosis, fibrosis, haemorrhage, distrophic calcifications, foamy/haemossiderin-laden macrophages), grouped in no response (<5%), poor (5-33%), moderate (33-66%), extensive response (>66%).
Results: We collected eight cases, six with both biopsy and surgical specimen. All biopsies showed well-differentiated foetal hepatoblastoma. Patients were between 5 months and 3 years. Patients were classified as PRETEXT II or III (5/3 cases); all cases underwent neoadjuvant chemotherapy, but different surgical approaches (hepatectomy,

segmentectomy, tumoural enucleation). Histologically three cases were classified as mixed epithelial-mesenchymal hepatoblastomas with well-differentiated foetal pattern, osteoid and bone formation (7-45% tumour area), one case was a mixed hepatoblastoma with crowded and embryonal patterns; three cases were well-differentiated foetal pattern hepatoblastomas. Two patients showed no response; one had poor response; three had moderate response; two had extensive response. All patients are alive and on follow-up.
Conclusion: Core biopsies made the diagnosis of hepatoblastoma correctly but failed to represent mesenchymal elements. In this series of cases the presence of mesenchymal elements (osteoid, bone formation and immature fibrotic tissue) did not relate to the extension of treatment response, suggesting that these are established neoplastic tissues. Imagiological extension of treatment response seems to correlate with better pathological response. Considering all the predictors, hepatoblastoma has a good prognosis and our series confirms the established literature.

PS-16Poster Session Soft Tissue and Bone Pathology
PS-16-004
Clinicopathological features of primary histiocytic neoplasms of bone: a two-centre retrospective study of 58 cases
H. Berber*, S. Ozduzgun Polat, S. Yüksel, S. Guresci, G. Kaygusuz
*Ankara University, Medical School, Pathology Department, Turkey

Background & objectives: Bone involvement is seen 90% in Erdheim Chester disease (ECD), less than 10% in Rosai Dorfman Disease (RDD). Single-system Langerhans cell histiocytosis (LCH) predominantly involves the bone. Herein, we describe two-centre experience of these rare entities focused on clinicopathological aspects.
Methods: Clinicopathological features (age, sex, symptoms, sites of involvement, BRAF immunohistochemistry) of 43 cases diagnosed at Ankara University between 2005-2023 and 15 cases diagnosed at Ankara Bilkent City Hospital were reevaluated and recorded retrospectively. Statistical analysis was performed using SPSS version 26. Descriptive analysis and comparative analysis were performed by using Chi-square and Mann-Whitney U tests.
Results: There were two cases with ECD and 56 with LCH. Mean age of ECD was 47.5 years, whereas for LCH it was 20.6 years. All ECD cases were women. LCH cases were 14 females and 42 males. Tibia and sacrum involvement was observed in ECD. Cranium, vertebra, femur were most affected sites in LCH. Commonest LCH form was unifocal bone involvement (60%). Unifocal form of LCH was more common in adults. Pain was the commonest symptom in LCH cases. Radiologically, multiple lytic/sclerotic lesions were observed in ECD and lytic lesions were frequent in LCH. 53% of LCH cases showed BRAF immunopositivity, whereas BRAF mutation was detected in 54.5% of cases.
Conclusion: Histiocytic neoplasms may present with bone involvement, especially LCH may cause a solitary lytic bone lesion. Even if these disorders are rare, they should have been considered in the differential diagnosis of primary bone lesions.

PS-16-005
Impact of comprehensive genomic profiling on the diagnosis and clinical management of mesenchymal tumours
A.B. Csepregi*, Z. Melegh, A. Kohánka, Z. Küronya, E. Soós, E. Tóth
*National Institute of Oncology, Hungary

Background & objectives: Comprehensive genomic profiling (CGP) is becoming increasingly important in the clinical management of different tumours. However, there are very few data available on the usefulness of CGP in mesenchymal tumours.
Methods: Between January 2022 and December 2023, we performed CGA analysis with Oncomine Comprehensive Assay Plus (OCAplus) on 63 mesenchymal tumours, representing 25 histologies. The analysis covered more than 500 unique genes for single-gene and multigene biomarker insights, including homologous recombination deficiency (HRD) and tumour mutational burden (TMB). Genomic DNA and total RNA were extracted from formalin-fixed paraffin-embedded tissue blocks.
Results: Fifteen out of 63 patients had potentially actionable alterations: 9 had specific genetic alterations suitable for targeted therapies, 2 had a high TMB (>10), and 4 had a high HRD score (≥16). Three patients received targeted therapy: one with a CDK4-amplified tumour (dedifferentiated liposarcoma) received CDK4 inhibitor, one patient with angiosarcoma showing a high TMB received immune checkpoint inhibitor therapy, and one with uterine leiomyosarcoma with a high HRD score received PARP inhibitor therapy. All 3 patients are currently alive. In 2 patients, there was refinement or reassignment of the diagnosis: MYOD1 mutation (sclerosing rhabdomyosarcoma) and MDM2 and CDK4 amplification (change of diagnosis from biphenotypic sinonasal carcinoma to parosteal osteosarcoma).
Conclusion: In our practice, a significant proportion of patients were prescreened with a smaller NGS panel. Despite this fact, we still found actionable alterations in 23,8% of the patients, which is in line with those reported in the literature (22-61%). Our results demonstrate that CGP can provide useful additional information and can be beneficial in the clinical management of patients with mesenchymal tumours. Consequently, CGP can be an important tool for detecting biomarkers that may represent therapeutic opportunities.

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PS-16-006
The wide morphological spectrum of myofibroblastoma: in-depth clinicopathological study of rare mammary and extra-mammary variants
F. D'Aquila*, G.G.M. Attanasio, G. Tinnirello, J. Farina, S. Salzano, F. Laudani, L. Salvatorelli, G. Angelico, G. Magro
*Department of Medical, Surgical Sciences and Advanced Technologies "G.F. Ingrassia", Anatomic Pathology, University of Catania, Italy

Background & objectives: Myofibroblastoma is a benign mesenchymal neoplasm composed of myofibroblastic cells that can manifest in both mammary and extra-mammary sites. The aim of this study is to investigate rare and diagnostically challenging morphological variants that require careful differentiation from malignant counterparts.
Methods: We retrospectively analysed 45 surgically-resected myofibroblastomas from the archives of the University of Catania. Immunohistochemical analyses included vimentin, α-smooth muscle actin, desmin, myogenin, h-caldesmon, S-100 protein, CD34, bcl-2, CD10, and cytokeratins (AE1/AE3 clone). Additionally, FISH analysis targeted FOX1 on 13q14.11.
Results: Macroscopically, all tumours were unencapsulated with well-circumscribed margins. Histologically, cases exhibited intersecting short fascicles of spindle cells, interspersed with hyalinized collagen bundles. Unusual morphological variants included: (i) Small round cell variant (1 oral cavity, 2 vulvo-vaginal); (ii) Epithelioid cell variant (6 breast, 4 vulvo-vaginal); (iii) Deciduoid-cell variant (1 breast); (iv) Atypical/bizarre cell variant (2 breast); (v) Lipomatous variant (1 breast with >50% adipocytic component); (vi) neurofibroma/shwannoma-like variant (2 breast; 1 vagina); (vii) myxoedematous variant (1 breast). Immunohistochemically, all cases showed positive staining for desmin and α-SMA. Positive staining for CD34, ER and PR was

also detected in most cases. In addition, all cases showed the 13q14 deletion by F.I.S.H.
Conclusion: This study offers a comprehensive analysis of myofibroblastomas, shedding light on their different clinico-pathological manifestations and emphasizing the significance of accurate diagnosis in distinguishing benign lesions from malignant counterparts. Although MFB is typically a bland-looking spindle cell tumour, rare cases may show marked intralesional and interlesional variability in morphology. Accordingly, several uncommon histologic variants may be observed. Our study emphasizes that the recognition of atypical/epithelioid/deciduoid morphology within MFBs is crucial to avoid confusion with other benign or malignant tumours.

PS-16-007

Semiquantitive assessment of synovitis across the disease trajectory of Rheumatoid Arthritis: cross sectional analysis of 1,361 ultrasound-guided minimally invasive biopsies
L. Coletto, S. Perniola, B. Tolusso, C. Di Mario, M.R. Gigante, L. Petricca, A.V. Pacucci, D. Bruno, R. Benvenuto, M.A. D'Agostino, E. Gremese, S. Alivernini, M. Gessi*
*Division of Pathology, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy

Background & objectives: Synovial tissue (ST) inflammation in Rheumatoid Arthritis (RA) shows high degree of heterogeneity which may underly variable response to treatments. To assess the reliability of a semiquantitative assessment of synovitis degree using H&E based tool to inform RA clinical management.
Methods: 1361 FFPE ST specimens were collected using minimally invasive ultrasound-guided procedure from patients with RA. For each patient, synovitis degree was determined using a based semiquantitative score (modified Krenn Synovitis Score - KSS). Each naive RA patient was treated according to a treat to target strategy and was followed every 3 months to assess remission achievement at 6 months follow-up.
Results: KSS was associated with the disease stage being significantly higher in naive RA and c/b-DMARDs resistant RA patients compared to RA patients in remission. Both naive and c/b-DMARDs resistant RA patients showed significantly higher degree of synovial lining layer hyperplasia, stromal cell density and inflammatory infiltrate (with higher rate of lymphocytes and plasma cells) when compared to RA patients in sustained remission. ROC curve analysis identified a cut-off value for KSS<5 enabling to differentiate, at baseline naive RA patients responding to first line c-DMARDs treatment. In particular, naive RA patients with baseline KSS<5 had a higher 6-months-FU remission rate (53.2%) compared to naive RA patients with KSS≥5 (34.2%).
Conclusion: Semi-quantitative synovitis degree is associated with all the phases of RA and enables to differentiate, at first medical evaluation, naïve-to-treatment RA who subsequently responded to first line cDMARDs treatment from those who failed, strongly supporting its predictive value as putative patient-based decision test tool.

PS-16-008
TRPS1 oncoprotein is a reliable complementary marker for immunohistochemical diagnosis in synovial sarcoma
F. Giner*, E. Medina-Ceballos, I. Machado, S. Navarro, E. Mayordomo Aranda, M. Espino, A. Llombart-Bosch
*University of Valencia, Spain

Background & objectives: TRPS1 (trichorhinophalangeal syndrome type 1) protein is shown to be expressed in synovial sarcoma (SS). Herein we describe the morphological and immunohistochemical profile of a series of SS in order to assess the usefulness of this antibody.
Methods: A retrospective observational study of 49 SS collected from two different institutions with clinical data and confirmed molecular SS translocation. Histology was classified as monophasic, biphasic or poorly differentiated according with WHO criteria. A large immunohistochemical study with several antibodies was performed using tissue microarrays.
Results: The most frequent morphological subtype was monophasic (65%) followed by biphasic (27%), only 4 tumours were undifferentiated (8%). All cases were positive for bcl2, CD99, CD56, FLI1, TLE1 and PDGFR alpha. All tumours also expressed focally epithelial markers such as EMA and pancytokeratin. TRPS1, H3K27me3, SS18-SSX and SSX-carbl were positive in 96% of cases and 29% of cases presented reduced INI1 expression. The expression appeared diffuse weak to intense in CDK4(94%), p53 (78%), BCOR (57%), NKX2.2(55%), MDM2(49%), CD117 (39%), p16(37%) and S100 (14%). Interestingly GLI1 expression was nuclear in 6 cases and cytoplasmic in 20 cases.
Conclusion: TRPS1 protein is a good marker for SS complementing the SS18-SSX fusion oncoprotein. Nevertheless, GLI1, NKX2.2 and BCOR can also be expressed in SS representing a challenge in the differential diagnosis with other sarcomas. Clinical data and patient outcome will be included in the final presentation.

PS-16-009
Importance of transthyretin-derived amyloidosis (ATTR) detection in Carpal Tunnel Syndrome (CTS)
C. Girleanu*, J. Bissonnette, P. Fleming, N. Bermingham, L. Burke
*Mater Misericordiae University Hospital, Ireland

Background & objectives: Transthyretin-derived amyloidosis (ATTR) leads to cardiac and neurological complications. Prompt diagnosis is warranted due to advancements in therapy. Carpal tunnel syndrome (CTS) is an early manifestation. We performed an audit to evaluate for ATTR in CTS cases with follow up.
Methods: A retrospective chart review following a COGNOS database search of CTS samples containing amyloid (confirmed by Congo Red) at CUH from 2008 to 2022 was performed. Data analysed included age, gender, amyloid distribution and sub-type classification (performed at the National Amyloidosis Centre, UK). Clinical charts were examined for pre-existing conditions, co-morbidities and subsequent morbidities in all subtyped cases.
Results: 126 cases of CTS were identified over 14 years (2008-2022). 21 cases displayed amyloid with appropriate birefringence on Congo Red analysis. Average age was 75 years (57 - 91 years) and a M:F ratio of 11:10. In 20 cases amyloid deposits were identified within the stroma and in one case both stromal and vascular deposits were present. In the 11 cases subtyped, including one case with known Monoclonal IgM Kappa Band paraprotein, all contained TTR amyloid subtype. Comorbidities were grouped into cardiac (6/11), GI (2/11), neurological (3/11). Two patients were subsequently referred for additional investigations due to cardiac amyloidosis. Family history was identified in one patient.
Conclusion: Given the therapeutic advances in management of ATTR amyloidosis and its known associations with various disease processes including cardiomyopathy and neurological disorders, its detection is very important. Our results indicate that all samples of CTS with positive Congo Red amyloid deposits could act as an early histological diagnosis for this entity and therefore subtype analysis should be performed on all cases.

PS-16-010
Hydatidic cyst of bone: an ongoing diagnostic problem in the 21st century
C.A. Gomez Gonzalez*, I. Tamsel, H. Kaya, S. Cagli, M. Sezak, B. Doğanavşargil
*Department of Pathology, Ege University Faculty of Medicine, Turkey

Background & objectives: Hydatidosis is a worldwide zoonosis that affects humans as an accidental intermediate host. Detection of hydatidic cysts is difficult as the symptoms are related to localization. Spinal and osseous hydatidosis set challenges for diagnosis and treatment, with high recurrence rates.
Methods: From 1999-2022, a total of 46 bone and spinal hydatidosis biopsies were evaluated. Age of presentation, gender, localization, symptoms, radiological findings, and history of recurrence were recorded. The cases where the bone involvement could not be confirmed were excluded. Pathology tissue sample type, localization, presence of scolex, cuticular membrane, and host reaction were noted.
Results: A total of 20 cases were enrolled in the study. Female: male ratio was 1:1. The Median age of presentation was 39,5 years old. Vertebral (n=7), paravertebral (n=3), pelvis (n=7), femur (n=1), humerus (n=1), and tibia (n=1) localization were noticed. Eight cases had recurrent disease; the average period of recurrence was 3 years. Biopsy samples were curettage %50 and excisional biopsy %50.
Conclusion: The clinical presentation of spinal and osseous hydatidosis is due to compression and mass effect. Recurrence is an expected outcome, usually observed in the spine in one upper or lower level about the primary site or extraosseous soft tissue. Hydatidosis is still a public health concern, although the patient's profession or living conditions weren't evaluated, as time evolves the decline of cases is less than expected. We aimed to increase awareness of the entity as delays in diagnosis and treatment affect its global eradication.

PS-16-012
Morton neuroma: an evaluation of the histopathological findings of 626 cases
F. Maclean*, V.Q.T. Ngo, A. Cheah, C. Vargas, J. Turchini, F. Bonar

*Douglass Hanly Moir Pathology, Australia
Background & objectives: Morton Neuroma (MN) is a painful condition affecting the forefoot. Its pathophysiology is controversial, with theories implicating chronic inflammation, chronic repetitive trauma, and nerve entrapment. We sought to clarify the situation by conducting a review of the histological findings.
Methods: A retrospective quantitative correlational study was performed, reviewing all cases diagnosed as MN or "interdigital neuroma" over a 3-year period at a single high volume musculoskeletal practice. The anatomical site and histopathololgical changes present were documented, including the presence of an associated bursa. A subset of cases was stained with immunohistochemistry for histiocytic markers (CD68, CD163 and PU1).
Results: A total of 626 cases of MN were identified, with the female to male ratio 3:1. Origin was predominately from the 3-4 (57%) or the 2-3 web space (27%). In all cases a nerve was identified, typically showing fibromyxoid change. Three cases showed an intraneural perineuriomalike proliferation. Reactive changes within the soft tissue, consistent with the effects of low grade repetitive trauma, was documented in all cases. In the majority (66%) an associated bursa was present, with the proportion increasing to 79% in cases reported by a sub-set of specialist pathologists. Only 2 cases of fungal bursitis demonstrated significant inflammation. All cases showed increased positivity for histiocytic markers.
Conclusion: This is the largest histopathological study to document the association between MN and bursae (which may be challenging to identify), together with changes in the background tissue associated with low grade repetitive trauma. In none of the cases was there evidence of a neoplastic process, and a significant inflammatory process was only identified in 2 infective cases. MN occurs most frequently in anatomical locations which are susceptible to compressive forces, which may be associated with footwear type.

PS-16-013
Gene fusions-associated mesenchymal tumours of the uterus: a morphologic, immunohistochemical and molecular analysis of 40 cases
I.A. Neculaescu*, A. Guerriero, B. Elena, C. Borga, L. Zanatta, M. Sbaraglia, A.P. Dei Tos
*University of Padua School of Medicine, Italy

Background & objectives: Gene fusions associated uterine mesenchymal tumours (GF-UMTs) are rare and morphologically heterogeneous. Clinical behavior is still not entirely elucidated. We herein describe the immunomorphologic and clinical features of a series of molecularly confirmed cases.
Methods: We retrieved a case series of UMTs (excluding smooth muscle tumours) from the archive of our institution and from the consultation files of one of the authors. All cases were tested for molecular alterations by FISH or RNA-based target NGS and, depending on the specific histology, for sex cord and epithelial markers, Cyclin-D1, BCOR, CD10, ER, PR, SMA and desmin.
Results: We described 40 clinically annotated cases of UMTs harbouring different fusion transcripts classified as follows: 21 high grade endometrial stromal sarcomas (HG-ESSs) of which 17 harbouring *YWHA*E-rearrangements, 2 *BCOR-ZC3H7B*, 1 *BCOR*-internal tandem duplication and 1 *BRD8-PHF1*; 14 low grade endometrial stromal sarcomas (LG-ESSs) of which 11 harbouring *JAZF1-SUZ12*, 2 *JAZF1-PHF1* and 1 *BRD8-PHF1*; 1 uterine tumour resembling ovarian sex cord tumours (UTROSCT) harbouring *ESR1-NCOA3*; 2 inflammatory myofibroblastic tumours (IMTs) *ALK*-rearranged and 2 sarcomas harbouring *COL1A1-PDGFB*.
Conclusion: GF-UMTs are rare, heterogeneous and diagnostically challenging. In the last decade molecular analysis have contributed to improve both classification and diagnosis. Some of these molecular alterations potentially represent a molecular therapeutic target. Additionally, as some GF-UMTs are still not well characterized clinically, molecular analysis may play a role in allowing better prognostic stratification.

PS-16-014
Clinico-pathological study of synovialosarcomas, series of 20 cases
W. Ouahioune*, N. MOULAI, M. Guermi
*Faculty Of Medecine Of Blida, Algeria

Background & objectives: Synovial Sarcoma (SS) is a rare malignant soft tissue tumour of uncertain histogenesis with variable epithelial differentiation. Our objective is to characterize the clinico-pathological criteria of SS according to the 5th edition of the WHO classification of soft tissue.
Methods: This is a retrospective study of 20 cases of SS collected at our Department of Pathology at Blida University Hospital over two years. We analysed age, sex, site, tumour size, histological subtype and grading of FNCLCC (Fédération Nationale des Centres de Lutte Contre le Cancer). We used a panel of antibodies for diagnostic purposes and others for differential diagnosis.
Results: The sex ratio was equal to 1. The average age was 34 years. In 70% of cases, SS was located at the extremities, 16% in the otorhinolaryngology region and 14% in the trunk. Tumour size ranged from 3 cm to 7 cm. The predominant histological subtype was the monophasic SS with spindle cells, grade 2 of FNCLCC in 65% of cases, followed by biphasic SS, grade 2 of FNCLCC in 30% of cases, and poorly differentiated SS with round cells, grade 3 of FNCLCC in 5% of cases. Expression of epithelial markers was positive in 95% of cases. BCL2, CD99, TLE1 were positive in 100% of cases.
Conclusion: Synovial Sarcoma is a rare sarcoma. The essential and desirable diagnostic criteria retained in the latest WHO classification are the monomorphic blue spindle cell sarcoma showing variable epithelial differentiation with diffuse and strong nuclear immunostaining for TLE1. The search for the SS18 - SSX1/2/4 gene fusion is a desirable criteria in selected cases. Our data are consistent with literature data except for head and neck location. Tumour size greater than 5 cm was the majority in our series.

PS-16-015

Establishment of an osteoarthritis model of slow progression in rats and proposal of a new therapeutic approach with collagen V

T. de Matos Lobo, V.D. Rodrigues de Souza, S. Carrasco, D. Levy, A. dos Santos Filho, S. Catanozi, Z.A. de Jesus Queiroz, L. Keren Ramos da Silveira, J. Alves Almeida, R. Fuller, V.L. Capelozzi, A.P. Pereira Velosa, W. R. Teodoro*

*Division of Rheumatology, Faculdade de Medicina da Universidade de São Paulo, Brazil

Background & objectives: Previously we showed increased collagen II expression by mesenchymal stem cells stimulated with collagen V (ColV). We developed an osteoarthritis model with slow cartilage degradation and hypothesize that ColV could have an effect on chondroprogenitor cells.

Methods: Osteoarthritis (OA) was induced in male Sprague Dawley rats (n=10) by partial meniscectomy. After 8 weeks, articular cartilage was collected, stained with HE and safranin-O/fast green and immunostained for types I and II collagen. For in-vitro evaluation, human chondroprogenitor cells from osteoarthritic cartilage were cultured and stimulated with ColV (50µg/ml and 100µg/ml) for 72 hours and immunostained with collagen II.

Results: Articular cartilage from induced osteoarthritis group showed increased collagen I expression and chondrocyte proliferation in the plateau compared to the control group (6.92 ± 3.08 vs 1.19 ± 0.58, p=0.01 and 55.95± 14.82 vs 40.60 ± 2.558, p=0.049, respectively). In addition, the OARSI score indicated a significantly higher degeneration index in the OA group compared to the control (2.20± 0.45 vs 0.40± 0.55, p=0.0002). In the vitro analysis, the cells stimulated with 50µg/ml and 100µg/ml of ColV presented collagen II increased expression compared to the control (30.6±6.24 vs 8.1±2.26 and 36.7±4.48 vs 8.1±2.26; respectively, p<0.0001).

Conclusion: The OA model with slow progression replicated morphological changes in articular cartilage similar to those found in early human disease. Additionally, ColV was effective in stimulated human chondroprogenitor cells in a dose-dependent manner, suggesting a new therapeutic approach to osteoarthritis. In this way, the OA model could be an important tool for studying the pathogenesis and therapies in OA, and especially the evaluation of intraarticular injection with ColV in vivo, which is necessary for establishing new therapeutic strategies.

PS-16-016

Osteochondral tissue changes induced by cigarette smoke exposure: the importance of TNF-α in these events

A. Fernandes Callera, A. Ferreira, A. Riani Moreira, F. de Almeida, A.L. Porfirio, L. Mattos, F. Lima, V.D. Rodrigues de Souza, A.P. Pereira Velosa, W. R. Teodoro*, F. Degobbi T Q S Lopes

*Division of Rheumatology, Faculdade de Medicina da Universidade de São Paulo, Brazil

Background & objectives: Smoking exposure induces a chronic inflammatory process, with presence of inflammatory chemokines, which leads to increased bone fragility as well as worsening of musculoskeletal diseases in smokers. We have evaluated experimentally the effects of TNF-αin bone and cartilaginous tissues.

Methods: Mice were exposed to cigarette smoke (CS), by once a day, 5 days a week, during 45 days. One smoker group received anti-TNF-αantibody (10mg/kg), administrated by intraperitoneal injection, once a week. Non-smoking and anti-TNF-αgroups were maintained in ambient air. Histological analyses were performed in femurotibial joints. TNF-α, RANKL and OPG expression were evaluated in bone homogenates by ELISA.

Results: CS exposure induced a decrease in subchondral bone area (p=0.02), a lower density of chondrocytes in cartilaginous tissue (p=0.001) and a decrease in the trabecular area (p≤ 0.05). Moreover, there was an increase in TNF-α(p=0.008) and RANKL (p=0.018) expression in smoking group compared with the others. The administration of TNF-αinhibitor was sufficient to revert changes observed in subchondral area as well as in cartilaginous tissue and in chemokines expression.

Conclusion: Our results reinforce the importance of CS exposure in the increase of fragility of bone and cartilaginous tissues, clarifying the important role of TNF-αas a mediator of inflammatory mechanisms in bone and cartilage tissues.

PS-16-017

Advancing bone research: a new cryoembedding method for in-depth analysis of large bone specimens

P. Ticha*, I. Pilawski, X. Yuan, S. Tulu, B. Coyac, J. Helms

*Charles University in Prague, Czech Republic

Background & objectives: In preclinical dental and orthopaedic studies, large animal models are commonly employed due to their size, enabling the testing of devices at a human-scale level. The challenge comes with the analyses of large animal bone tissues.

Methods: Large fresh mini pig bone specimens were cryopreserved with sucrose, infiltrated with polyethylene oxide and carboxymethyl cellulose, and frozen with hexane-dry ice. Cryosections were collected on transparent adhesive film positioned over the surface of the block and stained. The stained tissue section on the film was then inverted onto a water-based mounting medium-covered silane-coated glass slide. Imaging followed standard techniques.

Results: Large bone specimens are traditionally decalcified, and paraffin embedded, which disables evaluation of dynamic bone states. Alternatively, tissues are resin embedded, yielding very few tissue sections, and resulting in almost complete loss of protein antigenicity and enzyme activity. Besides the fact that current methods are destructive and largely limited to histological observations, they are time-consuming, requiring several months to process the specimens. Here, we have developed a method that allows to yield hundreds of high-quality large fresh frozen tissue sections amenable to cellular, molecular, and dynamic histomorphometric analyses e.g., measurement of mineral apposition rate. Remarkably, the entire process can be completed in just several days.

Conclusion: In sum, the approach enhances the translational value of large animal model studies. Besides that, the method represents logical means to minimize the number of animals in a study while simultaneously maximizing the amount of information collected from each specimen.

PS-16-018

Frequent and tricky lesion of jaw: review 117 cases of ameloblastoma diagnosed in a single centre

A. Toklu*, C.A.G. Gonzales, M. Sezak, A. Başduran, B. Koyuncu, A. Biçer, K. Öztürk, B. Doğanavşargil

*Ege University Faculty of Medicine, Department of Pathology, Izmir, Turkey

Background & objectives: Ameloblastoma is the most common odontogenic neoplasm along with odontoma. It has no sex predilection and may occur at any age. It behaves in a locally aggressive manner with tendency to recur although it is classified as a benign neoplasm.

Methods: We reviewed clinicopathological features of 117 cases evaluated with 158 biopsies between 2000-2023 years in a single pathology centre. Clinicopathological features were correlated by nonparametric tests.

Results: Sixty percent of the cases (n=70) were male and median age at admission was 42±18,1 year old. (range: 9-87 years old) The most common site was mandible (n=69, 59%). Recurrence was observed in 31 cases (26.5%), 71% (n=22) of them occurred in the mandible

and 58,1% (n=18) occurred in men. The earliest recurrence was in the first year of the treatment while the latest recurred 16 years after diagnosis (Median: 3 ±4,46 years). Nine cases (5.1%) recurred more than once, and lung metastasis was developed in one of them 3 years after the diagnosis. No significant correlation was found between recurrence and gender (p=0,815, chi-square) or localization (p=0,275, chi-square).
Conclusion: The age, gender and localization distribution of our cases are consistent with literature. The recurrence rate in our series is 26.5% and comparable with the previous series reporting a broad range of recurrence rates from 8% to 69.4%. Recurrence rates are reported to be higher in multicystic tumours and in cases that are incompletely removed however more powerful histological biomarkers or surgical techniques are required to predict disease outcome as its course is troublesome with multiple recurrences or even metastasis.

PS-17Poster Session Digital and Computational Pathology

PS-17-001
Closing the gap in the clinical adoption of computational pathology: an open-source workflow for the integration of deep-learning models into the laboratory information system
M. Angeloni*, D. Rizzi, S. Schön, A. Hartmann, F. Fraggetta, F. Ferrazzi
*Institute of Pathology, Friedrich-Alexander-Universität Erlangen-Nürnberg (FAU), Erlangen, Germany

Background & objectives: The clinical adoption of deep-learning (DL) models for computational pathology remains challenging. Here, we report a workflow that allows the integration of any DL model into the routine practice, leveraging open-source software and Health Level 7 (HL7) standards.
Methods: Development and testing of the workflow were carried out in a fully digitized Italian pathology department. A Python-based server-client system was implemented to interface the anatomy pathology laboratory information system (AP-LIS) with an external decision support system (DSS) through HL7 messaging. Open-source software WSInfer and QuPath were used to run DL model inference and visualize model predictions as coloured heatmaps.
Results: Basing on tissue type and staining, a DL model is configured to run as each new slide is scanned. In addition, pathologists can initiate the analysis by selecting the model on-demand. In both cases, an HL7 message is sent from the AP-LIS to the DSS, which extracts information about the slide identifier and the DL model to apply. Model inference is performed and the appropriate visualization heatmap in QuPath selected based on the classification model used. Finally, the DSS sends back model inference results to the AP-LIS. Upon analysis completion, the slide is marked in the AP-LIS and pathologists can visualize model predictions by opening the slide directly in QuPath.
Conclusion: Overall, the described workflow demonstrates that by using open-source digital pathology software and HL7 standards, it is possible to close the gap between the research field of DL models for computational pathology and the adoption of such models in the clinical practice. We believe that the developed integration workflow will provide guidance for the widespread adoption of DL models in routine environments, thus providing more concrete support to pathologists in their daily work.

PS-17-002
Artificial intelligence system for training pathologists to score gastric PD-L1
S. Badve*, H. Schildhaus, J. Rueschoff, G. Bänfer, B. Jasani, D. Lievlieva, F. Soares, F. Alchami, K. Schmitz, S. Schöniger, A. Tereshchenko, D. Calvopina, T. Lang, M. Karasarides, G. Kumar
*Emory University School of Medicine, USA

Background & objectives: PD-L1 assessment in gastric cancer (GC) using Combined Positive Scoring (CPS) is challenging as it entails assessments of expression on tumour and immune cells. We sought to develop and test the utility of an AI-based program to train pathologists.
Methods: We developed an AI software for training pathologists and examined pathologist concordance using intraclass correlation coefficients (ICC) and agreement rates with a reference score on whole slide images of 20 gastric cardia/gastro-oesophageal junction biopsies. Nine expert pathologists manually provided CPS assessments. After a 2-week washout period, they used AI assistance to provide assessments on the same whole slide images.
Results: In this two-step study, manual (non-AI) assessment of PD-L1 of 20 whole slide images by 9 expert pathologists (>10 years' experience) showed good inter-rater concordance (ICC 0.846). After 2-week washout, the Mind peak Gastric Cancer CPS AI software was used to assist the pathologist's evaluation. The software is applied to whole slide images. It classifies and highlights positive and negative tumour cells as well as immune cells. Agreement with the reference score increased from 91.1% without AI assistance (specificity/sensitivity 95.8%/88.0%) to 93.9% with AI assistance (97.2%/91.7%). The use of AI-assistance resulted in significant improvement in concordance (ICC 0.954).
Conclusion: AI-assisted evaluation of combined positive score for PD-L1 expression in GC resulted in dramatic improvement in the pathologists' inter-rater concordance and agreement rates as compared to the conventional assessment without AI assistance. This documents the utility of the AI system for use in CPS training and in guiding pathologists in making decisions at an individual cell level. Ultimately, this study shows the potential of AI assistance in training pathologists for challenging diagnostic tasks and providing for consistent "pathologist-approved „results.

PS-17-003
The impact on accuracy and reading time of artificial intelligence concurrent read vs second read prostate histology workflows
G. Bryson*, J. Blackwood, R. Campbell, L. Cottrell, J. Crosby, S. Fraser, J. Lee, A. McConnachie, H. Pitchamuthu, K. Rakovic, J. Salmond, J. Wilson
*NHS Greater Glasgow and Clyde, United Kingdom

Background & objectives: Artificial intelligence (AI)-based algorithms are available to assist pathologists in diagnostic and grading tasks. This study aimed to evaluate an FDA-cleared and CE-marked prostate cancer tool and assess the application of different read modalities and their impact on clinical workflows.
Methods: 400 whole slide images of prostate core needle biopsies from 400 patients, with challenging case mix (202 adenocarcinoma/ASAP and 116 benign) were reported by four pathologists using distinct reading protocols. Concurrent read (upfront/unrestricted AI access) and Second Read (standard practice unassisted followed by repeat reporting with AI access) were applied using a randomised crossover design including a washout between modalities.
Results: The use of AI assistance, for both Concurrent and Second Reads led to a significant increase in pathologists' sensitivity for adenocarcinoma/ASAP, compared with standard practice (Concurrent Read, +3.6%, p<0.001; Second Read, +3.3%, p<0.001).[MOU1] AI assistance improved Gleason Grading concordance (standard practice: Intraclass Correlation Coefficient (ICC) = 0.82; Concurrent read ICC = 0.86; Second read ICC = 0.84). Reading time was reduced by 23.8% in the Concurrent Read relative to standard practice. There was no significant difference in pathologists' performance comparing the two AI reading paradigms.

Conclusion: This study demonstrated that performance and diagnostic accuracy gains were unchanged when testing a Concurrent Read approach compared with a Second Read design, and that pathologists experienced efficiency gains (>20% timesaving) using a Concurrent Read modality. Improved consistency in Gleason Grading was also observed in the AI assisted reads. While bias and safety remain key considerations as AI systems are adopted into standard practice, the sequence in which pathologists consume AI outputs has a strong impact on potential efficiency benefits.

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PS-17-004

Clinical scoring and validation of a comprehensive AI-powered tumour content and lung macrodissection algorithm

W. Edelman, R. Wyatt, D. Mulkern, H. Moore, P. Caie*
*Indica Labs, United Kingdom

Background & objectives: Tumour content scoring is an integral part of the clinical workflow to ensure an accurate molecular result. This manual scoring, however, suffers from interobserver variability. We present an automated AI based algorithm which aims to standardise tumour content reporting.
Methods: 250 NSCLC cases were divided equally between five pathologists across unaffiliated institutions. Each pathologist annotated 1/5th of the cases for a region typically representative for macrodissection prior to molecular testing. Each pathologist scored all 250 cases for tumour content. We systematically compare the pathologists' scores against HALO Lung Macrodissect AI's automated quantification of tumour content in this external test cohort.
Results: Results show low interrater reliability (Fleiss kappa) between pathologists (kappa = 0.048); increasing slightly when adding the AI to the agreement calculation (kappa = 0.053). Those pathologists who are lung specialists (n =2) have the highest kappa values when comparing each to AI than non-specialists. Despite high variability between pathologist scores, AI estimates tumour content scoring similarly to the pathologists as a whole; low scores from pathologists' trend with low scores for the AI algorithm, and vice versa for high pathologists' scores. Further, our automated AI based algorithm performs within range of five pathologists' scores (81.2% of scores). As expected, an inverse relationship between score variance and agreement are observed.
Conclusion: Considering the poor agreement between pathologists, AI holds potential to reduce subjectivity in percent tumour scoring while potentially reducing the amount of rejected molecular tests in the clinic. Future work to evaluate pathologists' agreement in the presence of the AI tool's assistance will help evaluate the extent to which AI can improve interrater variability metrics. Macrodissection AI may help boost clinical standardisation for molecular testing through automated image analysis, AI-assisted tissue macrodissection region selection, and tumour content scoring.

PS-17-005

Pathology teaching forum: use of a digital platform at universities in Brazil

J. Carneiro Melo*, D. Nunes Oliveira, G. Brasileiro Filho, F. Toledo Bueno Pereira, G. Pozzan, S. Maria Macedo, G. Garcia Costa e Melo, R. Osterne Lima Verde, F. Guimarães Rodrigues, R. Santana de Lima
*University of Fortaleza, Brazil

Background & objectives: The online environment of the Pathology Teaching Forum (PEF) was created to provide teaching materials (video classes, microscopy, macroscopy and documents). The study aimed to evaluate the use of these materials by medical students at Brazilian universities.
Methods: This is a descriptive, observational, and cross-sectional study. In 2023.2, pathology professors from the medical course at five universities adopted the PFE teaching material in the classroom, and then administered a questionnaire via Google Forms containing questions about the effectiveness of the website material in the learning process.
Results: The majority of the 131 students were studying the fourth (33.6%) and third (29.8%) semesters, with an average age of 23.8 years, the majority were female (61%). 88.5% of students reported having learned about FEP with the teacher in the classroom, 16% accessed general pathology, 11.5% special pathology and 72.5% both. The microscopic study had 69.5% of accesses, videos 19.8% and macroscopy 10.7%. On a scale of 1 (lowest score) to 5 (highest score), 57.3% gave a score of 5 regarding the use of the platform in studies. 85.5% of comments were positive about their experience using the platform.
Conclusion: The PEF platform is an environment where all national professors can upload their materials for sharing. The use of the materials made available through the PEF by professors in the classroom was the principal impacting factor. The students' perception of using this tool was positive in the experience described in this study, which is relevant for encouraging the dissemination of this practice.

PS-17-006

3-Dimensional analysis of tumour buds using open-top light-sheet microscopy in lung and colon cancers suggests that many tumour buds are local invasions

O. Chamian*, E. Baraznenok, M. Maillard, H. Dawson, I. Zlobec, S. Berezowska, J.T. Liu, A. Janowczyk
*Department of Neuroscience and Department of Biochemistry, Case Western Reserve University, USA

Background & objectives: Tumour buds (TB) are spatially isolated clusters of <5 tumour cells at the invasive tumour front. TBs are associated with metastasis and recurrence. Current 2D histopathology cannot always distinguish between true TBs and entities connected to larger tumour masses (TMs).
Methods: 3D open-top light-sheet (OTLS) microscopy datasets of colorectal cancer (n=6) were stained with a fluorescent pan-cytokeratin antibody. A 2D thresholding algorithm was used to segment TBs and larger TMs in each 2D section. TB hotspots were chosen using TB counts. Merging 2D sections yielded 3D segmentations which were validated by pathologists. Putative TBs were assessed for connectivity to TMs.
Results: Our 6 samples showed that "true" TBs – i.e., objects which were not connected to any nearby TMs - made up 2/22(9.1%), 14/84(16.7%), 4/22(18.2%), 1/11(9.1%), 6/34(17.9%) and 3/20(15%) of the TBs assessed in 2D. In contrast, most objects (84.1% $\pm$ 3.5%) resembling TBs in 2D were revealed to be extensions of larger TMs in 3D. While true TBs are less common than one might expect when analysing 2D images, a linear regression relating putative TBs to true TB incidence revealed a strong positive correlation ($p < 0.0005$, r-squared = 0.98), suggesting 2D assessed putative TBs may act as surrogate for quantifying the abundance of true TBs.
Conclusion: Our results suggest quantification of true TBs is overestimated in conventional 2D histopathology, although we show a strong correlation between true TB and 2D TB counts. While the prognostic impact of distinguishing between putative and true TBs is presently unclear, future studies on patient survival, focusing on characterizing and quantifying true TBs in 3D, may facilitate improved patient stratification.

PS-17-007

Development of an automated artificial intelligence-based tool for fibrosis assessment in bone marrow biopsies

G. D'Abbronzo*, A. Ronchi, S. Lucà, E. Carraturo, A. Cioce, A. Sica, G. Svanera, R. Franco

*Pathology Unit, Department of Mental and Physical Health and Preventive Medicine, Università degli Studi della Campania "Luigi Vanvitelli", Naples, Italy

Background & objectives: A main step in evaluating bone marrow biopsies (BMBs) is fibrosis assessment that is currently evaluated by the human eye with significant interobserver variability. The aim of this study is to develop a computed tool for automated and objective fibrosis' assessment.
Methods: Fifty-fives BMBs were selected and stained with reticulin stain. Slides were scanned with a Ventana DP200 and exported as Whole Slide Images. A semantic segmentation model for evaluation of fibrosis according to WHO (MF0; MF1; MF2; MF3) was developed using a fully convolutional network based on InceptionV3 architecture. Performances of the models were compared with performances of an expert hematopathologist.
Results: The training trend of the model was generally positive, with a rapid convergence of the accuracy and the loss function values towards optimal levels (> 0.9 for the accuracy, <0.1 for the loss function). The remaining forty BMBs were evaluated by both the pathologist and the IA-based tools. Agreement between the model and hematopathologist was evaluated using Cohen's Kappa: general agreement was optimal (Cohen's K: 0.831); while agreement evaluated according to the different categories was optimal for MF0 (0.918) and MF3 (0.886) and substantial for MF2 (0.776) and MF1 (0.749). These results suggested the potential of our AI-based tool in improving accuracy and reducing subjectivity of fibrosis assessment in BMBs.
Conclusion: An objective evaluation of fibrosis in BMBs is mandatory for diagnosis of Philadelphia chromosome (Ph)-negative myeloproliferative neoplasms. However, this evaluation can be affected by interobserver interpretative variability based on pathologists 'experience. In this study we developed an automated system tools that could provide an objective fibrosis assessment beyond the experience of single pathologist.

PS-17-008
Implementing advanced quality control in digital pathology: integration of QC in diagnostic workflows
C. Riou*, C. Bertrand, J. Pomerol, M. Isaieva, R. Boukaroura
*France

Background & objectives: In digital pathology, artifact-related rejections of slides entail significant time loss and inefficiency. Our workflow introduces QC4scan, QC4AI, and QC4MB to detect and flag artifacts early, streamlining slide preparation and enhancing diagnostic and analytical processes.
Methods: QC4scan utilizes basic image processing to identify artifacts directly at the scanner. QC4AI and QC4MB, both based on Unets, serve distinct functions: QC4AI detects non-exclusive labels like air bubbles and tissue folds at 10x magnification, enhancing AI analysis, while QC4MB identifies exclusive labels for critical tissue types, optimizing tissue selection for DNA extraction from cancerous regions.
Results: Our QC algorithms demonstrate exceptional performance, with F1 scores exceeding 0.9 for detecting artifacts such as air bubbles, tissue folds, ink, and pen marks, enhancing both slide quality and AI analysis reliability. Dust detection, while slightly lower, still shows promising accuracy. For QC4MB, the ability to differentiate tumoural from non-tumoural tissues achieves an F1 score greater than 0.95, crucial for accurate DNA extraction from selected cancerous regions. These results, validated across TCGA datasets for breast, colon, ovary, lung, and prostate cancers, indicate a significant potential to decrease slide rejections and streamline the pathology workflow, though a full assessment of time efficiency gains is ongoing.
Conclusion: By integrating our advanced QC workflow into Tribun Health's Calopix diagnostic viewer, we have made these essential artifact screening tools available for clinical use, setting a new standard in digital pathology practices. This implementation not only flags artifice slides efficiently but also ensures that AI-driven analyses and subsequent biomedical testing are conducted on high-quality samples. The availability of such robust quality control in a clinical setting is pivotal, promising enhanced diagnostic accuracy and operational efficiency in digital pathology.

PS-17-009
Market access landscape for digital and computational pathology in EU6
A. Gkiokas*, E. Sheppard, H. Bannister, O. Ben Dhia, S. Tsantila, C. Decaudaveine, N. Yao, N. Farkas, K. Baden
*Alira Health, Switzerland

Background & objectives: Digital (DP) and computational pathology (CP) increases diagnostic efficiency and accuracy of in the lab. We analyse the market access landscape to understand funding and adoption of DP/CP in EU4, UK and Switzerland, and provide suggestions for improvement.
Methods: We reviewed reimbursement pathways and country policies in EU4, UK and Switzerland to identify gaps in market access and adoption of DP/CP. Findings were verified by external experts and recommendations were made to fill these gaps.
Results: DP/CP adoption enhances lab efficiency and addresses lab staff shortages. Despite benefits, high upfront costs coupled with lack of funding/reimbursement, and reluctance to change workflows hinder adoption. Amongst countries analysed, DP adoption is highest in UK where government funding enabled integration into leading centres. In other countries, DP is adopted by major hospitals and may not be fully implemented in all workflows. Overall, CP is less well-funded than DP. Leading laboratories in certain countries may use algorithms to analyse single biomarkers in clinical practice, but CP is mostly used in RUO settings. Use of advanced algorithms combining several patient parameters for prognosis or outcome prediction remains rare in clinical practice.
Conclusion: Wider uptake of DP/CP is needed to modernize lab workflows and enable precision medicine. Leading labs should share hands-on experience of switching workflows with the wider pathology community, demonstrating the added value of DP/CP in terms of patient and economic outcomes. Existing innovation funds can be used to generate clinical and economic evidence collected in local pilots, with the aim of securing funding and reimbursement especially for CP.

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PS-17-010
Comparative study of feature extractors for colorectal cancer pathology image classification using large-scale datasets and multiple instance learning
G. Hwang*, H. Yoon, D. Jeong, W.J. Cho, E.J. Lee, Y. Chong
*Deepnoid Inc., Republic of Korea

Background & objectives: Colorectal cancer (CRC) is a leading global health issue. This study evaluates different feature extractors in Multiple Instance Learning (MIL) models, which are increasingly used for analysing large-scale pathology images, demonstrating AI's potential in CRC analysis.
Methods: To compare the performance of four different feature extractors, ResNet, CTransPath, Lunit-DINO, and UNI, we used the Clustering-constrained Attention Multiple Instance Learning

(CLAM) as the aggregator. We used 5,056 Whole Slide Images (WSI) collected from five institutions for the training phase and 3,997 WSIs from two other institutions for external validation.
Results: To ensure accurate performance comparison, the same preprocessing and normalization procedures were applied across all data. The performance metrics used were Area Under the Curve (AUC) and accuracy (ACC). A total of 5,056 WSIs were categorized into training, validation, and test sets, comprising 4,044, 506, and 506 WSIs, respectively. We conducted external validation after selecting the best-performing model for each of the four feature extractors through 10-fold internal validation. The experimental results showed that the AUC for ResNet50, Lunit-DINO, CTrans-Path, and UNI were 0.9469, 0.9681, 0.9719, and 0.9713, respectively, and the ACC was 79.38%, 80.36%, 81.91%, and 86.06%, respectively.
Conclusion: The results of the study indicate that recently developed feature extractors demonstrate superior performance in the subtype classification of colorectal cancer (CRC). Consequently, we anticipate significant advancements in the accuracy and efficiency of large-scale pathology image analysis, fuelled by the ongoing conduct of more extensive and higher-quality research in this field.

Funding: This project, "Development of a Disease Classification Algorithm Program for Colorectal Cancer Pathology Tissue Images Based on Artificial Intelligence," was funded by the Industry-Academic Cooperation Foundation of The Catholic University of Korea.AUC of 93.54%, F1 score of 93.43%.

PS-17-011
Inline quality assessment of WSI in parallel to scanning operations reduces the rescan burden and expedites digital pathology adoption
J. Jain*, R. Gupta, P.P. Pellaru, A. Shah, A.A. Shaik, P. Perugupalli
*Pramana Inc, India

Background & objectives: Manual quality assessment (QA) of WSI post slide scanning is time consuming and costly. Furthermore, errors detected post scanning QA require rescans, causing delays in turnaround time (TAT). So, it's imperative to integrate an inline QA tool with WSI scanning.
Methods: One thousand H&E slides (1 year old) were digitised with Pramana HT scanners, using volumetric (3D) scanning with inline automated QA algorithm running parallel to scanning. The QA tool aids in inline evaluation of focus, stitching and other artefacts and initiates inline rescan when these errors were > 0.5 %. Slides flagged by the QA tool were subsequently manually evaluated.
Results: All 1000 slides were evaluated by an automated inline Quality Assessment tool, out of which 88% were deemed acceptable, and 12% were flagged for manual evaluation. In the manual QA group, approximately 1% of slides were rescanned, with an average delay of 24 hours in the lab workflow time including time consumed in manual slide evaluation, slide retrieval and rescanning. Meanwhile in the auto QA group, rescans were initiated inline for 15.9% of slides based on the real time inputs from QA tool, prolonging the scanning process by few seconds. If these slides were subjected to manual QA evaluation, the costs in both time and resources would have been significant.
Conclusion: Inline automated quality assessment of WSI is more efficient and cost effective than manual, post-scan evaluation, as it allows for inline rescanning of the affected areas, decreasing overhead turnaround time (TAT) delays. Parallel running of inline automated slide quality assessment tools with WSI scanning also facilitates downstream modification in the scanning process as per the clinical use case, thus making the digital pathology adoption seamless and cost effective.

PS-17-012
Multiple instance learning-based classification of subtypes of renal cell carcinoma using the largest dataset of whole slide images
D. Jeong*, G. Hwang, W.J. Cho, H. Yoon, J.S. Ra, C.K. Jung, Y. Chong
*Deepnoid Inc., Republic of Korea

Background & objectives: The rising incidence of renal cell carcinoma (RCC) necessitates precise histologic subtyping, but limited dataset in each subtype renders this task challenging, even with existing deep learning-based methods. Hence, we apply multiple instance learning (MIL) to classify subtypes of RCC.
Methods: We obtained 8,263 WSIs with its paired slide-level classification labels from ten different institutions. MIL requires only slide-level labels instead of patch-level labels, making it effective for training on large-scale WSI datasets. The WSIs were pre-processed to remove noise, extract foreground areas, and divide into patches.
Results: We used 7,040 WSIs for training and internal validation, comprised of 1,411 Normal, 4,074 Clear Cell Renal Cell Carcinoma (CCRCC), 1,026 Papillary Renal Cell Carcinoma (PRCC), and 529 Chromophobe Renal Cell Carcinoma (ChRCC) cases. Additionally, for external validation, 1,223 WSIs were used, including 428 Normal, 728 CCRCC, 37 PRCC, and 30 ChRCC cases. The performance of MIL showed promising results, achieving AUC of 99.79%, 97.71%, 94.39%, 82.27% for Normal, CCRCC, PRCC, and ChRCC, respectively. Moreover, the average performance across all classes showed ACC of 92.81%, AUC of 93.54%, F1 score of 93.43%.
Conclusion: Our findings suggest that the application of MIL models to WSIs can significantly improve the accuracy and efficiency of RCC diagnosis, in practice. These encouraging results in renal neoplasm detection highlight the potential for future advancements in RCC diagnosis and treatment, as it has shown better performance than any other RCC subtype classification task. We expect these improvements to aid diagnosis in clinical practice.

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PS-17-013
HIPPO: an explainable AI framework to uncover causal relationships and decision drivers in weakly-supervised digital pathology models
J. Kaczmarzyk*, J. Saltz, P. Koo
*Stony Brook University, USA

Background & objectives: Weakly-supervised deep learning is a powerful approach to infer slide-level labels from whole slide images, but the attention mechanism in these models has limitations. We propose HIPPO (Histopathology Patch Occlusion), a *post hoc* interpretability method to address this gap.
Methods: We developed HIPPO, an explainable AI framework for experimental investigation of tissue biomarkers *in silico*. HIPPO enables testing hypotheses about the importance of specific tissue patterns by allowing selective occlusion of regions in whole slide images and evaluating changes to the model's predictions. We also developed a label-free, greedy search algorithm to identify regions most important for a model's prediction.
Results: As a proof of principle, we evaluated the necessity and sufficiency of tumour regions for the detection of metastasis in lymph nodes using the CAMELYON16 dataset, which includes expert-drawn labels of tumours. We found that tumour regions are both necessary and sufficient, and that recent histopathology foundation models have variable ability to identify the metastatic regions using the attention

mechanism. Our greedy search algorithm consistently outperformed attention in identifying metastatic regions. Following this proof of principle, we extended analyses to datasets with less obvious tissue phenotypes, namely *TP53* mutation status prediction and survival prediction in pan cancer cohorts. Finally, we released all models developed as part of this study.
Conclusion: HIPPO allows deep learning developers and pathologists to better understand weakly-supervised model behaviour through counterfactual manipulations and direct localization of decision-making regions. Using HIPPO, we are able to complement attention-based interpretation and calculate the effect size of tissue regions given a model. Through the experimental identification of histopathology regions that drive model predictions, HIPPO will enable more transparent and trustworthy AI tools for precision oncology applications.

PS-17-014
Developing a multi-site, multi-cancer, real world dataset integrating digital pathology, spatial tumour-TIL maps, clinical phenotypes, and outcomes
J. Kaczmarzyk*, W. Chen, E. Durbin, D. Foran, R. Gupta, J. Hajagos, I. Hands, G. Harris, T. Insaf, T. Kurc, J. Levens, B. Qiao, J. Saltz, A. Stroup, K. Ward
*Stony Brook University, USA

Background & objectives: Tumour-infiltrating lymphocytes (TILs) play a key role in the response to cancer, but their prognostic value may vary across cohorts. We created a multi-site, multi-cancer immunooncology dataset linking spatial tumour/TIL maps with clinical variables and outcomes to investigate this.
Methods: Whole slide images (WSIs) of H&E-stained tumour sections from breast, lung, and prostate cancers were collected at three medical centres in the United States. Tumour and lymphocyte regions were identified using publicly available deep learning models, and TIL density was calculated. Clinical phenotypes and survival outcomes from cancer registries were linked to the tumour/TIL data.
Results: We have developed a real world, multi-institutional, multi-cancer dataset designed to explore hypotheses related to immunooncology, created by linking WSI tumour/TIL spatial maps with cancer registry data. Using deep learning patch prediction software developed in the context of this project, we analysed over 50,000,000 image patches from over 4,000 WSIs to generate tumour/TIL maps. Our dataset currently consists of 2,239 unique patients (1,005 in breast, 629 in lung, and 605 in prostate cancer). In preliminary analyses, we sub stratified breast, lung, and prostate cancer by subtype and assessed relationships between percent TILs and survival. We also document the fraction of TILs in breast, lung by subtype and in prostate by grade.
Conclusion: The development of our dataset of linked tumour/TIL and cancer registry data augments research on the prognostic value of TILs in breast, lung, and prostate cancer. The dataset can be used to study associations among TILs and tumour phenotypes, like Gleason grade in prostate cancer, hormone receptor status in breast cancer, and histologic subtype in lung cancer. In ongoing work, we are scanning and linking many additional cases to add statistical power to our real-world data immunooncology results.

PS-17-015
Generating highly accurate pathology reports from gigapixel whole slide images with HistoGPT
M. Tran, P. Schmidle, S.J. Wagner, V. Koch*, V. Luppberger, A. Feuchtinger, A. Böhner, R. Kaczmarczyk, T. Biedermann, K. Eyerich, S. Braun, T. Peng, C. Marr
*Germany

Background & objectives: Histopathology is considered the gold standard for identifying and characterizing diseases, in particular cancer, based on their morphological appearances. However, the process of analysing tissue samples including the final report of the microscopic findings is time-consuming, labour-intensive, and non-standardized.
Methods: We present HistoGPT, a vision-language model that generates medical reports based on digitized whole-slide images. To train HistoGPT, we collected a large multimodal dermatology dataset from Technical University of Munich with 6,000 paired WSIs and written pathology reports. HistoGPT consists of two components: a vision foundation model and a large language model, integrated via interleaved gated cross-attention blocks.
Results: We validate HistoGPT on one internal test set and five external publicly available cohorts to cover different countries, disease classes, scanner types, staining protocols, and medical procedures such as shave biopsies, punch biopsies, and excisional biopsies. We show that pathology reports generated by HistoGPT can match the quality of human-written reports, as shown by various natural language processing metrics and domain expert evaluations. In particular, we demonstrate that HistoGPT generalizes to five international cohorts and can predict tumour subtypes and tumour thickness in a zero-shot fashion.
Conclusion: Our work represents an important step toward integrating AI into the medical workflow. We envision a potential future, where pathologists can choose to have their own personal AI assistant to aid them in decision-making and help them process routine cases much faster. We publish code and weights so that the scientific community can apply and improve HistoGPT to advance the field of computational pathology.

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PS-17-016
Artificial intelligence-assisted interpretation of colonic biopsies from patients with inflammatory bowel disease
A. Levine*, O. Hadar, H. Lowes, J. Gildenblat, T. Mistry, D. Oukrif, C. Sagiv, M. Rodriguez-Justo
*University College London and University College London Hospitals NHS Foundation Trust, United Kingdom

Background & objectives: Inflammatory bowel disease (IBD) includes Crohn's disease and ulcerative colitis. Histopathological assessment of endoscopic biopsies is crucial for IBD diagnosis and monitoring. We aimed to develop an artificial intelligence (AI) tool to assist pathologists with colonic IBD biopsy interpretation.
Methods: H&E colonic biopsy slides were scanned at 40x (Hamamatsu) generating whole-slide images (WSI). These were annotated using DeePathology® STUDIO by gastrointestinal pathologists generating training and validation datasets. DeePathology® STUDIO was used to create deep learning algorithms for tissue region segmentation (Unet based model at 10x), crypt classification (MaskRCNN at 10x) and cell detection and classification (MaskRCNN at 40x).
Results: A total of 83 IBD and 22 normal WSI were examined and >4,500 training and validation annotations generated, including 2,339 tissue regions, 864 crypts and 1,153 inflammatory cells. F1 score, a weighted average of precision and recall, was used to assess algorithm performance. Tissue region segmentation was achieved with F1 scores of 0.87, 0.86, 0.71 and 0.65 for crypts, lamina propria, muscle and surface epithelium, respectively. Crypt classification was achieved with an F1 of 0.64 for structurally abnormal crypts and 0.78 for normal crypts. Detection and classification of neutrophils, plasma cells and eosinophils were achieved with F1 scores of 0.78, 0.75 and 0.77, respectively.

Conclusion: We have developed AI classifiers to assist pathologists interpreting colonic biopsies from IBD patients, accurately highlighting tissue structures and inflammatory cells, and identifying crypt architectural abnormalities. Further work is underway to generate additional training data to improve the existing algorithms, to co-localise inflammatory cells with tissue regions and to compare AI-derived estimates of disease activity/chronicity with pathologists' assessments. Ultimately, this approach will enable pathologists to interpret and extract objective metrics from normal and IBD colonic biopsies more efficiently and accurately.

Funding: This study was conducted as a collaboration between University College London Hospitals NHS Foundation Trust, DeePathology Ltd. and Pfizer. Pfizer is the study sponsor.

PS-17-017

The sonification of pathology: from slides to sound with AI-powered analysis

Y. Li*, T. Romagnoli, S. Lin, M. Cecchini
*Canada

Background & objectives: Image analysis software and data sonification can convert slides into sound representations, offering a new way to analyse tissue. We explore the potential of using sonification and AI to distinguish malignant cells from that of normal tissue.
Methods: We used image analysis software (QuPath) to extract features from a digital slide including average optical density, hematoxylin/eosin concentration, and saturation. The data was converted into sound using Two Tone. Gemini 1.5 analysed these sound representations to predict the transition points corresponding to transition between normal lung tissue and tumour.
Results: Sonification produced discernible signals with distinct audio characteristics that both humans and AI tools could distinguish. Gemini 1.5 demonstrated promising accuracy, correctly predicting the exact transition point in 14 out of 30 cases. While further refinement is needed, this highlights the potential of AI-assisted sonification in pathology analysis. From a previous study involving 14 human participants, the average number of correct responses was 20.6 out of 30 cases.
Conclusion: Sonification provides a unique multi-sensory approach to pathology analysis. Its integration with advanced AI models like Gemini 1.5 shows potential for future diagnostic applications. Further research will expand this method to diverse tissues and tumour types, aiming to improve machine learning algorithms for automatic identification of critical pathological features within sonified data.

PS-17-018

Commercial AI-assisted algorithms for HER2 assessment can predict HER2 amplification

M. Maniewski*, J. Borowczak, H. Andrusewicz, J. Dzierżawski, J. Starzyński, M. Zdrenka, P. Chudzińska, Ł. Szylberg
*Department of Tumour Pathology and Pathomorphology, Oncology Center in Bydgoszcz; Department of Obstetrics, Gynaecology and Oncology, Chair of Pathomorphology and Clinical Placentology, Collegium Medicum in Bydgoszcz, Poland

Background & objectives: Despite the recent advancement of AI-assisted algorithms, in some cases, HER2 assessment in breast cancer still requires additional in-situ hybridization tests. This study investigated whether AI-based algorithms can detect the presence of HER2 amplification.
Methods: We collected 100 archival samples from patients diagnosed with invasive breast cancer and medium HER expression (2+). 50 cases had HER2 amplification confirmed by FISH, and 50 lacked HER2 amplification. We reassessed the samples using two algorithms, uPath and VMScope, which were certified for HER2 assessment in breast cancer. All samples were also assessed by expert pathologists.
Results: The results between the original analysis and that performed by AI-algorithms diverged significantly. uPath classified the expression of HER 2 in 70% of cases as high (3+) and in 30% as medium (2+). No sample with HER2 amplification was considered to be of a low HER2 expression. VMScope classified 66% of samples with amplification as 3+, 26% as 2+, but also 8% as 1+. uPath reached 100% sensitivity and 9,09% selectivity for predicting HER2 amplification, while VMscope 89,8% and 80,0%, respectively. Both uPath and VMScope were more likely to classify samples with HER2 amplification as 3+ than pathologists (35 vs. 33 vs. 19, respectively).
Conclusion: Currently available AI-assisted algorithms showed high sensitivity for detecting HER2 amplification in breast cancer. Their use provides a cost-effective alternative to traditional HER2 assessment that may reduce the number of cases requiring FISH testing and shorten the time from diagnosis to treatment. However, their application into clinical practice requires further validation, as patients with low (1+) HER2 expression would be disqualified from targeted therapy.

PS-17-020

Convolutional neural network classifier for Helicobacter pylori detection in immunohistochemical staining of gastric mucosa

E. Musulen*, P. Cano, P. Lloret, D. Gil
*Pathology Department, Hospital Universitari General de Catalunya-Grupo QuironSalud and Josep Carreras Leukaemia Research Institute (IJC), Spain

Background & objectives: Identification of H.pylori(Hp) in gastric mucosa(GM) is a time consuming task in daily practice. Digitization of histopathological images allows their analysis using artificial intelligence methods. The objective is to design an AI algorithm to detect Hp in GM.
Methods: GM immunohistochemical staining were digitized to obtain whole slide images (WSI) of a series of negative and positive samples with low and high Hp density. Convolutional neural network (CNN) of three convolutional layers was designed. The model learns hierarchical features, recognizing simple shapes in the first layers and progressively more complex structures in the deeper layers consolidating this information for final classification.
Results: As Hp is located on the tissue surface, we detected the edges of the sample and defined 256x256 pixel windows cropped along the sample contour that were the input to the CNN for classification into positive or negative case. The percentage of positive windows determined the final diagnosis. Positive and negative annotated and unannotated tissue samples from 183 patients were used to test the algorithm in a 5-fold cross-validation. The 95% confidence intervals for specificity and sensitivity were, respectively, [99%,85%] and [98%,86%]. Validation on a new series of unannotated samples from 86 patients yielded a specificity of 86% and a sensitivity of 82% with only 14 misclassified.
Conclusion: Our CNN classifier is a useful tool for diagnosing Hp-associated gastritis that could be used in daily practice working with digital WSI. However, analysis of misdiagnosed cases shows that there is room for improvement. Many of the failures were patients with a very low density of Hp. This could be resolved by annotating more patches with low density, providing the classifier with more exposure to these types of cases during training.

PS-17-021

Quantitative markers hidden beyond radiological and pathological images: an artificial-intelligence-based integrative approach for predicting response to chemoradiation in locally advanced non-small cell lung cancer

L. Nibid*, G. Sabarese, M. Tortora, C. Ermanno, R. Sicilia, S. Ramella, P. Soda, G. Perrone
*Campus Bio-Medico, Italy

Background & objectives: Despite some advancements in personalized treatments, there are no available predictive biomarkers for chemoradiation in NSCLC. In this study, we developed a trimodal approach combining features computed from Pathomics (P), Radiomics (R) and clinical data (C) to predict chemoradiation outcomes.
Methods: We retrospectively selected a cohort of 33 patients (11 responders; 22 non-responders) with Locally Advanced stage NSCLC, treated with concurrent chemoradiation and with availability of tumour tissue slides obtained before treatment. Hand-crafted features from histological WSIs and CT scans were extracted and tested together with clinical data adopting a trimodal late-fusion learning framework. A leave-one patient-out cross validation approach was adopted.
Results: Overall, 112 experiments were performed with a combination of 7 modalities (P+R+C; P+R; P+C; R+C; P; R; C), 8 late fusion rules and 2 aggregation rules. The best performance was reached by the trimodal P+R+C late fusion framework, with the combination of Decision Templates late fusion and Feature Mean aggregation rule. In detail, the tool was able to correctly classify 20/22 non-responders (True Negative rate: 0.91) and 7/11 responders (True Positive rate: 0.64) with an accuracy of 0.82, F1 score of 0.702 and Precision of 0.778.
Conclusion: RadioPathomics trimodal late fusion framework was found to be a promising and highly specific test to early detect non-responder patients affected by locally advanced NSCLC. These data underline the need of an integrative multiomics approach to define new and more effective AI-based therapeutical strategies in NSCLC. Further studies are needed to enlarge the training set and to validate our results in a prospective cohort.

PS-17-022
Tissue Concepts: a supervised foundation model for computational pathology
T. Nicke*, J.R. Schaefer, H. Hoefener, F. Feuerhake, D. Merhof, F. Kießling, J. Lotz
*Fraunhofer MEVIS, Bremen/Lübeck, Germany

Background & objectives: Foundation models are an emerging technology to data-efficiently analyse tissue images and to automate time consuming clinical tasks. However, training these models is data- and resource-intensive. Additionally, their generalizability across centres or clinics outside their respective training domain remains challenging.
Methods: We compared two training strategies for foundation models, our novel supervised multi-task training, called "Tissue Concepts" (TC), and a self-supervised approach (CTransPath). Evaluation was based on the models' performance in differentiating cancer types in H&E-stained tissue sections across unseen centres. Three openly available, multi-centric datasets of colon, breast, and prostate sections were selected, resulting in ten clinically motivated evaluation tasks.
Results: Without fine-tuning the foundation models, we report the mean AUC on the test data. Results for prostate and colon cancer are calculated across centres, a fixed split is used for breast cancer. Although the proposed model was trained using only 6% of the data compared to the self-supervised model, both models show comparable performances. On average, both models yield similar results for differentiating normal from cancerous colon tissue (ours: 0.989, baseline: 0.992) and breast tissue (ours: 0.992, baseline: 0.997). When detecting prostate cancer, TC outperforms the self-supervised model (ours: 0.920, baseline: 0.826). Additionally, we find that both foundation models reduce the gap between cross-centre and within-centre evaluation.
Conclusion: Although Tissue Concepts was trained with only 6% of the data compared to the self-supervised model, both models show similar performance during evaluation. This shows that supervised multi-task learning is a data-efficient way of creating foundation models. Depending on their pre-training, foundation models are promising tools to overcome the performance differences between within-centre and cross-centre scenarios. Addressing these disparities is still crucial to improve usability and effectiveness of deep learning models in clinical settings.

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PS-17-023
Characterizing tumour heterogeneity through quantitative pathology features for lung cancer patients' survival prediction
P. Porwal, F. Dambandkhameneh, X. Li, Y. Nie, P. Ocampo*
*Personalized Healthcare, Data Analytics and Imaging, Genentech, Inc., USA,

Background & objectives: The prognostic stratification of patients into risk groups is crucial for optimizing therapeutic outcomes in lung cancer patients. We investigate if tumour heterogeneity is correlated with patient survival and response to immunotherapy beyond the extensively studied tumour infiltrating lymphocytes attributes.
Methods: Random field-of-views from tumour regions in Whole Slide Images (WSI) were used to extract quantitative pathology features and their heterogeneity from tumour cells at WSI level. These morphological heterogeneity features were used to train and test the Cox Proportional Hazards model for patient risk prediction. Model performance was evaluated via Kaplan-Meier stratification, Hazard Ratio (HR), and log-rank test p-value (p).
Results: Using two inhouse clinical trial datasets scaled at 20X from 1158 patients receiving immunotherapy, the CoXPH model was trained and tested across inter-trial atezolizumab constrained arms. The model was successful in distinguishing between low-risk and high-risk groups with statistical significance in all settings. Specifically, the model achieved $HR = 0.68$ and $p = 0.0027$ for one test arm, and $HR = 0.77$ and $p = 0.0300$ for the other test arm. The feature importance derived from the model highlights that heterogeneity derived from nuclear curvature, texture complexity and coarseness, and shape capturing information about its orientation and elongation had greater impact on model training and prediction.
Conclusion: These results indicate that characterization of tumour heterogeneity derived from H&E-stained digital pathology images alone can offer substantial prognostic value in identifying subgroups of patients that benefit more from immunotherapy. This study underlines the need for in-depth exploration of the complex role of tumour heterogeneity in immunotherapeutic response mechanisms. Our findings invite increasing attention towards integrating tumour heterogeneity features as a potential biomarker in risk stratification models.

PS-17-024
Artificial intelligence applications in placental health: creating a new diagnostic algorithm for placental delayed villous maturation, an enigmatic pathological condition
S. Quinones, D. Pelu Brezae, I. Ramírez, M. De Uribe Viloria*, V. Macarrón, E. Tornay, R.M. Regojo, C. Simon de Blas
*La Paz University Hospital, Spain

Background & objectives: Few isolated immature villi amidst mature ones are considered normal. However, widespread immature villi populations are defined as delayed villous maturation (DVM). The lack of

standardized criteria complicates the diagnosis. Our objective is to establish quantified limits using mathematical algorithms.
Methods: We analysed 80 photographs of full-term placentas (44 normal, 33 DVM) at 10X magnification. Villi edges and geometric patterns were detected using "Roboflow" label software. A supervised artificial intelligence model based in neuronal networks was used in the assistance for labelling the dataset. Statistics regarding villi area, perimeter, coverage percentages were obtained.
Results: The identified elements were classified into 5 categories: small villi (SV), medium villi (MV), trunk (T), fibrin (FB), and syncytial knot (SK). The number of MV (T-Student=3.023, P-value=0.005) and SV (T-Student=3.401, P-value=0.002) was significantly higher in normal placentas compared to pathological ones. However, the number of trunks (T-Student=-3.38, P-value=0.003) was significantly lower in normal placentas compared to pathological ones. No significant differences were found regarding the number of FB (T-Student=-1.242, P-value=0.224) and SK (T-Student=0.816, P-value=0.420). Considering aggregated MV and T, the area coverage resulted a 28% larger for pathological respect to normal ones (T-Student=-4.39, P-value<0.001). The area coverage by SV was significant smaller for pathological than normal ones (T-Student=4.13, P-value<0.001).
Conclusion: In recent years, DVM has been associated with heightened stillbirth risk in late third trimester. Furthermore, it exists a lack of prenatal diagnosis in this entity. While some cases exhibit clear histopathology, others manifest focal involvement or ambiguous histology, presenting diagnostic challenges. Developing these initial models could objectively define limits between normal and pathological states, enhancing understanding of defective placental maturation diseases as delayed villous maturation. Even more, the labelled database allows automatic classification for new images for diagnosis purposes.

PS-17-025
Precise 3D invasiveness detection for skin tumours diagnosis using X-ray virtual histology
G. Saccomano*, M. Pinamonti, F. Ciompi, D. Dreossi, F. Brun
*Department of Engineering and Architecture, University of Trieste, Trieste, Italy

Background & objectives: This study presents the application of X-ray virtual histology (XVH) to human skin tumours. By exploiting X-ray Phase-Contrast Computed micro-Tomography (XPCT), XVH aims to investigate elements and patterns of the disease, as well as track invasiveness in melanoma three-dimensionally.
Methods: 32 skin biopsies, including melanoma, non-melanoma skin cancers, and control tissues, were selected for XPCT investigation at Elettra Synchrotron (Trieste, Italy). An AI-tool depicted for semantic segmentation was employed to extract melanocytic lesions and identify the presence of ulceration. Data were analysed three-dimensionally and processed to assess the level of invasiveness of the tumour and correlate it with histological outcomes.
Results: XVH demonstrated to be able to differentiate non-melanoma skin cancers from malignant invasive melanoma by highlighting the most important pathological features (e.g. malignant melanocytes, nests, pagetoid melanocytosis, disorganized growth patterns, lymphocytic infiltrate). The designed AI model (dice score: 0.69, accuracy: 0.93, precision: 0.92) successfully identified the melanocytic lesion in all cases. The 3D visualization of the tumour allowed for assessing the extent of infiltration into surrounding tissue and identifying the exact area of epidermal loss in ulcerated melanoma. Moreover, the so-called Breslow thickness was computed three-dimensionally for each section providing a more accurate measurement that considers all the tissue embedded in paraffin.
Conclusion: The application of XVH offers significant advances in the diagnosis of human skin tumours thanks to its non-destructive nature. XVH has the potential to assist clinicians in accurately visualizing the depth of tumour invasion, enabling accurate staging and characterization of the cancer. For a wider accessibility of the technique beyond the limitations of synchrotron facilities, the integration of X-ray phase-contrast laboratory setups could improve the diagnostic capabilities and workflow efficiency for skin tumours diagnosis.

PS-17-026
A novel artificial intelligence-based score for assessing the prognostic value of intra-epithelial lymphocytes in oral epithelial dysplasia
A. Shephard*, H. Mahmood, S.E.A. Raza, A. Khurram, N. Rajpoot
*University of Warwick, United Kingdom

Background & objectives: Oral epithelial dysplasia (OED) poses a significant clinical challenge due to its potential for malignant transformation and the lack of reliable prognostic markers. Recent studies have highlighted the potential prognostic significance of peri-epithelial lymphocytes and intra-epithelial lymphocytes (IELs) in transformation.
Methods: We propose an artificial intelligence based IEL score from Haematoxylin and Eosin (H&E) stained Whole Slide Images (WSIs) of OED tissue slides; calculated as the number of IELs per 100 dysplastic epithelial cells. We determine the prognostic value of our IEL score on a large digital dataset of 219 OED WSIs (acquired using three scanners), compared to pathologist-led clinical grading.
Results: Our IEL scores demonstrated significant prognostic value through univariate survival analyses (Hazard Ratio HR = 1.65, C-index = 0.67, $p < 0.001$), when compared to both the WHO (HR = 2.39, C-index = 0.70, $p < 0.001$) and Binary (HR = 8.20, C-index = 0.74, $p < 0.001$) grading systems. In multivariate analyses, the IEL score was shown to improve both the Binary (HR = 1.88, C-index = 0.81, $p < 0.001$) and WHO (HR = 1.66, C-index = 0.76, $p < 0.001$) grading systems. Nuclear analyses confirmed the positive association between higher IEL scores, and both more severe OED ($p < 0.05$), and malignant transformation ($p < 0.001$).
Conclusion: Our study contributes to the growing evidence affirming the role of immune cell infiltration as a potential prognostic indicator in OED, with a specific emphasis on the significance of IELs, and our IEL score. Additional validation through prospective multi-centric studies is warranted to confirm the clinical utility of IELs. By elucidating the molecular mechanisms underlying the interactions between immune cells and dysplastic epithelial cells, we may reveal innovative paths for personalized diagnostic and therapeutic strategies in head and neck oncology.

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PS-17-027
AI analysis of thyroid fine-needle aspiration liquid-based cytology study
X. Sun*, S. Tian, H. Cao, W. Xiong
*Landing Med, China

Background & objectives: To test Landing Med's AI of thyroid fine-needle aspiration liquid-based cytology samples stained with Pap and H&E.
Methods: 231 thyroid FNA liquid-based cytology samples were prepared with 131 and 100 stained with Pap and H&E respectively. Slides were scanned as Whole Slide Images then analysed with AI. Three cytopathologists made diagnosis according to the Bethesda criteria. Normal or benign cases were considered negative while others were diagnosed as positive. The sensitivity and specificity of the diagnosis were calculated.
Results: 131 Pap-stained slides were diagnosed as 74 positive and 57 negatives under microscopic diagnosis. 71 and 72 positives out

of 74 were diagnosed from two cytopathologists, with sensitivities of 96% and 97%, respectively. 54 and 48 were found as negatives among 57 cases, with specificities of 94% and 82%, respectively. In the 100 H&E-stained samples, there were 64 positives and 36 negatives under microscopic diagnoses. 63, 64, and 63 positives out of 64 were diagnosed by three cytopathologists using AI analysed images, with sensitivities of 98%, 100%, and 98%, respectively. 30, 29, and 30 negatives were found among 36, with specificities of 83%, 80%, and 83%, respectively.
Conclusion: After processing thyroid fine-needle aspiration samples stained with two different methods, the sensitivity of pathologist diagnosis was over 95%, and specificity was over 80% using AI analysis. This study confirms that AI analysis can be used for both Pap and H&E-stained thyroid FNA liquid-based cytology samples.

PS-17-028
Utilizing artificial intelligence for detecting nodal metastasis in head and neck squamous cell carcinoma
B. Martin, E. Olkhov-Mitsel, J.T. Chao, T. Truong*
*Precision Diagnostics and Therapeutics Program, Sunnybrook Health Sciences Centre, Toronto, Department of Laboratory Medicine and Pathobiology, University of Toronto, Canada

Background & objectives: Assessing lymph nodes in oral squamous cell carcinomas (OSCC) is crucial for staging and prognosis. In this study, we developed and validated a deep learning approach to identify nodal metastases in OSCC resection specimens.
Methods: 444 digital whole-slide images (WSI) from 625 lymph nodes were analysed. Using three convolutional neural networks, pre-trained on an 11,467 WSI cancer dataset, our pipeline detects and classifies nuclear-dense tissue as lymphoid or non-lymphoid. A second model screens for neoplastic regions and a third verifies neoplastic nuclei. Algorithm performance was evaluated for sensitivity, specificity, and predictive values, benchmarked against pathologist's annotations.
Results: The initial model demonstrated high sensitivity (95%), specificity (88%), positive predictive value (PPV; 93%), and negative predictive value (NPV; 91%) in classifying lymphoid tissue and achieved 100% accuracy in identifying primary tumour sites (ranging in size from 13.2 to 17.1 mm). Additionally, our pipeline detected metastatic tumour deposits in lymphoid tissue with 93% sensitivity, 75% specificity, 23% PPV, and 99% NPV. The size of largest tumour deposits ranged from <0.1-to-5.5 cm. We intentionally designed the pipeline to achieve the highest possible sensitivity and NPV at the expense of higher false positive rate, thus lowering the overall specificity and PPV.
Conclusion: Our three-model approach has achieved high sensitivity in identifying tumour deposits in lymph nodes of OSCC specimens, albeit with compromised precision. Future work includes fine tuning the model to further improve performance metrics and external validation with prospective cases in routine pathologist workflow. The potential application of the model in detecting other tumours in lymph nodes can also be assessed.

PS-17-029
Whole slide image-based application for optimization of immunohistochemical staining protocol
C. Ohnishi, E. Yanagita, D. Frosina, R. Serrette, P. Ntiamoah, A. Jungbluth, Y. Yagi*
*Memorial Sloan Kettering Cancer Center, USA

Background & objectives: Development of new IHC staining protocols involves comparison of variable assay conditions, tissues, subjective evaluation of staining. We develop a whole slide image (WSI) based application that supports stable protocol evaluation by quantifying and visualizing differences in staining between protocols.
Methods: Slides were stained employing different assay conditions using different primary antibody dilutions, primary incubation times, as well antigen retrieval modifications. All slides were digitized at 0.46 μm/pixel. Target regions are automatically detected, and then the intensity of DAB membranous staining is obtained from WSI. IHC staining is adjusted to achieve high target antigen reaction and low background staining.
Results: Three selected different protocols were compared by analysing the same core from different slides which consist of a spleen carrier tissue and 5 mm cores of five different seminomas. The lower dilution slide tends to have a higher DAB intensity. Comparing the histogram peak values, the difference in DAB intensity between slides B and C is 1.03 times, but the difference in background is 2.07 times. This result suggests that the protocol on slide B may provide superior contrast. We compared the results with the technician's visual evaluation and confirmed a consensus which protocol was considered best.
Conclusion: Our application is able to quantify the immunostaining differences of various protocols and allows for the selection of the optimal protocol. We are currently optimizing our application for the analysis non-membranous proteins. Since the basis of image analysis has been constructed, once the protocol is optimized, our application and the control slides can be applied to automated evaluation in a clinical setting, such as intensity-based score classification.

PS-17-030
A new method of artificial-intelligence-based automatic identification of grade and invasion in urothelial carcinomas
S. Zurac*, B. Ceachi, L. Nichita, M. Cioplea, C. Popp, L. Sticlaru, M. Bușcă, A. Cioroianu, A. Vilaia, J. Gerald Dcruz, P. Mustățea, C. Dumitru, V. Cauni, A. Bastian, C. Mogodici
*Department of Pathology, Colentina University Hospital, Bucharest, Romania; "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

Background & objectives: Urothelial carcinoma (UC) requires histopathologic reporting of several parameters. In most of the cases, the pathologist must examine 4-6 slides but cases with more than 10 slides are not uncommon. An automated method for histopathological analysis is more than welcome.
Methods: We selected from our archives 105 patients (100 UC; 5 cystitis); one slide/case was scanned, obtaining whole slide images (WSIs). We performed a pixel-per-pixel semantic segmentation of 21 selected areas/WSI for several classes (high-/low-grade tumour, invasion, emboli, stroma, vessels, smooth muscle, etc). We trained an Intern Image model using dice coefficient (DCC) and intersection-over-union (IoU) as metrics for our model performance.
Results: UC patients were predominantly males (72%), average age 66.04years, 46%low-grade UC/ 54%high-grade UC, 42% noninvasive/ 58%invasive (28%pT1 and 30%pT2 or above). There were, on average, 3.93paraffin blocks/case (1-17 paraffin blocks/case). The data set obtained after annotation was arbitrarily separated in training (57.18%), validation (21.37%) and test set (21.44%). The results on test set are high-grade tumour (0.66 DCC/0.49 IoU), low-grade tumours (0.82 DCC/0.70 IoU), stroma (0.84 DCC/0.73 IoU), vessels (0.75 DCC/0.60 IoU) and LVI (0.77 DCC/0.62 IoU). We evaluated each patch of the test set; apparently low DCC and IoU scores are consequences of human inability in precise drawing of the classes and/or impossibility of annotation of very small vessels.
Conclusion: When diagnosing large cases of UC (10-20 blocks or more) a pathologist will experience fatigue, diminished attention, and sometimes postpones examination

Our model identifies high-/low-grade tumour, invasion, emboli, and smooth muscle and highlights them on a heat map. The pathologist analyses highlighted areas, thus shortening the time required by

microscopic analysis. The results of our model are encouraging; its integration promises to improve the diagnostic accuracy, reduce the time taken for analysis, and potentially lead to better patient outcomes.

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PS-17-031

Classification of craniofacial bone tumours using deep learning models

G.S. Hosseini Japalagh*, T. Kleijn, W. H. Schreuder, K. Szuhai, M. Witjes, K. van Langevelde, R. Hemke, D. Savci-Heijink, A. J.H. Suurmeijer, G. Diercks, U. E. Flucke, L. Hiemcke-Jiwa, J. Bovée, D. Baumhoer, A. Cleven
*University Medical Center Groningen, The Netherlands

Background & objectives: The accurate diagnosis of craniofacial bone tumours is challenging; radiological and morphological features may overlap. We aimed to develop an innovative deep learning model as a diagnostic tool to classify craniofacial bone tumours based on whole-slide-images of HE slides.
Methods: We collected a well-characterized discovery cohort (n=157) of craniofacial bone tumours. The method involved these steps:(1) annotation, segmentation into tiles. (2) data splitting and stratification into 70% data training, 15% testing, and 15% validation. (3) ResNet-50V2 pretrained architecture on ImageNet was used as base model, transfer learning applied, model trained with early stopping callback using data augmentation and class weighting.
Results: Our deep learning model showed tumour class predictions with high accuracy for all subtypes (including 28 cemento-osseous dysplasias, 22 cemento-ossifying fibromas, 26 fibrous dysplasias, 37 psammomatoid ossifying fibromas, 10 juvenile trabecular ossifying fibromas, 8 low-grade osteosarcomas, and 26 high-grade osteosarcomas) with high AUROC (>0.90) and Precision-Recall (>0.90) scores. Notably, low-grade osteosarcomas demonstrated the best AUROC (1.0) and Precision-Recall score (1.0).
Conclusion: We achieved an accurate diagnosis in more than 90% of craniofacial bone tumours using deep learning models including the often-challenging diagnosis of low-grade osteosarcoma. Our next step is to validate our deep learning model on non-annotated slides of other craniofacial bone tumours. Furthermore, to better understand the patterns used by our deep learning model for prediction of tumour subtypes, our next step is to visualize in heat maps on WSIs morphological areas of importance for classification.

PS-18Poster Session Head and Neck Pathology

PS-18-002

Critical evaluation: the Imperative of head and neck specialist review in multidisciplinary team meetings

A. Ali*, U. Kiriwandeniya
*FRCPath, United Kingdom

Background & objectives: Head and Neck and thyroid cases are traditionally reported by general pathologists in various District General Hospital settings in the UK and globally. This practice has always resulted in a questionable accuracy of the report, potentially impacting patient management.
Methods: We conducted a prospective audit to assess changes in diagnoses when cases are reviewed by Head and Neck specialists before finalising the report for MDT review. The audit comprised of 200 consecutive cases and the diagnoses were compared between the primary report issued by the general pathologists and the final report issued by the specialist Head and Neck pathologists.
Results: The results revealed clinically and statistically significant discrepancies in certain areas, which were thoroughly analysed within this audit. These findings underscore the importance of utilising specialist Head and Neck expertise whenever accessible.
Conclusion: In conclusion, our study underscores the crucial necessity of Head and Neck specialist review in Multidisciplinary Team Meetings (MDT), emphasising the vital role of specialist expertise in ensuring accurate diagnoses and optimal patient care in Head and Neck pathology.

PS-18-004

Diffuse sclerosing subtype of papillary thyroid carcinoma: a tertiary care cancer centre experience

S. Bhatia*, N. Mittal, S. Rane, K. Rabade, M. Bal, A. Patil
*Tata Memorial Center, India

Background & objectives: Diffuse sclerosing subtype of papillary thyroid carcinoma (DSS-PTC) is uncommon, aggressive, and clinically mimics a goitre. Recent studies show a relatively worse prognosis in paediatric patients. The study aims to evaluate the clinicopathologic features in the Indian subcontinent.
Methods: Retrospective study of 10 years duration (January 2014-December 2023). All cases were confirmed histologically. Clinicopathologic details were noted from electronic medical records. A total of 19 cases (5 males,14 females, M:F ratio 0.35:1) were evaluated. Mean age was 39 years (range 17-67 years). Swelling of the neck was the commonest symptom; followed by hoarseness of voice.
Results: Nineteen cases with imaging findings included diffuse lesions with focal nodularity and calcifications in 100%cases;73.6% had multifocal/multicentric lesions, involving bilateral lobes (42 %) (right>left). All cases underwent total thyroidectomy. Histologically, sclerosis (100%), psammomatous calcification (73.6%), squamous metaplasia (42%), lymphocytic infiltrate (89.4%); oncocytic features (42.15%) and tall cell morphology in 36.8%cases noted. Extrathyroidal extension was observed in 68.4% (macroscopic 15.7%; microscopic 84.2%); lymphovascular invasion in 52.6%. Central compartment nodal involvement was observed in 100% cases; nearly half had bilateral neck node involvement. All cases received radioactive iodine at least once, while 2 cases additionally received radiotherapy. Median follow-up of the cohort was 15 months (1-72 months). Distant metastasis, to the lung, at presentation, was observed in 10.5 %. Local recurrence to the neck on follow-up was observed in 2 cases (2 and 54 months, respectively), both with gross extrathyroidal extension and tall cell morphology.
Conclusion: DSS-PTC is a rare subtype of PTC characterized by female preponderance, multicentricity, extrathyroidal extension, and lymph nodal metastasis at presentation. Distant metastatic rate is five times more than classical PTC, thus requiring workup for the same. Histological features of diffusely infiltrative PTC with sclerosis, psammomatous calcification, and lymphocytic infiltrate will confirm the diagnosis. Though DSS-PTC is considered to be an aggressive variant, total thyroidectomy along with lymph nodal dissection with upfront distant metastasis screening, followed by radioactive iodine and radiotherapy (wherever needed) have shown a favourable outcome.

PS-18-005

Ex vivo confocal microscopy imaging in head and neck tumours

O. Casiraghi*, N.I. Ben Romdhane, I. Breuskin, M. Abbaci
*Gustave Roussy Cancer Campus, Paris-Saclay University, Department of Biopathology, F-94805, Villejuif, France; Surgery and Pathology Photonic Imaging group, Gustave Roussy, Villejuif, France

Background & objectives: Fluorescence Confocal microscopy (FCM) providing high-resolution, real-time images from fresh surgical

specimens in the pathology workflow could optimize pathologists' practice. We evaluated the technical feasibility of FCM for ex vivo extemporaneous examination of ENT surgical specimens (protocol, image quality).
Methods: Thirteen patients with surgery were included, and one to five tissue samples of 2cm2 were randomly selected for FCM imaging. The samples were stained by topical application of acridine orange at 0.025% and fast green at 0.067%. Away from the image acquisition, two pathologists (PT1 and PT2) interpreted FCM images as tumoural (benign or malignant) versus non tumoral (normal tissue).
Results: Twenty-four samples were imaged and blindly interpreted by PT1 and PT2, without clinical or location information. These interpretations were compared to the diagnosis performed on the corresponding Hematoxylin-Eosin-Safran (HES) slides obtained after paraffin embedding. All head and neck squamous cell carcinoma (HNSCC) and non-tumoural tissue were recognized. However, without location indication (particularly for salivary glands, nasal and ethmoid cavities), we noted three major discrepancies. It corresponded to a pleomorphic adenoma interpreted on the FCM image as HNSCC, an intestinal-type adenocarcinoma interpreted on the FCM images as pleomorphic adenoma, and a meningothelial meningioma interpreted on the FCM image as a HNSCC.
Conclusion: Inclusions will pursue to allow a robust statistical analysis (in progress). For the second part of the study, lesion location will be provided to the pathologists. At this stage, the analysis by FCM seems to be a very promising technique. It could eventually replace the frozen section because its diagnostic reliability seems at least equivalent to that of conventional HE sections, provided that location is available for the pathologist. Furthermore, its speed processing (5 minutes) constitutes a major asset.

PS-18-006
Intranodal benign thyroid inclusions: a series of 41 cases emphasizing the morphologic criteria and the application of BRAF VE1 immunohistochemistry
Y. Chuang*, Y. Kuo, J. Hang
*Taipei Veterans General Hospital, Taiwan

Background & objectives: Intranodal benign thyroid inclusions (BTIs) cause diagnostic challenges. The study aims to identify the incidence of BTIs, to evaluate the utility of BRAF VE1 immunohistochemistry (IHC), and to recognize histopathologic features in distinguishing metastatic papillary thyroid carcinoma (PTC) from BTIs.
Methods: Cases of BTIs were categorized into (A): thyroidectomy due to PTC with regional lymph node (LN) dissection, (B): thyroidectomy due to benign disease with incidental LN sampling, and (C): surgery due to other head and neck cancers with cervical LN dissection. BRAF VE1 IHC was performed on all cases. The histopathologic features of BTIs and metastatic PTCs were compared.
Results: A total of 41 cases were identified, including 33 in Group (A), 4 in Group (B), and 4 in Group (C). The incidence of BTIs was 4.2% (33/792) in Group (A). They were found in central neck LNs only (level VI) in 35 cases, lateral neck LNs only (level IB-V) in 5 cases, and both in 1 case. BRAF VE1 IHC was positive in all metastatic PTCs while negative in all BTIs. Papillae, undulating luminal border, pseudoinclusions, nuclear grooves, and chromatin alterations were significantly less common in BTIs than in metastatic PTCs ($P < 0.001$). To differentiate metastatic PTCs from BTIs, presence of intranuclear pseudoinclusions had the highest specificity (100%).
Conclusion: Benign thyroid inclusions (BTIs) are encountered in several types of surgical specimens. They can appear in central neck or lateral neck lymph nodes, even coexisting with metastatic PTCs in the same lymph node. A combination of histopathologic features and BRAF VE1 IHC result is useful to render the diagnosis of BTIs.

PS-18-007
Prognostic relevance of tumour microenvironment features in lip squamous cell carcinomas: focus on poorly differentiated clusters and tumour budding
S. Ekmekci*, Y. Adalı, A. Tavukcu, Y. Pekcevik, İ. Cukurova, Ü. Küçük
*Izmir Provincial Health Directorate, Izmir City Hospital, Department of Pathology, İzmir, Turkey

Background & objectives: The prognostic importance of tumour microenvironment characteristics, such as poorly differentiated clusters (PDCs) and tumour budding (TB), is increasingly recognized in oral malignancies. This study aims to investigate the prevalence and prognostic implications of PDCs and TB in lip squamous cell carcinomas (SCC).
Methods: The study included 40 patients diagnosed with lip SCC. Tumour sections were reassessed for tumour invasion depth (TID), lymphovascular invasion (LVI), peritumoural fibrosis (PTF), perineural invasion (PNI), presence of necrosis, TB, and PDCs. The severity of these histopathological features was quantified based on the number of cell groups observed in the most active area under 200x magnification and categorized as mild, moderate, or severe.
Results: Among the cases studied, 38(95%) were located on the lower lip and 2(5%) on the upper lip. Histologically, 37 cases (92.5%) were moderately differentiated and 3 (7.5%) were well-differentiated. TB was classified as mild in 29 cases (72.5%), moderate in 8 cases (20%), and severe in 3 cases (7.5%). PDCs were observed as mild in 72 cases (67.5%), moderate in 6 cases (15%), and severe in 7 cases (17.5%). Statistical analysis revealed no significant associations between TB or PDCs and survival, gender, age, location, degree of differentiation, TID, PTF, PNI, LVI, or lymph node metastasis ($p>0.05$). However, a statistically significant increase was found in TID, PNI, and lymphocytic response in cases with PDCs ($p=0.005$, $p=0.000$, and $p=0.000$, respectively).
Conclusion: This analysis confirms the presence of PDCs and TB in lip SCC and identifies a significant association between PDCs and indicators of aggressive tumour pathology, including increased TID, PNI, and lymphocytic response. These findings emphasize the critical role of microenvironmental factors in the pathology of lip cancer and highlight the need for further studies to explore how these histopathological features could influence tailored therapeutic strategies.

PS-18-008
Tonsillar localization of mucosal leishmaniasis mimicking oropharyngeal malignancy: diagnostic challenges
M. Errani*, M. Ortalli, S. Varani, R. Albertini, L. Amorosa, E. Pasquini, P. Rinaldi, A.R. Lombardi, M. Del Vecchio, V. Gaspari, M.P. Foschini
*University of Bologna School of Medicine, Bologna, Italy

Background & objectives: Mucosal leishmaniasis (ML) is a rare variant of tegumentary leishmaniasis. Clinical manifestations are variable and tends to overlap with those of head and neck tumours. To improve knowledge on ML, three cases of tonsillar leishmaniasis are described.
Methods: This series consists of three adult patients, 2 males and 1 female, aged 42 to 62 years old, living in northeastern Italy. Tissues obtained by biopsies or tonsillectomy were formalin fixed and paraffin embedded (FFPE) according to routine procedures. Histochemical and immunohistochemical studies were performed on an automated auto stainer. Real-Time PCR for Leishmania DNA was performed at the Unit of Microbiology.
Results: All patients presented tonsillar pain. Fibrolaryngoscopy and CT scan showed right tonsillar swelling and enlargement, suggesting malignancy. Incisional biopsies, followed by tonsillectomy, were

performed. On histology giant cells and non-necrotizing granulomas were seen in all cases. Histochemical staining (Giemsa, PAS after diastase digestion and Ziehl-Neelsen) failed to reveal any possible etiological microorganism. CD1a revealed intracytoplasmic structures suggestive for Leishmania amastigotes in 2/3 cases. Biopsies tested positive for Leishmania DNA in all cases, confirming the diagnosis of tonsillar leishmaniasis.
Conclusion: While ML is not uncommon in endemic areas, a pure tonsillar localization of Leishmania is a rare finding. By searching on PubMed, only two cases of tonsillar leishmaniasis were found. Overall, ML is poorly recognized and underdiagnosed in the Mediterranean Europe. Since the overlap in clinical presentation of isolated ML and tumours, leishmaniasis should be considered in the differential diagnosis of head and neck cancer in patients from - or who report travelling to - endemic areas.

PS-18-009
Epstein-Barr virus associated lymphoproliferative disorders in oral cavity and oropharynx
M. Gómez Tena*, M. Gomà Gallego, N. Vicente, J. Bosch, J. Azcarate, A. Vidal, M. Pané Foix, B. Kaliullayev, I. Blazquez, A. Domingo, J. Martinez, J. Rodriguez, F. Climent
*Hospital Universitari de Bellvitge, Spain

Background & objectives: Epstein-Barr Virus positive mucocutaeous ulcer (EBVMCU) is a lymphoproliferative disorder that affects skin and mucosae of immunosuppressed individuals. It resolves spontaneously or after reducing immunosuppression. Involvement of oral mucosae by EBVMCU represents a diagnostic challenge for pathologists unexperienced in hematopathology.
Methods: A clinicopathological review of nine cases diagnosed as EBV associated lymphoproliferative disorders (EBVLPD) presenting as an ulcer in the oral cavity and oropharynx between 2015 and 2023.
Results: A series of 9 patients(8male/1female), median age of 71 years-old(range:31-92). The causes of immunosuppression were old-age (3), iatrogenic(4), HIV infection (1) and primary immune deficiency(1). Six cases displayed a mixed lymphoid population with scattered large, atypical cells. After staging, half of these cases were diagnosed as EBV associated diffuse large B cell lymphoma (EBV+DLBCL) due to presence of dissemination. The rest had a self-limited course. Three cases were made up of an atypical diffuse monotonous lymphoid proliferation and were first diagnosed as aggressive EBV+ lymphomas. There was no evidence of progression and they resolved spontaneously. Despite the disparities in the morphology the atypical cells were positive for B-cell markers, CD30 and EBER.
Conclusion: Our case series proves the morphological heterogeneity of EBVLPD involving the head and neck areas. Clinical history and radiologic staging are crucial for distinguishing EBVMCU from EBV+ lymphomas. The suspicion and understanding of this entity are of utmost importance in order to avoid diagnostic errors that may lead to over-treatment in patients with immunosuppression.

PS-18-010
A head-to-head comparison of four systems for oral epithelial dysplasia grading and prognostication
P. Hankinson*, M. Clark, H. Walsh, A. Khurram
*University of Sheffield, United Kingdom

Background & objectives: The World Health Organisation (WHO) oral epithelial dysplasia (OED) grading system is the current gold standard. Other grading systems have been proposed including the binary, 2-point and 6-point systems. We aim to assess these four grading systems.
Methods: Five-year follow-up data was collected for 137 patients with OED to determine malignant transformation. Archived slides were independently reviewed by three clinicians. WHO, binary, 2-point and 6-point grades/scores were assigned to each case. Light's kappa coefficient (LKC) was used to calculate inter-observer reliability. Kaplan-Meier and Cox regression survival analyses were used to assess each grading system's correlation with malignant transformation.
Results: The WHO, Binary, 2-point and 6-point grading systems had a LKC of 0.42, 0.31, 0.17 and 0.41 respectively. Kaplan-Meier and Cox regression survival analyses showed stratification of malignant transformation risk by grade in all systems except the 2-point system. The risk of malignant transformation was not significantly raised for moderate OED (WHO), while severe OED had a hazard ratio (HR) of 13.7 ($p = 0.018$). The high-risk category for the binary and 6-point systems had HR of 5.8 ($p = 0.038$) and 8.7 ($p = 0.047$) respectively.
Conclusion: The 6-point grading provided superior risk stratification when compared with WHO, binary and 2-point grading. Despite limited practical experience of its use, it has comparable inter-observer reliability with the widely used WHO grading system.

PS-18-011
An evaluation of high-risk HPV in squamous cell carcinoma of the lip in a South African cohort
S. Harbor*, J. Schneider, M. Sanderson, A. Afrogheh
*National Health Laboratory Service, South Africa

Background & objectives: High-risk human papillomavirus (HR-HPV) is a known risk factor for oropharyngeal squamous cell carcinoma (OPSCC); however, its prevalence in squamous cell carcinoma (SCC) of the lip remains unclear. We investigated HR-HPV prevalence in South African patients with lip SCC.
Methods: Fifty cases of SCC of the lip and 50 controls were tested for HR-HPV using p16 immunohistochemistry (IHC) and HR-HPV DNA PCR. Cases showing both p16 equivocal/positive and HPV DNA PCR positivity were further evaluated for the expression of HPV-16 and HPV-18 mRNA transcripts using reverse transcription quantitative real-time polymerase chain reaction (RT-qPCR) to confirm transcriptionally active HPV.
Results: p16 IHC was positive in 22% (n=11) and equivocal in 4% (n=2) of the SCC cases. One p16-positive case also showed positivity for HPV-16 DNA and HPV-16 E6/E7 mRNA transcripts (HPV prevalence rate of 2%). The HPV-positive case was non-keratinising and occurred in an 80-year-old female. The two p16 equivocal cases were HR-HPV DNA positive and mRNA PCR-negative. p16 was found to have a positive predictive value (PPV) of 9%.
Conclusion: This study indicates that HR-HPV might not play a major role in the pathogenesis of lip SCC (2% prevalence). Soley utilising p16 is insufficient to establish HR-HPV infection at this site, due to its low PPV. The combination of p16 IHC and DNA PCR correlates with a transcriptionally active virus. Although HPV E6/E7 mRNA is the gold standard, it is not widely accessible in low-income countries and may be reserved for cases with unequivocal p16 IHC in these settings.

PS-18-012
Tumour budding assessed according to the International Tumour Budding Consensus Conference recommendations correlates with prognosis in oral squamous cell carcinoma
M. Hermanova*, M. Herman, K. Kopecka, P. Liptakova, J. Michalek, R. Pink, I. Staniczkova Zambo, J. Zapletalova
*First Department of Pathology, Faculty of Medicine, Masaryk University and St. Anne´s University Hospital Brno, Czech Republic

Background & objectives: Tumour budding (TB) was suggested as a prognostic factor in oral squamous cell carcinoma (OSCC) but lacks a standardized scoring system. This study aimed to evaluate TB in OSCC using the scoring recommended by International Tumour Budding Consensus Conference (ITBCC).

Methods: The study included 114 patients with resected OSCC. TB was scored in hematoxylin and eosin-stained whole tissue slides of resection specimens according to ITBCC criteria and assigned to budding groups Bd1-3. Associations between TB and clinicopathological parameters were examined and survival rates analyses were performed by the Kaplan-Meier method. Prognostic value of TB was assessed by Cox regression analysis.
Results: TB was low (Bd1) in 52.6%, intermediate (Bd2) in 23.7%, and high (Bd3) in 23.7% of cases. Tumour budding scores assessed as continuous and categorized variables were significantly associated with UICC/AJCC pT, pN, stage, and differentiation (all $p<0.0001$), and significantly correlated with lymphovascular invasion ($p=0.0002$), perineural invasion, and pattern of invasion ($p<0.0001$). TB was significantly associated with reduced overall survival (OS), disease specific survival (DSS), and disease-free survival (DFS), (all $p<0.0001$). The Cox analyses showed intermediate and high budding scores according to ITBCC to be an independent prognostic factor for OS (HR=5.18; 95%CI 2.61-10.56; $p<0.0001$), DFS (HR=4.22; 95%CI 2.39-7.46; $p<0.0001$), and DSS (HR=7.52; 95%CI 2.85-19.87; $p<0.0001$).
Conclusion: International Tumour Budding Consensus Conference scoring system represents a simple, reliable, and reproducible method to evaluate tumour budding in oral squamous cell carcinomas. Tumour budding, according to ITBCC criteria, showed to be an independent prognostic factor in resected oral squamous cell carcinomas, and its inclusion into the histopathological reporting guidelines should be considered.

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PS-18-013
Poorly differentiated thyroid carcinoma: a clinicopathological study
M. Johari*, K. Rabade, S. Rane, N. Mittal, M. Bal, A. Patil
*Tata Memorial Centre, Homi Bhabha National Institute, Mumbai, India

Background & objectives: Poorly differentiated thyroid carcinoma (PDTC) is an uncommon but aggressive thyroid cancer. Turin's proposal defines the diagnostic criteria; however, the MSKCC group has suggested alternative criteria. We present the clinicopathological features of PDTC cases diagnosed at our institute.
Methods: This is a retrospective study of all cases of PDTC diagnosed at our institute between January 2011 and July 2022, identified in pathology archives. All slides were retrieved and reviewed, and clinical details were obtained from electronic medical records. Cases fulfilling Turin's proposal were included in the study and were further analysed using MSKCC criteria (necrosis, ≥5 Mitoses 5/2mm square).
Results: Eighty-two cases were included in the study with the age range 18-77 years (mean 53.8 years), and a female-to-male ratio of 2.04:1. Thirty-eight of sixty-seven cases (56.7%) had metastasis at the initial presentation. The tumour size (available in 45 cases), ranged from 1.7-11 cm (mean 5.8 cm). Histologically, a differentiated component was associated with PDTC in 18 cases, capsule with invasion in 20 cases (focal in 5, extensive in 15), lymphovascular invasion (LVI) in 74 cases, and extrathyroidal extension (ETE) in 23 cases. Lymph node dissection was available in 45 cases, 14 of them had metastasis. Sixty-eight cases fulfilled MSKCC criteria and showed a higher incidence of LVI and ETE.
Conclusion: PDTC, a subset of high-grade follicular cell-derived non-anaplastic thyroid carcinoma, is a rare tumour, and there has been disagreement over its diagnostic criteria. While Turin's consensus criteria are the standard to define PDTC, several studies have shown MSKCC criteria to be equivalent to Turin's criteria. Our retrospective study of 82 cases is the largest series in the Indian subcontinent analysing clinicopathological parameters in PDCT, along with the correlation of MSKCC criteria with Turin's proposal.

PS-18-014
HMGA2 immunoexpression in epithelial myoepithelial carcinomas
A. Kakkar*, S. Saifi, R. Kumar
*All India Institute of Medical Sciences New Delhi, India

Background & objectives: A proportion of epithelial myoepithelial carcinomas (EMCs) have been proven to originate from pre-existing pleomorphic adenomas (PAs), which harbor rearrangements in *PLAG1* and *HMGA2* genes. We aimed to assess a cohort of EMC for HMGA2 immunostaining and *HMGA2* gene rearrangements.
Methods: Cases of EMC diagnosed between 2014 and 2023 were retrieved. Histomorphological features were reviewed for evidence of pre-existing PA. Immunohistochemistry was performed using HMGA2 rabbit monoclonal antibody in a dilution of 1:800. Unequivocal nuclear staining of moderate to strong intensity was considered as positive. Fluorescence in situ hybridization (FISH) was performed using HMGA2 break apart probe.
Results: Nineteen EMC cases were included. Of these, nine had histological evidence of a pre-existing PA; two biopsies and three consult cases with a single block submitted could not be assessed for the same. Diffuse strong HMGA2 positivity was identified in six EMCs i.e. 31.6%. Two of the HMGA2 immunopositive cases showed evidence of a pre-existing PA. HMGA2 staining was not identified in five EMC cases known to have *PLAG1* rearrangements. *HMGA2* FISH was available in five cases: three showed rearrangement (60%), one (20%) showed amplification, and one had normal signal pattern.
Conclusion: A subset of EMCs harbour *HMGA2* rearrangements and show HMGA2 immunopositivity, supporting their status as carcinomas ex PA. Histological evidence of a pre-existing PA may or may not be evident. HMGA2 immunopositivity and gene rearrangement are mutually exclusive with *PLAG1* rearrangement in EMCs, similar to PA. Further genetic testing is indicated in the normal *PLAG1*/ normal *HMGA2* group of EMCs to ascertain the pathways to its pathogenesis.

PS-18-015
Nasal polyposis: clinico-histological factors of recurrence
S. Kanoun*, M. Triki, R. Hammami, C. Chaari, I. Charfeddine, T. Sellami Boudawara, S. Makni
*Department of Pathology, Habib Bourguiba University Hospital, Sfax, Tunisia

Background & objectives: Nasal polyposis (NP), a chronic benign inflammatory disease, often recurs post-treatment. The EPOS 2020 classification defines two polyposis endotypes based on tissue eosinophil infiltration that have distinct outcomes. This study investigates factors of post-surgical recurrence using the updated EPOS classification.
Methods: This was a retrospective study of 100 NP cases undergoing surgery at Habib Bourguiba University Hospital, Sfax, Tunisia from 2013 to 2020. Slide reviews identified parameters based on literature review, with tissue eosinophil percentages derived from ≥4 random high-power fields (×400), averaging multiple field percentages. We examined clinical and histopathological factors influencing post-surgical recurrence through univariate and multivariate statistical analysis.
Results: Univariate analysis showed that asthma ($p=0.003$), aspirin intolerance ($p=0.001$), Widal triad ($p=0.001$), tissue infiltration of polyps by eosinophils greater than 20% visualized by high-power field ($p=0.036$), and poor compliance with postoperative local corticosteroid therapy ($p=0.001$) were significantly associated with the occurrence of polyp recurrence after surgery. In multivariate analysis, the importance of tissue infiltration by eosinophils as a percentage ($p=0.014$) and poor

compliance with postoperative corticosteroid therapy (p=0.001) were independent factors associated with the occurrence of recurrence.
Conclusion: Elevated levels of eosinophils in histological samples may indicate an ongoing inflammatory process that could contribute to recurrence after surgery. Thus, it is important to classify the NP based on their endotype. Identifying patients at high risk of recurrence allows for the implementation of targeted preventive measures and personalized follow-up protocols, potentially improving long-term outcomes. In this context, clinical and histological parameters hold promise as prognostic tools.

PS-18-017
Verrucous carcinoma of the larynx - a clinical and pathologic study of 34 cases
W. Mokni*, Z. Nfikha, I. Bahri, N. Abdessayed, B. Sriha, M. Mokni
*Department of pathology, Farhat Hached University Hospital, Sousse, Tunisia

Background & objectives: Laryngeal verrucous carcinoma (LVC) is a rare variant of squamous cell carcinoma, representing 1,3% of all laryngeal carcinomas. It is characterized by exophytic growth and good outcome. The purpose of this study was to report our experience with this disease.
Methods: The databases of the Cancer Registry of Central Tunisia were used for the identification of patients. Clinical presentation, age, gender distribution, diagnosis, treatment, and outcome of 23 cases of LVC diagnosed between 1993 and 2023 were reviewed retrospectively.
Results: Our series included 34 patients aged between 30 and 84 years, with a mean age of 57.6 years. The sex ratio M/F was 33/1. They all presented with hoarseness. The most frequent site of origin was the glottis. Tumour size ranged from 0.7 to 4 cm. 10 patients underwent total laryngectomy with bilateral functional lymph node dissection. 4 cases of partial laryngectomy for pTis or pT1aN0 LVC were noted. No data available for the remaining 20. In patients with data available, 8 were staged as pT1aN0, 4 as pT3N0, 3 as pT4aN0, 1 as pT2N0 and 1 as pTis. Recurrence as a moderately differentiated SCC occurred in one case.
Conclusion: LVC presents different clinical, pathological, and survival outcomes when compared with classic laryngeal squamous cell carcinoma. In cases with no evidence of chorion invasion on biopsies, further resections are needed to differentiate LVC from squamous verrucous hyperplasia. The glottic location of most LVC leads to the detection of this lesion at its early stages. Surgery remains the gold standard of treatment. Future studies are needed to better understand the biology of LVC and its related prognostic outcomes.

PS-18-018
Salivary gland tumours are epigenetically regulated by THOR methylation
A. Paiva-Correia*, J. Apolónio, P. Castelo-Branco, H. Hellquist
*Faculty of Medicine and Biomedical Sciences, University of Algarve, Campus de Gambelas, Faro, Portugal

Background & objectives: The methylation of the hypermethylated oncological region (THOR) of human telomerase reverse transcriptase (hTERT) may forecast the aggressive behaviour of tumours. Our objective was to evaluate THOR as a biomarker of recurrence/malignant transformation of salivary gland pleomorphic adenomas (PA).
Methods: We analysed THOR methylation in 114 FFPE samples of parotid tumours and adjacent tissues, by quantitative pyrosequencing. Specific TERT promoter mutations (TPM) were analysed by Sanger sequencing. Samples were distributed in 7 cohorts (non-neoplastic parotid tissue, tissue adjacent to PA, PA tissue, tissue adjacent to recurrent PA (rPA), tissue from rPA, tissue adjacent to carcinomas, and carcinoma tissue).
Results: The overall THOR methylation status showed marked differences between the 7 cohorts. A significantly higher THOR methylation was found in malignant tissues when compared with non-neoplastic tissues and no difference was found between non-neoplastic tissue and benign tumours. On average, THOR methylation in rPA was closer to carcinoma than to normal tissue, was similar in rPA and tissues adjacent to rPA, and higher in adjacent tissues to carcinomas than in non-neoplastic tissues. A subset of PA shows adjacent tissue epigenetic alteration which might indicate that those are the ones prone to recur/develop malignancy (5-15 %). TPM were not found.
Conclusion: We showed, for the first time, that THOR methylation differentiates normal from carcinogenic tissue and may be viewed as a malignancy biomarker in parotid gland tumours. Epigenetic heterogeneity in PA was evidenced through identification of epigenetic alterations in a subgroup of PA adjacent tissues with normal histology. In fact, adjacent tissues to carcinoma, which look histologically normal, are not epigenetically normal but show THOR hypermethylation. Absence of TPM indicates that these tumours regulate telomerase expression mainly epigenetically rather than genetically.

PS-18-019
Diagnosing hyalinizing trabeculae tumour: a single institution experience
P. Radia*, L. Collins, I. Bagwan, P. Mitra, G. Hall
*United Kingdom

Background & objectives: Hyalinizing trabeculae tumour (HTT) is a rare, follicular cell derived neoplasm, considered low risk. We present the clinical, fine needle aspirate (FNA) and pathological findings of all HTT that presented at Guy's Hospital over a 17-year period.
Methods: We conducted a retrospective review of the Guy's Hospital NHS Foundation Trust Head and Neck pathology databases to identify any HTT diagnosed between 2007 and early 2024, including cases referred from external hospitals. For all cases, relevant clinical information, FNA diagnosis, radiological and pathological findings, treatment modality and follow up were obtained.
Results: We identified four patients who were diagnosed with HTT from a total of 87,132 head and neck / thyroid cases that were reported over this time period. All were women, between 48-77 years old (mean age 56.5 years old). The preoperative FNA diagnoses ranged from suspicious of malignancy (Thy4, n=2), to suggestive of a follicular neoplasm (Thy3f, n=1). In one case, the FNA diagnosis was Thy1 after multiple attempts, but the ultrasound was reported as U3/U4. All patients had background lymphocytic thyroiditis. The histological features were typical for HTT in all cases. Follow up shows no evidence of recurrence or locoregional disease. No further surgical or non-surgical treatment was performed.
Conclusion: HTT is an extremely rare thyroid neoplasm, classified as low risk with a favourable prognosis. Our findings highlight the difficulty in pre-operative diagnosis, in particular when the ultrasonographic features and fine needle aspiration cytology of HTT can resemble those of malignant thyroid tumours. Correct diagnosis is essential to ensure patients are not overtreated.

PS-18-020
A novel ultrasound-enhanced fine-needle biopsy method increases yield in vivo setting
M. Rehell*, M. Naukkarinen, Y. Le Bourlout, S. Ranjan, J. Kelppe, J. Rautava, J. Tarkkanen, T. Atula, H. Nieminen, K. Aro
*Department of Otorhinolaryngology - Head and Neck Surgery. University of Helsinki and Helsinki University Hospital, Finland

Background & objectives: Fine needle aspiration biopsy (FNAB) has limited cell/tissue fragment yield. Ultrasound-Enhanced FNAB (USeFNAB) utilises the same technical features as FNAB but adds

an ultrasonically vibrating needle tip with electric power. The method improves the sample mass by 2-6 times.
Methods: We included patients who underwent lymph node removal under general anaesthesia. The enlarged lymph nodes (N = 10) were sampled in vivo with 3 techniques: USeFNAB, FNAB, core needle biopsy (CNB). The samples were weighed and the yield, tissue area on the slide, and quality of the tissue fragments were quantified by two pathologists. Early and late complications were registered.
Results: On average, USeFNAB collected 49.76 mg, FNAB 36.18 mg, and CNB 5.76 mg. USeFNAB showed an increase in mass of 1.38x and 8.64x compared to FNAB and CNB, respectively. The tissue area on the slides increased 2.28x and 5.39x compared to FNAB and CNB. The sample quality remained good with all methods. There was a small hematoma in three lymph nodes immediately after sampling, but no subsequent complications were found.
Conclusion: USeFNAB provides considerably improved tissue yield compared to those obtained with FNAB or CNB. The quality of the USeFNAB samples remained the same as that of FNAB. USeFNAB brings the potential to improve the representativeness of the sample and the diagnostic accuracy. The method is safe in real clinical work.

PS-18-021
Molecular heterogeneity in mucosal melanoma of the head and neck region
C. Ricci*, L. Di Sciascio, D. de Biase, B. Corti, E. Pasquini, G. Molteni, A. Tarsitano, A.M. Baietti, L. Amorosa, A. D'Errico, M. Fiorentino, G. Tallini, D. Massi, S. Ihrler, M.P. Foschini
*Italy

Background & objectives: Limited data are available on the molecular profile of mucosal melanoma of the head and neck (MM-H&N) region. The aim of the study was to analyse a series of MM-H&N applying an in-house developed NGS panel for identifying targetable biomarkers.
Methods: In total, 57 samples of MM-H&N from 27 patients were collected and reviewed to confirm the diagnosis and exclude metastases. Cases were analysed using a multi-gene NGS panel comprising 28 genes involved in the melanoma pathogenesis. Molecular data were obtained from multiple/sequential samples (incisional biopsy, excisional biopsy of the primary tumour, residual tumour/relapses, metastases), when available.
Results: In 50/57 (87.7%) samples from 25/27 (92.6%) patients the material was suitable for NGS. Overall, a total of 25/50 (50%) samples showed a wild type (WT) status. The most frequently detected mutations involved RAS (KRAS and NRAS) (7/50, 14%), TP53 (3/50, 6%), KIT (3/50, 6%) and BRAF (3/50, 6%) genes; notably, all BRAF (p. Asn581Ile) mutated samples were from one patient with a long clinical history of relapsing desmoplastic MM-H&N, mixed-type (5 residual tumour/relapse). 4/11 (36.4%) patients with multiple/sequential samples and at least two suitable for NGS showed discordant molecular results: patient #1 (KRAS/TP53), patient #12 (WT/GNA11/NRAS), patient #21 (WT/BRAF), and patient #24 (WT/KIT).
Conclusion: Our data confirm the unique molecular profile with the predominant role of RAS family genes mutations in MM-H&N. Notably, a subset of patients with multiple/sequential samples showed discordant molecular results. These data suggest that NGS analysis of all available tissue samples may be required for the most appropriate therapeutic planning in MM-H&N patients.

PS-18-022
Detailed analysis of NANOG expression in head and neck precancerous and cancerous lesions: an approach using QuPath digital image analysis
Y. Sung*, S. Ahn, W. Oh, Y.J. Lee, J. Sim, Y. Kim
*Anam Hospital, Republic of Korea

Background & objectives: The grading criteria for head and neck (H&N) precancerous lesions is obscure, leading to low observer reproducibility. In this study, we performed NANOG immunohistochemical (IHC) staining on H&N dysplastic lesions and quantitatively evaluated their expression using QuPath digital image analysis.
Methods: Tissue from 68 patients diagnosed with oral/laryngeal dysplasia or invasive carcinoma was classified into four groups through a central review: normal (NL), low-grade dysplasia (LG), high-grade dysplasia (HG), and invasive carcinoma (CA). After performing NANOG IHC, the scanned IHC images were annotated by group. Subsequently, the intensity of NANOG expression for each group was quantitatively evaluated using QuPath.
Results: NANOG immunostaining revealed predominantly cytoplasmic staining patterns in both dysplastic and invasive carcinoma areas, but it also stained normal submucous glands and ciliated cells. Using the 'cell detection' tool in QuPath, the NANOG staining intensity (measured as mean optical density per cytoplasm; mOD) of cells within each group was evaluated. The results showed a gradual increase in mOD from NL through LG to HG, followed by a decrease in CA compared to HG (NL: 0.06 ± 0.02, LG: 0.09 ± 0.03, HG: 0.18 ± 0.08, CA: 0.16 ± 0.07). Significant differences in mOD were observed in the pairwise comparisons of NL- LG, LG-HG, and HG-CA ($P < 0.001$, all).
Conclusion: Currently, there is no established biomarker to aid in the grading H&N dysplastic lesions. In this study, to minimize tissue heterogeneity, cases diagnosed with dysplasia or cancer were annotated into NL, LG, HG, and CA groups through central review. Subsequently, we quantitatively confirmed differences in NANOG expression across these groups. Notably, the differences in NANOG intensity between the groups were also visually discernible. This suggests that NANOG IHC could enhance the accuracy and improve diagnostic reproducibility of H&N dysplastic lesions.

PS-19Poster Session Molecular Pathology

PS-19-001
Comparation between two different sequencing technologies using automated target enrichment based on hybrid capture in lung cancer samples
I. Abdulkader Nallib*, R. Pérez-Becerra, T. Pereira Ares, I. Lesende Rodríguez, J.R. Antúnez López, J. Cameselle Teijeiro, M. Sánchez Ares
*Department of Pathology, Clinical University Hospital of Santiago de Compostela, Health Research Institute of Santiago de Compostela, Galician Healthcare Service (SERGAS), Santiago de Compostela, Spain. School of Medicine, University of Santiago de Compostela, Santiago de Compostela, Spain

Background & objectives: Identification of genomic alterations from formalin-fixed paraffin-embedded (FFPE) samples using next-generation sequencing (NGS) is very important for cancer-targeted therapy today. In order to achieve a higher efficiency, we compared the sequencing metrics of the DNBSEQ-G99 (MGI) with the NextSeq550 (Illumina).
Methods: DNA from 240 FFPE samples of lung cancer was extracted, and libraries were prepared using the SureSelect XT HS Target Enrichment system using the Magnis NGS Prep System (Agilent Technologies) following the manufacturer's protocol. The same libraries were sequencing in both instruments and the variants and metrics were compared using the same in house bioinformatic pipeline.
Results: The same molecular alterations were detected in both platforms. Sequencing time is lower in the DNBSEQ-G99 than in the NextSeq550 for a 2x75 bp run (6 hours vs 18 hours). Nevertheless, for MGI assay it was necessary to use the conversion kit from MGI to make the final libraries compatible with the DNBSEQ-G99, which meant 5 more hours until obtaining the DNA nanoball for sequencing. Illumina

platform only needs an additional half an hour for the denaturalization of the libraries before sequencing. The duplicate ratio was highly variable from 15% to 60% depending on the DNA input. The average duplicate ratio was 34.3% for DNBSEQ-G99 and 39.6% for Nextseq550.
Conclusion: Our study demonstrates the fully compatibility between the Magnis and the DNBSEQ-G99. These results suggest that the performances of the DNBSEQ-G99 platform is comparable to that of the Illumina NextSeq550 platform and support the potential applicability of the DNBSEQ-G99 in precision oncology. We also show a slightly improvement increasing the number of data available for analysis and allowing a shorter turnaround time for diagnosis.

PS-19-002
Excellent inter-rater agreement between pathologists in reporting morphological characteristics of frozen tumour tissues in a multicentric international cancer genomic study
B. Abedi-Ardekani*, G. Roshandel, A. Nikmanesh, F. Ghasemi-Kebria, M. Sotoudeh, F. Azmoudeh-Ardalan, H. Saffar, S. Serra, J.Y. Scoazec, S. Ferlicot, V. Gaborieau, P. Brennan
*Int Agency for Research on Cancer (IARC/WHO), France

Background & objectives: Genomic studies prioritize frozen tissues that are challenging for pathologists. We report a successful pathology workflow of frozen tissues and the agreement between pathologists for rating tumour characterizations and purity in one of the largest international cancer genomic studies.
Methods: 4000 frozen tumour tissues of seven cancers are whole genome sequenced in the Mutographs project (https://www.mutographs.org/) after pathology evaluation led by the International Agency for Research on Cancer (IARC/WHO) with six external pathologists. Inter-rater agreements were measured by the Cohen's Kappa Coefficient (K) and the Intraclass Correlation Coefficient (ICC) and their 95% confidence intervals (CI) for tumour type and tumour purity, respectively.
Results: Of 6,374 processed frozen cancer tissues, 35.5% were excluded for whole genome sequencing following microscopic evaluation by pathologists based on the predefined inclusion and quality criteria. Our findings showed high agreement between pathologists who independently evaluated the quality and microscopic features such as tumour type and grade, and percentage of cellular elements of the same tumour tissue, by applying digital pathology (K=0.86; 95%CI: 0.80 - 0.91). The agreement of non-simultaneous report of the tumour type on frozen and FFPE tissues by the same pathologist was 0.77 (95% CI: 0.75 - 0.79). We also found an excellent agreement between pathologists for rating tumour purity in frozen tissues (ICC=0.75;95% CI 0.72-0.77).
Conclusion: Our data demonstrate the critical role of pathologists in cancer genomic studies. Regardless of incurred freezing artifacts imposing more difficulties in microscopic evaluation of frozen tissues, our results showed the importance, feasibility, and reliability of assessing tumour characteristics of frozen tissues as well as estimating tumour purity in high agreement between pathologists. Such evaluation prevents performing sophisticated expensive genomic analyses on low quality tissues. This success owes an excellent well-structured and organized teamwork between pathologists in this complex study.

Funding: Mutographs project funded by Cancer Research UK (CRUK), cancer grand challenges program.

PS-19-003
Single-nucleotide polymorphism (SNP) analysis as a valuable ancillary tool for the diagnosis of biliary duct carcinomas
E. Albertini*, T. Maloberti, L. Miranda, A. D'Errico, D. de Biase, F. Vasuri
*IRCCS Azienda Ospedaliero-Universitaria di Bologna, Italy

Background & objectives: The pathological diagnosis of extrahepatic bile duct malignancies is often made difficult due to the scarcity of material available. Our aim was to apply a new technique of multiple single-nucleotide polymorphism (SNP) analysis as a diagnostic help for pathologists.
Methods: Fourteen paraffin embedded ERCP biopsies were selected, 5 morphologically positive for infiltrative biliary carcinoma, 9 negatives. Chromosomal aneuploidy and chromosomal partial loss of heterozygosity(pLOH) were evaluated using a laboratory developed NGS panel targeting 1800 SNPs throughout the entire genome. SNPs with an allele frequency (VAF) between 40 and 60% were considered "stable", while SNPs with a VAF <40% or ≥60% were considered "unstable".
Results: The most represented unstable chromosomes were Chr. 6, 10, 17 (nr. 4 cases each), followed by Chr. 3, 11, 20, 21 (nr. 3). Other recurrent pLOHs were observed in Chr.1, 5, 9, 12, 18 and 22 (2 positive cases each). Four out of five (80%) positive cases showed aneuploidy and the fifth one had pLOH in chr. 11 and 20. The most frequently aneuploid chromosomes were chr. 3, 6, 21 and 22 (50% each). Other aneuploid chromosomes were chr. 9, 10 and 18 (25% each). Aneuploidy was never found in negative cases, with 100% specificity and 80% sensibility. pLOH was observed in some benign cases instead, showing no diagnostic specificity.
Conclusion: SNPs analysis can be a valuable alternative to FISH in the analysis of bile duct biopsies, intercepting frequent alterations different from the canonical chr. 3, 7, 9 and 17 abnormalities. The NGS analysis allows also to couple the SNPs study with the assessment of the mutational status, providing highly informative results. On the other hand, we found that pLOHs are present also in benign epithelium: SNPs instability configuring aneuploidy, but not pLOH, helps pathologists in the diagnosis of biliary carcinomas.

PS-19-004
Prevalence and clinical impact of the tight junction protein claudin-3: a tissue microarray study involving more than 14,000 samples from 133 human tumour types
S. Büyücek, F.B. Ergüven, N. Gorbokon, N. Schraps, M. Lennartz, F. Viehweger, F. Lutz, E. Bady*, G. Sauter, R. Simon, M. Kluth, S. Steurer, S. Minner, T.S. Clauditz, M. Freytag
*Institute of Pathology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

Background & objectives: Claudin-3 is a tight-junctions protein regulating intercellular permeability. Altered claudin-3 has been linked to tumour progression in multiple tumour types and considers an attractive drug target candidate. However, systematic studies are lacking.
Methods: To comprehensively determine the prevalence of claudin-3 expression in cancer, a tissue microarray containing 14,966 samples from 133 different tumour types and subtypes as well as 608 samples of 76 different normal tissue types was analysed by immunohistochemistry.
Results: Claudin-3 immunostaining was observed in 7,919 (67.4%) of 11,753 analysable tumours, involving 96 of 133 tumour categories. Claudin-3 positivity was most frequent (≥95% of sample positive) in adenocarcinomas (uterus, ovaries, breast, thyroid gland, prostate, lung, cervix, and colon), and in neuroendocrine tumours/carcinomas of various origin. Less frequently positive tumour types included clear cell renal cell carcinomas (RCCs) (69.9-97.1%), pancreatic adenocarcinomas (67.0%), urothelial cancers (22.8-63.8%), and squamous cell carcinomas of various origin (4.5-43.2%). Reduced claudin-3 expression was strongly linked to adverse tumour features and poor outcome (p=0.02 each) in clear cell RCC. In non-invasive urinary bladder cancers, claudin-3 expression increased from low (1.3%) to high grade (17.4%, p<0.0001).
Conclusion: Claudin-3 is abundantly expressed in most tumour types of epithelial origin. The clinical impact of claudin-3 expression

depends on the tumour type. While loss of claudin-3 expression parallels progression and adverse prognosis of renal cell cancers, claudin-3 upregulation is linked to development of high-grade disease in non-invasive urinary bladder cancer.

PS-19-005

Early insights gained in Canadian non-small cell lung cancer biomarker testing following the introduction of a novel integrated biomarker external quality assurance scheme

K. Bisson*, A. Beharry, J. Garratt, J. Won, B. Sheffield
*Department of Laboratory Medicine - William Osler Health System, Canadian Pathology Quality Assurance - assurance qualité canadienne en pathologie (CPQA-AQCP), Canada

Background & objectives: Ensuring timely access to high quality and easily interpretable biomarker reports is fundamental in oncology. Towards improving equitable access to biomarker testing across Canada, we developed an integrated approach to biomarker quality assurance assessing accuracy, turnaround time and report clarity.
Methods: Three challenge specimens were made using non-small cell lung cancer (NSCLC) tissue and paired with clinical vignettes to mimic referred-in cases. Participants were to provide all required molecular testing (immunohistochemistry, gene sequencing, etc.) and submit final reports for each case once completed. Reports were assessed by molecular pathologists and medical oncologists who recommended a treatment based on vignettes and reports.
Results: Thirteen Canadian laboratories participated in this exercise. Overall biomarker testing accuracy was achieved with one exception. The turnaround time ranged from 5-57 (median 25) calendar days. Only two laboratories (15%) submitted reports within 2 weeks. Four laboratories (31%) resulted their biomarkers in more than a month. Only three of thirteen laboratories (23%) received an optimal status wherein they provided timely (<21 days), accurate and easily interpretable biomarker reports leading medical oncologist assessors to gold standard treatment. One laboratory (8%) failed due to a critical incorrect *EGFR* result in case 1, three (23%) received a suboptimal status due to inappropriately long turnaround times and the remaining (69%) received an adequate status.
Conclusion: This report summarizes the valuable insights gained from the first NSCLC exercise following a novel approach to biomarker testing external quality assurance in Canada. Through assessment beyond analytical accuracy, including specimen management, reporting clarity and overall turnaround time, significant quality gaps were identified. Ongoing external quality assurance in this style will help laboratories identify performance concerns in comparison to other laboratories, in the hopes of improving their overall quality and remediate these observed gaps.

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PS-19-006

The structure of germline variants in pancreatic cancer in Moscow patients

T. Yanova, A. Danishevich, N. Bodunova*, M. Byakhova, V. Galkin, M. Makarova, S. Gadzhieva, D. Isaeva, I. Khatkov
*Moscow Clinical Scientific Center named after A.S. Loginov, Russia

Background & objectives: Pancreatic cancer (PCa) has a multifactorial etiology, approximately 10-15% of patients have some genetic predisposition. PCa is often detected at advanced stages and therefore may have limited therapeutic approaches. Genetic testing has the potential to change surveillance and treatment practices.
Methods: Blood samples from 39 patients with pancreatic cancer who underwent examination and treatment at The Loginov Moscow Clinical Scientific Center were analysed. The average age was 63 years (42-84 years). All patients underwent genetic, psychologist's counselling, whole genome sequencing (WGS). WGS was performed to identify clinically significant genetic variants associated with PCa and other hereditary diseases with similar phenotypic manifestations.
Results: In the group of patients with PCa, the detection rate of germline mutations was 28.2% (11 out of 39). According to our study results, pathogenic variants in the following genes were detected in the examined patients: NBN (chr:8g.89971214del), BLM (chr15:g.90761015C>T), SEC23B (chr20:g.18543095C>T), NTHL1(chr16:g.2046238 G>A), MUTYH (chr1:45332803T>C), ATM (chr11:g.108312424G>T); likely pathogenic - CHEK2 (chr22:g.28695219G>A), MSH3 (chr:g.80670157 C>T); and variants of uncertain clinical significance MEN1 (chr11:g.64805655G>A), MLH3 (chr14:g.75048943T>G), APC (chr5:g.112840896A>G), BARD1 (chr2:214745742-214745744del). Some genes are known to be associated with the development of PCa, while the association with others remains unclear.
Conclusion: The performed WGS analysis allowed to identify mutations associated with hereditary tumour syndromes. For the ATM, BRIP1 genes, an association with the development of pancreatic cancer is known, while other genes need to be studied. According to the literature, the most common hereditary syndromes with increased risk of PCa - BRCA1/2 - associated cancer (20%). However, no variants in BRCA1/2 were identified in our study. Our results will contribute to the study of the hereditary nature of PCa.

PS-19-007

Increased MAL2 expression confers poor prognosis in women with triple-negative breast cancer

J. Borowczak*, M. Maniewski, M. Zdrenka, W. Socha, K. Gostomczyk, H.A. Andrusewicz, J. Łysik-Miśkurka, T. Nowikiewicz, Ł. Szylberg, M. Bodnar
*Clinical Department of Oncology, Oncology Center in Bydgoszcz; Center of Medical Sciences, University of Science and Technology in Bydgoszcz, Poland

Background & objectives: Triple-negative breast cancer (TNBC), due to its lack of hormonal and HER2 receptors, shows inherent resistance to most therapies. MAL2 overexpression may confer treatment resistance, including anti-PD-L1 agents. This study explores the role of MAL2 in TNBC patients' prognosis.
Methods: 111 samples were collected from 73 patients with TNBC and stained for MAL2 and PD-1 expression. Patients' clinical data, including follow-up time, overall survival and clinicopathological features of TNBC were collected. The analysis was expanded by including data extracted from The Cancer Genome Atlas (TCGA).
Results: We found no correlation between MAL2 expression, clinicopathological features of TNBC, and PD-1 expression. High MAL2 expression was associated with lower 5-year survival rates (71.33% vs. 89.59%, $p = 0.02$). Lymph node invasions, disease recurrence, and low MAL2 (HR 0.29 [CI95% 0.087 - 0.95]; $p<0.05$) predicted longer patients' survival. In the TNBC TGCA cohort, patients with high MAL2 expression had significantly higher 5-year survival (87.25% vs. 55.45%, respectively). In this group, high MAL2 expression was an independent prognostic factor of shorter patient survival. The results from the TCGA cohort aligned with the TMA cohort results.
Conclusion: MAL2 is overexpressed in TNBC, and high MAL2 predicts unfavourable prognosis in triple-negative breast cancer independently of PD-1 levels and TNBC clinicopathological features. While we found no direct correlation between the expression of PD-L1 and MAL2, both proteins partake in tumour immunoregulation and may be intertwined in mediating tumour immunity. Considering its role in tumour immune escape and therapy resistance, targeting MAL2 appears

to be a promising therapeutic target, Nevertheless, its clinical utility needs to be verified in further trials.

PS-19-008

BRCA1/2 testing in prostate cancer: adequacy of presurgical biopsies and surgical resections

R. Bruno*, A.M. Poma, G. Alì, L. Galli, E. Sammarco, M. Pacini, R. Bartoletti, C. Ugolini, P. Faviana
*Unit of Pathological Anatomy, University Hospital of Pisa, Pisa, Italy

Background & objectives: Metastatic castration-resistant prostate cancer (mPC) harbouring BRCA1/2 alterations may respond to PARP inhibitors. BRCA1/2 testing is recommended on tumour tissue to identify both germline and somatic variants. We aimed to evaluate feasibility of BRCA1/2 testing on presurgical biopsies and resections.
Methods: BRCA1/2 testing was performed on 37 consecutive mPC. DNA was purified from formalin-fixed paraffin-embedded presurgical biopsies and macrosections from resections. DNA was evaluated using a fluorometer and a quantitative real-time PCR assay. NGS test was performed by an amplicon-based gene panel on Ion-Torrent platform. Two-way ANOVA with post-hoc t-test was used to assess effect of sample characteristics on NGS test.
Results: Fourteen presurgical biopsies and 23 resections were included. Two pathogenic variants (7.14%) and two variants of unknown significance (VUS) in BRCA2 and two VUS in BRCA1 were identified. Overall, 29.7% of cases failed the test; more than 90% had a 3-to-5-year storage time. Biopsies failure rate was 21.4%, 12 samples (85.7%) had a 3-to-5-year storage time with a 16.6% failure rate. Resection failure rate was 39%, 18 samples (78.26%) had a 3-to-5-year storage time with a 50% failure rate. As expected, DNA fragmentation differed between biopsies and resections; however, DNA fragmentation significantly dropped after 3 years only in surgical resections ($p=0.04$).
Conclusion: BRCA1/2 testing is mandatory for mPC and should be performed on tumour tissue. However, progression occurs after several years; macrosections are required for histological diagnosis and metastasis biopsy is mostly unfeasible. Tissue storage time and fixation procedures can increase DNA degradation, with macrosections undergoing over-fixation more frequently than standard blocks. Although preliminary, our results suggest that presurgical biopsies, even if not fully representative of the entire tumour, may be considered for BRCA1/2 testing, especially when DNA from resections is inadequate.

PS-19-009

QIAGEN clinical decision support software provides rapid and accurate interpretation of gBRCA variants in a clinical lab setting

K. Bungartz*, R. Salazar, B. Turner
*QIAGEN Digital Insights, Germany

Background & objectives: PARP inhibitors target cancers with deficiencies in homologous recombination repair pathways and are of clinical importance for tumours harbouring BRCA mutations. QIAGEN Digital Insights (QDI) conducted a study to identify patients who may benefit from PARP inhibitor treatment.
Methods: In collaboration with select pharmaceutical companies, QDI identified ten diagnostic laboratories within Europe conducting routine gBRCA NGS analysis and onboarded them to QIAGEN Clinical Insight Interpret (QCII), QIAGEN's clinical decision support software (CDS) platform. Each lab conducted a minimum of 48 retrospective germline analyses using QCII and compared time and accuracy of analysis with existing in-house methods.
Results: A total of 553 tests were completed in the study. QCII was reported to save time for 72% of the tests. Moreover, QCII provided automatic variant assessment that agreed with manual classification of variants in 93% of cases. In the majority of cases, QCII was estimated to save time even in the event of interpretation dispute. Of the 90 specific variant changes reported, 13 were downgraded from likely pathogenic or pathogenic (LP/P) and 3 were upgraded to LP/P by the user from the QCI I computed classification.
Conclusion: Based on study conclusion interviews, QCII is a CDS that saves labs time while providing reliable standardized variant assessment. A number of partner sites are currently considering incorporating QCI I into their routine NGS interpretation workflow.

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PS-19-010

MLH1 loss as secondary hit, a pan-cancer analysis of The Cancer Genome Atlas (TCGA) data

S. Burgermeister*, L. de Leval, E. Missiaglia
*Institute of Pathology, Department of Laboratory Medicine and Pathology, Lausanne University Hospital and University of Lausanne, Switzerland

Background & objectives: Alterations in the DNA mismatch repair genes, including MLH1, lead to a microsatellite instability (MSI) phenotype and high tumour mutational burden (TMB). We investigated the impact of deletion of MLH1 locus on tumour TMB, when combined with other driver alterations.
Methods: Mutations, copy number variations (CNV) and clinical information from 6348 solid tumours, (including lung, breast, kidney, colorectal, etc.) were obtained from TCGA. Samples were separated based on MLH1 mutation and/or CNV status. Presence of driver alterations occurring in tumour suppressor genes (TSG) located in the 3p arms was assessed. Non-synonymous TMB was compared between those groups.
Results: 90 cases presented with MLH1 copy number alterations (CNAs). The median TMB in tumours with a biallelic deletion of MLH1 locus was significantly lower than in those with a monoallelic deletion and a pathogenic mutation of the MLH1 gene (classic MSI) (2.6 vs 28.7, $p<0.001$). Among the former group, 41% (24/58) showed a concomitant pathogenic mutation on TSGs located in the 3p arms, namely VHL, SETD2, BAP1 or PBRM1, as well as deletion of the second allele of the TSG. This proportion of driver alterations in TSGs was significantly higher than in the classic MSI group (13% 2/15, $p<0.05$).
Conclusion: Our study supports the hypothesis that a subset of tumours showing biallelic deletion of MLH1 locus might be the result of a late event, occurring upon loss of the 3p arm as second hit on other TSG driver mutations. This is supported by the lower TMB, and higher proportion of mutations in TSG located nearby MLH1 gene. This event is probably not a main driver in the tumorigenesis of those tumours and may have clinical implication for immunotherapy stratification.

PS-19-011

Hereditary cancer syndromes in Moscow patients with malignant neoplasms: WGS project results

M. Byakhova*, M. Makarova, A. Semenova, M. Nemtsova, D. Chernevskiy, O. Sagaydak, M. Belenikin, N. Bodunova, A. Danishevich, I. Khatkov, D. Kanner, A. Shabunin, D. Protsenko, V. Galkin, S. Gadzhieva
*City clinical oncology hospital No. 1, Russia

Background & objectives: Between October 2022 and March 2024, as part of a scientific project, 1800 WGS were performed for patients with malignant neoplasms: breast, ovarian, pancreatic, endometrial, gastric, colorectal cancer, and neuroendocrine tumours.
Methods: 1800 patients with malignant neoplasms and suspected (HCS) whole genome sequencing (WGS) were performed. WGS: 30x, PCR-free protocol, DNBseq-T7, EVOGEN LLC; bioinformatics analysis accelerators: EVA Pro, EVOGEN, Russia; MegaBOLT, MGI, China. The variant classification was made according to

ACMG criteria. Sanger sequencing validation for all significant findings (446 samples, 515 variants).
Results: According to the results of 1800 WGS, pathogenic variants were identified in 310 patients (17.2%), likely pathogenic – in 51 (2.8%), variants of uncertain clinical significance – in 122 (6.8%), potentially clinically significant structural variants (copy number variation, deletions) – in 21 (1.2%). Thus, significant variants were identified in 21.2% of patients. Among the most significant identified HCS, causing a high risk of cancer of various localizations, one should highlight 219/1800 (12.2%) cases: hereditary breast and ovarian cancer (BRCA1, BRCA2, PALB2), Lynch syndrome (MLH1, MSH2, MSH6, PMS2), adenomatous polyposis syndrome (APC), Cowden syndrome (PTEN), Li-Fraumeni syndrome (TP53), melanoma and pancreatic cancer syndrome (CDKN2A), Hippel-Lindau syndrome (VHL), neurofibromatosis type I (NF1).
Conclusion: WGS is an important instrument to discover causative genetic variants in patients with different malignant neoplasms, to develop and implement personalized programs for the treatment and early detection of cancer. Grants: Moscow Department of Health financial support

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PS-19-012
Intra-tumour heterogeneity: demonstrating the importance of robust tissue validation for use in External Quality Assessment (EQA)
M.H. Cheetham*, N.L. Wolstenholme, S.J. Patton
*EMQN CIC, United Kingdom

Background & objectives: Intra-tumour heterogeneity (ITH) is well described; sub-populations of cells with distinct genomic and phenotypic alterations exist within the same tumour. This is important to characterise, where present, when providing an EQA scheme using patient tumour tissue to ensure accurate assessment.
Methods: In 2023, EMQN sent three FFPE samples to participants of its 'PIK3CA testing in breast cancer' EQA scheme for genotyping and reporting of clinically actionable PIK3CA variants using their routine methodologies. One of the patient-derived tumour tissue blocks was provided by a local biobank and sectioned in-house to generate 150 x 10uM curls, one for testing by each participant.
Results: Previous genotyping of this tumour indicated that there were not clinically actionable PIK3CA variants present. Recent validation of two FFPE curls from the block confirmed this. One-hundred and thirty laboratories returned results to EMQN for analysis and assessment. This analysis involved 'mapping' genotypes submitted - each FFPE curl tested had a unique identifier defining its vertical position within the tissue block. The majority of participants reported a PIK3CA 'wild type' result as expected, but areas of tumour heterogeneity were noted by the presence of two different clinically actionable low-level PIK3CA variants as reported by participants. This was demonstrated and visualised by use of a 'heat map'.
Conclusion: Whilst tumour heterogeneity is well researched and is documented in the literature, we present clear and unique evidence of it through EQA scheme participation data. Implications for patients may need to be considered where licensed therapeutics are available. However, with the advent of liquid biopsy testing, a comprehensive picture of the tumour's genetic landscape is more easily accessible, thus enabling faster, clearer treatment decisions and outcomes for patients.

PS-19-013
KRAS-mutated non-squamous non-small cell lung cancer. Comprehensive analysis of co-mutations and PDL1-expression
V. Cristóbal Redondo*, V. Pedrero Castillo, R. Roca, S. Ortuño, N. Martínez-Banaclocha, C. Alenda González, I. Aranda López
*Dr.Balmis General Universitary Hospital of Alicante. Department of Pathology. Institute for Health and Biomedical Research, Alicante, Spain

Background & objectives: Recent advances have drastically changed the treatment landscape for KRASG12C-mutated non-small cell lung cancers, renewing interest in KRAS oncogenic driver and its variants. The aim of this study is to explore KRAS and KRASG12C co-mutations, PDL-1 expression and clinicopathological features.
Methods: Genomic alterations were identified by NGS (Oncomine Comprehensive Assay, 161 unique cancer driver genes) in 523 patients from our Institution, 372 non-squamous non-small cell lung cancers (NS-NSCLC). Medical records and histopathological data were retrospectively reviewed. PDL-1 was available in 296. Cases were stratified into KRAS and KRASG12C-mutated. Results were correlated and significant differences were calculated with $\chi 2$ or Fisher's tests.
Results: KRAS mutation was detected in 143/372 (38.4%), 89 males (62.2%) and 54 females (38.8%), with a median age of 64 years. Statistical analysis showed a significant difference in tobacco smoking (medium/heavy smokers, defined as $\geq$ 15 pack-years, p=0.001), stage (advanced disease, p=0.012) and PDL1 expression (higher, p=0.025). TP53 (42.7%), STK11 (12.6%), SMARCA4 (11.9%), ARID1A (8.4%) and NOTCH3 (7%) were the most frequent co-occurring mutations. EGFR was found in only one case (0.7%), ALK in 2.1% and ROS1 in none. KRASG12C was the most common variant identified (64 cases; 44.8%). KRASG12C-mutated patients had lower levels of smoking (p=0,006) and a lower tendency to have mutations in MAP2K2/MEK, P53, NF1 and SETD2.
Conclusion: Our study confirmed that KRAS and P53 were the most frequent mutations in NS-NSCLC. Within KRAS-mutant cohort, we observed a lower degree of smoking in KRASG12C, which was the most common KRAS-subtype detected, and remarkable variations in PDL1 expression and co-mutations (P53, STK11, SMARCA4 or ARID1A). These findings may explain the different biological behaviours. A better understanding of KRAS co-mutations is essential for an adequate therapeutic approach, such as immunotherapy or KRAS specific inhibitors.

PS-19-014
Retrospective assessment of the usefulness of comprehensive genomic analysis for identifying targetable therapeutic options for solid tumours
A.B. Csepregi*, Z. Melegh, L. Báthory-Fülöp, T. Strausz, M. Szőke, Z. Küronya, E. Soós, E. Tóth
*National Institute of Oncology, Hungary

Background & objectives: Comprehensive genomic analysis (CGA) is becoming an increasingly accessible option for the clinical management of solid tumours. Our aim was to assess the usefulness of an extended molecular genetic panel, concentrating on finding targetable therapeutic options for advanced solid tumours.
Methods: We performed CGA using the Oncomine Comprehensive Assay Plus on 232 different solid tumours over a period of two years (2022-2023). The analysis included more than 500 unique genes for single-gene and multigene biomarker insights. Genomic DNA and total RNA were extracted from formalin-fixed paraffin-embedded tissue blocks. Next-generation sequencing was performed on a Thermo Fisher Ion S5 platform.
Results: Among the 232 solid tumours assessed, 19 (8.2%) had targetable mutations. In 6 patients, mutations suitable for on-label therapy were identified, while in another 13 patients, we found mutations suitable for off-label therapy. Based on our results, on-label therapy was initiated in one patient, and off-label therapy was initiated in 3 patients. The patient who received on-label therapy (lung adenocarcinoma, MET inhibitor therapy) died of the disease. Two patients who

received off-label therapy (extrahepatic cholangiocarcinoma, HER2 inhibitor therapy; dedifferentiated liposarcoma, CDK4/6 inhibitor therapy) are still alive. The third patient (embryonal carcinoma of the testis, MET inhibitor therapy) died of the disease.
Conclusion: Our study aimed to assess the usefulness of an extended panel from the perspective of targetable mutations in solid tumours. We detected targetable mutations in 8.2% of the patients. However, all the mutations detected in our study are included and therefore detectable by smaller 50 or 160 gene panels, such as Oncomine Focus or Comprehensive Assay v3. Hence, we believe, an extended panel may have little advantage over smaller panels if we consider solely their ability to detect targetable mutations.

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PS-19-015
mRNA gene-based models fail to predict breast cancer metastases to axillary lymph nodes: a negative study
L. Dalton*
*Dalton Pathology Research, USA

Background & objectives: A pertinent question is whether a contemporary gene-based model can predict lymph node involvement in breast cancer, potentially altering surgical strategies and overall treatment options. Additionally, embedded feature selection might identify genes associated with increased metastatic potential.
Methods: mRNA expression in three breast cancer datasets was studied: N=3114 Sweden Cancerome Analysis Network (SCAN); N=1895 METABRIC and N=749 TCGA. Three datasets yielded 6 permutations of train/test. With genes as predictors and lymph node status (LNS) as label, gradient boosting was used to build predictive models (R xgboost). For comparison, grade was also evaluated. Datasets had 15,900 genes in common.
Results: Area under curve (AUC) of receiver operator curves was the favoured performance metric. With LNS as response variable the 6 possible inter-institutional train/test permutations had AUC's ranging from 0.51-0.55 (median=0.535). AUCs in this range are in keeping with coin flips. The AUCs for grade ranged from 0.65-0.90 (median=0.845). Genes having highest variable importance in prediction of LNS included: EPN3, HOXC10, SNX1, LNPEP, PDCD1LG2, and BCL2A1. None corresponded to individual AUC's exceeding 0.55. A literature review selection FOXC1 also had AUC<0.55 in all datasets. For grade, the gene having highest variable importance was AURKA in both TCGA and METABRIC. The AUC for AURKA was greater than 0.77 for all 3 datasets.
Conclusion: Gradient boosting is highly regarded for building prediction models. Here, the "positive" results with respect to grade prediction was supportive. The negative results are blamed on the genes. Numerous studies have claimed that specific gene expressions indicate increased metastatic potential. In this study, none answered the call. Clearly, outlining the complexities of cancer spread to neighbouring tissues, let alone distant sites, will be extremely difficult. Additional studies of what doesn't work might be helpful. mRNA expression was not helpful.

PS-19-016
Molecular genotyping on liquid biopsies for assessment of resistance mechanisms to osimertinib in patients with EGFR-mutated non-small-cell lung cancer
I. Demidova*, A. Barinov, A. Gorokhov, E. Reutova, F. Moiseenko, K. Laktionov
*Moscow City Oncology Hospital 62, Russia

Background & objectives: Resistance to Osimertinib in advanced EGFR-mutated non-small-cell lung cancer (NSCLC) is a challenge either in terms of molecular diagnosis or in therapeutic management. Understanding of the main resistance mechanisms is a critical step to define optimal treatment strategy.
Methods: This is a retrospective analysis on a cohort of consecutive patients treated with Osimertinib for an advanced EGFR-mutated NSCLC both in first- or second-line setting. Next-generation sequencing (NGS) analysis was conducted for plasma samples of patients at the time of progression. We performed concordance analysis between primary mutations in tissue and plasma and analysed possible mechanisms of secondary resistance.
Results: Sixty-two advanced EGFR-mutated NSCLC patients treated with Osimertinib in first- (n = 18) or in second line (n = 44) were included. We managed to perform successful NGS on liquid biopsies in 67.7% of patients who experienced progression. Acquired resistance mechanisms were classified as EGFR-dependent in 37.5% of patients, with high-level EGFR amplification (21%), EGFR C797S (9.3%), G724S (n = 2) and rare deleterious mutation of EGFR extracellular domain (NM_005228.5(EGFR): c.323G>A (p.Arg108Lys) . In seven patients (16%), we revealed EGFR-independent mechanisms: MET amplification (n=2), RAS/MAPK pathway mutations (n=3), ERBB2 amplification (n=1) and RET-CCDC6 fusion (n=1). The mean concordance rate between tissue and plasma for the primary EGFR activating mutations was 93%.
Conclusion: Resistance to Osimertinib demonstrated to be highly heterogeneous, with EGFR-dependent pathway aberrations as the main mechanism. Plasma genotyping is a relevant diagnostic tool, which might successfully substitute tissue analysis for the study of primary mutational status and acquired resistance.

PS-19-017
Spatial characterization of CD8+ tumour infiltrating lymphocytes in homologous recombination deficient and proficient high-grade ovarian carcinomas
E. Dorca*, S. Villatoro, A. Vidal, X. Matias-Guiu, M. Vaquero
*Hospital Universitari de Bellvitge, Spain

Background & objectives: Homologous recombination is a mechanism of DNA repair and a common event in ovarian carcinomas, harbouring better prognosis and response to platinum-based therapies and PARP-inhibition. The aim of this study is to characterize CD8+Tils distribution in HRD/HRP high-grade ovarian carcinomas.
Methods: 86 high-grade ovarian tumours have been identified, selecting an FFPE block and obtaining 8 scrolls x10um for DNA extraction and a tissue cut for CD8 immunostaining. HRD status has been determined with Myriad MyChoice-CDx-panel. Slides have been scanned at 40x. Semantic segmentation of tumour/stroma has been applied by using Qupath.v.04.3 (MLP algorithm) and "fast cell counts" for identification of CD + cells.
Results: A total of 86 cases have been analysed, 42 of which shown homologous recombination deficiency, while 38 proficiency and 6 were inconclusive. According to the spatial distribution of CD8 Tils (iTils/sTils), we have classified the tumours into 3 known immunophenotypes (16 Immune-infiltrated, 52 Immune-excluded and 18 Immune-Desert). Excluding the inconclusive cases we have found that HRD carcinomas are associated with higher intratumoural Tumour Infiltrating Lymphocytes (iTils) counts and a higher prevalence of Infiltrated immunophenotype (p-value of 0.05 and 0.027 respectively). TMB and BRCA1/2 mutational status have not shown statistical association with any concrete mmunophenotype and/or higher levels of iTils nor sTils.

Conclusion: Homologous recombination deficient carcinomas are correlated with high levels of intratumoural-CD8 lymphocytes, showing and therefore with an immune-infiltrated immunophenotype. Manual or computational-assisted morphological immunophenotyping of high-grade ovarian cancers could emerge as a potential surrogate biomarker for detecting those cases with high probability of harbouring HRD deficiency.

PS-19-018

Molecular diagnostics of undifferentiated round cell sarcomas

A. Druy*, A. Panferova, I. Sidorov, D. Konovalov
*D. Rogachev National Medical Research Center of Paediatric Haematology, Oncology and Immunology, Russia

Background & objectives: Undifferentiated round cell sarcomas with BCOR aberrations, CIC rearranged, and sarcomas with EWSR1-non-ETS rearrangements often present diagnostic challenges due to their rare occurrence and morphological similarity to Ewing sarcoma.
Methods: The study included 41 tumours with morphological diagnoses: undifferentiated round cell sarcoma, sarcoma with BCOR aberrations, CIC-rearranged sarcoma, sarcoma with EWSR1-non-ETS rearrangement, and Ewing sarcoma without EWSR1:FLI1 and EWSR1:ERG. All samples were tested using RT-PCR for common EWSR1 and BCOR rearrangements, RNA sequencing and Nano string digital barcoding for gene expression profiling (GEP).
Results: Ten of 14 morphologically recognized BCOR-sarcomas harboured BCOR::CCNB3 fusion, two - BCOR ITD, and two failed to identify the molecular driver but clustered together with BCOR sarcomas in Nano string GEP assay. In 8 other cases initial diagnosis was changed to BCOR-sarcoma because of presents BCOR::CCNB3 (n=6), BCOR::MAML3, YWHAE-NUTM2B and corresponding GEP. Five of 19 samples diagnosed as CIC-sarcoma were confirmed by detection of CIC::DUX4 (n=3), CIC::NUTM2B, CIC::DUX4L28. Five additional cases had CIC-specific GEP. In 6 cases diagnosis was changed because of BCOR::CCNB3 (n=2), CRTC1::SS18, HEY1::NCOA2 and unspecific GEP (n=2). Three cases were not diagnosed due to poor quality of the material.
Conclusion: The results show that histological diagnosis for these tumours is challenging and requires molecular genetic verification. Nano string digital barcoding is a rapid and extremely effective method for detection of CIC-and BCOR-rearranged sarcomas because of highly specific GEP.

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PS-19-019

Prevalence and clinicopathologic features of driver mutations in follicular nodular disease

M. Errani*, L. Cardisciani, F. Chiarucci, E. Solaroli, A. Repaci, S. Coluccelli, T. Maloberti, A. De Leo, D. de Biase, G. Tallini
*University of Bologna School of Medicine, Bologna, Italy

Background & objectives: Follicular nodular disease (FND) is new terminology (WHO-2022) representing the pathologic correlate of multinodular goitre (MNG). The aim of this study is to characterize prevalence and histologic features of these nodules with clonal mutations in a contemporary series of cases.
Methods: One-hundred-sixteen unselected, thyroid nodules diagnosed as FND/MNG were retrieved from the anatomic pathology archive of Maggiore Hospital in Bologna (Italy). Mutational hot spots for the most relevant genes altered in thyroid tumours were analysed using a laboratory developed NGS panel. Blinded to molecular results, clinicopathologic features of all nodules were reviewed.
Results: Five cases were excluded because molecular analysis was unsatisfactory, five because they were reclassified as NIFTP. Overall, 21/106 (19.8%) nodules carried clonal driver mutations: H-RAS,3/106(2.8%); K-RAS,1/106(0.9%); N-RAS,9/106(8.5%); TSHR,3/106(2.8%); PTEN,2/106(1.8%); EIF1AX,2/106(1.8%); DICER1,1/106(0.9%). RAS (H-, K-, N-RAS) mutations occurred in 13/21 mutated cases (61.9%). Mutations (overall) correlated with: (i) micro follicles, p=0.03; (ii) nuclear atypia-quality (Nuclear score according to Nikiforov et al 2016), p=0.01; (iii) nuclear atypia-quantity (percentage of overall nuclear atypia), p=0.01; (iv) nuclear atypia-overall score (Nuclear atypia-quality value multiplied by nuclear atypia-quantity value), p<0.01; (v) papillary architecture, p=0.49 (not-significant). RAS mutations showed similar correlation with the above histologic features. No correlation was found between mutation and age, sex and tumour dimension.
Conclusion: Clonal driver mutations are not uncommon in nodules of FND, supporting the new "follicular nodular disease" term proposed by the WHO. All mutations identified are RAS-like or have been associated with follicular-patterned tumours. RAS mutations have the highest prevalence, but other mutations occur in small subsets of cases. Mutated nodules tend to display microfollicular architecture and/or nuclear atypia, which may have implications for preoperative diagnosis of thyroid nodules.

PS-19-020

Subclassification of atypical spitzoid tumours using a diagnostic algorithm based on the methylation status

J.F. González-Muñoz*, B. Sánchez-Sendra, C. Monteagudo
*Department of Pathology. Hospital Clínico Universitario of Valencia. Biomedical Research Institute INCLIVA, University of Valencia, Spain

Background & objectives: Current molecular techniques used to classify spitzoid tumours are not capable of predicting the clinical behaviour of Atypical Spitzoid Tumours (AST) in comparison to Spitz nevus (SN) and spitzoid melanoma (SM). DNA methylation may be useful for classifying spitzoid lesions.
Methods: Genomic DNA was obtained from 40 formalin-fixed paraffin-embedded (FFPE) tumour samples from patients with spitzoid lesions (12 SN, 19 AST and 9 SM). DNA methylation status was studied using Reduced Representation Bisulfite Sequencing (RRBS). Differential methylation analysis was performed for each individual cg site and a predictive model was constructed using independent logistic regression.
Results: 224 cg sites were differentially methylated between SN and SM. Using binary logistic regression, 7 cg sites (located in genes MYO1D, TEKT4P2 and PMF1-BGLAP) with a p-value<0.02 were used for the construction of a predictive algorithm. Methylation of these cg sites in SM was higher than in SN, but the AST methylation levels were scattered. The predictive algorithm classifies 100% of the SN and SM samples properly (100% sensitivity and specificity). The algorithm also allows the subclassification of AST according to their potential risk of clinical aggressiveness: 52.63% were classified as tumours behaving like an SN, whereas 47.37% were classified as behaving like an SM.
Conclusion: Based on the methylation status of seven cg, we propose a diagnostic algorithm with high predictive power to properly classify SN and SM, predict the risk of AST according to their similarity to the methylation levels of benign and malignant spitzoid tumours and, therefore, anticipate the potential clinical outcome of these patients.

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PS-19-021

Prevalence of MTAP deficiency in human cancer: a tissue microarray study on 17,078 cancers from 149 different tumour types

N. Gorbokon*, K. Teljuk, N. Schraps, K. Möller, S. Büyücek, M. Lennartz, F. Viehweger, C. Fraune, C. Bernreuther, S. Steurer, R. Simon, G. Sauter, F. Lutz, T.S. Clauditz, M. Kluth
*Institute of Pathology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

Background & objectives: The S-methyl-5′-thioadenosine phosphorylase (MTAP) gene is located at chromosome 9p21, a region that is prone to deletions in many tumour types. MTAP expression loss offers therapeutic options in tumour cells that depend on a functional MTAP gene.
Methods: To study the relationship between MTAP expression loss and gene copy numbers in different human tumour types, a tissue microarray containing 17,078 samples from 149 different tumour entities was analysed by immunohistochemistry (IHC) and fluorescence in-situ hybridization (FISH).
Results: At least one case with a complete MTAP expression loss was observed in 87 of 149 (58%) tumour categories. MTAP staining was most commonly lost in neuroendocrine neoplasms of various sites (up to 80%), Hodgkin's lymphoma (38%), mesothelioma (24-30%), bilio-pancreatic adenocarcinomas (9-36%), and urothelial neoplasms (19-29%). Comparison with 9p21 FISH data from 2,153 tumours identified homozygous 9p21 deletions in 90-100% of cases with MTAP expression loss in malignant melanoma, urothelial neoplasms, mesotheliomas, pancreatic cancers, ovarian and endometrioid cancers, hepatobiliary carcinomas, as well as squamous cell carcinomas of various origin. Tumour types with frequent MTAP loss but without 9p21 deletion included neuroendocrine tumours of various origin and Hodgkin's lymphoma.
Conclusion: Our data provide a comprehensive overview on MTAP expression in cancer and show a strong link between MTAP expression loss and homozygous 9p21 deletions in most tumour entities. The absence of 9p21 deletions in other entities with frequent MTAP expression loss reveals that other mechanisms can cause significant MTAP downregulation. These findings demonstrate various diagnostic applications for MTAP IHC and identify cancer types for MTAP guided therapy.

PS-19-022
The usefulness of NGS in the treatment of cholangiocarcinomas: our experience
D. Guerrero*, I. Amat, M.d.R. Mercado, R. Beloqui, I. Fernández De Los Reyes, L. Jiménez-Goñi, A. Córdoba
*Department of Pathology, Spain

Background & objectives: Cholangiocarcinomas (CCA) are heterogeneous tumours that arise from epithelial cells of the biliary tract. The use of NGS for the analysis of established and emerging biomarkers is crucial in this type of cancer, characterized by its aggressiveness.
Methods: We include 46 patients diagnosed with CCA between 2019 and 2024. Macrodissected tumour areas were selected by pathologist and DNA was extracted from formalin-fixed, paraffin-embedded sections. Targeted DNA-RNA-based Next Generation Sequencing (NGS) was conducted by the Oncomine™ Precision Analysis-OPA (Genexus, ThermoFisherScientific) panel to analyse single nucleotide variants (SNVs), insertions/deletions (indels), copy number variations (CNVs) and fusions in 50 genes.
Results: Nine patients (19.6%) displayed actionable biomarkers (Tier I), 8 cases (17.4%) with pathogenic variants of IDH1 and one patient (2.2%) with FGFR2-BICC1 fusion. One patient displayed a variant of unknown clinical significance in the IDH1 gene. Other pathogenic and probable pathogenic variants were also found in KRAS (26.1%) and PIK3CA (8.7%), among other. Clinical data demonstrates the usefulness of NGS based in simultaneous DNA/RNA analyses.
Conclusion: The use of DNA/RNA NGS panels is essential to detect patients that are candidates for directed therapies.

PS-19-023
Clinicopathological characteristics and genotypes of MUTYH mutated colorectal cancer patients in the Turkish population
I. Guzelis*, A. Subasioglu, A. Akder Sari
*Izmir Katip Celebi University Ataturk Training and Research Hospital Pathology Department, Turkey

Background & objectives: Approximately 5-6% of colorectal cancers are a part of a hereditary cancer syndrome. MUTYH is a DNA base excision repair gene, and its mutation can lead to polyposis and colorectal cancer. MUTYH may interact with the DNA mismatch repair system.
Methods: Patients who were tested with large hereditary cancer panels in the genetic department and found to have MUTYH mutation were retrieved from the archive data. Among these patients, those who had colorectal cancer were included in the study. The clinicopathological features of these cases were investigated.
Results: Eleven colorectal cancer patients 10 with pathogenic and 1 with likely pathogenic MUTYH mutations were included in the study. The mean age was 52 years, with 8 cases being male. Among the cases, 4 had c.800C>T p.P267L, 2 had c.1353_1355delGGA p. E452del, 1 had c.1087C>T p.Q363, 1 had c.452 A>G p.Y151C, 1 had c.631G>A p.V211I, 1 had c.1353_1355delGGA p. E452del, and 1 had c.650 G>Ap.R217H mutations. Ascending colon was the most common site. Seven cases had polyposis, with a polyp count ranging from 36 to 130. Two cases were found to be MSH2-deficient. In both of the MSH2-deficient cases, the tumours were located in the ascending colon, and one had >100 polyps.
Conclusion: This study demonstrates the clinicopathological features of MUTYH-mutated colorectal cancer in the Turkish population. Given that MUTYH mutation is rare in colorectal cancers, we believe that our findings could contribute to identifying potential clinical and therapeutic implications for individuals with this mutation.

PS-19-024
Differential expression PSMD10 gene mRNA in liver tissue and blood plasma of patients with cirrhosis and hepatocellular carcinoma
M. Jangavadze*, Z. Bedinashvili, N. Goishvili, K. Tsomaia, I. Khakhutaishvili, I. Kirvalidze
*TSU Aleqsandre Natishvli Institut of Morphology, Georgia

Background & objectives: The early diagnosis of hepatocellular carcinoma (HCC) is vital for the patient survival. Gankyrin/PSMD10 plays an important role in HCC carcinogenesis. The aim - to investigate the feasibility of plasma circulating Gankyrin mRNA as a potential biomarker for HCC.
Methods: Blood samples from patients with HCC (n=32), metastatic HCC (n=5), cirrhosis (n=7), hepatitis C virus+ (HCV+; n=5) and healthy individuals (n=5) were evaluated. The expression of Gankyrin/PSMD10 RNA was analysed in tumour tissue samples from patients with HCC (tumour and adjacent; n=32), cirrhosis (n=5) and normal tissues (n=5). RT-qPCR was performed using p28/Gankyrin and human 18S ribosomal RNA.
Results: In patients with cirrhosis, HCV+ and healthy individuals, Gankyrin/PSMD10 RNA was not detected in serum. The mean ΔCq in HCC group was 11.69±1.6, and in patients with metastatic HCC it was 10.16±0.4. A statistically significant difference in the ΔCq was found between the groups (P<0.0002;). A significant difference in the Gankyrin expression level was found in the tissue samples. The 2-ΔΔCq mean for Gankyrin/PSMD10 in HCC, HCC

ADJ T, cirrhosis and control group was 418.5±220.6, 78.68±49.40, 20.62±11.32 and 1.02±0.23, respectively. The differences between groups were statistically significant (P<0.001).
Conclusion: Expression of Gankyrin RNA is significantly increased in HCC compared with that in normal and cirrhotic tissues. In the tumour adjacent liver tissue, the Gankyrin RNA level was higher than that in the cirrhotic liver tissues. Gankyrin RNA was not detectable in the plasma of healthy individuals, its expression was increased in the plasma of patients with HCC. The detection of Gankyrin RNA in LB can be used for screening, monitoring, and early detection of tumour recurrence.

PS-19-025
Detection of neurofibromatosis type 1 mosaicism: the Erasmus MC, Rotterdam experience
E. Korpershoek*, R. van Minkelen, S.A. van Dijk, L.M. Elemans, L. Meerstein-Kessel, T. van Ham, M. Nellist, E.J. Dubbink, M. van Vliet, W. Taal, Y. van Ierland
*Department of Clinical Genetics, Erasmus MC, University Medical Center Rotterdam, The Netherlands

Background & objectives: For optimal patient care and counselling, it is important to detect NF1 mosaicism. In this study, we evaluated screening methods - performed at the departments of Clinical Genetics and Pathology and outcomes of patients suspected of having NF1 mosaicism.
Methods: Patients with a heterozygous germline NF1 mutation were excluded. Genetic screening was performed for 64 patients, who were referred by the Erasmus MC departments of Clinical Genetics and Neurology, for germline testing of the NF1 gene. From 17 of these patients, 1-3 tissue samples (neurofibromas or café-au-lait macules (CALMs)) were analysed using targeted NGS of the NF1 gene.
Results: Genetic screening methods included Sanger sequencing (n=45) and/or targeted Next Generation Sequencing (tNGS) (n=16), MLPA (n=64), RNA sequencing (n=5), whole exome sequencing (n=1), and mutation-specific PCR test (n=3). NF1 mosaicism was identified in 14 of the 64 patients (22%). In 10 of these 14 patients NF1 mosaicism was detected in germline DNA (5 by Sanger sequencing, 2 by MLPA-analysis, 3 by tNGS analysis (no NF1 mutations were identified by prior Sanger sequencing)). In addition, in 4 patients NF1 mosaicism was only identified in neurofibroma or CALM tissue samples.
Conclusion: Identification of NF1 mosaicism is important to tailor clinical follow-up regimens and inform patients on transmission risks and family planning. Although less likely, these patients might be still able to transmit the disease to their offspring. Our results show that tNGS of germline DNA and DNA derived from tissue samples, such as neurofibromas and CALMs, improving the detection and diagnosis of NF1 mosaicism.

PS-19-026
Next-Generation Sequencing (NGS) for lung squamous cell carcinoma (LSCC): insights from a pilot study performed at a Portuguese university hospital centre
N.J. Lamas*, C. Vilasboas, T. Santos, X. Wen, J.R. Vizcaíno, F.E. Costa
*Centro Hospitalar Universitário de Santo António (CHUdSA), Portugal

Background & objectives: Squamous cell carcinoma is the second most frequent lung cancer type, mainly occurring in smokers. Over the past years, immunotherapy has become an efficacious treatment modality. Less is known about targeted therapies since reflex NGS testing is not routinely performed.
Methods: To thoroughly understand the molecular landscape of LSCC we retrospectively collected primary LSCC cases from April 2022 until April 2024, which underwent routine Next-Generation Sequencing (NGS) testing using middle-sized lung cancer-directed panels in the Genexus (Thermo-Fisher Scientific) or MiSeq (Illumina) platforms. Genetic changes identified were correlated with clinical and histopathological data, PD-L1 status and patient outcome.
Results: Our pilot study included 25 patients, with a preponderance of male patients (n=24, 96%) and a mean age of 70.0 years-old (±7.2). The majority of the cases were diagnosed in lung biopsy specimens (n=21, 84%). Fourteen patients (56%) had passed away at the end of the study. Genetic abnormalities were found in most of the cases (n=22, 88%). None had changes in the RNA study. The most frequently genetic alteration found was on the TP53 gene (n=21, 84%), followed by PIK3CA (n=3, 12%). PD-L1 expression was positive in 15/25 cases (60%). Seven cases (28%) harboured potentially actionable genetic variants (EGFR p.L858R, PIK3CA p.E542K, PIK3CA p.Q546E, FGFR3 p.S249C and ERBB2 p.S310F).
Conclusion: We were able to characterize the most relevant molecular changes in a cohort of LSCC patients. In nearly one third of the cases, we found genetic variants that are potentially targetable with specific drugs, which further support the emerging trend towards systematic NGS testing for LSCC. NGS testing in these cases will help to better understand the molecular landscape and possibly sediment the idea of reflex NGS testing for LSCC similarly to what has been done for lung adenocarcinoma.

PS-19-027
Prevalence of CA19-9 (Sialyl-Lewis A) antigen expression in human cancers: a TMA study involving 7,827 tumours from 73 human tumour categories
N. Schraps, S. Steurer, K. Möller*, F. Viehweger, N. Gorbokon, M. Kluth, T.S. Clauditz, S. Büyücek, R. Simon, G. Sauter, F. Lutz, M. Lennartz, M. Freytag
*Institute of Pathology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

Background & objectives: Carbohydrate antigen 19-9 (CA19-9, Sialyl-Lewis A), is a cell surface glycoprotein with a role in cell-to-cell recognition and a potential therapeutic target. However, the prevalence of CA19-9 in different human tumour types is poorly documented.
Methods: To determine the prevalence CA19-9 expression in different human cancer types, a tissue microarray containing 7,827 samples from 73 different tumour types and subtypes as well as 608 samples of 76 different normal tissue types was analysed by immunohistochemistry (IHC).
Results: CA19-9 immunostaining was observed in 2,412 (36.4%) of 6,629 analysable tumours including 21.0% with weak, 7.5% with moderate, and 7.9% with strong staining intensity. CA19-9 positivity was found in 63 (86.3%) of 73 tumour categories, and 42 (57.5%) tumour categories contained at least one strongly positive case. CA19-9 positivity was most frequently positive in pancreatic adenocarcinomas (92.0-93.2%), ovarian carcinomas (41.4-82.9%), hepato-biliary cancers (38.4-82.8%), colorectal carcinomas (72.2%), and endometrial carcinomas (64.9-71.4%). Tumour types with less frequent CA19-9 positivity included breast cancers (27.3-38.1%), prostate cancers (15.5-31.6%), renal cell carcinomas (21.2-52.5%), thyroid carcinomas (11.1-56.1%), and squamous cell carcinomas of various origin (8.3-50.0%).
Conclusion: CA19-9 expression occurs in a broad range of human tumour categories, most frequently in adenocarcinomas originating from various organs. CA19-9 immunohistochemistry is not suitable for the distinction of cancers of different sites of origin.

PS-19-028
P-PROFILER: refining criteria for homologous recombination deficiency (HRD) in pancreatic ductal adenocarcinoma (PDAC)
N. Pfarr*, C. Kling, M. Koppermann, E. Mayr, K. Merkl, A. Jacob, A. Terron Kwiatkowski, A. Muckenhuber, Q. Heiss, Y. Wagner, M. Walker, S. Chakraborty, K. Schwamborn, M. Quante, S. Lange

*Institute of Pathology, Technical University of Munich, School of Medicine & Health, Munich, Germany

Background & objectives: HRD is used for treatment stratification in ovarian cancer, defined by BRCA1/2-deficiency and/or a genomic instability score (GIS) ≥42. Its accuracy for other cancers including PDAC remains unknown. This study aims at refining HRD criteria for PDAC.
Methods: In the P-PROFILER study, GIS will be assessed in 250 PDAC samples from clinically well-characterized patients with metastatic disease at initial diagnosis applying the Illumina TruSight™ Oncology 500 HRD panel. This panel also detects single nucleotide variants in 523 cancer-associated genes including 29 HRR-genes, fusion/rearrangements, copy number variations and other metabiomarkers such as tumour mutational burden or microsatellite instability.
Results: Of 194 PDAC samples sequenced so far, 181 met quality criteria, with a mean GIS of 16.9 ± 13.0 (SD). 6% were classified as HRD (+) applying the current criteria. 60% of these harboured pathogenic/likely pathogenic (P/LP) BRCA1/2 variants. In contrast, 14% of all analysed PDAC samples had ≥ 1 P/LP variant in any of the known HRR-genes. In this subgroup, the mean GIS was 26.6 ± 22.4 (SD). 63% of patients received platinum-containing first line therapy (1L-platin) and 37% gemcitabine-based regimens (1L-gem). Progression-free survival was significantly longer in patients with HRD (+) PDAC treated with 1L-platin compared to HRD (+) receiving 1L-gem and patients with HRD (-) PDAC treated with either regimen.
Conclusion: These preliminary results underscore the rarity of pathogenic BRCA variants in PDAC, along with a lower GIS. Few tumours were classified as HRD-positive per existing criteria. Instead, the identification of P/LP variants in other HRR-genes that are associated with a lower GIS point towards the existence of BRCA-independent mechanisms in pancreatic cancer HRD and argues for refined HRD-criteria for this entity. An adapted GIS threshold is under evaluation using this cohort's clinical data.

Funding: Funded by Illumina

PS-19-029
Exploring the synergistic role of BRAF, NRAS and TERT promoter mutations in papillary carcinoma thyroid: insights into immune microenvironment dynamics through PD-L1 and PD-1 analysis
C. Rana*, I. Makkar, P. Ramakant
*KGMU Lucknow, India

Background & objectives: This study presents a comprehensive analysis of PDL1 and PD1 expression levels in Papillary thyroid carcinoma (PTC) and their associations with BRAF, NRAS and TERT promoter mutations, either occurring independently or in combination.
Methods: This is a retrospective cohort study of patients diagnosed with papillary thyroid carcinoma (PTC). Formalin-fixed paraffin-embedded tissue was used for DNA extraction. The presence of the BRAF V600E, NRAS and TERT mutation were determined using PCR-based assays followed by Sanger sequencing. PD-L1 and PD-1 immunohistochemical expression was also performed and analysed.
Results: A total of 83 cases were analysed in which BRAFV600E, NRAS, and TERT promoter mutations were observed in 25 (30.1%), 12 (14.4%), and 7 (8.4%)) cases respectively. PD-L1 was expressed in 38 (45%) cases. Patients with PD-L1 expression had more advanced disease in terms of extrathyroid extension, lymphovascular invasion, lymph involvement, and perinodal extension. These patients also had higher tumour-infiltrating lymphocytes and PD-1 expression. BRAFV600E and TERT co-mutation were seen in 4 cases all of which showed poor clinical outcomes and or histopathological features. Apart from having an advanced disease, the anaplastic transformation was seen in two of these cases.
Conclusion: Our findings provide valuable insights into the molecular and clinical characteristics of PTC, highlighting the significance of PD-L1 expression, BRAFV600E mutation, NRAS mutation, and TERT promoter mutation in driving disease progression and influencing patient outcomes. These findings may have implications for risk stratification, treatment selection, and the development of targeted therapeutic approaches in PTC. Further studies are warranted to validate these findings and elucidate the underlying mechanisms driving the observed associations.

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PS-19-030
Validation of the OncoDEEP kit comprehensive genomic panel on the MGI chemistry
S. Lefevre, S. Sauvage*, K. Ashour Garrido, J. Hong, A. Terradez, K. Eycken, J. Vanbellinghen
*OncoDNA SA, Belgium

Background & objectives: OncoDEEP® is a comprehensive gene panel (CGP) allowing the assessment of variants and genomic signatures in 638 genes. Implementation in alternative sequencers to Illumina, such as MGI platform, makes the solution more cost-effective, which is crucial for CGP routine use.
Methods: 92 samples were processed using the OncoDEEP® kit and sequenced on a DNBSEQ-G400 with FCL flowcell. Those samples were a mix of clinical (55) and control (37) samples allowing the validation of both variant/fusion calling and genomic signatures. In addition, DNA inputs ranging from 6 ng to 100 ng were tested.
Results: The QC metrics passed the thresholds (depth>350x and uniformity>85%) ensuring high quality data at the recommended DNA inputs (30-100 ng). On the 92 samples, most variants were detected. Triplicates of HD832 control showed that all variants were detected, except for three under threshold detection at low DNA input of 6 ng. All fusions were detected, except one at 6 ng. Genomic signatures showed expected results with 100% of concordance for HRD results (11 positive and 9 negative), 100% of concordance for MSI samples (8 positive and 27 negative), and 91.4% of concordance for TMB (3 discordant out of 35 samples, all near the threshold).
Conclusion: The OncoDEEP® is a cost-effective, end-to-end solution, based on Twist Bioscience technology and Illumina sequencing, offering a full characterization of the tumour. MGI platform was shown to be an alternative to Illumina by generating high quality data. All variants and fusion detected, as well as the calculation of genomic signatures were comparable to those using an Illumina platform. This allows the reduction of sequencing costs, increasing the cost-effectiveness of the OncoDEEP® solution, and therefore making CGP more accessible to patients.

PS-19-031
Refining MRD assessment in CLL patients: validating and testing of an NGS-based method
S. Tsuriel*, V. Hannes, Y. Bornstein, Y. Harishanu, D. Hershkovitz
*Tel Aviv Sourasky Medical Center, Israel

Background & objectives: Minimal residual disease (MRD) measurement, pivotal in CLL treatment, is predominantly conducted via flow cytometry (FC) in peripheral blood. Its sensitivity remains uncertain, particularly when tumour cells are absent in peripheral blood.
Methods: A recent CLL liquid biopsy protocol, that enables tumour clone identification in both blood and cell free DNA (cfDNA) using NGS, was published. We tailored this method for IonTorrent platform,

assessing 20 patients for validation and tracking 17 in remission. Tumour DNA in buffy coat and cfDNA were examined for tumour DNA, compared with FC for each participant.
Results: For validation, 17 samples from active CLL patients and three negatives were used. Results showed complete concordance between FC and the new method, the method got comparable results with both cfDNA and buffy coat. Among remission cohort, agreement was strong (82%), in one of the discrepancy cases where NGS detected positivity despite FC negativity, disease recurrence was detected months later. The ongoing study tracks patient progress, providing crucial insights into the methodology's accuracy and prognostic value.
Conclusion: The method demonstrates promising efficacy, offering an additional avenue for MRD assessment. The predictive value of this method as well as cut-off values for optimal sensitivity and specificity require further comprehensive research and longer follow-up to ascertain its potential.

PS-19-033
Detection of FGFR3 mutations and fusions in bladder cancer samples: Comparison of the MODAPLEX FGFR panel with therascreen FGFR Kit
R. Weissbach*, R.M. Wirtz, A. Weber, T. Schubert, M. Waldner, E. Veltrup, R. Hake, S. Eidt, J. Graff, V. Grunwald, T. Ecke
*BIOTYPE GmbH, Dresden, Germany

Background & objectives: Molecular testing of FGFR3 in bladder cancer will become clinical routine. The objective of this study was to evaluate the concordance of FGFR3 mutation and FGFR2/3 fusion detection between therascreen and the MODAPLEX FGFR kits as an alternative PCR test.
Methods: Formalin fixed paraffin embedded (FFPE) tumour tissues from 82 TURB samples were prospectively collected as part of the Bladder BRIDGister. RNA from FFPE tissues was extracted using commercial kits and consequently assessed using following kits, therascreen FGFR (Qiagen GmbH, Hilden) and MODAPLEX FGFR (BIOTYPE GmbH, Dresden) according to manufacturer's instructions.
Results: A total of 80 samples were available for comparative analysis. Both PCR-based FGFR test systems concordantly identified S249C (n=11), R248C (n=2) and G370C (n=1) mutations and FGFR3:TACC3 (n=2) gene fusions. Results for Y373C were partially discrepant as therascreen FGFR detected 7 mutations, while MODAPLEX FGFR detected 3 mutations. Further examination of the 4 discrepant Y373C cases by SNaPshot and Uromonitor FGFR test revealed that the therascreen FGFR led to 3 false positive results (excluded from concordance analysis). Additionally, samples with a gene fusion FGFR3:JAKMIP1 (n=1) and a mutation FGFR3 K650E (n=1) were identified that aren't characterized using therascreen FGFR. Overall, the Sensitivity was at 95% with a Specificity of 100%.
Conclusion: The MODAPLEX FGFR panel allows the stratification of bladder cancer patients by determination of the FGFR3 mutational and FGFR2/3 fusion status. The PCR-based FGFR assessment by MODAPLEX FGFR panel and therascreen FGFR kit is highly concordant (78/79). The MODAPLEX assays enable fast, local FGFR assessment in a multiplexed one-step approach within few hours. Moreover, utilizing the MODAPLEX FGFR panel can effectively prevent false positive results generated by the therascreen kit.

PS-19-034
The Idylla™ IDH1-2 Mutation Assay Kit demonstrates high sensitivity and specificity for detection of IDH mutational status in glioma
R. Werner, C.K. Hand, L. Burke*, M. Jansen, L. Favre, S. Tran, R. Mertaniemi, T. Vaisanen, M. Linea, S. Truelsen, S. Mrabet-Dahbi, D. Salas Díaz, C. Teixido, N. Shelestovich, H. Tabibian-Keissar
*Dept of Histopathology Cork University Hospital, Ireland; Department of Pathology, School of Medicine, University College Cork, Ireland

Background & objectives: With the evolution of precision medicine, IDH inhibitors are essential for managing glioma patients with targetable mutations. IDH1-2 have emerged as key diagnostic and prognostic markers in these malignant brain tumours. Thus, rapid assessment of IDH mutation status is necessary.
Methods: The Idylla™ IDH1-2 Mutation Assay Kit (RUO) is a fully automated assay detecting five IDH1 mutations in codon R132, four IDH2 mutations in codon R140, and six IDH2 mutations in codon R172 within 95 minutes. Centres from Europe, US, Israel, and Thailand evaluated its performance in a global multicentre study using FFPE tissue samples and extracted DNA genomic material.
Results: Each centre aims to test 10 to 15 samples pre-analysed by routine reference technology (Immunohistochemistry, Next Generation Sequencing, or Polymerase Chain Reaction), with a final target of analysing at least 150 samples. Intermediate analysis, based on data from 7 out of the 13 centres, was conducted on 94 samples, comprising 69 FFPE tissue samples and 25 extracted DNA samples. These samples encompassed 57 IDH1 mutations, 9 IDH2 mutations, and 28 samples without IDH1 or IDH2 mutations. The Idylla™ assay produced a valid result in 99% (93/94) of cases, demonstrating 98.5% sensitivity (65/66), 100% specificity (27/27), and an overall concordance rate of 98.9% (92/93).
Conclusion: The Idylla™ IDH1-2 Mutation Assay demonstrates high sensitivity and specificity in detecting IDH1-2 mutations in gliomas across real-world clinical settings. The rate of development of targeted treatments and biomarkers has led to increased demand for rapid results in the clinical diagnostic laboratory. This system is easily integrated into pathology laboratories, facilitating fast turnaround time of IDH1-2 results to clinicians. The implementation of this time-saving assay with minimal hands-on time and easily interpretable report will enhance cancer care for glioma patients.

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PS-20Poster Session Pulmonary Pathology

PS-20-001
Lymph node dissection quality with new pathological criteria in oncologic surgery: does robotic-assisted surgery do better?
A. Deceuninck *, P. Thiebaut, M. Bubenheim, S. Aguir, B. Bottet, A. Dujon, M. Couralet, J. Melki, M. Sarsam, J. Sabourin, F. Guisier, J. Baste, N. Piton
*Department of Pathology, UNIROUEN, INSERM U1245, CHU Rouen, Normandy University, Rouen, France

Background & objectives: Robot-assisted thoracic surgery (RATS) seems to improve the surgical precision of nodal dissection compared to video-assisted surgery (VATS), but its benefits on the pathological quality have never been assessed, which was the aim of our study.
Methods: Consecutive RATS and VATS lobectomies for cancer performed at Rouen University Hospital by surgeons accustomed to both approaches were included (May - November 2023). We assessed the following parameters for each lymph node dissection: the number of stations and lymph nodes dissected, the volume and size of fragments, the macroscopic integrity of the capsule, and microscopically, the lymph node surface.
Results: Twenty patients each underwent RATS and VATS. RATS showed significant superiority over VATS in dissected mediastinal lymph node stations (4.8 vs. 4.1, $p = 0.02$), number of nodes (7.7 vs. 6.05, $p = 0.02$), and fragment size (22.8 mm vs. 20.2 mm, $p = 0.04$). However, no significant differences were found in fragment volume (0.49 ml vs. 0.47 ml, $p = 0.44$), number of lymph nodes with intact capsules (2.1 vs. 2.1, $p = 0.45$), and total microscopic observable surface (553 mm^2 vs. 398 mm^2, $p = 0.07$). Notably, in station 7, RATS group had significantly larger lymph node fragment volumes (1.32 ml vs. 0.44 ml, $p = 0.02$).

Conclusion: Our study demonstrated that RATS lymph node dissection provides larger fragments than VATS, which is new information. Additionally, it was associated with more dissected lymph node stations and more lymph nodes compared to VATS, in line with recent data. However, no statistically significant difference was found for more subtle, microscopic quality criteria.

PS-20-002

Lung cancer in Syria - a multicentre retrospective study

D. Alshaar*
*Syrian Arab Republic

Background & objectives: Lung cancer is a public health concern with increasing incidence anticipated, particularly with emerging smoking methods and lack of regulations among youth. Lung cancer is a public health concern with increasing incidence anticipated, particularly with emerging smoking methods and lack of regulations among youth. We aim to explore epidemiology and pathology of lung malignancies concerning age, gender, and regional distribution in Syria. We aim to explore epidemiology and pathology of lung malignancies concerning age, gender, and regional distribution in Syria.
Methods: The research was carried out at three prestigious centres in Syria, Al-Assad University Hospital and Albairouni University Hospital in Damascus, and Tishreen University Hospital in Lattaki, involving patients diagnosed with malignant lung masses from early 2017 to mid-2023. The study encompassed a total of 5348 patients, with data collected on patients' age, gender, tumour type, and place of residence.
Results: Male cases accounted for 81.7% while the remaining 18.3% were female, with a mean age of 59.77 years ranging from 18 to 95 years old. The majority (74.2%) of lung malignancies were NSCLC followed by neuroendocrine neoplasms (20.3%). Adenocarcinoma was the commonest type among NSCLC with an incidence rate of 44.1%, followed by squamous cell carcinoma which occurred in about 22.8% and large cell carcinoma comprising less than 2%. The highest incidence rate was in the coastal regions at 47.7%, followed by Damascus and Rural Damascus at 24.5%.
Conclusion: The mean age of the study patients was slightly lower than the age reported in studies from neighbouring countries. Furthermore, this study revealed a higher incidence of lung cancers in coastal regions compared to other areas.

PS-20-003

Occupational interstitial lung diseases: what is it, why is it important, and when should I think of it?

R. Ayadi*, R. Yaiche, E. Braham, I. El Hadhri, I. Bouassida, M. Affes, O. Ismail, B. Hamdi, A. Ayadi
*Department of Pathology, Abderrahmen Mami Hospital, Tunisia

Background & objectives: Interstitial lung diseases (ILD) caused by exposure to toxic inhalants in the workplace (occupational ILD) are potentially reversible diseases. Many different agents are reported to cause it. The aim is to better understand the clinicopathologic features of this entity.
Methods: We retrospectively analysed clinicopathological data of 22 patients with occupational ILD identified from pathological reports and surgical files at Abderrahman Mami Hospital on a period of 23 years, from 2000 until 2023.
Results: There were 17 male and 5 female patients with a mean age of 50,35 years. Clinically patients reported almost respiratory symptoms. The diagnosis was suggested on chest CT with diffuse infiltrative pneumonia in all cases. The diagnosis was made on surgical pulmonary biopsy in all cases and on bronchoalveolar lavage fluid (BALF) (n=4). Silicosis was the most common aetiology (n=14), followed by berylliosis (n=4) and hypersensitivity pneumonitis (n=4). Microscopic examination showed small nodules of fibroblasts and histiocytes with abundant silica birefringent with polarization, nonnecrotizing granulomas (berylliosis). hypersensitivity pneumonitis showed airway centred (peribronchiolar) change, interstitial cellular infiltration, poorly formed nonnecrotizing granulomas, foamy macrophages in alveolar spaces and organizing pneumonia.
Conclusion: Occupational ILD is a rare disease that is difficult to diagnose and treat. In general, it is thought that the diagnosis of this entity requires both cytological histological examinations. Although the list of occupational exposures that may cause ILD continues to grow, emphasizing the need for ongoing vigilance and effective preventive measures. An interprofessional team effort including pathologists and pulmonologists is mandatory to assess the diagnosis.

PS-20-004

Nuclear texture and size are good differentiators between adenocarcinoma and squamous cell carcinoma of the lung

A. Bloomberg*, D. Hershkovitz, S. Tsuriel, R. Hagage, J. Brazowski
*Tel Aviv Sourasky Medical Center, Israel

Background & objectives: Accurate histological distinction between squamous cell carcinoma and adenocarcinoma of the lung is important for treatment decisions but can be difficult. Identifying the most significant parameters for distinguishing between SqCC and adenocarcinoma could enhance the development of machine learning tools.
Methods: We analysed 167 adenocarcinoma and squamous cell carcinoma cases using an automated nuclear segmentation tool. We extracted 655 features from segmented nuclei. Statistical analysis identified parameters differentiating between the two cancer types, which we categorized into size (75, 12%), colour (90, 14%), density (15, 2%), nuclear texture (225, 34%), and cytoplasm texture (250, 38%).
Results: 237,384 segmented nuclei were analysed. 170 (26%) showed statistically significant difference larger than 10% between the groups. Interestingly, 43% and 40% of size and nuclear texture parameters showed significant difference between the groups, respectively, compared to less than 20% of colour, density, and cytoplasm parameters ($p<0.001$). Additionally, 70% of parameters based on standard deviation were associated with >10% difference between the groups compared to less than 26% of parameters that were based on mean, median and 10th and 90th percentile ($p<0.001$).
Conclusion: Our findings demonstrate that size and nuclear texture features are the primary differentiators between lung cancer histological types. Additionally, parameters based on standard deviation were better differentiators as well. These results identify the most significant parameters for distinguishing between squamous cell carcinoma and adenocarcinoma, potentially improving diagnostic accuracy. This work could also inform the development of ML applications to streamline the diagnostic process in lung cancer.

PS-20-005

Evaluation of changes after neoadjuvant therapy of lung cancer

M. Çağlayan*, B. Yaman, K. Turhan, A. Veral, D. Nart
*Ege University Faculty of Medicine Department of Medical Pathology, Turkey

Background & objectives: The use of neoadjuvant therapies prior to surgical resection, measuring radiographic and pathological response compared to adjuvant therapy, has the potential to alter microscopic tumour appearance. We investigate pathologic assessment of the effects of neoadjuvant therapy with the survival.
Methods: In our centre, 58 patients with non-small cell lung carcinoma between 2000 and 2022 were included in the study. Viable tumour rate, necrosis rate, stroma rate and inflammation intensity were evaluated. The relationship of these changes with prognosis was evaluated statistically.
Results: 22 cases were diagnosed as adenocarcinoma (37.9%), 30 cases as squamous cell carcinoma (51.7%) and 6 cases were classified as

others (10.3%). Pathologic assessment of the extent of residual viable tumour did not vary between subtypes. There was a positive correlation between viable tumour rate and lymph node metastasis(p:0.01). The estimated survival time in the group with a viable tumour rate of ≤10% (148.7±28.6 months) was longer than in the group with >50% viable tumour rate of (77±27 months) (p:0.055). The group receiving radiotherapy in addition to neoadjuvant chemotherapy (n:8) had a lower viable tumour rate (p:<0.001).
Conclusion: This study including lung cancer patients treated with neoadjuvant therapy found evidence that measurable pathological changes attributable to chemotherapy and/or radiotherapy predicted survival.

PS-20-006
Real-world insights from France, Italy, Spain, and Austria for the investigation of common (exons 19, 21) and rare (exons 18, 20) EGFR mutations in lung cancer
S. Cheloni*, X.B. Bustillo, L. Staehli, D. Constantin, G. Morales, S. Lima, L. de Visser, F. Hodeib, R. Dowlati
*SOPHiA GENETICS, France

Background & objectives: Identification of exon-specific EGFR mutations can guide the appropriate treatment of lung cancer with tyrosine kinase inhibitors (TKIs) or alternative therapies (Hou, et al. Biomark. Res.2022;10:21). We examine NGS EGFR testing practices in France, Italy, Spain, and Austria.
Methods: The SOPHiA DDM™ Platform (SOPHiA GENETICS SA, Switzerland) was used to analyze pseudonymized real-world genomic profiles (Q4 2021 – Q3 2022) across 27 institutions. Aggregated anonymized statistical data were obtained from 18 SOPHiA GENETICS somatic oncology NGS panels capable of detecting *EGFR* alterations from RNA or DNA.
Results: Between 2022 and 2023, 17,433 individuals across France, Italy, Spain, and Austria were tested with SOPHiA GENETICS NGS panels capable of detecting EGFR alterations. There were 1,268 EGFR mutation-positive profiles, of which approximately 27% (n = 345) had lung cancer; >25% (n = 99) of these had non-small cell lung cancer (NSCLC). The variant breakdown in EGFR mutation-positive lung cancer profiles was: exon19del, >40%; exon21mut, >30%; exon20ins, >10%; exon20mut, >5%; exon18mut, >5%. Co-mutations of the EGFR gene were observed in a subset of the population.
Conclusion: This analysis provides new insights into the occurrence of specific alterations in exons 18, 19, 20, and 21 in EGFR in lung cancer patients, and NGS testing practices across France, Italy, Spain, and Austria. The comprehensive characterization of the molecular epidemiology of EGFR variants and their prevalence are crucial to identify the NSCLC patients that are most likely to benefit from TKIs or alternative therapies.

PS-20-007
PD-L1 expression in driver-mutated metastatic non-small cell lung cancer
V. de Jager*, B.N. Cajiao Garcia, M.A. Hempenius, C.C. Kuijpers, L.C. van Kempen, E. Schuuring, A.J. van der Wekken, S.M. Willems
*Department of Pathology and Medical Biology, University of Groningen, University Medical Center Groninngen, Groningen, The Netherlands

Background & objectives: Specific (targetable) driver aberrations in patients with non-small cell lung cancer (NSCLC) are associated with poor response to mono-immunotherapy. Our objective was to determine the prevalence of high programmed death-ligand 1 (PD-L1) tumour proportion score (TPS) (≥50%) in driver-mutated NSCLC.
Methods: Clinical data of all patients diagnosed with metastatic non-squamous NSCLC in the Netherlands in 2019 were retrieved from the Netherlands Cancer Registry and linked to pathology reports of the Dutch Nationwide Pathology Databank (Palga). From the pathology reports, PD-L1 expression was retrieved, as well as mutational status for the following genes: EGFR, KRAS, BRAF, MET, ERBB2, ALK, ROS1 and RET.
Results: In preliminary analysis, PD-L1 immunohistochemistry was performed in 3,392 patients with metastatic NSCLC. Among these patients, 42.4% had negative PD-L1 TPS (<1%), 22.8% had low PD-L1 TPS (1-49%) and 34.6% had high PD-L1 TPS (≥50%). Below-average high PD-L1 TPS (≥50%) were observed in patients with an ERBB2 mutation (13.0% of cases), EGFR mutation (22.6%) or RET fusion (26.7%). Above-average high PD-L1 TPS (≥50%) were observed in patients with a KRAS mutation (39.6% of cases), ROS1 fusion (40.7%), ALK fusion (42.6%), BRAF mutation (51.5%) or MET exon 14 skipping mutation (65.0%).
Conclusion: Large variation in PD-L1 expression was observed in patients with NSCLC with predictive driver mutations. Above-average high PD-L1 TPS (≥50%) scores were observed in patients with specific targetable driver aberrations, including BRAF mutation, MET exon 14 skipping mutation, ALK fusion or ROS1 fusion. Real-world follow-up data studies are needed to examine the outcome of patients with (metastatic) driver-mutated NSCLC with low or high PD-L1 TPS who are treated with (chemo-)immunotherapy after first-line targeted therapy.

Funding: This work was financially support by a shared grant ('Landelijke implementatie predictieve analyses bij longkanker op regionaal niveau') from AstraZeneca, Bayer, Pfizer, Lilly, MSD and Roche. None of these sponsors had a role in the design of the study, data collection, data analysis, interpretation of data, manuscript writing, or the decision to publish the results.

PS-20-008
Predictive biomarker testing rates in patients with metastatic non-small cell lung cancer in The Netherlands
V. de Jager*, B.N. Cajiao Garcia, C.C. Kuijpers, G.H. de Bock, W.J. Maas, W. Timens, L.C. van Kempen, A.J. van der Wekken, E. Schuuring, S.M. Willems
*Department of Pathology and Medical Biology, University of Groningen, University Medical Center Groninngen, Groningen, The Netherlands

Background & objectives: Predictive biomarker testing in patients with metastatic non-small cell lung cancer (NSCLC) is mandated by (inter)national guidelines. This study's objective was to determine guideline-adherent biomarker testing rates in the Netherlands in 2019 and to examine associations with demographic/clinical factors.
Methods: The cohort comprised all patients diagnosed with metastatic non-squamous NSCLC in the Netherlands in 2019. Clinical data of the Netherlands Cancer Registry were linked to pathology reports of the Dutch Nationwide Pathology Databank (Palga). Data extracted from these reports included sample type, diagnosis, and molecular testing status of predictive biomarkers.
Results: Among 3,877 included patients, overall molecular testing rates for non-fusion predictive biomarkers (EGFR, KRAS, BRAF, ERBB2, MET) ranged from 73.9 to 89.0%. Molecular testing for fusion-drivers (ALK, ROS1, RET, NTRK1/2/3) ranged from 12.6% to 63.9%. Guideline-adherent testing of EGFR, KRAS and ALK was performed in 85.2% of patients, with regional rates ranging from 76.0% to 90.8%. Based on binary logistic regression analyses, factors associated with guideline-adherent biomarker testing included lower age (odds ratio (OR)=1.05 per one year decrease), female sex (OR=1.36), diagnosis of adenocarcinoma (OR=2.48), availability of histological tumour material (OR=2.46) and clinical stage of

metastatic disease. Non-clinical factors included diagnosis at academic centre (OR=1.87) and patient's region of residence.
Conclusion: Regional differences in guideline-adherent predictive biomarker testing were observed in patients diagnosed with metastatic NSCLC in the Netherlands in 2019. Optimization of the chain-of-care for NSCLC patients in the Netherlands is needed to facilitate equal access to guideline-indicated care.

Funding: This work was financially support by a shared grant ('Landelijke implementatie predictieve analyses bij longkanker op regionaal niveau') from AstraZeneca, Bayer, Pfizer, Lilly, MSD and Roche. None of these sponsors had a role in the design of the study, data collection, data analysis, interpretation of data, manuscript writing, or the decision to publish the results.

PS-20-009
Exploratory evidence maps for the WHO Classification of Tumours 5th edition: tumours of the lung
C. Giesen*, R. Cierco Jimenez, J. del Águila Mejía, S. Armon, N. Myles, G. Goldman, F. Campbell, T. Lee, A. Bres, L. Bouanzi, I. Cree, D. Lokuhetty
*IARC/WHO, France

Background & objectives: Tumour pathology research is progressing, assessing citations and identifying levels of evidence (LOE) based on study design in 5thedition WHO Classification of Tumours (WCT-5) is a timely requirement. We performed exploratory maps for lung tumours of WCT-5 for future editions.
Methods: Citations were extracted from the lung tumours chapter of WCT-5 and imported and coded in EPPI-Reviewer. Maps were plotted using EPPI-Mapper. Final evidence maps displayed tumour types(columns), tumour descriptors(rows) and LOE based on study designs (dots using a four-colour code). LOE were assigned in accordance with criteria from the Centre for Evidence Based Medicine (CEBM) of the University of Oxford.
Results: We included 1434 studies addressing 51 tumour types cited in the lung tumours chapter of the WCT-5 for Thoracic Tumours. Overall, 87.7% (n=1257) references were labelled as low LOE, and 4.1% (n=59) were labelled high LOE for lung tumours. The tumour with the highest number of references was invasive non-mucinous adenocarcinoma of the lung (n=215; 15.0). The tumour presenting the highest proportion of high LOE was colloid adenocarcinoma of the lung (n=11; 18.2%). Based on the tumour descriptor, the heading with the highest number of cited evidence was under Prognosis and Prediction section (n=273; 19.0%). Histopathology yielded 2.5% (n=50) and Immunohistochemistry 7.5% (n=152) citations.
Conclusion: This study represents an initial step in EU grant 101057127 funded WCT Evidence Gap Map (WCT-EVI-MAP) project, aiming at assessing existing evidence for different tumour types and tumour descriptors and LOE in WCT-5. We observed that, when applying CEBM LOE, most studies were coded as low LOE in the lung tumours in WCT-5, with heterogeneity across assessed areas. We plan to improve on the cited evidence for lung tumours in the next edition of the WCT based on these findings.

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PS-20-010
MTAP deficiency closely correlates with p16 status in non-small cell lung cancer but is unrelated to tumour aggressiveness or patient prognosis
N. Gorbokon*, K. Teljuk, N. Schraps, K. Möller, S. Büyücek, M. Lennartz, F. Viehweger, C. Fraune, C. Bernreuther, R. Simon, G. Sauter, F. Lutz, T.S. Clauditz, M. Kluth, S. Steurer
*Institute of Pathology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

Background & objectives: S-methyl-5′-thioadenosine phosphorylase (MTAP) and cyclin dependent kinase inhibitor 2A (CDK2A, p16) are often co-deleted on chromosome 9p21 in non-small cell lung cancer (NSCLC). MTAP expression loss offers therapeutic options in tumour cells that depend on functional MTAP.
Methods: To study the clinical impact of MTAP and p16 (co-)alterations in lung cancer, a tissue microarray containing 470 adenocarcinomas and 235 squamous cell carcinomas was analysed by immunohistochemistry (IHC) for expression of MTAP and p16.
Results: MTAP expression was lost (0+) in 13.2%, weak (1+) in 45.4% and strong (2+/3+) in 41.4% of 423 interpretable adenocarcinomas (ADC), and 0+ in 25.8%, 1+ in 46.4% and 2+/3+ in 27.8% of 209 interpretable squamous cell carcinomas (SQCC) of the lung. MTAP deficiency was strongly linked to absence of p16 expression in ADC ($p<0.0001$). However, both MTAP deficiency and p16 expression loss, either alone or in combination, were unrelated to parameters of tumour aggressiveness, including pT status, pN status, histological grade, and patient survival, in ADC and in SQCC. In 40 analysed mesotheliomas, a MTAP loss was seen in 45% ($p<0.0001$ for adenocarcinoma vs. mesothelioma).
Conclusion: Loss of MTAP expression occurs in 13.0-25.0% of NSCLC irrespective of tumour extent or metastasis stage. These findings identify a potential application of MTAP IHC in NSCLC for diagnosis of malignancy and the identification of possible therapeutic options. The strong link between loss of MTAP and p16 is in line with genomic co-deletion as the major cause for MTAP/p16 deficiency.

PS-20-011
Evaluation of different grading systems among primary pulmonary adenocarcinomas: architectural grade combined with STAS is superior to others – a single centre study
F. Hegedus*, Z. Széll, N. Zombori-Tóth, J. Furák, T. Zombori
*University of Szeged, Hungary

Background & objectives: Regarding pulmonary adenocarcinomas, several grading proposals have been introduced in the past decade. We aimed to evaluate and compare the prognostic effect of these grading schemes on overall survival (OS) and recurrence-free survival (RFS) in a single centre study.
Methods: Our retrospective study included patients diagnosed with stage I-III lung adenocarcinoma who underwent surgery between 2004 and 2013 at the Department of Surgery, University of Szeged. Morphological patterns were recorded and revised on digitalized slides. As statistical analyses, univariate and multivariate Cox proportional hazard models, Kaplan-Meier analysis and log rank test was applied.
Results: Altogether 304 patients were included in our study. In multivariate analysis of OS, type of surgery (HR:1.80 95%CI:1.07-3.02, p=0.025), architectural grade combined with spread through air spaces (STAS) (HR:4.37 95%CI:1.88-10.19 $p<0.001$), lymphovascular (HR:1.86 95%CI:1.13-3.08 p=0.014), and vascular spread (HR:2.067 95%CI:1.02-4.25 p=0.045) were independent prognostic factors. In the multivariate analysis of RFS, stage (HR:2.55 95%CI:1.42-5.67 p=0.003) architectural grade combined with STAS (HR:2.41 95%CI:1.23-4.73 p=0.010) and vascular spread (HR:2.41 95%CI:1.29-4.50 p=0.005) were proven as independent prognosticators. In a subgroup analysis excluding the adverse factors (vascular spread, stage III) the architectural grade combined with STAS preserved its prognostic impact on OS and RFS.
Conclusion: Most grading systems of pulmonary adenocarcinoma take into consideration the architectural features; however, some of them focus on nuclear features or STAS. We have compared the available grading systems and have proven that all of them have prognostic role

on survival. The architectural grade combined with STAS was superior to others even in subgroup analysis where adverse factors were omitted.

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PS-20-012

Analytical performance of a diagnostic immunohistochemical assay for MET protein (c-Met) in non-small cell lung cancer

L. Inge*, B. Admire, T. Foutch, T. Landowski, M. Lopez-Schultz, K. Gordon, M. Kapdia, L. Zhang, A. Mistry, A. Hotson, S. Bheddah, M. Li, L. McKee
*Roche Diagnostics Solutions, USA

Background & objectives: The MET/c-Met protein is a membrane tyrosine kinase receptor found overexpressed in 35-72% of non-small cell lung cancers (NSCLC) and is a potential target for therapy. This study evaluated the analytical performance of a MET IHC assay for NSCLC.
Methods: FFPE NSCLC specimens were stained with an investigational anti-MET IHC assay using clone SP44 (Roche) on a Benchmark ULTRA instrument. MET protein expression was determined as the percentage of tumour cells with membrane and/or cytoplasmic staining at a strong (3+) intensity. Repeatability and intermediate precision, inter- and intra-reader precision studies were performed by pathologists (n=3) and compared to determined agreement.
Results: Western blot and peptide competition data demonstrated that the SP44 clone specifically recognized the MET protein within NSCLC cell lines and FFPE tissue. Analytical repeatability and intermediate precision assessments showed >95% overall percent agreement (OPA). Intra-reader precision assessment showed a >98% OPA and inter-reader precision showed a >95% OPA. Assessment of concordance between matched primary and metastatic NSCLC samples showed >90% OPAs.
Conclusion: Overexpression of the MET protein in NSCLC provides an actionable target for antibody drug conjugate (ADC) based therapies, such as telisotuzumab vedotin, requiring a robust and reproducible immunohistochemistry (IHC) assay to detect MET protein overexpression to ensure accurate patient identification. Our results demonstrate that the SP44 MET Assay is a robust and reproducible assay for the detection of MET protein overexpression in NSCLC.

PS-20-013

Tumour budding in lung squamous cell carcinoma: a single centre validation study comparing tumour budding assessment using conventional light microscopy and digital whole slide images

M. Keyter*, M. Maillard, S. Berezowska
*Department of Laboratory Medicine and Pathology, Institute of Pathology, Lausanne University Hospital and University of Lausanne, Switzerland

Background & objectives: Tumour budding (TB) is of prognostic value in lung squamous cell carcinoma (LUSC). As digital pathology is increasingly used in routine diagnostics, we aimed to compare TB assessment using conventional light microscopy (LM) and digital whole slide imaging (WSI).
Methods: Randomly selected 110 tumours from consecutive patients with LUSC who underwent surgical resection between 2005-2020 (N=212). H&E-stained sections and WSI were evaluated. TB was assessed according to International Tumour Budding Consensus Conference (ITBCC) guidelines as: low (Bd1) = 0-4 buds, intermediate (Bd2) = 5-9, and high (Bd3) ≥ 10 buds. Intra-rater reliability was assessed using Cohen's Kappa coefficient.
Results: Peritumoural budding (PTB) was mostly low using conventional LM (Bd1=93; Bd2=14; Bd3=3) and WSI (Bd1=91; Bd2=14; Bd3=5). Agreement across all three categories was 83.6%, with an intra-rater reliability assessment score of 0.422 (Cohen's kappa coefficient). Agreement of intratumourally budding (ITB) across all three categories using LM (Bd1=98; Bd2=7; Bd3=5) and WSI (Bd1=98; Bd2=10; Bd3=2) was 88.1%, with an intra-rater reliability assessment score of 0.473. Selection of different "hotspot" areas using LM vs WSI occurred in 30% of cases, leading to a different TB-assessment in 7%: PTB = 36 cases {8/36 (22%) different category, 28/36 (78%) same category}; ITB = 31 cases {7/31 (23%) different category, 24/31 (77%), same category}.
Conclusion: We show moderate reproducibility in TB assessment across two different diagnostic platforms (LM vs WSI), based on a single intra-rater comparison. Differences in intraobserver reproducibility in preitumoural and intratumourally assessment were due to decreased reproducibility in cases with borderline bud-counts, especially between low and intermediate categories. Although selection of different "hotspot" areas on LM versus WSI occurred in 30% of the cases, it resulted in a different classification of TB across the two platforms in only 7%.

PS-20-014

mTOR pathway hyperactivation in POU2F3-positive primary and brain metastatic small cell lung carcinoma

I. Krencz*, D. Sztankovics, F. Szalai, D. Moldvai, A. Sebestyén, J. Pápay
*Department of Pathology and Experimental Cancer Research, Semmelweis University, Hungary

Background & objectives: POU2F3-positive SCLCs represent about 10% of all SCLCs and are characterised by distinct biological features and cell origin. Despite the high frequency of mTOR pathway alterations in SCLC, there is no clear evidence of subtype dependency of mTOR pathway activation.
Methods: The expression of POU2F3, phospho-mTOR (active form of the mTOR kinase), phospho-S6 (downstream target of mTORC1), Rictor (scaffold protein of mTORC2), and phospho-Akt (downstream target of mTORC2) was analysed by immunohistochemistry in 50 primary and 50 brain metastatic SCLCs. The H-score method was used to assess the immunoreactions. A case with a POU2F3 H-score higher than 50 was considered POU2F3-positive.
Results: The prevalence of POU2F3 positivity was 12% in the primary SCLCs and 6% in the brain metastatic SCLCs. In the primary tumours, POU2F3 expression showed a significant positive correlation with the expression of phospho-mTOR (R=0.443, p=0.001) and Rictor (R=0.418, p=0.003). The expression of all the studied mTOR pathway markers were higher in the POU2F3-positive cases. Despite the lower number of POU2F3-positive tumours, similar results were observed in the brain metastases: POU2F3 expression showed a significant positive correlation with the expression of phospho-mTOR (R=0.547, p<0.001), phospho-S6 (R=0.490, p<0.001), and phospho-Akt (R=0.292, p=0.040), and the expression of the mTOR pathway markers was also higher in the POU2F3-positive brain metastases.
Conclusion: Accumulating evidence suggests that each subtype of SCLC has specific therapeutic vulnerabilities. Based on our results, POU2F3-positive SCLCs are characterised by hyperactivation of the mTOR pathway, which may provide a therapeutic opportunity in this distinct subtype of SCLC.

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PS-20-015

Ultrastructural changes of lung tissue under conditions of experimental obesity and smoking

Y. Kuzyk*, O. Mazur
*Danylo Halitsky Lviv State Medical University, Ukraine

Background & objectives: Obesity can cause respiratory disorders caused by adipose tissue accumulation and numerous cytokines produced by adipocytes. Smoking is associated with a wide range of lung diseases with diffuse changes in the lung tissue and a decrease in the respiratory volume.
Methods: Modelling of experimental obesity and smoking was carried out, with the determination of isolated and combined effects on lung tissue in sexually mature male rats. The total sample consisted of 120 rats divided into four groups: the control group (n=30), rats under tobacco smoke (n=30), experimentally obese rats (n=30), and experimentally obese rats simultaneously exposed to tobacco smoking (n=30).
Results: The conducted study of experimental obesity and smoking in rats shows pronounced pathomorphological changes already in the first months after the action of these factors. The main ultrastructural change observed in both obesity and smoking is increased collagenization of bronchial walls. Distinctive changes in the experimental group of smokers are pronounced destruction of type 2 alveolocytes, haemorrhages, thrombus formation, and arteriosclerosis. In the group of experimental obesity, an increase in the secretory activity of the epithelium with the accumulation of secretory granules was observed. The identified ultrastructural features of the lungs in the groups of experimental obesity and the combination of obesity with smoking did not differ qualitatively.
Conclusion: In the analysis of ultrastructural changes, it was established that chronic bronchitis, emphysema, focal pneumosclerosis, and signs of pulmonary hypertension developed in rats in the presence of experimental alimentary obesity. However, it should be noted that changes in the lungs did not qualitatively differ with the simultaneous use of experimental obesity and smoking.

PS-20-016

Challenging diagnosis of serious pulmonary fungal infections: report of 145 cases

F. Loued*, R. Ayadi, E. Brahem, R. Yaiche, B. Hamdi, O. Ismail, S. Ben Slama, A. Ayadi
*Department of Pathology, Monji Slim Hospital, 2070, Tunis, Tunisia

Background & objectives: Pulmonary fungal infections are less common than bacterial infection, but they have recently gained increasing importance. They are historically associated with a high mortality. The aim is to disseminate the recent advances in the diagnosis of this disease.
Methods: This retrospective study included all patients with a pathologically confirmed diagnosis of a fungal infection of the lung at our department of pathology between 2004 and 2023.
Results: There were 95 male and 50 female patients, aged between 7 and 80 years with a mean age of 48. The clinical history consisted of pulmonary tuberculosis (n=28), diffuse interstitial lung disease (n=4), pulmonary hydatid cyst (n=4), lung adenocarcinoma (n=2), transplanted medullar aplasia, broncholithiasis and Wegener's disease in one case each. The diagnosis was made on surgical resection (n=103), bronchoalveolar lavage fluid (n=29) and bronchial biopsy (n=8). Bronchoalveolar lavage fluid was useful in the diagnosis of all cases with pneumocystosis and 2 cases with Candidiasis. The rest of the diagnosis was histo-pathological. Final diagnoses were Aspergillosis (65, 51%), followed by Pneumocystosis (18, 62%), Mucormycosis (7, 58%) and Candidiasis (3, 45%).
Conclusion: Diagnosis of lung fungal infections is challenging due to its nonspecific clinical presentation, the limitation of laboratory testing, and the similarities of radiographic and laparoscopic findings compared to other diseases. The cytology examination must be completed with bacteriological and histo-pathological studies, mainly when the clinic presentation suggests the diagnosis.

PS-20-017

Pathologic assessment of resected stage III non-small cell lung cancer after neoadjuvant chemotherapy: identification of new prognostic factors

F. Lunardi*, A. Ferro, L. Vedovelli, S. Tzorakoleftheraki, C. De Chellis, F. Pezzuto, F. Fortarezza, M. Schiavon, F. Rea, G. Pasello, F. Calabrese
*Italy

Background & objectives: Non-small cell lung cancer (NSCLC) patients undergoing neoadjuvant chemotherapy before surgery represent an ideal setting to identify prognostic/predictive factors. The aim of the study was to investigate the prognostic role of clinico-pathological features, taking advantage of morphometry and artificial intelligence-AI.
Methods: Seventy stage III NSCLC patients undergoing surgery after neoadjuvant chemotherapy were studied. Histopathological evaluation of surgical specimens included in addition to the tumour bed (according the 2020 IASLC statement) a granular evaluation of additional histological parameters and a morphometrical quantification of the stromal components (fibrosis/inflammation). An AI-algorithm of the different inflammatory cell components on immunohistochemistry-stained whole-slide images was also applied.
Results: Major pathological response (MPR) and complete pathological response were related to DFS and OS but, in addition, also vascular/perineural/pleural infiltration and Ki-67 were useful in stratifying the study population. Concerning the tumour bed stromal components, only morphometrical quantification highlighted the prognostic role of fibrosis and inflammation, particularly when distinguishing CD4+ and FOXP3+ cells and mainly in adenocarcinomas. We finally identified a ClinPATH combined score that included blood lymphocyte count at baseline and the more significant morphological, morphometrical and AI-derived parameters (such as perineural/vascular infiltration, Ki-67, fibrosis %, MPR, WHO grading, CD4+ and FOXP3+ cells). This combined score showed a better predictive value both for DFS and OS.
Conclusion: The precise computer-assisted quantification of stromal components and the AI-mediated identification of the different inflammatory cell types highlighted the importance of a granular and more objective evaluation of the tumour bed, in particular fibrosis and inflammation. This could become even more crucial for the standardization of the pathological assessment in case of neoadjuvant immunotherapy.

PS-20-018

Enhancing idiopathic pulmonary fibrosis diagnosis and subtyping through multidisciplinary integration and a machine learning-based approach

G. Maggioni*, F. Lunardi, F. Pezzuto, L. Vedovelli, C. Giraudo, E. Balestro, M. Schiavon, A. Fattori, A. Labani, M. Ohana, R. Kessler, S. Hirshi, M. Chenard, F. Rea, F. Calabrese
*Italy

Background & objectives: Usual interstitial pneumonia (UIP), the characteristic pattern of idiopathic pulmonary fibrosis (IPF), may be detected in other fibrotic forms. Our study aims to evaluate IPF diagnosis accuracy according to the new guidelines and to identify additional parameters in UIP/IPF subtyping.

Methods: 1180 slides (from explants or lung biopsies) of 96 IPF patients in Padova and Strasbourg were reviewed according to 2018-2022 guidelines. Fourteen additional morphological parameters were graded in all specimens. Unsupervised clustering and variable importance analysis were conducted. Machine learning (Boruta algorithm) was employed to identify morphological patterns and key clinical features associated with IPF and other interstitial lung diseases.
Results: Our study revealed that a substantial number of patients were previously misdiagnosed as UIP-IPF (39%). We found that additional morphological parameters (e.g. the number of lymphoid aggregates, presence of germinal centres, ratio of plasma cells to lymphocytes, the peribronchial metaplasia and abortive granulomas), organized into novel diagnostic criteria, were significantly helpful in distinguishing non IPF-UIP, particularly connective tissue disease (CTD) and fibrotic hypersensitivity pneumonitis (F-HP) (the most common). The machine-learning algorithm and the derived decision tree diagram showed that morphological parameters chosen by the pathologists had better performance (AUC 88.4% vs AUC 63.3%) than those chosen by the mathematical model alone.
Conclusion: The new 2018-2022 guidelines, combining clinical, radiological, and pathological data have improved UIP-IPF diagnosis. The evaluation of additional morphological parameters plays a crucial role in identifying non-IPF-UIP, such as CTD and F-HP. Machine learning offers a promising tool for integrating diagnosis and guiding treatment for challenging conditions.

PS-20-019
Lack of immunohistochemical orthopaedia homeobox protein (OTP) expression is associated with adverse outcome in pulmonary carcinoid tumour patients
J. Niinimäki*, S. Mononen, T. Kaprio, J. Arola, T. Vesterinen
*University of Helsinki, Finland

Background & objectives: Expression of orthopaedia homeobox protein (OTP) has shown promise as an independent prognostic biomarker in pulmonary carcinoid (PC) tumours. Our study aimed to corroborate this finding and evaluate the performance of novel monoclonal OTP antibodies.
Methods: A retrospective analysis of 164 PC patients treated at Helsinki University Hospital (Helsinki, Finland) between 1990 and 2020 was conducted. Tissue microarray (TMA) slides, derived from formalin-fixed, paraffin-embedded primary tumour samples, were immunohistochemically stained using one previously utilized polyclonal and two recently developed monoclonal OTP antibodies. Manual scoring was performed on digitized TMA slides.
Results: Absence of OTP expression was significantly associated with shorter disease-specific survival (DSS) and disease progression ($p < 0.001$ for each antibody). Five-year DSS ranged from 73.3% to 78.8% in patients lacking OTP expression compared to 90.8% to 94.1% in OTP-expressing patients. Absence of OTP expression, AC subtype, metastatic disease, Ki-67 proliferation index >1%, and larger tumour size were associated with adverse outcomes in the univariable Cox regression model. In multivariable analysis, only absence of OTP expression and lymph node involvement at diagnosis predicted a poorer prognosis. Interobserver reliability between raters was excellent (ICC 0.971–0.983), with good concordance among all three OTP antibodies (ICC 0.831–0.951, Kappa 0.800–0.937).
Conclusion: The novel monoclonal OTP antibodies demonstrated similar performance as the previously utilized polyclonal antibody, thereby aiding the integration of OTP staining into routine diagnostics. Although OTP immunohistochemistry lacks the ability to reliably subtype PC tumours, its absence strongly correlates with aggressive disease progression and shorter disease-specific survival in PC patients. Consequently, incorporating OTP immunohistochemistry into PC tumour diagnostics can effectively identify patients at risk of relapse, necessitating intensified follow-up.

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PS-20-020
SMARCA4 deficient non-small cell lung carcinoma: immunohistochemistry and molecular genetic study
G. Raskin*, A. Fedorova, M. Mukhina, A. Drui, A. Chernev, L. Zavalishina
*Dr. Berezin Medical Institute, Russia

Background & objectives: Mutation of SMARCA4 in non-small cell lung carcinoma (NSCLC) is associated with poor prognosis and resistance to standard treatments. The aim of investigation was to study molecular and morphological features of SMARCA4 deficient lung tumours.
Methods: We studied 189 cases of undifferentiated and/or poorly differentiated NSCLC by immunohistochemistry (IHC) with antibodies to SMARCA4, SMARCA2. Molecular genetic study of ROS1, ALK, EGFR and BRAF using PCR and FISH methods was carried out in 14 cases with identified loss of SMARCA4. Also, 20 cases of SMARCA4-deficient tumours were evaluated with next-generation sequencing (NGS: 82 gene panel).
Results: We identified 41 (22%) cases with a loss of SMARCA4 expression. Tumour types comprised 12 cases of SMARCA4-deficient undifferentiated tumours and 29 cases SMARCA4-dNSCLC. 12 of 32 cases demonstrated complete or partial loss of SMARCA4/SMARCA2. 26 SMARCA4-deficient tumours were negative for TTF1 and/or P63. Mutations of ROS1, ALK, EGFR and BRAF were not detected in our study. NGS analysis was performed in 14 tumours. Inactivating mutations in the SMARCA4 gene were revealed in all cases. These mutations were represented by likely pathogenic variants and variants of uncertain significance. The most frequent co-mutated gene in SMARCA4-deficient tumours was gene TP53. Mutations such as BRCA1, NRAS, APC, ARID1A, CDKN2A were also found.
Conclusion: We demonstrated that SMARCA4-deficient lung tumours are quite common. Additionally, 37,5% of SMARCA4-deficient tumours showed loss of SMARCA2. Mutations of SMARCA4, which were revealed by NGS, have also accompanied by negative IHC staining that confirm its efficiency.

PS-20-021
YAP-1 expression in stromal cells could impact on chemoimmunotherapy efficacy in SCLC patients
G. Sabella*, G. Centonze, E. Roca, M. Gentili, B. Bodini, A. Fabbri, D. Lorenzini, A. Mangogna, E. Tosoni, A. Cucinella, G. Pruneri, A. Santo, M. Milione
*Switzerland

Background & objectives: Small-cell lung cancer (SCLC) is an exceptionally lethal malignancy for which more effective therapies are urgently needed.
Previous studies have classified SCLC patients by RNA-sequencing clustering analysis to identify who could benefit from immune checkpoint blockades.
Methods: Retrospective series of 48 SCLCs was included in the study. Patients were stratified according to received treatment [chemotherapy (CT) vs immunochemotherapy (IO-CT)] and associations with immunohistochemicalmarkers and clinico-pathological features were evaluated, including correlation with Overall Survival (OS) and Progression Free Survival (PFS). We aimed to explore whether YES-associated protein 1 (YAP-1) could be a potential biomarker of response to immunochemotherapy.
Results: Overall, 22 CT and 26 IO-CT treated patients were included in the study. IO-CT patients were significantly younger (p=0.004), presented with an intermediate prognostic EPSILoN score (p=0.02), an

ECOG=0 (p=0.005) and less in need of age-specific management (G8 geriatric score) (p= 0.007) than those treated with only CT. Within the IO-CT group, OS and PFS of poor EPSILoN score patients tended to be worse compared to intermediate and best score. Moreover, our findings revealed elevated intra- and extra-tumoural expression of YAP-1 in stromal cells among all SCLC patients; interestingly among IO-CT group Kaplan-Meier analysis showed a significant association between the stromal immunoexpression of YAP-1 and a poor PFS.
Conclusion: Our preliminary results suggest that stromal expression level of YAP-1 protein was negatively correlated with efficacy of chemoimmunotherapy, contributing significantly to the disease progression.

PS-20-022
Collagen V-induced nasal tolerance enhances lung tissue IL10, preventing alveolar damage in an experimental COPD model
F. Santos Zambon Robertoni*, A.P. Velosa, L. de Mendonça Oliveira, L. Keren Ramos da Silveira, Z.A. Jesus Queiroz, T. de Matos Lobo, S. de Morais Fernezlian, C. Machado Baldavira, M. Notomi Sato, V.L. Capelozzi, F. Degobbi T Q S Lopes, W. R. Teodoro
*Division of Rheumatology, Faculdade de Medicina da Universidade de São Paulo, Brazil

Background & objectives: Collagen type V (Col V) is a highly immunogenic protein, and its autoimmunity may be involved in the pathogenesis of COPD. We evaluate autoimmunity against Col V in COPD by examining Col V-induced nasal tolerance effects in an experimental model.
Methods: Male C57BL/6 mice were split into 3 groups: one exposed to CS for 4 weeks (CS), one tolerated with Col V and exposed to CS for 4 weeks (CS/Tol), and one kept in filtered air for the same period (CT). We conducted structural evaluations, analysed T-cell immunophenotyping in the spleen and the inflammatory/regulatory cell balance in the lung parenchyma.
Results: Col V-induced tolerance prevented emphysema development, significantly reducing Lm (p=0.0032), and minimizing structural changes in elastic and collagen fibers. Tolerance group (CS/Tol) had a significant increase in systemic Treg (p=0.0465, compared to CT) and a higher prevalence of regulatory cell profile in lungs, characterized by increased expression of FOXP3+ (p=0.034, compared to CS) and IL10+ (p=0.0034, compared to CT). The immunosuppressive effect of tolerance eventually overcame the inflammation resulting from cigarette smoke, therefore protecting the lung parenchyma from damage.
Conclusion: These results suggest that Col V autoimmunity indeed plays a role in the development of COPD as induced tolerance to it was able to prevent COPD onset in this murine experimental model, and this effect is probably due to IL10 action.

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PS-20-023
Effects of cumulative association resulting from different combinations of epithelial-mesenchymal transition proteins and clinical variables on NSCLC behaviour
C. Machado Baldavira, T. Gutierrez Prieto, C. Silvério Faria, A. Ab'Saber, T. Takagaki, W. R. Teodoro*, V.L. Capelozzi
*Division of Rheumatology, Faculdade de Medicina da Universidade de São Paulo, Brazil

Background & objectives: We hypothesized that the association of different epithelial-mesenchymal transition (EMT) proteins occurs on malignant cells of tumour, facilitating invasion and metastases. We investigate the effects of diverse combinations of EMT proteins that yield power on lung histology, and molecular biology.
Methods: Using immunohistochemical staining and the QuPath software, we characterized and quantified the expression of proteins that are part of the EMT event: DSP, SPP1, ITGB1, VIM, CDH1, MAP1B, and MMP9. These expressions were valued in tumours from a cohort of 61 patients diagnosed with NSCLC, in early clinical stages (I to IIIA).
Results: We found a high VIM and CDH1 expression and a low expression of DSP, SPP1 and ITGB1. A correlation was found between, DSP and MMP9, SPP1 and VIM, and VIM and MAP1B. High expression of DSP expression was found in squamous cell carcinomas, while a high SPP1 and VIM expression correlated with T1-2 stages and tumours ≤3.4 cm. A high expression of ITGB1 correlated with adenocarcinoma, and tumours >3.4 cm. The Cox multivariate analysis, controlled for N stage and local or distant metastases, ITGB1 DSP, SPP1, demonstrated a high risk of death for male patients in pathological stage IIIA and tumours harboured low expression of ITGB1.
Conclusion: In the current NSCLC study, our results demonstrated that cumulative EMT proteins itself cannot be clinically defined as a sufficient cause for risk of death; rather, the way that EMT components are expressed determines the potential behaviour of a given tumour.

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PS-20-024
Collagen V α1 chain oral tolerance attenuates the lung fibrosis and vascular reactivity in systemic sclerosis model
A.P. Velosa*, T. de Matos Lobo, Z.A. Jesus Queiroz, A. Dos Santos Filho, V.D. Rodrigues de Souza, J. Alves Almeida, S. de Morais Fernezlian, C. Machado Baldavira, L. Keren Ramos da Silveira, S. Catanozi, W. Paganelli Rosolia Teodoro, V.L. Capelozzi
*Division of Rheumatology, Faculdade de Medicina da Universidade de São Paulo, Brazil

Background & objectives: We hypothesize that autoimmunity to collagen V (COLV) α1 chain [α1(V)] is involved with the pulmonary extracellular matrix damage in systemic sclerosis (SSc). Thus, we investigated the effects of oral tolerance to COLV and α1(V) on lung from SSc model.
Methods: SSc model was induced in C57BL/6 mice (n=12) immunized with COLV emulsified in Freund's adjuvant (IMU-COLV). Two groups of animals received oral treatment, respectively with COLV/10μg and α1(V) chain/50μg diluted in saline, 5 days before the first immunization with COLV. The non-treated IMU-COLV mice received oral saline. The pulmonary remodeling and vascular reactivity were accessed by immunofluorescence, immunohistochemistry and histomorphometry.
Results: After 60 days, lung parenchyma of IMU-COLV mice showed prominent inflammatory response and collagen deposition around small vessels, bronchioles, and interstitium. The oral treatment with COLV/10μg and α1(V)/50μg minimized the inflammatory response and collagen deposition in lung parenchyma when compared to IMU-COLV (p=0.0046 and p=0.0015, respectively). Low deposition of collagen type I in lung parenchyma occurred in IMU-COLV treated with α1(V)/50μg compared to non-treated group (p=0,0194) and the group treated with COLV/10μg (p=0,0009). Interestingly, the group treated with α1(V)/50μg showed low amount of COLV in relation to non-treated group (p=0,0278). Furthermore, both COLV/10μg (p<0,0001) and α1(V)/50μg (p=0,0084) oral treatments were effective in reducing vascular reactivity by Factor VIII+ immunostaining.
Conclusion: In the current experimental SSc, our results demonstrated that oral tolerance induced by α1(V) chain can modulate lung parenchyma fibrosis, defined as a sufficient cause for experimental SSc; rather, the way that fibrillar and vascular components of the extracellular matrix are present determines the potential of repair.

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PS-20-025

Primary intrathoracic liposarcoma: an extremely rare malignant tumour involving the thorax

R. Yaiche*, R. Ayadi, E. Braham, I. El Hadhri, I. Bouassida, I. Mallek, O. Ismail, S. Ben Slama, A. Ayadi
*Abderrahmane Mami Hospital, Tunisia

Background & objectives: Primary intrathoracic liposarcoma (PIL) is extremely rare, accounting for 2.7% of all liposarcomas. The intrathoracic location of this malignancy is poorly reported in the literature. The aim of our study is to better understand the clinicopathologic features of this entity.
Methods: We retrospectively analysed clinicopathological data of 12 patients with primary intrathoracic liposarcoma identified from pathological reports and surgical files at Abderrahman Mami Hospital on a period of 23 years, from 2000 until 2023.
Results: Patients were mostly males (sex-ratio=2) with a mean age of 62years.The chief complaint was chest pain (75%). Seven tumours occurred in the anterior mediastinum (58%), followed by pleural cavity (25%) then the chest wall (17%). Tumour mean size was 180 mm. The diagnosis of PIL was confirmed histologically on surgical specimens (10 cases) or pleural biopsies (2 cases). Half of cases were of mixed histological subtype, associating a well-differentiated lipoma-like sclerosing component and a myxoid one. Myxoid, dedifferentiated and well-differentiated morphologies were found respectively in three, two and one case. All patients were treated surgically with satisfying postoperative outcome. Two cases developed recurrence and no metastasis were noted.
Conclusion: PIL is a rare subtype of intrathoracic sarcoma which can mimic various neoplastic and non-neoplastic lesions with different prognostic and therapeutic outcomes. Therefore, an accurate diagnosis and a correct classification is of great clinical significance for a better management of the disease.

PS-21Poster Session Thymic and Mediastinal Pathology

PS-21-001

Micronodular thymoma with lymphoid stroma: an extremely rare subtype of thymic neoplasm

R. Ayadi*, I. El Hadhri, E. Braham, R. Yaiche, I. Bouassida, M. Affes, O. Ismail, S. Ben Slama, A. Ayadi
*Department of Pathology, Abderrahmen Mami Hospital, Tunisia

Background & objectives: Micronodular thymoma with lymphoid stroma (MTLS) is an extremely rare subtype of thymic neoplasm. It accounts for approximately 1%-5% of all thymomas and is rarely reported. To better understand this entity, we reviewed clinicopathological data of patients with MTLS.
Methods: We report 4 cases of MTLS, treated in our institution from 2004 to 2023. The clinical features, histopathology findings and treatment are discussed. The diagnostic was made on resected chirurgical specimens. Hematoxylin and eosin-stained sections were studied and immunohistochemically stained using cytokeratin, TdT, CD3, CD20 were done to confirm the histopathological diagnosis.
Results: There were 2 male and 2 female patients, aged between 62 and 73 years with a mean of 66. There was no history of myasthenia gravis or autoimmune disease. All patients presented with chest pain. Computed tomography of the chest showed an anterior medisatinal mass. All patients underwent asurgical resection and radiotherapy was performed after operation. Microscopic examination showed two components: a nodular epithelial component and mature lymphoid cells with prominent germinal centres. Of the nodular structures, the epithelial cells had a spindle to round appearance, with bland euchromatic nuclei and plump cytoplasm. Mosaoka was in stage I (n=1) and stage II (n=3). The patients had a successful postoperative recovery.
Conclusion: The micronodular thymoma with lymphoid stroma, according to the new WHO classification, is infrequently tumour and is currently considered to be a borderline tumour with good prognosis, rare recurrence and metastasis.

PS-21-002

Exploratory evidence maps for the WHO Classification of Tumours 5th edition for tumours of the thymus

R. Cierco Jimenez*, C. Giesen, J. del Águila Mejía, S. Armon, N. Myles, G. Goldman, F. Campbell, T. Lee, A. Bres, L. Bouanzi, I. Cree, D. Lokuhetty
*IARC/WHO, France

Background & objectives: Research in tumour pathology is ever-changing. Therefore, assessment of existing evidence in WHO Classification of Tumours 5th edition (WCT5) and identifying levels of evidence (LOE) will improve future editions. We aimed to perform exploratory maps for tumours of the thymus in WCT5.
Methods: We extracted citations from this chapter, imported and coded them in EPPI-Reviewer. The maps were plotted using EPPI-Mapper. Our final evidence maps displayed tumour types (columns), tumour descriptors (rows) and LOE according to study designs (dots using a four-colour code). LOE were assigned in accordance with criteria from the Centre for Evidence Based Medicine (CEBM) of the University of Oxford.
Results: We included 677 studies addressing 25 tumour types cited in the thymus chapter of the WCT5 for Thoracic Tumours. Overall, 80.8% (n=547) references were labelled as low LOE based on study design only, and 2.2% (n=15) were labelled as high LOE for thymus tumours. The tumour with the highest number of references was squamous cell carcinoma (n=93; 13.7%). The tumour presenting the highest proportion of high LOE was type AB thymoma (n=4; 1.4%). By tumour descriptor, the heading with the highest number of cited evidence was Epidemiology (n=186; 28.0%), and the lowest were Clinical Manifestations, Other (n=10; 1.5%), Diagnostic Molecular Pathology (n=11; 1.7%) and Prognosis and Prediction (n=13; 2.0%).
Conclusion: This study represents a first step in the WCT EVI MAP project (funded by the EU Horizon grant 101057127), which aims to assess existing evidence for different tumour types and tumour descriptors and LOE. We observed that, when applying CEBM LOE, most studies were coded as low LOE based on study design. We also observed great heterogeneity throughout all assessed areas. Based on these findings we plan to improve on the cited evidence in the next edition of the WCT.

Funding: The overall project, International Agency for Research on Cancer, and beneficiaries are funded by the European Commission (HORIZON grant no. 101057127).

PS-22Poster Session Cytopathology

PS-22-001

Role of EBUS-TBNA of mediastinal lymph node in the diagnosis of silicosis

I. Bağcı*, E. Dündar, F. Alataş, P. Şener
*Eskişehir Osmangazi University, Turkey

Background & objectives: Silicosis is a preventable occupational disease, diagnosed clinically, caused by chronic exposure to silica crystals. We evaluated the clinicopathological concordance of cases considered suspicious for silicosis by histomorphological and polarized light microscopic examination of FNAB materials of mediastinal lymphadenopathies.
Methods: FNAB materials with detection of crystalloids via polarized light microscopy evaluation in our department, were scanned with

the automation system. Clinical data of the cases were obtained from the automation system and patient files, and cases, which is clinically diagnosed with silicosis, were determined. Cytoblock preparations of these cases were re-evaluated histomorphologically.
Results: Clinical data were obtained for 63 of 140 cases scanned by polarized light microscopy. Fifty of these cases (79.4%) had crystals and 30 of them diagnosed with silicosis. Three patients were diagnosed with concomitant tuberculosis. Twenty-one of the patients (42%) resided in the Eskişehir-Kütahya-Bilecik region and 24 of 38 patients with occupational data (%63,2) worked in the ceramics, construction, and foundry sectors, which are risk factors. In 48 of cases with crystals (96%), histomorphologic examination revealed histiocyte aggregates containing anthracotic pigment accumulation. Fibrosis, hyalinization, and necrosis were present in 15, 7 and 5 of them, respectively. In the other 2 cases, poorly formed granulomas were noted.
Conclusion: Silicosis is diagnosed clinically by evaluation of radiological imaging and respiratory function tests of patients with long-term exposure. Although not necessary for definitive diagnosis, pathological examination of FNAB materials can support the diagnosis and exclude differential diagnoses, such as malignancies and infectious processes. Therefore, evaluation of crystalloids via polarized light microscopy in FNAB materials of mediastinal lymphadenopathy cases with histiocyte aggregates containing anthracotic pigment accumulation, necrosis and/or fibrosis, would be guiding in terms of the clinical management of these cases.

PS-22-002
Thyroid fine needle aspiration cytology: validation of the 2024 RCPath reporting guidelines in an independent UK tertiary centre cohort
J. Coelho Lima*, S. Appukutty, J. Chan, A. Duckworth, L. Heptinstall, N. Patel, M. O'Donovan, A. Marker
*Department of Histopathology, Addenbrooke's Hospital, Cambridge University Hospitals NHS Foundation Trust, United Kingdom

Background & objectives: To review thyroid fine needle aspiration cytology (FNAC) reporting in a UK tertiary centre and assess reproducibility of the 2024 Royal College of Pathologists' (RCPath) FNAC guidelines, particularly the expected 'Thy' category risk of malignancy (ROM), in this independent cohort.
Methods: All consecutive thyroid FNAC reported at Addenbrooke's Hospital (Cambridge, UK) between January 2021 and December 2022 were reviewed. The proportion of cases assigned a 'Thy' category and discussed at multidisciplinary team meeting (MDM) as well as the ROM were compared to RCPath standards. The ROM was calculated based on available histopathological diagnosis over a maximum follow-up period of 38 months.
Results: 328 thyroid FNAC from 287 patients were reported [female n=238 (83%); mean age±SD = 49±16 years]. The proportion of cases assigned to each 'Thy' category was as follows: Thy1 25.6%; Thy2 13.4%; Thy3a 32.6%; Thy3f 21.3%; Thy4 0.9%; Thy5 5.5%; no 'Thy' assigned 0.6%. Further treatment discussion at MDM was recorded for 98%, 100%, and 100% of Thy3, Thy4, and Thy5 cases, respectively. The ROM for each category (RCPath 95%CI ROM) was as follows: Thy1 8.6% (5%-22%); Thy2 2.8% (3%-9%); Thy3a 11.7% (20%-31%); Thy3f 22.2% (24%-39%); Thy4 100% (70%-87%); and Thy5 100% (97%-100%). Thy3a cases showing cytological atypia had higher ROM compared to those with architectural atypia (26.5% vs. 12.5%).
Conclusion: The proportion of 'Thy2' cases was lower than expected, likely reflecting local practice of not performing FNAC for clinically and sonographically 'benign' nodules. Overall, the percentage of cases discussed at MDM and the ROM associated with each 'Thy' category was in line with the RCPath recommendations. The higher ROM observed for Thy3a cases with cytological atypia is also expected by the RCPath. Our data corroborates the use of the 2024 RCPath thyroid FNAC guidelines in an independent, real-life UK cohort.

PS-22-003
Worrisome features in thyroid FNAC – malignancy not confirmed. Bethesda V cases revisited
J. Dušková*, J. Jiskra, J. Kovářík, D. Nováková Kodetová
*Charles University, Czech Republic

Background & objectives: The introduction of the NIFTP diagnosis and subsequently published second edition of TBSRTC reduced the risks of malignancy in the categories BIV - BVI. Follow-up analysis of six-year material focusing on unconfirmed suspicions.
Methods: In the years 2017-2022, during the validity of the 2nd edition of the Bethesda classification, we used diagnostic category B V in 105 cases. Follow up was obtained from 12 collaborating endocrinologists. Histopathological correlates were included in the teaching collection. In cases of unconfirmed suspicion, we analysed the source of the worrisome features and the possibility of additional investigations.
Results: The suspicion of malignancy was confirmed in 82% of cases, unsurprisingly most often, but not exclusively, in various subtypes of papillary carcinomas. Focusing on not confirmed suspicions, in our group of patients oncofollicular lesions without signs of invasion were three times diagnosed in cases suspicious for medullary carcinoma (twice with a near- complete necrosis of the nodule after FNA). Intrathyroidal parathyroid adenoma with nuclear features of papillary carcinoma was found in two cases. Twice, regressive changes in follicular nodular disease were the source of suspicion.
Conclusion: To optimize the treatment of patients with thyroid nodules: Education of the clinicians in getting sufficient material for both the immunocytochemistry and molecular techniques must continue. Interdisciplinary approach and standardized reporting are the state of art. In reporting suspicious cytomorphology patterns broader differential diagnosis provided may initiate proper use of additional diagnostic tools.

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PS-22-005
Endoscopic ultrasound-guided fine needle aspiration of pancreatic neuroendocrine tumours and impact of rapid on-site evaluation: single centre experience
I. Guvendir*, O. Sahin, I.E. Zemheri
*Kartal Dr. Lütfi Kırdar City Hospital, Department of Pathology, Turkey

Background & objectives: Endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) is a highly sensitive and accurate method for identifying pancreatic neuroendocrine tumours (PanNETs). However, research on grading and assessing the Ki67 proliferation index in FNA samples is limited.
Methods: This study analysed 335 EUS-FNA cases performed between 2016 and 2022, of which 12 cases of PanNET were further evaluated. The morphology, Ki-67 index, and grading (G) of cell blocks (CB) obtained from the PanNET aspirations were compared to those of the resected material.
Results: Out of 12 PanNET's with rapid on-site evaluation(ROSE), in aspiration and CB,7 (58.3%) cases were G1,while 5 (41.7%) cases were G2.On the other hand, resection of these cases,6 (50%) were diagnosed as G1,5(41.7%) cases were G2,and 1 case(8.3%) was G3.The average ki67 index in CB was 2.92(min: 1-max: 10), while in resections it was 4.67(min: 1-max: 22).Only 2(16.6%) showed a discordance between grade and ki67, resulting in an overall concordance of over 80%.On average,1.83 needle passes were made(range: 1-3), while the average number of slides and cell blocks were 9.33(range: 1-24) and 2.17(range: 1-6),respectively. There were no

significant differences in the number of passes, slides, or cell blocks between the consistent and discordant groups.
Conclusion: Optimal counting techniques and sensitivity for Ki67 are crucial in grading PanNETs in both aspiration and resection materials. The grade and Ki67 index demonstrated high concordance when comparing CB and resection, and was not affected by the number of passes, slides, or cell blocks. But still, ROSE can be a valuable tool for diagnosing rare pancreatic lesions, particularly in low-volume centres.

PS-22-006
Usefulness of pancreatic fine needle aspiration - a comparison with histological diagnosis using the new WHO reporting system, a tertiary centre experience
J. Martins Gama*, C. Courelas, J. Pimentel, A.L. Alves, G. Fernandes, M.A. Cipriano
*Unidade Local de Saúde de Coimbra, Portugal

Background & objectives: Fine needle aspiration (FNA) is an essential tool in the diagnosis of pancreatic lesions. We attempted to find the diagnostic yield of this method and how it compares with the surgical specimen, applying the new WHO Cytology Reporting System.
Methods: A retrospective transversal study was completed using archival slides and the digital medical records from the 404 patients to whom pancreatic FNAs had been performed between 2012-2023, a total of 420 pancreatic FNAs. 16 patients had more than one FNA. 259 FNAs were from our institution and 69 FNAs were from a different institution, with no information about follow-up.
Results: From the 420 FNAs, 314 of the diagnoses were made in a cell block and 106 in a conventional smear only. 87 FNAs were deemed nondiagnostic (20.7%): 21 were conventional smears, and 66 were cell blocks. The remaining 333 were adequate. The cases were distributed as follows: benign/negative for malignancy in 69 (16.4%), atypical in 1 (2%), pancreaticobiliary neoplasm low risk/grade (PaN-low) in 6 (1.4%), pancreatic neoplasm, high risk/grade (PaN-High) in 5 (1.2%), suspicious for malignancy in 2 (0.5%) and malignant in 250 (59.5%). Forty-four patients were submitted to surgery. There was a cytology-histology agreement in 39 with a Cohen's kappa agreement of 0.785 (substantial).
Conclusion: Using the new WHO reporting system there is a substantial agreement between cytology and histology. In our series, under one-fifth of the FNAs were deemed non-diagnostic, but almost 60% were positive for malignancy.

PS-22-007
Comparison of cytoplasmic and nuclear expression loss of MTAP immunohistochemistry in pleural effusion cytologies and correlation with homozygous deletion of p16/CDKN2A
N.S. Şeker, O.F. Mülkem*, E. Tekin, G. Ak, M. Metintaş, S. Metintaş, E. Dündar
*Eskisehir Osmangazi University, Turkey

Background & objectives: Pleural mesothelioma (PM) is a common cause of death in some parts of world. There are no specific rules in the literature for MTAP immunohistochemistry evaluation. Our aim in this study is to evaluate MTAP loss in every aspect.
Methods: We discussed pleural cytology samples of cases with histopathologically PM diagnoses. Cell blocks prepared from these materials were subjected to fluorescent in situ hybridization for p16/CDKN2A homozygous deletion. We further categorized MTAP loss into nuclear and cytoplasmic loss and whether it was focal or diffuse. We also evaluated the correlation. We use IBM SPSS 21 program for statistical analysis.
Results: This study included 48 cases of PM. The mean age of the cases was 65.6±10 years. There was no significant gender predominance. We observed MTAP loss in a total of 21 cases. MTAP nuclear loss was usually diffuse (n=14). MTAP cytoplasmic loss was usually focal (n=18). MTAP nuclear and cytoplasmic loss was consistent with each other (kappa value=1), but not with focal or cytoplasmic loss (kappa=0.5). We found 33 cases with p16/CDKN2A deletion. 15 of the 33 cases of PM with MTAP loss also had p16/CDKN2A deletion in cases with p16/CDKN2A deletion, nuclear loss detected diffusely (n=11/15); also, cytoplasmic loss commonly detected focally (n=13/15).
Conclusion: In English literature, we did not find a study in which the degree of MTAP staining loss was recorded. With this study, we think that it is not healthy to use MTAP immunohistochemistry alone in the diagnosis of mesothelioma, but it can be taken into consideration when the cytoplasmic or nuclear loss is focal or nuclear. However, we think that it should always be correlated with p16/CDKN2A deletion and evaluated together with other markers known in the literature.

PS-22-008
Assessment of HPV vaccination status and its relationship with HPV-associated lesions in young women
C. Padrão*, J. Tinoco, C. Ribeiro, A. Ferreira, M.G. Gasparinho
*Hospital Prof. Dr Fernando Fonseca, Portugal

Background & objectives: HPV causes most cervical cancers. HPV vaccines provide protection against intraepithelial neoplasia and HPV16/18-associated carcinomas in young women. The incidence of HPV in Portugal was 19.4% before vaccination was introduced in 2008. Its real effectiveness is not known in Portugal.
Methods: Squamous intraepithelial lesions and squamous cell carcinoma diagnoses from cervical cytology samples were retrieved from the files in our department between 2016 and 2023, from women born from 1990 to 1998, eligible for HPV national vaccination plan and cervical screening. We also collected clinical data concerning vaccination status and age of first intercourse.
Results: From 491 cases, we found 1 squamous cell carcinoma (non-vaccinated), 18 HSIL (3 with complete vaccination, 2 incomplete and 13 non-vaccinated) and 78 LSIL (37 with complete vaccination, 5 incomplete and 34 non-vaccinated). From the 48 cases of lesions in vaccinated women, we could find the age of first intercourse in 26 cases. In 12 women it happened before the vaccination (2 HSIL and 10 LSIL), in 14 after it (1 HSIL and 13 LSIL). Diagnosis was rendered at a mean of 25,37 years-old (range 18 – 31 years-old). In vaccinated women, mean age of vaccination was 16,48 years-old (range 12 – 30 years-old). 3 women were vaccinated after diagnosis.
Conclusion: Vaccines provide partial protection against LSIL and HSIL. We had at least 1 HSIL and 13 LSIL cases of vaccinated people that theoretically only had contact with the virus after vaccination. This retrospective study represents a population that was selected for hospital evaluation, and we couldn't establish global vaccine coverage, posing limitations. Nonetheless, it highlights the continued importance of cervical screening cytology until high vaccination coverage significantly lowers virus prevalence and, thus, cervical squamous lesions.

PS-22-009
Malignancy rates for Bethesda III-IV thyroid nodules: a single institution retrospective study of the correlation between fine-needle aspiration cytology and histopathology
M. Rezola*, P. Aguirre, D.X. Ugas, I. Bernal, Y.P. Rodriguez, J.W. Comba, A. Ordoñez, S. De Burgos, A. Val-Carreres, M. Carrillo, M. Hidalgo, I. Ruiz
*Spain

Background & objectives: Reported malignancy rates for Bethesda III-IV categories have considerable variability among institutions. The aim of this study is to establish a possible association between these cytological categories and malignancy rates in patients treated at a single institution.

Methods: A retrospective analysis of 2879 thyroid fine-needle aspiration cytology (FNAC) were performed at the Hospital Universitario Donostia over from 2020 to 2023. The nodules of 254 patients were classified as Bethesda III - IV. A correlation between the FNAC results and the histopathological analyses, performed by surgical treatment or biopsy, was made including clinical follow-up.
Results: Of 2879 FNAs analysed, 218 were diagnosed as Bethesda III and 36 IV. Surgery or biopsy was performed in 60.5% of III cases with a 25.5% malignancy rate, ranging 16-32% by year. About 66.6% of IV cases underwent surgery or biopsy with a 32.5 malignancy rate, ranging 22-50% by year.
Conclusion: The risk of malignancy described for Bethesda III - IV nodules is comparable within the literature, ranging from 13 to 30% for category III and 23-24% for category IV. As some degree of subjectivity exists between the distinction of these categories, it is important to agree on unanimous cytological criteria for their categorization and estimate the rates of malignancy, at each institution. Adding molecular tests could be helpful to accurately identify thyroid lesions that require surgical intervention.

PS-23Poster Session Pathology in Favour of Developing Countries

PS-23-001
Diagnostic value of neutrophil lymphocyte ratio, platelet lymphocyte ratio and systemic immune-inflammation index in prostate cancer

A.C. Ablaza*, A.B. Asanion
*Baguio General Hospital and Medical Center, Philippines

Background & objectives: Systemic inflammation is linked to solid tumour development, including prostate cancer (PCa). Identifying cost-effective and accessible inflammatory biomarkers offers potential for improving PCa diagnosis affordably and reducing unnecessary biopsies. Our study assesses their diagnostic value in suspected PCa patients.
Methods: This six-year cross-sectional study involved patients with suspected PCa, documenting their age, histopathologic diagnosis, serum prostate-specific antigen (PSA) level, and complete blood count (CBC)-derived neutrophil lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR), and systemic immune-inflammation index (SII). Diagnostic value was evaluated using specificity, sensitivity, positive predictive value (PPV), negative predictive value (NPV), and receiver operating characteristic (ROC) curve analysis.
Results: The study included 79 patients, categorized into PCa and non-PCa groups based on histopathology. CBC parameters showed minimal variation between groups, resulting in little differences in inflammatory biomarkers derived from this test. PSA levels were substantially higher in the PCa group than the non-PCa group. PSA displayed high sensitivity and NPV but low specificity and PPV, while NLR, PLR, and SII showed low sensitivity, specificity, and PPV but high NPV in PCa diagnosis. Only PSA demonstrated a significant difference ($p < 0.003$) between the two groups, whereas NLR, PLR, and SII did not ($p > 0.05$). ROC curve analysis revealed weak discrimination for NLR, PLR, and SII and strong discrimination for PSA.
Conclusion: Despite controversial findings in studies on inflammatory biomarker diagnostics, our research concurs with several authors in identifying NLR, PLR, and SII as inferior to PSA for PCa diagnosis. Although easily derived from an inexpensive CBC, they are susceptible to influences like inflammation and infection. Variations in the time intervals between blood test and surgery may also affect results. Further research on their relationship with PCa progression is recommended to assess biomarker levels in early and advanced disease stages.

PS-23-002
Survey-based evaluation of pathology services within Romania's healthcare system

M.M. Köteles*, G. Olteanu
*County Emergency Hospital Bihor, Romania

Background & objectives: Insufficient funding, outdated legislation, and lack of standardization within pathology services (PS) in Romania's Public Health System (PHS) impede the integration of basic and advanced diagnostic techniques. Our study was designed to evaluate the state of PS in the PHS.
Methods: A survey consisting of 10 questions was distributed through emails, the national society of pathology WhatsApp Group and postal letters to PS from the PHS. Eight questions were designed to assess the available equipment, diagnostic techniques, and the number of pathologists, and two questions were meant to establish the satisfaction for the current infrastructure and with the funding received.
Results: A total of 153 Pathology Services (PS) were identified, with 69 (45.1%) responding to our request, and 63 out of 69 (91.3%) completing our questionnaire. Among respondents, over 88% reported having tissue processors, microtomes, and tissue embedding stations. Regarding staining equipment, 15.87% used only manual staining kits, 41.27% used automatic stainers, and 39.68% had both. 47.62% of PS reported having cryostats for frozen sections. Less than 40% reported having automatic immunohistochemical staining systems and other advanced equipment. On average, 3.7 pathologists worked in the PHS laboratories. Satisfaction ratings ranged from 1 to 10, with less than 33% rating satisfaction below 5 and over 67% rating it above 5.
Conclusion: The lack of dedicated funding for the infrastructure of PS within Romania's PHS is the first consequence of outdated and inapplicable laws. The first step towards finding solutions to this problem is assessing the current status of the country's PS. Our study raises important questions about the future open collaboration between PS, the possibility of digitalisation, and the improvement strategies that must be implemented to optimize quality patient care.

PS-23-003
Clinical and pathological features of fusion oncogene associate papillary thyroid cancer of China

H. Li*
*Fujian Provincial Hospital, China

Background & objectives: RET and NTRK gene fusion are markers linked to radiation-induced papillary thyroid cancer (PTC) and targets for treatment of PTC. Understanding the characteristics of fusion oncogene-associated PTC (FO-PTC) is crucial for clinical management. This article summarizes the clinicopathological features of FO-PTCs.
Methods: 590 cases of PTCs, including 46 FO-PTCs (13 NTRK/PTC and 33 RET/PTC), underwent genetic testing from 2019 to 2024 were included. Patients' ages ranged from 9 to 70 years, with a median of 38 years. 36 were female and 10 were male. The female-to-male ratio is approximately 4:1. Clinicopathological parameters and molecular changes were analysed. Data from the TCGA were studied.
Results: Compared with BRAFV600E PTCs, FO-PTCs tend to occur in younger patients($p=0.0041$) and have large tumour size. FO-PTCs exhibit a multinodular growth pattern and show extraperitoneal thyroid invasion, infiltrating glandular lobes and lymph node metastasis. Histology has limited diagnostic value due to its broad morphologic spectrum. All tumours display typical PTC nuclear features, and significant pale, translucent cytoplasm is commonly seen. In FO-PTCs, RET and NTRK gene fusion are the most common fusion genes, accounting for 5.6% and 2.2% of cases, respectively. The predominant fusion genes in NTRK-PTCs are CCDC6 (42.1%) and NCOA4 (47.4%). In NTRK-PTCs, ETV6-NTRK3 is the predominant fusion gene. Additionally, two previously unreported fusion genes were identified.
Conclusion: RET and NTRK gene fusions are rare in disseminated PTC. FO-PTCs have varied morphologies and invasive behaviour, making them easily misdiagnosed. Genetic testing is crucial for accurate

diagnosis and guiding treatment of advanced PTC. The release of radioactive wastewater from Japan has posed significant challenges for thyroid cancer prevention and treatment in China. It is important to remain vigilant about the high incidence of radiation-induced PTC in the coming decades. Further research is necessary for comprehensive understanding in the future.

PS-23-004

Primary effusion lymphoma: a clinicopathologic study from an HIV/AIDS endemic province of South Africa

G.B. Nhlonzi*, N. Moagi, A. Mwazha
*Ampath Laboratory Pietermaritzburg, South Africa

Background & objectives: Primary effusion lymphoma (PEL) is a rare and distinct subtype of a high-grade non-Hodgkin diffuse large B-cell lymphoma that predominantly presents as body cavity lymphomatous effusion. We described the histopathological spectrum of PEL in a South African public sector.
Methods: 10 years retrospective laboratory-based study, from January 2010 to December 2019 which reviewed and reappraised clinical presentation, laboratory data, histomorphology, immunohistochemical profiling and bone marrow aspirate and trephine of all the patients diagnosed as PEL in our centre. Stata16 software was employed for data analysis. The study was approved by the University of KwaZulu-Natal's Biomedical Research Ethics Committee.
Results: Ten patients were diagnosed with primary effusion lymphoma in the period under review. Eight patients had solid variant of primary effusion lymphoma involving lymph nodes. One patient had concurrent Kaposi sarcoma. Eight patients were male, and two patients were female. The patients' age ranged from 26 years to 51 years (mean 36 years). Seven patients were HIV positive, and the HIV status was unknown in three patients. The CD4 count ranged from 137 (16%) to 348 (22%) in 6 patients. Three patients with bone marrow aspirate and trephine biopsies, demonstrated no evidence bone marrow involvement by the tumour. The histopathological diagnosis was based on the WHO classification of hematolymphoid tumours.
Conclusion: Primary effusion lymphoma is dominated by extravacitary solid variant in our community and occurs in young patients who are HIV-positive. All our patients were lost to follow-up. It is uncertain whether all patients died prior to being referred to haematology clinic or sought alternative medicine. Two PEL cases involved either pleural cavity or abdominal cavity exclusively. In two cases, there was either associated multicentric castleman disease or Kaposi sarcoma underscoring the pathogenetic role of Human Herpesvirus 8 in PEL.

PS-23-005

Assessment of Ki 67 proliferative index in breast cancer tissue using visual scoring android application by IKWG – a closer step to better analytic validity?

N. Radhakrishnan*, P.P. Kasukurti, S. Naskar, S.M. Kamath, C.D. Wilfred, M.G. S R
*Department of Pathology, Ramaiah Medical College, Bengaluru, India

Background & objectives: IKWG introduced Visual scoring Android Application (APP) and proposed a standardized scoring method to ensure consistency in Ki 67 scoring. Our study aims to examine the reproducibility of global Ki67 score by the APP with the aid of smart phones.
Methods: 71 Ki67 immunostained hormone receptor positive trucut biopsies of breast cancers were retrospectively collected and scored by two observers independently using institutional hotspot method (HS) and global method by APP (GW). For 10 cases, multiple high-quality images taken in smart phone were uploaded in QuPath software for digital image analysis (DIA), in the absence of whole slide scanner (WSS).
Results: The GW scores of Ki67 PI obtained is categorized into low, intermediate, and high categories based on 2015 St. Gallen's guidelines. The overall intra-class correlation between inter-observer values by HS is 0.819 (good) whereas it is 0.971 (excellent) by global method. The overall mean difference by HS is five times greater than global weighted APP scores, which is statistically significant. Between the observers, cases exhibited 21.8% categorical shift in HS and 12.5% while using APP. The average Ki67 values obtained from multiple high-quality images by DIA using QuPath software for 10 selected cases showed increased concordance with APP scores when compared to HS scores.
Conclusion: The study highlights the significant inter-observer variability in HS when compared to GW scores by the APP and demonstrates the use of smart phone images in DIA in the absence of WSS. The concordance of results using DIA obtained from smart phone images illustrates the effective standalone use of visual scoring APP in bringing consistency to KI 67 PI and its potential to broaden the prognostic role of Ki67 as a companion diagnostic tool in resource limited countries like India.

PS-23-006

Cervical cytopathology insights in underserved communities: perspectives from a humanitarian initiative in Cabo Verde

V. Salgado*, R. Luís
*Department of Pathology, Unidade Local de Saúde São José, Portugal

Background & objectives: Cervical cytology, whether through liquid-based or conventional smears, significantly reduces cervical cancer rates. The 'Portugal Para África' project sought to facilitate screening in Ilha do Maio, Cabo Verde, enabling state-supported treatment access for underserved women.
Methods: Women aged 20-65 without screening in the previous 3 years or over 65 who had never been screened were selected across the five island health facilities. General Practitioners performed conventional smears, which were handed to a Pathology resident for manual Papanicolaou staining and microscopic evaluation in a field laboratory. The process, from sampling to review, took about 30 minutes.
Results: A total of 73 exams were performed in 5 days, encompassing patients aged 21-70 years old; 7 samples were deemed inadequate (3 irreparably broken slides and 4 incorrectly stained specimens). The remaining 66 samples were assessed according to The Bethesda System for Reporting Cervical Cytology (TBSRCC) criteria and classified as follows: 42 NILM (63.6%), 8 ASC-US (12.1%), 4 ASC-H (6.1%), 4 LSIL (6.1%) and 8 HSIL (12.1%). The Pathology resident consulted on rare occasions with a Senior Pathologist, by telepathology (via exchange of pictures of selected microscopic fields). Women with a diagnosis of intraepithelial lesion were referred to a Gynaecologist and received financial aid from the local government.
Conclusion: Our series presents a higher percentage of squamous intraepithelial lesions than reported by other authors; notably, no malignancies were identified. These results may stem from the geographical isolation of the island within the archipelago, impacting vaccination rates and healthcare access. TBSRCC criteria allowed for rapid examination with structured reports from a Resident. Besides offering immediate medical aid, Humanitarian projects are also a good way to educate and empower the population, providing awareness and instituting good practices.

PS-23-007

Diagnostic utility of TRPS1 and GATA3 antibodies in various metastatic and primary tumour entities of breast and non-breast origins

H. Sahin Ozkan*, Ç. Çelikel, H. Kaya
*Marmara University, Turkey

Background & objectives: TRPS1 (Trichorhinophalangeal syndrome 1) immunohistochemistry (IHC) has been suggested as a diagnostic

marker for breast carcinoma (BC), however its specificity and potential role in differential diagnosis of metastatic tumour of unknown primary have not been well-established.
Methods: Tissue microarrays were created using a 3mm punch per case. Immunoreactivity score (IRS) was calculated by multiplying a variable representing the percentage of positive cells by a variable representing the staining intensity. The IRSs were categorized as negative (0-1), low-positive (2), intermediate-positive (3-4), high-positive (6,9). Also, institutional next-generation sequencing RNA fusion panel results were examined for TRPS1 and/or GATA3-partnered fusions.
Results: A total of 173 cases, of which 47 were BC, were evaluated. Non-breast cases included 24 different tumour entities. Intermediate to high-positivity of TRPS1 distinguished BCs from other tumours with 95%sensitivity and 85%specificity.Only TRPS1-negative BC case was a triple-negative apocrine BC, which was high-positive with GATA3.Only 1 BC was GATA3-negative,which was an adenoid cystic carcinoma (AdCCa) and high-positive with TRPS1.When intermediate to high-positivity of TRPS1 and GATA3 antibodies were combined, sensitivity and specificity were 93%and 98%.All urothelial carcinomas were negative with TRPS1. 50%of pancreatobiliary adenocarcinomas were high-positive with GATA3, while all were TRPS1-negative. An oral AdCCa was TRPS1-positive, GATA3-negative. 30%of lung and 25%of prostatic adenocarcinomas were low-positive with TRPS1. 78%of osteosarcomas and 71%of chondrosarcomas were high-positive with TRPS1.
C**onclusion:** TRPS1 has high sensitivity and specificity for BC, especially in combination with GATA3. It is a reliable marker for distinguishing BC from urothelial carcinoma. It is also more specific than GATA3 when differentiating pancreatobiliary cancers from BC. New markers are needed to differentiate salivary gland AdCCa from its breast counterpart, since they both show TRPS1-positive, GATA3-negative immune-profile. It is also important to keep in mind that both bone metastasis of BC and the primary bone tumours may highly express TRPS1.

PS-24Poster Session Digestive Diseases Pathology - GI

PS-24-001
Spectrum of appendiceal neoplastic lesions: an institutional review

S. Akhtar*, R. Yadav, P. Das, S. Rawat, M.D. Ray, H. Bhattacharjee, K. Kataria, R. Panwar
*AIIMS, New Delhi, India

Background & objectives: Appendix gives rise to several neoplasms, many causing pseudomyxoma peritonei and these behave differently from colorectal carcinomas. We aimed to study the spectrum of appendiceal neoplasms and grade and stage them as per WHO and PSOGI classifications.
Methods: Cases with a diagnosis of appendiceal neoplasm over a period of last 9 years were retrieved and reviewed. Variables including age, gender, tumour location, tumour type, clinical status, diagnosis, and treatment were collected from the records. Slides were reanalysed in detail for tumour type, grade, and stage as per the WHO/ PSOGI classifications.
Results: A total of 188 patients with a diagnosis of appendiceal neoplasm were included. Mean age was 43.6 years. Of the 188 patients, 115 were females (62.5%). The main symptom was abdominal pain, and few patients were diagnosed incidentally on imaging. 124 cases were classified as low-grade mucinous neoplasm (65.95%), 3 high grade mucinous neoplasm (1.59%), 29 adenocarcinoma including mucinous adenocarcinoma (15.42%), 5 goblet cell adenocarcinoma (2.65%), 4 serrated lesion of appendix (2.12%) and 21 neuroendocrine neoplasm (11.17%). One case of appendiceal granular cell tumour (0.53%) and one ganglioneuroma (0.53%) were also identified.
Conclusion: Appendiceal neoplasms more commonly affect adult females and can present with a variety of clinical manifestations ranging from incidental lesions to widely metastatic abdominal masses. Low grade mucinous neoplasms are the most common amongst them followed by adenocarcinomas and neuroendocrine neoplasms. Their nomenclature, grading and staging differs from rest of colorectum which forms the backbone of treatment decision and prognostication for these patients.

PS-24-002
Lymph node threshold in colorectal cancer: surgeons' perspectives and practices

B.K. Aktas*, N. Padmanabha, Y. Chornekyy, O. Yilmaz
*Turkey

Background & objectives: Current guidelines from the AJCC and the College of American Pathologists recommend examining at least 12 lymph nodes in colorectal cancer cases. This study explores surgeons' views on yields below this threshold, assessing their beliefs and expectations.
Methods: A voluntary 19-question survey was administered by email to colorectal and general surgeons to assess clinical, pathologic, and molecular factors that affect low lymph node yield. The survey had 168 respondents, including colorectal surgeons (58%) and general surgeons (32%) from academic and non-academic centres. 73% of respondents had more than 10 years of experience in surgery.
Results: The majority of the surgeons (71%) find suboptimal lymph node yields uncommon, yet 29% report them as frequent. While 92% consult pathologists in such cases, consensus on additional node requests or fat submission is absent. Nearly half (49%) believe treatment decisions are rarely affected by low yields, with 48% linking more nodes to better outcomes. Uncertainty persists about the role of clinical, surgical, and molecular factors in enhancing yields. Fifty-six percent consider prior treatments like chemotherapy/radiation, and 47% point to specimen characteristics such as length and sidedness as influential, but most dismiss mismatch repair status, age, or BMI as significant factors.
Conclusion: While the magic number of "12" LN appears to be the central dogma for CRC LN harvests, the above survey underlines a variable spectrum of expectations and interpretations of LN yield among surgeons. The overarching message for pathology is that thoughtful communication among surgeons and pathologists is critical to understanding the idiosyncrasies around individualized care and nuances around factors that may influence LN yield, with the ultimate hope of best-managing resources and optimizing patient care.

PS-24-003
Ultra-short coeliac disease: "proximate" biopsy is required for "ultimate" explanation

A.R. Akur*, E.N. Kozan, C.T. Kırsaçlıoğlu, Z. Kuloğlu, A. Akpinar, B. Savaş, A. Kansu Tanca, A.I. Soykan, A. Ensari
*Ankara University School of Medicine, Pathology Department, Turkey

Background & objectives: Ultra-short coeliac disease (USCD) has recently appeared in the literature to designate coeliac cases showing mucosal pathology only in the duodenal bulb(D1). We, therefore, evaluated clinicopathological features of USCD to stress the significance of duodenal bulb biopsy in clinical practice.
Methods: Sixty-four USCD cases (46 children, 18 adults) with isolated D1 involvement and age/sex-matched 70 classical CD (cl-CD) cases (46 children, 24 adults) showing both D1 and distal duodenum(D2) involvement were evaluated for symptoms (typical/atypical), serology, histology including Marsh types, and CD3 IEL counts in a statistically comparative manner. Additionally, correlation between clinicopathological features and serology was assessed for each group.

Results: Mean ages of paediatric and adult patients were 9.37, 37.09 years with a female predominance of 64.13%, 61.9%, respectively. In all patients, typical symptoms (53.84%;21.73%), seropositivity (95.45%;82.97%), Marsh 3 histology (77.14%;33.12%), and higher CD3 IEL count (45%;38.98%) were significantly more frequent in the cl-CD group than in the USCD group (p=0.0089;0.0493;0.012;0.021, respectively). Diarrheal (50%) was the prevailing presenting symptom in paediatric cl-CD while screening endoscopy (43.75%) was more common in children with USCD (p=0.031). Seropositivity was more common in cl-CD than the USCD both in paediatric (p=0.0009) and adult groups (p=0.0001). CD3 IEL count was significantly lower in paediatric USCD (39.59%) than cl-CD (45.42%) (p=0.04) and was positively correlated with histologic Marsh types (F=5.27; p=0.0099).
Conclusion: The non-negligible prevalence of USCD within CD, along with its association with atypical, milder symptoms at initial presentation indicates the significance of a high level of suspicion and extensive sampling for accurate diagnosis. High frequency of parameters associated with severe disease such as elevated tTg-IgA, Marsh Type 3 histology and higher IEL counts in cases with extensive duodenal involvement compared to USCD, suggests that USCD may represent an early stage of CD, thus further assisting in preventing late complications.

PS-24-004

Exploring the prognostic value of blood cell ratios and C-reactive protein in gastric cancer: insights into molecular subtypes and tumour immune microenvironment

J.C. Almeida*, A.C. Bravo, J.R. Silva, D. Marques, C. Neto do Nascimento, X. Wen, L. Mascarenhas-Lemos, M. Cravo, F. Carneiro, I. Gullo
*Department of Pathology, Centro Hospitalar Universitário de São João (CHUSJ), Porto, Portugal; Faculty of Medicine of the University of Porto (FMUP), Porto, Portugal

Background & objectives: Lymphoplasmacytic-rich and neutrophilic-rich tumour immune microenvironment (TMI) have been described in Epstein-Barr-virus-associated (EBV+) and microsatellite-unstable (MSI-high) gastric cancer (GC), respectively. Aim: to explore associations between EBV+/MSI-high status, TMI, peripheral blood cell ratios, tumour serum biomarkers and prognostic outcomes in GC.
Methods: A multicentric series of GC patients submitted to neoadjuvant chemotherapy (NAC) (n=58) or surgery alone (n=82) was selected retrospectively. Clinicopathological variables were collected, including serum biomarkers (1-3 months before NAC/surgery and 3 months after surgery): neutrophils/lymphocytes/monocytes/platelets count; C-Reactive-Protein (CRP)/CA125/CA19.9/CEA levels. Neutrophil-to-lymphocyte-ratio (NLR) was calculated. EBV (EBER-ISH) and MSI (multiplex-PCR) status and TMI morphology (lymphoplasmacytic- versus neutrophilic-rich) were assessed.
Results: The series encompassed 7/140 EBV+ (5.0%) and 38/140 MSI-high (27.1%) GCs, characterised by lymphoplasmacytic-rich (EBV+:71.4% vs EBV-:5.3%, p<0.001) and neutrophilic-rich (MSI-high:28.9% vs MSS:2.0%, p<0.001) TMI, respectively. Prior to surgery, patients who underwent NAC harboured lower NLR compared to those submitted to surgery alone (3.05 vs 2.53, p=0.021). Pre-operative NLR and post-operative CRP levels were lower in neutrophilic-rich TMI GC (p=0.015 and p=0.006, respectively). Serum tumour biomarkers (CA125, CA19.9, CEA) were not related to morphological features or molecular subgroups (p>0.05). Overall, GC patients with CRP lower than median value(<1.1mg/dl) showed better overall survival (p=0.032), even when stratified by type of therapy (NAC versus surgery), MSI status and presence of neutrophilic-rich TMI.
Conclusion: This study contributes to the growing body of evidence of blood-based biomarkers as predictive markers of GC prognosis. A reduction of systemic pro-inflammatory status after surgery (e.g. CRP<1.1md/dl) might contribute to better overall prognostic outcomes of GC patients. Moreover, we observed that GC patients with neutrophilic-rich TMI, a morphologic feature associated with MSI-high status, had lower levels of neutrophils in peripheral blood (low pre-operative NLR). Possible explanations include neutrophil sequestration within the tumour microenvironment and/or consumption by the tumour.

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PS-24-005

Predictors of neoplastic progression in gastro-oesophageal lesions indefinite for dysplasia

V. Angerilli*, F. Galuppini, S. Brignola, G. Businello, B. Filippin, G. Pennelli, V. Guzzardo, J. Gasparello, P. Parente, A.P. Dei Tos, S. Realdon, A. Fantin, E.V. Savarino, M. Fassan
*Department of Medicine, Surgical Pathology Unit, University of Padua, Padua, Italy

Background & objectives: Current understanding of the risk of neoplastic progression in patients with Barrett's oesophagus with indefinite for dysplasia (BE-IND) and gastric indefinite for dysplasia (G-IND) remains limited. This study aims to identify the predictive histologic hallmarks and biomarkers of neoplastic progression.
Methods: Patients with confirmed BE-IND and G-IND, no previous evidence of dysplasia/cancer and follow-up of ≥6 months were included. The rate of neoplastic progression was calculated, and the multivariate Cox regression model adjusted for demographic and histologic features was used to identify risk factors for progression. MLH1, IMP3, Cyclin-D1, AMACR and p53 were evaluated as immunohistochemical markers of progression in G-IND.
Results: A total of 719 patients diagnosed with IND (158 BE-IND and 561 G-IND) were identified, out of whom 395 were excluded due to follow-up<6 months. Progression rates were 4.4 per 100 person-year for BE-IND and 1.6 per 100 person-year for G-IND patients. Progression was observed only in IND of hyperproliferative intestinal metaplasia (HIM) type. OLGA stage (III-IV vs 0-II) proved to be the only risk factor at univariate and multivariate Cox regression analysis (HR: 48.37, CI95%: 6.30-371.41, p<0.001) for G-IND. As for BE-IND, none of the demographic and histologic features at T0 were associated with disease progression. None of the immunohistochemical markers were useful for stratification of G-IND patients.
Conclusion: IND is a challenging diagnosis for pathologists and implies an increased risk for neoplasia, especially in BE patients, without providing definitive information for patient management. It is crucial to identify markers of neoplastic progression for risk stratification. While no IHC marker proved to be a robust predictor of progression, neoplastic progression of BE- and G-IND was strongly associated with IND of HIM type and, in the gastric setting, OLGA staging system resulted useful to identify patients requiring a tighter follow-up.

PS-24-006

Expression and prognostic value of PD-1 and PD-L1 in colorectal carcinoma

R. Aouadi*, I. Helal, F. Khanchel, R. Hedhli, E. Ben Brahim, R. Jouini, A. Chadli Debbiche
*La Rabta Hospital, Tunisia

Background & objectives: Programmed cell death protein-1 (PD-1) and its ligand PD-L1 are immune checkpoint molecules representing therapeutic targets and potential prognostic biomarkers in various types of cancer. We aimed to evaluate PD-1 and PD-L1 expression and prognostic value in colorectal carcinoma.

Methods: A retrospective study was carried out involving 104 cases of colorectal carcinoma diagnosed between 2014 and 2016. Tissue microarrays were used for immunohistochemical study. PD-1 expression was considered high if stained cells represented 10% or more of the stromal surface. PD-L1 expression was assessed using combined positive score (CPS) with a cutoff of 1%. A survival analysis was carried out.
Results: There were 60 men and 44 women with a mean age of 61 years old. PD-1 staining was observed in all cases and involved only immune cells. PD-1 expression was low in 76 cases (73,1%), and high in 28 cases (26,9%). There was no significant association with survival (p= 0,474). PD-L1 staining was observed in 58 cases (55,7%), involving mainly immune cells. Tumour cells were stained in only 3 cases. Fourteen cases (13.5%) had a CPS ≥1 and were therefore considered PD-L1+. The overall survival was superior in PD-L1+ patients. PD-L1 expression was significantly associated with survival in both univariate and multivariate analysis (p=0,039 and p=0,008 respectively, HR =0,186).
Conclusion: The mortality rate of colorectal cancer remains high worldwide, highlighting the importance of finding new prognostic markers and therapeutic options. In this context, PD-1/PD-L1 pathway is currently used as a therapeutic target for immune checkpoint inhibitors. Our study shows that PD-L1 expression may also be an independent prognostic factor associated with survival.

PS-24-007
Dysplasia in IBD: obvious and not so obvious
A.T. Bol*, E. Gedik, B. Savaş, A. Ensari
*Ankara University, Medical School, Pathology Department, Turkey

Background & objectives: Nonconventional dysplasia's have recently been described in ulcerative colitis (UC), posing difficulty in diagnosis for both endoscopists and pathologists. We set out to identify nonconventional dysplasias in UC, with their clinical characteristics, to improve our recognition of the entity.
Methods: We retrospectively examined colorectal resections of 50 UC cases (28 females, 22 males) with a mean age of 38.4, a mean disease duration of 7.0 years. All slides were examined for types of nonconventional dysplasia including hypermucinous (HMD), crypt cell (CCD), goblet cell-deficient (GCD), Paneth cell differentiation (PCD), serrated-like dysplasias (SLD), besides conventional dysplasias. Disease extension, site and pattern of colitis, initial biopsies were also assessed.
Results: Dysplasia was observed in 84% of cases; 95.2% of these were nonconventional type, including CCD (60%), HMD (26%), PCD (26%), GDD (20%), SSL (16%), and mixed in 56% of the cases. Left colon was most commonly involved (63.3% of HMDs, 51.6% of CCDs, 42.85% of GCDs, 38.46% of PCDs, 60% of SLDs). The disease duration was significantly longer in cases with SSL(p=0.01). A moderate correlation was found between disease duration and dysplasia frequency (r=0.54, p<0.01). In cases with dysplasia at multiple locations, the disease duration was 8.1 years, longer than the 5.36 years observed in cases with dysplasia at a single location (p=0.16). Dysplasia was present in the biopsies of 56% cases showing dysplasia in resection.
Conclusion: Our findings reveal the high prevalence and multiplicity of non-conventional dysplasias in UC, which were previously unknown to us. We found a significant correlation between the frequency of dysplasia and the duration of this chronic inflammatory disease. Although nonconventional dysplasias are typically low-grade, they can progress to colorectal carcinoma and require total excision. Therefore, increasing awareness of the pathologist and determining the clinical characteristics in coordination with clinicians seem to be crucial for early diagnosis and better disease management.

PS-24-008
Immune microenvironment in rectal adenocarcinoma after chemoradiation therapy
M. Omer, D. Yang, W. Cao*
*Rhode Island Hospital, USA

Background & objectives: Immune microenvironment is gaining increasing importance in malignancy. Programmed death-ligand 1 (PD-L1) expression in rectal adenocarcinomas after chemoradiation therapy was poorly understood. This study examined PD-L1 expression in the residual rectal adenocarcinomas after chemoradiation therapy.
Methods: We queried our records for rectal adenocarcinomas diagnosed from 2009 to 2021 and treated with chemoradiation therapy. Forty-three cases were included. Clinicopathological parameters were recorded. Immunohistochemical staining for PD-L1, CD3, CD4, and CD8 was performed. PD-L1 membranous expression in >1% of tumour cells were considered positive.
Results: Our cohort included 27 males and 16 females. The average age was 61.3 ± 1.6. Sixteen percent (7/43) cases were PD-L1 positive. In PD-L1+ tumours, PDL1+ lymphocytes (11.8±4.9/HPF) and CD3+ lymphocytes (136.4±28.4/HPF) in the stroma were significantly higher than PDL1- tumours (PDL1+ 3.3±1/HPF; CD3+ 88.8±8.9/HPF). In tumours with stromal PDL1+ lymphocytes >2/HPF, the pretreatment tumour size (measured by CT or MRI) was much smaller (4.4±0.1 cm vs 6.7±0.2 cm), PDL1+ tumour cells were significantly higher (1.4±0.1 vs 0.05±0.01/100 tumour cells) than in tumours with PDL1+ lymphocytes <=2/HPF. CD3+ lymphocytes in the tumour and stroma and CD8+ lymphocytes in the stroma were significantly higher than in tumours with PDL1+ lymphocytes <=2/HPF.
Conclusion: PD-L1 was expressed in 16% of rectal adenocarcinomas after chemoradiation therapy. Our findings indicate that PD-L1 checkpoint blockade may still be useful in rectal adenocarcinomas after chemoradiation therapy.

PS-24-009
Utility of cutting deeper levels on endoscopically observed polyps that display no histologic correlates on initial sections
J. Castellano*, V. Jones, L. Vaickus, A. Suriawinata, M. Lisovsky, B. Ren
*Department of Pathology, USA

Background & objectives: Pathology regularly receives colonoscopy samples labelled "polyp", that display no histologic correlate for a polyp on initial sections. We aimed to investigate what proportion of these would show relevant findings on additional, deeper-cut levels.
Methods: From December 2020 to June 2023, we performed additional levels on colonoscopy specimens seen as polyps endoscopically, but which histologically displayed no microscopic correlate for a polyp on initially cut sections. We compared the results of performing two regular "steps" (cut at intervals of 80-100 microns per step), with two "deep steps" (cut at intervals of approximately 200 microns per step).
Results: A total of 797 polyps were examined during the study period. Of these, 426 had two "step" cuts, and 371 had "deep steps" performed. Overall, histologic correlates for polyps were found in 224 (28%) of samples in subsequent levels. 120 (15%) were tubular adenomas, and 86 (11%) were hyperplastic polyps. When looking at the sub-groups of "steps" and "deep steps", in the "deep steps" group, a significantly higher number of tubular adenomas was found; 75 of the 371 polyps in this group (20%) proved to be tubular adenomas on deep steps, compared with 45 of 426 (10%) in the "steps" group (p<0.001).
Conclusion: Based on our findings, up to 20% of endoscopically observed polyps with no histologic corelates for a polyp on the initial section will reveal a tubular adenoma on subsequent deeper sections. We therefore recommend at least two additional sections, cut at intervals of at least 100 microns on all such cases.

PS-24-010

Increased expression of RPS4X and RPL31 in hepatic metastasis of primary left-sided colon cancer

M.S. Chang*, H. Park, S. Byeon, E. Shin
*Seoul National University College of Medicine Boramae Hospital, Republic of Korea

Background & objectives: Metastasis to liver is a critical driver of colon cancer-related mortality. A half of patients with primary colon cancer accompany hepatic metastasis at diagnosis or shortly after diagnosis. We aimed to find hepatic metastasis-related molecular markers in left-sided colon cancer.
Methods: From 11 patients of left-sided colon cancer with synchronous hepatic metastasis, we constructed tissue microarray containing 22 cores of colon and metastatic cancer. Using Digital Spatial Profiling System, (GeoMx® Human Whole Transcriptome Atlas), we quantified RNA expression of 18,883 genes simultaneously in 44 ROI of two tissue compartments defined by fluorescence colocalization: pan-cytokeratin+ and CD45+. Immunohistochemistry was performed for validation.
Results: Digital Spatial Profiling results revealed that 18 markers increased in hepatic metastatic cancer cells than in primary colon cancer cells, while one marker decreased in hepatic metastatic cancer cells (p value < 0.05, and FDR < 0.05). RNA expression of 15 ribosomal proteins (RPS4X, RPL31, RPL24, RPL32, RPL9, RPL4, RPS6, RPS25, RPL36A, RPL37, RPL14, RPL29, RPL12, RPLP2 and RPL35A) belonged among the top statistically significant increased markers in hepatic metastatic cancer cells. On immunohistochemistry for RPS4X and RPL31—the most statistically significant two markers in Digital Spatial Profiling results—were more expressed in hepatic metastatic cancer cells than in colon cancer cells (p value < 0.05).
Conclusion: Increased expression of RPS4X and RPL31, and further, the upregulation of ribosome complexes may play a crucial role in hepatic metastasis of left-sided colon cancer. It may provide a new strategy for developing drugs against hepatic metastasis of primary left-sided colon cancer.

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PS-24-011

Neutrophil-to-lymphocyte ratio is an effective and sensitive predictive maker of early appendiceal perforation in in acute appendicitis

L. Chen*, J. Bao, F. Chen, J. Ding, T. Zhu, Q. Chen
*Department of Laboratory Medicine and Pathobiology, University of Toronto, Canada

Background & objectives: To investigate the predictive value of neutrophil-to-lymphocyte ratio (NLR) for early perforation of the appendix in patients with acute appendicitis (AA).
Methods: 280 patients with the first attack of AA within 48 hours and not yet treated with antibiotics were included in this study retrospectively; divided into two groups by the presence or absence of perforation. The clinical data, inflammatory indexes, and NLR were compared between two groups. The predictive value of inflammatory indexes on the early appendiceal perforation was explored.
Results: Patients in the perforated group were older, with higher blood WBC, NEU% and NLR, lower LYM% and PLT, higher serum CRP and PCT, and longer hospitalization time. Multivariate regression analysis revealed that high WBC, NEU%, NLR, CRP, PCT, and low LYM% were independent risk factors for early appendiceal perforation. The ROC curves revealed that the predictive value of WBC, CRP, and PCT for early appendiceal perforation was low. NLR, LYM%, and NEU% had a higher predictive value, with AUC values of 0.947, 0.928, and 0.920, respectively. NLR had the highest predictive value. The diagnostic Cut-off value of NLR is 10.83 with a sensitivity of 0.963, and a specificity of 0.850.
Conclusion: NLR can be used as an effective and sensitive predictive maker of early appendiceal perforation in AA patients. It is easy to generate from existing routine clinical laboratory testing for AA and can be included in complete blood count (CBC) as a routine or add-on value.

PS-24-012

Mucosal healing in ulcerative colitis - helpers versus toxic lymphocyte cells

A. Coman*, L. Dragostin, A. Vilaia, M. State, C. Popp, L. Nichita, M. Cioplea
*Department of Pathology, Colentina University Hospital, Bucharest, Romania

Background & objectives: Endoscopic mucosal healing is an important goal of treatment in ulcerative colitis (UC). The aim of this study is to identify the relationship between CD4+ (main inflammatory cells in UC) and CD8+ (with pro-inflammatory effects) lymphocytes during mucosal healing.
Methods: We included, in a retrospective study, 20 patients with UC that achieved endoscopic mucosal healing. Expression and patterns of distribution of CD4+ and CD8+ T lymphocytes were analysed using immunohistochemistry on biopsies from the mucosal healing period and from a previous or subsequent activation of the disease. Histologic activity was assessed according to the Geboes score criteria.
Results: Endoscopic mucosal healing was correlated with a low Geboes score (ranging between 1.3 and an outliner with a score of 5.2, and an average of 2.A1), while during disease activity Geboes score was ranging between 1.3 and 5.4 with an average of 3.3. The number of CD8+ intraepithelial lymphocytes (IELs) was significantly greater than the number of CD4+ IELs in periods of disease activity, as well as during mucosal healing ($p<0.01$ in both cases). In regard to patterns of distribution, CD8+ cells had a scattered pattern in both intervals, while CD4+ cells had a predominantly nodular distribution in mucosal healing, while being scattered during periods of disease activity.
Conclusion: Greater CD8+ lymphocytes involvement and higher CD8+/CD4+ distribution can have a meaningful impact on understanding the pathogenesis of ulcerative colitis, as well as future treatment options for lymphocytes targeting medications.

PS-24-013

Medullary carcinomas of the non-ampullary small intestine: association with coeliac disease, mismatch repair deficiency, programmed death-ligand 1 expression, and favourable prognosis

G. De Lisi*, C. Guerini, C. Klersy, F. Grillo, G. Nesi, G. Arpa, E. Quaquarini, D. Furlan, M. Fassan, P. Parente, M. Paulli, S. La Rosa, A. Di Sabatino, A. Vanoli
*Anatomic Pathology Unit, Department of Molecular Medicine, University of Pavia, Pavia, Italy

Background & objectives: Gastrointestinal medullary carcinoma (MC) is a rare histologic subtype of adenocarcinoma. As non-ampullary small bowel MCs are poorly characterized, we aimed to analyse their clinic-pathologic and immunohistochemical features, and to compare them with remaining small intestinal adenocarcinomas.
Methods: Surgically resected small bowel adenocarcinomas (SBAs) collected through the Small Bowel Cancer Italian Consortium were classified as MCs (defined as carcinomas with $\geq$50% of tumour surface fulfilling the typical histologic criteria of MC, including solid syncytial architecture, pushing margins, and prominent lymphoid infiltrate) or non-medullary SBAs. The two groups were compared in terms of clinic-pathologic and immuno-molecular features.

Results: Eleven small bowel MCs and 149 non-medullary SBAs were identified. Ten MCs harboured mismatch repair deficiency (MMRd) while one was Epstein-Barr virus positive. Compared with non-medullary SBAs, MCs exhibited a strong association with coeliac disease ($p<0.001$), and showed less frequently lymphovascular invasion ($p=0.04$), cytokeratin 20 expression ($p=0.024$), and p53 overexpression ($p=0.034$), whereas higher rates of MMRd ($p<0.001$) and programmed death-ligand 1 positivity by both tumour proportion score (TPS >1%) and combined positive score (CPS>1) were seen in MCs ($p<0.001$ for both). Survival analysis revealed a better prognosis of MC patients compared to remaining cases ($p=0.02$).
Conclusion: Our study highlights that, pathogenetically, small bowel MCs are related to MMRd (91%) or Epstein-Barr virus infection (9%) and that they represent a distinct histologic subtype, with peculiar features compared to remaining SBAs, including associations with MMRd, programmed death-ligand 1 expression, and a better prognosis, in keeping with findings from colorectal and ampullary MCs. Furthermore, an interesting link between small bowel MCs and coeliac disease emerged.

PS-24-014
Metaplastic oxyntic mucosa in autoimmune gastritis: a complex lesion without apparent precancerous features of intestinal type
T.S. Driva*, S. Sakellariou, E. Theochari, G. Gadetsakis, N. Kavantzas, I. Delladetsima
*First Department of Pathology, Medical School, National and Kapodistrian University of Athens, Athens, Greece

Background & objectives: Metaplastic changes of oxyntic mucosa in autoimmune gastritis (AIG) are still a matter of investigation. Our study aims to explore subtypes of pyloric and intestinal metaplastic epithelium and gain further insight into their cellular origin and prognostic value.
Methods: 147 gastric biopsies showing histopathological changes of AIG, negative for H. pylori infection, were examined retrospectively regarding the presence and type of metaplasia. Immunohistochemistry for CDX2, MUC5AC, MUC6, chromogranin and Ki67 was performed and 2 double immunostaining assays for MUC5AC-CDX2 and MUC6-CDX2 were applied in 15 cases.
Results: Pyloric-type metaplasia was seen in 98.6% (145/147) and intestinal metaplasia (IM) in 81.6% (120/147) of the cases. IM was complete (type I) in 99.1% (119/120) and incomplete (type II) in 0.04% (5/120) of the cases. No changes of epithelial dysplasia were noted while in one case a signet-ring cell carcinoma was diagnosed. MUC5AC-positive cells prevailed over MUC6-positive cells. Biphenotypic gastric mucous cells co-expressing MUC5AC-CDX2 and MUC6-CDX2 were detected in all cases examined, indicating mucous-to-intestinal cell transdifferentiation. Biphenotypic MUC5AC-CDX2-positive cells exceeded numerically MUC6-CDX2-positive cells. Metaplastic intestinal cells showed markedly high Ki67 expression followed by metaplastic mucous cells.
Conclusion: In AIG, transdifferentiation of MUC5AC- and to a lesser extent of MUC6-expressing metaplastic cells plays a contributory role in the generation of IM, which is almost exclusively complete. The absence of epithelial dysplasia and the presence of complete IM seems to deprive the proliferative metaplastic mucosa of a potential precancerous nature, suggesting a non-carcinogenic impact of the autoimmune inflammatory microenvironment.

PS-24-015
Implementation of the IBD-DCA for ulcerative colitis: a single institution experience
D. Egong*, M. Hanly, E. Mcgrath, M.B. Cotter, G. Cullen, J. Sheridan, G. Doherty, K. Sheahan
*Department of Histopathology, St Vincent's University Hospital, Ireland

Background & objectives: The advent of the IBD-Distribution, Chronicity, Activity (DCA) histological scoring for ulcerative colitis echoes the importance of histological assessment. We captured the IBD-DCA reporting uptake in St Vincent's University Hospital (SVUH), with a prospective validation against commonly used endoscopic scores.
Methods: IBD biopsies reported from August 2022 to July 2023 were extracted from the SVUH laboratory information system. Quality of reports were assessed against the DCA template. The corresponding UC Endoscopic Index of Severity (UCEIS) and Mayo Endoscopic Score (MES) from the first six months were prospectively recorded. Correlation between the endoscopic scores and IBD-DCA was quantified using Kendall's tau coefficient.
Results: Of the 291 total cases reported, rectal biopsy was most frequently performed (83.5%). The IBD-DCA components were reported for each biopsied site in 221 (75.9%) cases. 9 of 138 (6.5%) cases with histological evidence of erosion/ulceration were deemed normal on the corresponding endoscopic examination. Notable tau correlations included UCEIS vascular pattern with histological chronicity ($\tau = 0.3891$), UCEIS erosions/ulceration with histological activity ($\tau = 0.3252$), total UCEIS with histological activity ($\tau = 0.3450$). MES showed the strongest correlation with histological distribution ($\tau = 0.3450$). All p-values < 0.001.
Conclusion: We showed an encouraging uptake of this simple histological reporting template in UC cases in daily routine use. Our data suggest that the IBD-DCA score adds to finding not already apparent on endoscopy, which may be clinically actionable. We intend to advance to the next step by studying the usefulness of our reports to our physician colleagues.

PS-24-016
Venous invasion detection in colorectal cancer resections: is routine elastic stain cost effective?
A. Elmahs*, M. Avery, M. Elgoweini
*University Hospital Crosshouse, United Kingdom

Background & objectives: International collaboration on Cancer Reporting and Royal College of Pathologists datasets stress the prognostic importance of vascular invasion in colorectal cancer resections. We estimated costs and efficacy of elastic stain in venous invasion detection in these cases in our department.
Methods: From January to November 2023, we received 110 colorectal cancer resection specimens. On average, 6 blocks were taken from each tumour. Elastic stain was performed to all tumour slides at an average cost of £3.5 per slide in our department. Intramural and extramural venous invasion were recorded.
Results: The cases were reported by different pathologists. Venous invasion was identified in 77 out of 110 cases (70%). Of these, extramural venous invasion, with or without intramural venous invasion, was present in 46 cases (42%). Exclusive intramural venous invasion was seen in 31 cases (28%). The average cost of elastic stain application was £21 per case.
Conclusion: The routine application of elastic stain showed that the detection of venous invasion in our reported cases exceeded the minimally accepted published national standard which is at least 30%. It also offered a simple and cost-effective way for enhancing diagnostic accuracy leading to better patient management.

PS-24-017
Error rates in colonic biopsy reporting
H. Evans*, D. Snead
*United Kingdom

Background & objectives: Colon biopsies are a common pathological specimen, yet the volume and type of errors in their reporting is

unknown. Our aims were to quantify error rates in colonic biopsies, consider if rates varied with reporting modality and encourage safer reporting.
Methods: 752 colonic biopsy specimens were reviewed on light microscopy (LM) and digital pathology (DP) by four consultant pathologists from three UK centres. Each specimen was reviewed by all pathologists on both modalities, equating to 6016 diagnoses. The pathologist's diagnosis was compared to the ground truth determined by consensus review. Clinically important differences (CID) were those that would alter patient management.
Results: There were 226 CID between a pathologist's diagnosis and the ground truth, equating to 3.8% of all specimen diagnoses. There was a marginally higher rate of errors seen in DP (52.7% compared to 47.3% on LM). The rate of diagnostic errors made by each consultant was fairly uniform (ranging from 21.2- 28.8%).
The most common areas for errors were the type of serrated polyp (25.7% of errors) and the grading of dysplasia in a polyp (23.5%). Although rare, there were instances where adenocarcinoma was missed and reported as high-grade dysplasia (0.9%), or more concerningly as low-grade dysplasia (0.8%). Other errors were seen in inflammatory bowel disease, microscopic colitis, and microorganisms.
Conclusion: This work highlights areas of ongoing diagnostic complexity, such as the inter-observer variability in the diagnosis of serrated polyps, as well as the grading of dysplasia in adenomas, both of which can have prognostic implications. This data suggests that DP has a slightly higher error rate than LM, so caution should be applied particularly when introducing this new modality for the diagnosis of colonic biopsies.

PS-24-018
Assessment of pathological lymph nodes response to neoadjuvant therapy in locally advanced colorectal carcinomas
L. Fernández Ariati*, Á. López-Janeiro, J. Arredondo Chaves, E. Miraval Wong
*Clínica Universidad de Navarra, Spain

Background & objectives: Neoadjuvant therapy (NAT) for locally advanced colon carcinomas (LACC) is increasingly used, however, a standardized pathological lymph nodes response (PLNR) is lacking. We aimed to find a significant cut-off point for PLNR regarding disease-specific survival (DSS) and disease-free survival (DFS).
Methods: We reassessed 51 colectomies from patients with LACC receiving NAT (2009 to 2020). Using QuPath v0.5.1 software, we calculated a global percentage for PLNR (total tumour area/total tumour bed). Cut-points for DFS and DSS were adjusted using the surv_cutpoint function from the R package survminer, and Kaplan-Meier (KM) analysis was conducted. Clinicopathological variables were assessed using Fisher's exact test.
Results: Mean age was 63.3 years (42-84 years). Fifteen cases (29.3%) had at least 1 lymph node with tumoural bed and/or tumoural cells. Optimal cut-off point was 1%, categorizing PLNR as partial/poor (PPR) (residual tumour >1%, n=11, 21.5%) and total/near-complete (TNCR) (residual tumour 0-1%, n=4, 7.8%). A third group named truly negative lymph nodes (TNLN) (n=36, 70.7%) was also used to build KM curves. The groups did not show differences regarding ypT, pathological tumoural response and NAT. PPR group showed a higher proportion of lymphovascular invasion, perineural invasion and ypN1b-2b ($p<0.05$). Both DSS and DFS showed a poorer outcome for the PPR group, being only DSS statistically significant ($p=0.018$).
Conclusion: This study proposes the first cut-off point for PLNR in this novel group of patients with LACC treated with NAT. We provide insight into the prognostic significance of analysing PLNR using a global percentage. However, since the TNCR group had only 4 patients, these results are still limited and we cannot assure the independent nature of PLNR assessment as a prognostic factor, highlighting the importance of conducting studies involving more patients.

PS-24-019
Tumour regression grading scores are not associated with regression of the lymph node metastases in patients with oesophagogastric adenocarcinoma after neoadjuvant chemotherapy
C. Glava*, I. Nikolopoulos, S. Smparounis, D. Riga, M. Theochari, P. Papakostas, F. Seretis, N. Memos, T. Triantafyllou, D. Theodorou, G. Kafiri
*Department of Pathology, Hippocratio General Hospital of Athens, Greece

Background & objectives: Neoadjuvant chemotherapy is the standard treatment option for locally advanced gastro-oesophageal/gastric adenocarcinoma. Tumour-regression-grading (TRG) systems categorize histopathological cancer-regression after treatment on primary tumour, but none estimates regression in the lymphnodes (LNs). The aim of this study was to investigate LN cancer-regression.
Methods: Hematoxylin-Eosin slides of LNs harvested during curative resection after FLOT therapy, were evaluated. Patients were pooled into two groups, based on Mandard-TRG-score as: TRG-low: TRG1-TRG3 and TRG-high: TRG4-TRG5. Ratios were calculated for: %of remittent LNs out of total LNs (remission ratio), %of negative remittent LNs out of negative LNs (negative remission ratio) and %of positive LNs out of total LNs (positive ratio).
Results: Sample sizes were adequate to account for normal distribution of all three ratios calculated, and Levene's test for Equality of Variances validated the presence of homogeneity of variance. Three independent samples tests for the three ratios were performed. A power analysis resulted in 91% power accounting for an effect size of 0.8.70 patients, Male:Female=60:10, GEJ:gastric=48:22, TotalLNs 10-69(mean 30), PositiveLNs 0-47(mean 3), NegativeLNs 8-50(mean 27), Positive-remitted-LNs 0-13(mean 1), Negative-remitted-LNs 0-14(mean 1). None of the three t-tests revealed statistical significance regarding the TRG-grouping and the LN ratios studied (remission ratio TRG-low 0.07 ± 0.129 vs TRG-high 0.075 ± 0.124, $p=0.436$, positive ratio TRG-low 0.06 ± 0.148 vs TRG-high 0.10 ± 0.174, $p=0.142$, negative remission ratio TRG-low 0.06 ± 0.116 vs TRG-high 0.047 ± 0.094, $p=0.303$).
Conclusion: While the pathology reports from the LNs prove some degree of tumour regression, TRG systems do not predict the actual effects of FLOT in the LNs harvested during curative resection. This finding could be attributed to clonality of tumour or the possibility that FLOT does not equally affect primary tumour and lymphatic metastases. We propose that a modified version of Mandard system be introduced, involving lymphatic status. Such a system would more accurately reflect prognosis and survival of these patients.

PS-24-020
Gastrointestinal stromal tumours presenting as a synchronous or metachronous tumour
C.A. Gomez Gonzalez*, B. Doğanavşargil, M. Sezak, M. Calik, O. Bozbiyik, T. Akalin
*Department of Pathology, Ege University Faculty of Medicine, Turkey

Background & objectives: Gastrointestinal stromal tumours (GISTs) may present as a part of a clinical syndrome or as synchronous/metachronous tumours accompanying other primary neoplasms. The previous data usually focus on the histological type of the accompanying tumours. We searched the histopathological features of coexistent GISTs.
Methods: 60 cases were retrieved from a cohort of 440 GIST cases diagnosed between 2000-2023 having synchronic (ST)/metachronous tumours (MT) accompanying GIST.ST is defined as a case diagnosed in the same operation session or less than 6 months. Demographic data,

initial biopsy date, and tumour location were noted for both tumours; cellular type, size, and risk assessment were added for GISTs and correlated with non-parametric tests.
Results: The median age was 67,17 years with 53% male cases. Most common GIST localizations were stomach (56,7%) and small bowel (31,7%), high-risk tumours constituted 21.7%. Accompanying tumours were GI-located (58.3%) or non-GI-located (41.7%), mostly epithelial (73,3%) but haematological (8,3%) and benign tumours were also observed (8,3%). ST were more frequent than MT (40 cases vs 20), more frequently accompanied by GI primaries (p=0,001, chi-square) and more frequently classified as "low-risk tumours" with coincidental discovery in operation specimens (p=0,022). Although spindle cell tumours dominated our series; the mixed-epithelioid cell tumours were more frequent among MT (20% vs 12.5 %, p=0.44). Epiteloid morphology was also more frequent among GISTs accompanying non-GI primaries (80% vs 20%).
Conclusion: GISTs can accompany many epithelial tumours ranging from prostatic to lung tumours, haematological malignancies, or multiple primaries. The accompanying GIST cases in our series mostly represented "incidentally" found spindle cell tumours carrying no increased risk for disease progression. Larger series and further molecular studies are required to reveal their pathogenetic relationship with other tumours.

PS-24-021
Clinicopathological and molecular features of genome stable-like colorectal cancers
L. Jin, H. Jin, Y. KIm, N. Cho, J. Bae, J.H. Kim, G.-H. Kang*
*Seoul Natl Univ College of Medicine, Republic of Korea

Background & objectives: Colorectal cancers (CRCs) are traditionally divided into tumours with either chromosomal instability (CIN) or microsatellite instability (MSI). Genome-stable CRCs (GS CRCs) were defined as tumours lacking both CIN and MSI. The clinicopathological features of GS CRCs are not well defined.
Methods: A total of 437 CRCs were analysed for copy number variation (CNV) statuses in 8 genes (ARID1A, EGFR, FGFR1, KDM5B, MYBL2, MYC, SALL4, and SETDB1) using droplet-digital PCR. CRCs that showed CNV in ≤ one gene and no MSI were defined as GS-like CRCs. Clinicopathological and molecular features of GS-like CRCs were compared with those of CIN-like CRCs.
Results: 4.6% of the CRCs were classified as GS-like CRCs, whereas 88.1% and 7.3% were classified as CIN-like and MSI-H CRCs, respectively. Compared with CIN-like CRCs, GS-like CRCs exhibited a preponderance toward the right colon (65.0% vs. 26.5%, P=0.001) and tended to have hypo chromatic nuclei. The nuclear optical density was significantly lower in GS-like CRCs than in CIN-like or MSI CRCs. Survival analysis showed no difference between the three subtypes. KRAS and PIK3CA mutations were more frequent in GS-like CRCs than in CIN-like CRCs (68.4% vs. 28.0%, P<0.001 and 43.8% vs. 14.3%, P=0.006, respectively). GS-like CRCs showed a higher frequency of KRT7 expression than CIN-like CRCs (20.0% vs. 4.8%, P=0.020).
Conclusion: Through our study, the GS-like subtype was found to comprise a minor proportion of CRCs and have proclivity toward proximal bowel location, hypo chromatic tumour nuclei, aberrant KRT7 expression, and a high frequency of KRAS and PIK3CA mutations.

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PS-24-022
Clinicopathological spectrum of primary anorectal mucosal melanoma: a proposal for survival-prognostic model based on 66 resected cases
R. Kaushal*, S. Yadav, T. Agarwal, M. Bal, K. Deodhar, M. Ramadwar, A. Saklani
*Tata Memorial Hospital, India

Background & objectives: Anorectal melanoma is an uncommon and aggressive malignancy with poor median survival rates. In this study, we aimed to determine the prognostic variables (including clinicpathologic parameters) of anorectal melanoma who underwent surgery and to derive an optimal staging system.
Methods: A total of 66 operated cases of anorectal melanoma from 2013 to 2022 were included. Clinical and treatment details were obtained from the electronic medical record. Pathological parameters evaluated included histological type, tumour depth, level of anorectal wall invasion, vertical and radial growth phase, mitotic rate, surface ulceration, lymphovascular invasion, perineural invasion, satellitosis, tumour infiltrating lymphocytes, and lymph node status.
Results: The median age was 54 years. Tumour epicentre was anorectal junction (41), rectum (17) and anal canal (8). Median tumour dimension and thickness were 4.5 mm(7-150mm) and 13.5 mm(1-23mm), respectively. APR was performed in 92% of cases. Growths were predominantly ulceroproliferative 47% (31/66). Histomorphology was epithelioid (45%, n=30), spindled (7.6%, n=5) and mixed (47%, n=31). Amelanotic cases were 27%(n=18). Invasion into muscularis propria and beyond was seen in 47 patients (71%). Pagetoid spread and junctional activity was seen in (21%, n=14/66) cases. Lymph node metastasis was seen in 61% (37/66). OS and RFS at 2 years were 66% and 29%, respectively, with a median follow-up of 25 months. Tumour size (4.5cm, p= <0.036) and thickness (13mm, p= <0.046) showed statistically significant correlation of OS.
Conclusion: Anorectal melanoma is an aggressive neoplasm, and patients usually present at an advanced stage. These patients have a higher frequency of lymph node metastasis and distant metastasis and an overall poor survival rate.

PS-24-023
Performance evaluation of a deep learning-based, real-time gastric cancer detection system through confocal laser endomicroscopy
S. Kim*, H. Cho, D. Moon, S.M. Heo, J. Chu, H. Bae, S. Choi, Y. Jo, K. Hwang, H. Choi
*Department of Pathology, Ajou University School of Medicine, Republic of Korea

Background & objectives: There has been a persistent demand for a modality in real-time histologic imaging, distinct from frozen section technique. The confocal laser endomicroscopic system (CLES) has demonstrated its efficacy in real-time imaging, but its application in human gastric tissue remains constrained.
Methods: 7,480 tumour and 12,928 normal images were obtained from 43 gastric cancer specimens through CLES. A deep learning (DL) model was developed by using a two-stage model of EfficientNet V2. The standalone performance was evaluated by 100 images, compared to those of four pathologists. Another 100 images were utilized to assess the model's value as complementary tool for the pathologists.
Results: The performance evaluation of the trained DL model in the internal validation dataset, comprising 3,686 CLES images, demonstrated an AUROC of 1.000 for both detecting tumours and differentiating histologic subtypes. In the external validation dataset, the model demonstrated noteworthy proficiency in distinguishing between tumour and normal images, yielding accuracy, specificity, and sensitivity of 0.990, 0.982, and 1.000, respectively, achieving superior performance compared to any performance by pathologists. Performance enhancement of interpreting CLES images by using DL model was also observed for all pathologists. DL-assisted revision could lead to the accuracy improvement from

0.74 to 0.97, 0.63 to 0.85, 0.78 to 0.79, and 0.65 to 0.76, in each pathologist.
Conclusion: We developed an AI model tailored for the real-time and automated detection of cancer cells within CLES images for the first time. The remarkable performance of the model suggests its potential utilization as a standalone modality for instantaneous histologic assessment and as a complementary tool for pathologists' interpretation.

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PS-24-024
The role of S100A4, α-SMA, and fibroblast markers in depicting the tumour microenvironment in stage-III colorectal cancers
K. Kolçak*, M.F. Tekin, Ç. Çelikel
*Marmara University Pendik Hospital, Turkey

Background & objectives: In colorectal carcinoma, the tumour microenvironment (TME) is a significant factor influencing tumour behaviour. Research has focused on cancer-associated fibroblasts(CAFs) for TME assessment.
Our study aims to evaluate TME using immunomarkers(S100A4/α-SMA/fibroblast) and to reveal their relation with histopathological features and molecular data.
Methods: Patients diagnosed with clinical stage-III colorectal carcinoma at the Marmara University Department of Pathology between 2012 and 2018, and who did not receive neoadjuvant therapy, were selected for inclusion in the study. The cases were classified based on desmoplasia type (mature, immature, intermediate) and severity (0-3). The intensity and staining percentage of immunomarkers (S100A4, α-SMA, fibroblast) were used to calculate histoscores(0-300).
Results: Out of 179 cases, 95 (53.1%) were male, and 84 (46.9%) were female, with an average age of 61.1 years. The staining of S100A4 in epithelial cells, fibroblasts, and inflammatory cells was evaluated separately and found to have no significant correlation with histopathological factors (lymphovascular/perineural invasion, desmoplasia type/severity, tumour budding (TB) score) or molecular data (microsatellite instability, KRAS, NRAS, BRAF mutation status). Comparison of α-SMA with desmoplasia score revealed a significant difference attributed to low h-scores in cases lacking desmoplasia (p: 0.03). Furthermore, α-SMA indicated low h-scores in cases featuring perineural invasion (p: 0,02). Although not statistically significant, intratumourally fibroblast h-scores were lower in cases with microsatellite instability (p: 0,059).
Conclusion: Publications suggest that increased density of CAFs and immature desmoplasia enhance TB, lymphovascular/perineural invasion, and possibility of metastasis. In our study, we found no correlation between desmoplasia type/severity and staining scores of the applied markers. Decreased α-SMA density signifies desmoplasia and perineural invasion, but S100A4 and fibroblast immunomarkers did not align with routine histomorphological parameters. Although our results do not show any concordance with the literature in assessing TME impact, this might be due to selected-patients being limited to stage-III cases.

PS-24-025
Quantitative real-time PCR for detection of Helicobacter pylori and its clarithromycin resistance from gastric biopsies - when the negative can be turned positive
A. Biró, A. Kurucz, Á. Jakab, I. Szirtes, G.M. Buzás, V. Papp, A. Szijártó, A. Kiss, É. Kocsmár, G. Lotz*
*Semmelweis University, Department of Pathology, Forensic and Insurance Medicine, Hungary

Background & objectives: The diagnostic accuracy of detecting Helicobacter pylori (HP) and its clarithromycin susceptibility (Cla-susc) from gastric biopsies by immunohistochemistry (IHC) and fluorescence-in-situ-hybridization (FISH) compared to isolated DNA-based polymerase chain reaction (PCR) methods is still controversial and needs to be investigated.
Methods: Formalin-fixed paraffin-embedded (FFPE) gastric tissue samples from 209 patients with clinical request for HP diagnostics were collected. Tissue sections were stained by Helicobacter IHC and Cla-susc FISH. DNA was isolated from further sections and Fluorescence Resonance Energy Transfer (FRET)-based quantitative-PCR (qPCR) was performed using a custom designed primer amplifying a sequence containing 122 bp from 23SrRNA gene of the bacterium.
Results: Out of the 209 FFPE gastric biopsy specimens, 108 was diagnosed by IHC and FISH as HP-positive and 101 as HP-negative. Quantitative-PCR detected the bacterium from 102 out of 108 immunohistochemically and FISH tested HP-positive cases and 25 out of 101 cases HP-negative by IHC. The qPCR melting point analysis identified 34 clarithromycin susceptible, 5 heteroresistant, 1 homoresistant (and 2 HP-negative) samples out of the 42 cases Cla-susceptible by FISH and 4 clarithromycin susceptible, 19 heteroresistant, 8 homoresistant (and 2 HP-negative) samples out of the 33 cases Cla-heteroresistant by FISH, moreover no Cla-susceptible, 2 heteroresistant, 29 homoresistant (and 2 HP-negative) samples out of the 33 cases homoresistant by FISH.
Conclusion: Among the cases positive for HP by IHC/FISH, qPCR performed adequately in detecting both Helicobacter pylori and its clarithromycin susceptibility status. However, a substantial proportion (25%) of cases with negative Helicobacter IHC result was found to be HP positive by qPCR. Helicobacter occurs discontinuously on the gastric mucosa and is therefore not always histologically detectable in the obtained biopsy specimen(s), only by PCR from soluble DNA, which is therefore recommended in cases negative by IHC.

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PS-24-027
Multiplex immunohistochemistry analysis of CTLA4, PD-L1, LAG3 and tumour microenvironment components in relation to MMR status in colorectal carcinoma
S. Naumov*, N. Krakhmal, S. Vtorushin
*Siberian State Medical University, Russia

Background & objectives: The relationship of immune checkpoints (ICP) in the microenvironment of colorectal cancer is a current challenge. In this study, we comprehensively evaluated CTLA-4, PD-L1, LAG3; CD3+, CD8+ lymphocytes, CD163+ macrophages in the tumour core and invasive margin using multiplex IHC.
Methods: We studied 50 tissue samples from patients who did not receive neoadjuvant therapy: 16 samples of colorectal carcinoma with dMMR status and 34 samples with pMMR status. Tumour samples were stained with antibodies to LAG3, CTLA4, PD-L1 proteins, to CD3+, CD8+ lymphocytes, and CD163+ macrophages followed by the optimization of multiplex immunofluorescence examination.
Results: Research results revealed significant differences in the expression of each protein among dMMR tumours compared to pMMR carcinomas: CTLA-4 (p=0.011), PD-L1(p=0.004), LAG3 (p=0.013). Evaluation of PD-L1 expression in pMMR carcinomas showed predominance of its expression in the tumour core (p=0.008), whereas there were no differences in PD-L1 expression in different compartments of dMMR carcinomas (p=0.187). We noted a significant

predominance of CD163+ macrophages and CD3+ and CD8+ lymphocytes in the tumour core (p=0.007) and in the invasive tumour margin (p=0.007; p=0.041) in dMMR carcinomas, respectively. Evaluation of the immunoreactivity index showed its predominance among dMMR tumours (p=0.008).
Conclusion: The study showed that there was an increased expression of CTLA-4, PD-L1, LAG3, higher rate of CD3+ and CD8+ lymphocytes in the invasive margin in dMMR tumours and the predominance of CD163+macrophages in the tumour core. We established the predominance of PD-L1 expression in the tumour core of pMMR carcinomas but there were no differences in its expression among the same compartments in dMMR tumours. Expression of the studied ICP and tumour microenvironment depends on the MMR status.

PS-24-028
Artificial Intelligence (AI)-powered tertiary lymphoid structures recognition on hematoxylin and eosin slides
G. Serna, J. Ros, X. Guardia, R. Fasani, S. Mauchanski, F. Gallego, J. Jimenez, E. Elez, P. Nuciforo*
*Molecular Oncology Group, Vall d´Hebron Institute of Oncology, Spain

Background & objectives: Tertiary lymphoid structures (TLS) significantly influence tumour immunity and patient outcomes across cancers. Accurate TLS detection is challenging, necessitating advanced methods. Our study leverages AI for precise TLS identification on hematoxylin and eosin (HE) slides for precision oncology applications.
Methods: One slide/case was cut and sequentially stained with HE followed by multiplexed immunohistochemistry (mIHC) using a custom-made panel targeting seven TLS-associated immune cells markers. mIHC was used to accurately annotate TLS on HE images (mIHC-TLS) and train an AI model (AI-TLS). In parallel, TLS were assessed by a pathologist directly on HE slides based on morphology (path-TLS).
Results: Tumour tissues from 57 patients with colorectal cancer (CRC) were retrospectively selected and divided into training (41) and test (16) sets. The training set containing >300 mIHC-annotated (CD3, CD4, CD8, CD20, CD21, CD23, and Ki67) TLS was used to develop an AI model which was a 305K iteration DeepLabv3+ model with a loss of 0.006 and an error rate of 0.3%. In the whole cohort, median TLS were 13, 9, and 2 for AI-TLS, mIHC-TLS, and path-TLS, respectively. Path-TLS only moderately correlated with AI-TLS (R2=0.495) and mIHC-TLS (R2=0.546). The AI-TLS model showed high correlation with mIHC-TLS, achieving R2 values of 0.939 and 0.957 in training and test sets, respectively.
Conclusion: We developed an AI model for TLS quantification using mIHC-annotated HE images. Our model operates on plain HE slides precisely identifying TLS in CRC samples, being superior to pathologist-based assessment reflecting the AI's capacity to discern complex histological patterns in HE stains. By transcending the need for IHC panel analysis for TLS identification, the model offers a cost-effective method for enhancing tumour-immunology understanding and aiding patient stratification for immunotherapy, setting a new benchmark in the pathological assessment of cancer.

PS-24-029
GNAS mutation induces increased invasiveness in colorectal cancer cells, which can be suppressed by phosphodiesterase 4 inhibitors
P. Nummela*, S. Zafar, A. Ganesan, I. Ukkola, A. Ayo, W. Wahbi, E. Naakka, P. Laakkonen, T. Salo, A. Ristimäki
*Applied Tumour Genomics Research Program, University of Helsinki and HUS Diagnostic Center, Helsinki University Hospital, Finland

Background & objectives: GNAS mutation is recurrent in colorectal cancer (CRC) with a prevalence of 5%. It is known to activate cAMP-dependent signaling pathways and associate with poor prognosis in CRC, but its functional effects in CRC cells have been less studied.
Methods: We utilized CRC cells edited with GNAS R201C/+ mutation by CRISPR/Cas9 technology (HCT116 GNASmt cells) and analysed their molecular and functional features using cAMP ELISA, migration assay, invasion assay, and mouse xenograft model, both in the absence and presence of phosphodiesterase 4 (PDE4) inhibitors. Further, we analysed the xenograft tumours with image analysis (vitality), immunohistochemistry, qPCR, and Western blotting.
Results: HCT116 GNASmt cells were more migratory and invasive in vitro than the parental cells. At molecular level, GNASmt cells showed increased cAMP levels, which could be further elevated by inhibiting the activity of cAMP hydrolysing PDE4 enzymes. In functional assays, PDE4 inhibition suppressed the invasion of GNASmt cells without an effect on parental cells. PDE4 inhibition also drastically impaired the growth of HCT116 GNASmt xenografts in mice. The PDE4 inhibitor treated GNASmt tumours further showed decreased amount of vital tumour area. We also verified overexpression of PDE4D subtype in the GNASmt tumours as compared to the parental ones.
Conclusion: GNAS mutation increases cAMP levels and invasiveness of CRC cells. However, further elevation of cAMP by blocking its breakdown using PDE4 inhibition suppresses the invasion of GNAS-mutated CRC cells. PDE4 inhibition thus provides a potential way to keep these CRC tumours in control. Currently, PDE4 inhibitors have been approved for the treatment of various inflammatory conditions.

PS-24-030
PD-L1 expression correlates with epithelial-to-mesenchymal transition (EMT) and exhibits improved prognostic outcomes in microsatellite stable colorectal cancer (MSS-CRC)
B. Palomar De Lucas*, N. Tarazona, F. Gimeno-Valiente, J.F. González-Muñoz, M. Huerta, D. Moro, A. Cervantes, C. Martínez-Ciarpaglini
*Department of Pathology. Hospital Clínico Universitario of Valencia. Biomedical Research Institute INCLIVA, University of Valencia, Spain

Background & objectives: PD-L1 expression has been suggested as a prognostic biomarker in certain CRC studies. However, controversy surrounds the directionality of this association. We aim to assess the prognostic significance and transcriptomic profile in MSS-CRC cases based on PD-L1 status.
Methods: We retrospectively evaluated a series of 124 surgically resected mismatch repair-proficient CRC cases. Formalin-fixed paraffin-embedded (FFPE) samples were stained for CD3, CD4, CD8, CD163 and PD-L1. RNA sequencing (RNAseq) was conducted after tumour dissection. A 96-custom gene panel for nCounter assay was used to obtain the CMS (Consensus Molecular Subtypes). Differential expression analysis was carried out by DESeq2.
Results: Positive PD-L1 expression (>1% positive immune cells) was significantly correlated with pN (p=0.015), pT (p=0.014) clinical stage (p=0.015), tumour-associated stroma (TS) (p=0.012), tumour-budding (TB) (p=0.004), CD3 (p=0.0061) and CD163 (p=0.0067) content. CMS4 (mesenchymal subtype) cases were enriched in PD-L1 negative tumours (p= 0.001). PD-L1 positivity was an independent prognostic factor strongly correlated with enhanced disease-free survival probability (HR 0.18, CI 0.06-0.49, p=0.000). RNA-seq analysis unveiled 320 genes exhibiting differential expression about PD-L1 status. Notably, there was a pronounced upregulation observed in members of the Cadherin family (PCDH10, PCDHA3, PCDHA9, CDH4, CDH7, PCDHA7, CDH16), along with a significant enrichment of biological pathways associated with cell adhesion in PD-L1 positive cases.

Conclusion: According to our results, PD-L1 positive MSS-CRC cases comprise a distinct group of tumours associated with a better prognosis, epithelial phenotype and stronger immune response. Recently, PD-L1 expression has been shown to play a role in regulating

epithelial-to-mesenchymal transition in a subset of cancers. The overexpression of cell-binding pathways observed in PD-L1 positive tumours in our cohort, along with the enrichment of TS, TB and CMS4 in PD-L1 negative cases, lends support to this idea.

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PS-24-031

Digital evaluation of intratumoural lymphocytic infiltrate profile in microsatellite inestable colorectal carcinomas: does the lost protein matter?

C. Perello-Fabregat*, M. Sant, J. Linares, N. Mulet, P. Osorio, G.A. Martín-Small, K. Matute-Molina, I. Beleña, M. Jimeno
*Hospital Germans Trias i Pujol, Spain

Background & objectives: Immune response related to the two main groups (MutSa and MutLa) in microsatellite inestable (MSI) colorectal carcinoma (CRC) have been barely studied. We analysed with digital technology the intatumourally lymphocytic infiltrate (ILI) in them as well its prognostic impact.
Methods: Ten cases of MSI CRC (5 of each group) were recruited. Immunohistochemistry was performed with CD3 and CD8, and two slides of each per case were digitalized. Image analysis was made with QuPath v.0.4.3 software. We retrieved the ILI 3-tier grading from diagnosis reports. All patients were diagnosed at stage II or III, with an average follow-up of 38 months.
Results: ILI counting was centred on the tumour core and on the infiltrative front, both at hot spots and at 5 random fields, of which an average was calculated. ILI density and distribution in each group were analysed and compared between groups and then correlated to disease free survival (DFS) (R v.4.2.3 software). The descriptive analysis has demonstrated a distinct distribution of ILI with a higher density both for CD3 and CD8 in the tumour core and in the infiltrative front in MutSa group. Comparison based on the 3-tiered ILI classification showed significant differences between the two heterodymer groups (Fisher's test, $p<0,05$). The DFS was similar in both groups.
Conclusion: MSI CCR tumours are usually treated as a homogenous group, hence the particularities between MutSa and MutLa has been scarcely described. Our study has demonstrated an evident greater lymphocytic reaction in the first one, both in the tumour core and in the infiltrative front. Differences in ILI landscape could have impact on immune therapy response and could also influence survival. We are currently working on expanding the case series to confirm these preliminary findings and obtain more robust results.

PS-24-032

Immunohistochemical assessment of tumour budding in stage II colon cancer – Bd0 as a prognostic marker

M. Pihlmann Kristensen*, U. Korsgaard, S. Timm, T. Frøstrup Hansen, I. Zlobec, S. Kjær-Frifeldt, H. Hager
*Department of Pathology, Vejle Hospital, University Hospital of Southern Denmark, Denmark

Background & objectives: Tumour budding, a prognostic biomarker in stage II colon cancer, is traditionally evaluated using H&E staining. This study aimed to assess the prognostic significance of tumour budding using immunohistochemistry (IHC) in a contemporary cohort of stage II colon cancer patients.
Methods: Tumour budding was evaluated in a retrospective population-based cohort comprising 493 patients with stage II colon cancer using IHC, following the H&E-based guidelines proposed by the International Tumour Budding Consensus Conference (ITBCC). Correlation between H&E-based and IHC-based tumour budding was assessed using a four-tired scoring system that included a zero budding (Bd0) category. Survival analyses explored the prognostic significance.
Results: IHC-based tumour budding evaluation yielded significantly higher bud counts compared to H&E ($p<0.01$). The IHC tumour bud count was on average 16 buds higher and the disparity between the staining methods escalated with increasing bud count. In total, 21 patients were identified as having a complete absence of tumour budding and categorized as Bd0 based on IHC. The Bd0 tumours were associated with significantly improved recurrence-free survival (HR=5.19, 95% CI 1.27-21.16, p=0.02) and overall survival (HR=4.47, 95% CI 1.10-18.27, p=0.04) in a multivariate analysis, when compared to tumours with budding. The Bd0 category demonstrated a 100% predictive value for the absence of recurrence.
Conclusion: IHC-based tumour budding evaluation in stage II colon cancer provides additional prognostic information. Our findings indicate that Bd0 tumours display a lower level of aggressiveness in colon cancer compared to tumours that exhibit any degree of budding. The absence of tumour budding is associated with a favourable prognosis and may serve as a potential marker for identifying patients with no risk of recurrence. This is significant in a clinical setting when making the decision regarding adjuvant chemotherapy.

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PS-24-033

(Phospho)Proteomic analysis reveals vulnerabilities in refractory metastatic colorectal cancer

M. Marinucci, G. Boot, M. Lazzari, C. Esposito, C.K. Ng, L. Terracciano, O. Kollmar, S. Piscuoglio*
*IRCCS Humanitas Research Hospital, Italy

Background & objectives: Proteomic networks are crucial for cellular homeostasis maintenance, and aberrant regulation is implicated in cancer development and progression. Understanding the alterations underlying these pathways may provide a way to design therapeutic interventions in human cancer.
Methods: We performed (phospho)proteomic analysis and ex-vivo drug testing on a cohort of refractory metastatic colorectal cancer (mCRC) tissues and matched patients-derived organoids (PDO) to identify new putative druggable biomarkers. State-of-the art bioinfomartic algorithms were used to analyse the data. The mCRC tissues with their matched PDOs were normalised to a pool of 6 colon mucosa tissues.
Results: GSEA identified upregulation in MYC, cell cycle, and MTORC1 signalling pathways in mCRC tissues and PDO, while kinase enrichment analysis highlighted an increase in Casein Kinase II (CKII) activity. Our ex-vivo experiments showed that silmitasertib-mediated CKII inhibition reduced cell viability in our PDO models; however, the anti-tumoural effect was overall modest. Interestingly, our data showed that higher resistance to silmitasertib was correlated with higher mTORC1 pathway activities, suggesting a relationship between the 2 pathways. Moreover, resistant PDO lines presented the highest EGFR pathway signalling basal activity and increased MAPK signalling post-treatment. Strikingly, the CKII inhibition combined with trametinib-mediated MEK blockade resulted in a synergistic interaction leading to enhanced antitumour activity.
Conclusion: Taken together, our findings propose the silmitasertib and trametinib combination as a new therapeutic opportunity for refractory mCRC patients and strengthen the use of PDO as a suitable model for drug screening.

PS-24-034

A rare subset of colorectal carcinomas with microsatellite instability and KRAS mutations

E. Rabaux, J. Grosjean, F. Marguet, A. Lamy, J.-C. Sabourin*
*Rouen University Hospital Normandy University, France

Background & objectives: Sporadic microsatellite instability (MSI)-colorectal carcinomas (CRC) are generally associated with BRAF mutations but do not disclose KRAS mutations. Hereditary MSI-CRC do not disclose BRAF mutations but may disclose KRAS mutations. We aimed to analyse MSI-CRC with KRAS mutations.
Methods: We searched the clinical data warehouse of our centre for patients with CRC (Proficient or Deficient for the MisMatch Repair system pMMR/dMMR) and KRAS status. KRAS mutations were characterized by molecular biology, and microsatellite status by both immunohistochemistry (4 antibodies MLH1, PMS2, MSH2 and MSH6) and molecular biology (Replication Error Test). Genetic analysis was performed for Lynch syndrome.
Results: Between 2009 and 2024, 6380 cases of CRC were identified. Among them, 10.7% were dMMR and only 15 cases (8 men and 7 women) were KRAS mutated, representing 0.2% of all CRC cases. KRAS mutation was mainly present in exon 2 (73%) and the most frequent mutation was c.35G>A (35%), then c.38G>A (27%). As expected, no double BRAF-KRAS mutations were found. Histologically, these 15 cases did not present any dMMR specificity (i.e. mucinous or signet-ring cell differentiation, Crohn-like inflammatory reaction) but presented dirty necrosis in the lumen of the glands (57%). They were histologically similar to pMMR mKRAS CRC. Lynch syndrome was diagnosed in 6 of the 13 cases tested.
Conclusion: dMMR mutated KRAS CRC are very rare tumours and are mainly associated with Lynch syndrome. They do not disclose the histological features usually described in dMMR CRC but are morphologically similar to mutated KRAS pMMR CRC. This distinct morphology could be a pitfall for artificial intelligence (AI) algorithms seeking to establish MMR status on hematoxylin and eosin-stained slides as these AI algorithms are trained with tumours presenting the usual morphology of dMMR CRC.

PS-24-035

Effectiveness of upper endoscopic screening in patients with head and neck neoplasia – results from a prospective cohort study

M. L. Sacramento*, M.S. Brito, B. Marinho, J. Afonso, F. Carneiro, R. Morais, I. Gullo
*Pathology Department, Centro Hospitalar Universitário de São João, Porto, Portugal; Faculty of Medicine of the University of Porto, Porto, Portugal

Background & objectives: Patients with head and neck neoplasia (HNN) are at an increased risk of developing synchronous/metachronous gastro-oesophageal neoplasia (GEN) due to shared risk factors. Aim: to prospectively evaluate the outcomes of upper endoscopic screening in a cohort of patients with HNN.
Methods: A prospective cohort of patients diagnosed with HNN (2020-2023) underwent screening oesophago-gastroduodenoscopy (time from HNN diagnosis to endoscopy: median=4 months; range=0-20 months). Non-epithelial HNNs were excluded. Clinicopathological features were collected. GEN detected during the screening program and respective synchronous/metachronous HNNs were analysed by RNA in situ hybridization for EBV (EBER) and immunohistochemistry (p16). IBM SPSS was used for statistical analysis.
Results: The series included 48 patients (males: 83.3%; median age: 64 years). GENs were detected in nine patients (n=9/48, 18.8%), encompassing six (n=6/48, 12.5%) oesophageal lesions (squamous dysplasia: n=4; squamous cell carcinoma (SCC): n=2, pT1a and pT1b) and three (n=3/48, 6.25%) gastric neoplasias (gastric adenoma: n=1; gastro-oesophageal-junction adenocarcinoma: n=1, pT1b; gastric adenocarcinoma: n=1, pT1b). The risk of developing GEN was higher in females (50.0%) compared to male patients (12.5%; p=0.013) but was not related to frequency/quantity of smoking/alcohol consumption. Strong-diffuse p16 expression was observed in two SCCs from two patients (vocal cord: n=1; oesophagus: n=1) and the gastric adenocarcinoma was EBV+. During the follow-up, recurrence/progression of GEN was not observed.
Conclusion: This study highlights the importance of routine endoscopic screening for individuals diagnosed with HNN, particularly in identifying early-stage synchronous/metachronous GEN that may benefit from endoscopic curative-intent treatment. The detection of an EBV+ gastric adenocarcinoma in a patient with p16+ HNN SCC underscores the potential role of viral infections (HPV/EBV) in high-risk, immunocompromised populations in neoplasia development and the need for further molecular studies to elucidate these relationships in order to improve patient care.

PS-24-036

Relevance of the new tumour budding Bd0 category in pT1 colorectal carcinomas

K. Saez de Gordoa*, M. Rodrigo, I. Archilla, M. Daca-Álvarez, J.J. Aguirre, L. Alarcón-Molero, M. Cámara Jurado, C. González-Lois, I. Machado, C. Martínez-Ciarpaglini, D. Naranjo, N. Papaleo, M. Pellisé, M. Cuatrecasas Freixas, o.b.o.t. EpiT1 Consortium
*Pathology department. Hospital Clinic. University of Barcelona. Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Spain

Background & objectives: pT1 colorectal carcinoma (CRC) is usually treated by endoscopy. Subsequent surgery depends on the presence of histological features associated with lymph node metastasis (LNM), including tumour budding (TB). The new Bd0 TB category is defined by the absence of TB.
Methods: A retrospective multicentre study including 2,430 pT1 CRC was held and 738 cases treated by endoscopy and subsequent surgery were selected. Haematoxylin-eosin (H-E) preparations were scanned, and 20 gastrointestinal pathologists evaluated high-risk histological features for LNM. Clinical and histological data were collected and correlated to TB, using Pearson's Chi-square for categorical variables and analysis of variance for continuous variables.
Results: TB was zero (Bd0) in 414 cases (56.10%), low (Bd1) in 197 cases (26.69%), intermediate (Bd2) in 62 cases (8.40%), high (Bd3) in 41 cases (5.56%), and in 24 it was not evaluable (3.25%). The presence of any TB (Bd1, Bd2 or Bd3) was significantly related to rectal tumours, with high histological grade, presence of lymphovascular invasion, perineural invasion, higher grade of poorly differentiated clusters and affected margins. The presence of TB conferred a higher risk for LNM, being 14% in cases with any TB, compared to 6.76% LNM in Bd0 cases (p-value < 0.001).
Conclusion: The presence of TB is associated with histological high-risk factors for LNM and with the presence of LNM. Nevertheless, more than half of pT1 CRC have Bd0, which can be feasibly assessed with H-E. Therefore, the introduction of the Bd0 category would allow to identify patients at lower risk for LNM.

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PS-24-038

Microsatellite instability in gastric precancerous lesions

M. Stepanchenko*, A. Shimanskaya, A. Kononov, S. Mozgovoi, V. Rubtsov, M. Parygina, E. Pomorgailo
*Omsk State Medical University, Russia

Background & objectives: Microsatellite instability (MSI) is a state of genetic hypermutability caused by a defect in DNA mismatch repair

(MMR) system. It's often found in cancers including gastric adenocarcinoma. Modern data suggest, that MSI may occur at the stage of precancerous lesions.
Methods: Gastric mucosal specimens with chronic gastritis (n=25) and dysplasia (n=75), gastric cancer (n=100) and distant zone specimens (≥10 mm from histological tumour border, n=100) were assessed for MSI (NR-21; NR-24; NR-27; BAT-25; BAT-26) and MMR status (anti-MLH-1, G168-15; anti-MSH2, DBM15.82; anti-MSH6,44; anti-PMS2, A16-4; Diagnostic BioSystems, USA). Fisher's exact test was used for comparing groups data, considered significant differences – $p<0.05$.
Results: All cases with chronic gastritis and indefinite for dysplasia (n=25), were classified as MMR-proficient and microsatellite stable (MSS). When assessing MSI and MMR status in samples with low and high-grade dysplasia (n=50), MMR deficiency(dMMR) was found in 4 cases (8%), MSI – in 3 cases (6.5%). 15 dMMR cases (15%) were found in gastric cancer specimens, MSI was detected in 10 samples (10%). In 2 cases (2%) of distant zone samples dMMR was detected in the foci of intestinal metaplasia, all cases turn out to be MSS. When comparing the distribution of MMR and MSI in gastric cancer and dysplasia cases no significant differences were found (p=0,12, and p=0,55).
Conclusion: Detection of MSI in precancerous lesions indicates the potential of MSI testing to assess the risk of microsatellite-associated gastric cancer development with assessment of the MMR-system proteins showing to be more sensitive method Determination of microsatellite instability and MMR deficiency is advisable for the differential diagnosis in cases indefinite for dysplasia. Its detection may indicate the formation of definitely neoplastic rather than regenerative lesion and probably indicates the need for a repeat biopsy to exclude low- or high-grade dysplasia.

PS-24-039
Improvements of diagnostic approach of gastric epithelial dysplasia via implementation decision support sustem with immunohistochemical markers
M. Stepanchenko*, S. Mozgovoi, A. Kononov, A. Shimanskaya, M. Parygina
*Omsk State Medical University, Russia

Background & objectives: In the last edition of WHO classification (2019), the terms indefinite dysplasia, intramucosal carcinoma and suspicion for invasive carcinoma are used for correctly definition of marked precancerous lesions. Gastric epithelial dysplasia/intraepithelial neoplasia has had low level of reproducibility between pathologists.
Methods: Selection of diagnostic patterns was identified by examining of three diagnostic signs of gastric epithelial dysplasia: epithelial atypia, differentiation gradient/cell maturation and histoarchitectonic disorganization. In order to evaluate an agreement level of specialists the assessment of Cohen's kappa (k) was carried out in group of pathologists with collection of hematoxylin-eosine stained histological slides and additional evaluation of Ki-67 and P53 expression.
Results: Evaluation of the level of reproducibility of each pattern and the final diagnosis were carried out in remote mode by 15 pathologists. A poor level of agreement was found general k = 0.2. The most reproducible diagnostic patterns (κ greater than 0.4) were: pseudostratification, gland branching and mitoses. Poorly reproducible (κ less than 0.2) were: loss of polarity of nuclei, lateralisation, and hyperchromia of nuclei. The final list of decision support system included verbal designation of patterns with images. After comments and discussion (master class) n the expert agreement increased to general k= 0.63 and k=0,79 after add Ki-67 and P53 markers.
Conclusion: A schematic representation of diagnostic patterns, the application of which is described by the algorithm of actions, is support in making a diagnostic decision. The testing of the pictograms and algorithm allowed to reach a good level of agreement. Usage of the proposed combinations of tissue and cellular patterns and immunohistochemical markers would be appropriate approach to increase the accuracy and, most importantly, the reproducibility of diagnosis. Such approach probably reflects the new education standard for pathologists.

PS-24-040
Temporal shifts in gastric cancer dynamics: time series analysis (pre-pandemic and pandemic) in a county hospital in Western Romania
I.-A., Traila*, M. Marasescu, A. Muresan, R. Cornea, C. Suciu, A. Dema, D. Szilagyi, C. Lazureanu, M. Cornianu, S. Taban, A. Vaduva
*Pathology Department, "Pius Brinzeu" Emergency County Clinical Hospital Timisoara, Romania

Background & objectives: The influence of the Coronavirus Disease on gastric cancer is closely unknown. The purpose was to examine the impact of COVID-19 on patients surgically treated for stomach cancer as a time-series analysis of the presentation stage in both datasets.
Methods: We studied gastric cancer patients diagnosed during the COVID-19 pandemic restrictions period and the corresponding pre-pandemic period two years before. The study included 112 cases from the pre-pandemic period and 99 cases from the pandemic period. Data were processed in Python with the pandas, matplotlib, and NumPy libraries.
Results: Analysis of the pre-pandemic and pandemic datasets suggests that the difference between the two periods is insignificant, although slightly reduced in the pandemic period. The mean age was 65 in both datasets, with an SD ± 11.14. Histological grade 3 tumours were predominant in both groups. Over time, analysis of the pT criteria revealed a higher prevalence of pT4a (43 pre-pandemic, 38 pandemic) followed by the pT3 stage. The monthly average number of cases peaked at 12 cases/month in March 2020, followed by a sharp decline during lockdown (April - May 2020). Throughout the alert period, cases ranged from 1 to 5 per month.
Conclusion: Our study reveals that the COVID-19 pandemic hasn't affected patients' access to medical services to diagnose and treat gastric cancer. Moreover, the aggressivity criteria analysed over time didn't significantly differ between the two datasets. We propose to continue the study by collecting post-pandemic data to analyse the pandemic's influence on gastric cancer after the restriction period and to simulate, with machine learning methods, the evolution of gastric cancer cases if the pandemic didn't exist.

PS-24-041
Robust prognostic signature in colon cancer by studying ectopically expressed genes using machine learning
S. Valmary-Degano*, A. Spinelli, A. Vitte, F. Chuffart, M. Laverrière, J. Abba, S. Rousseaux, S. Khochbin, E. Bourova-Flin
*Univ. Grenoble Alpes, Inserm U1209, CNRS UMR5309, Institute for Advanced Biosciences, Department of Pathology, Grenoble Alpes University Hospital, France

Background & objectives: Colon cancer (CC) ranks third in cancer frequency and second in cancer-related deaths. Despite screening, late diagnoses limit treatment options. Early prognosis prediction is crucial. Our objective is to discover new prognostic biomarkers in CC for a better treatment guidance.
Methods: Epigenetic deregulations in tumours lead to aberrant gene activation associated with an unfavourable prognosis. Based on these findings, we developed a machine learning pipeline named "ectopy", which aims to discover a panel of robust prognostic biomarkers from transcriptomic data. These biomarkers are combined in a Gene Expression Classifier (GEC) that stratifies patients according to the number of aberrant activations.
Results: By applying the "ectopy" method, we found that 748 tissue-specific genes, normally silent in healthy colon tissues, become

aberrantly activated in CC. Among these, the aberrant activations of 4 genes were significantly associated with a poor survival prognosis across two independent datasets (n=964). Using these 4 genes, we created a GEC tool capable to predict individual prognosis for each patient. The GEC was successfully validated in a third independent CC cohort (n=177). Additionally, multivariate analyses demonstrated that the GEC provides independent and complementary information alongside already known risk factors in CC, such as tumour stage, grade, lymph node status, and KRAS mutation.
Conclusion: The GEC signature effectively identifies patients with poor prognosis, independently of other prognostic criteria. In particular, the GEC helps to evaluate treatment decisions for hyperthermic chemotherapy in stage IV. In earlier stages, it highlights aggressive forms of CC for which the treatment can be intensified. Future prospects of this project involve RT-qPCR analysis of a new Grenoble Alpes University Hospital cohort, as well as the development of an immunohistochemical test for routine clinical use.

PS-24-042
Impact of extending the original criteria in the chemoradiotherapy for oesophageal cancer followed by surgery study (CROSS) regimen on treatment outcome in locally advanced oesophageal cancer (EC) patients
H. Wang*, R. Verhoeven, V. Oppedijk, I. Nolte, B. van Etten, G. Hospers, J. Plukker, G. Kats-Ugurlu
*The Netherlands

Background & objectives: CROSS regimen is currently offered to EC patients beyond the eligibility criteria. This national population-based study assessed the safety in implementation regarding treatment outcome when extending these criteria i.e. pathological complete response (pCR), overall survival (OS) and disease-free survival (DFS).
Methods: Data of 5061 EC patients from the Dutch Cancer Registry (2015-2022) with cT1N+/T2-4aN0-3/M0 disease were divided into the original group (n=1958) and extended group (n=1348). Primary outcome was OS. Secondary outcomes were pCR, DFS, post-operative morbidity and mortality. Chi-square and Likelihood ratio tests compared categorical variables, Kaplan-Meier displayed OS and multivariate Cox regressions assessed prognostic factors for OS and DFS.
Results: The OS, both determined after neo-adjuvant chemoradiotherapy (OS-nCRT) and after curative intended surgery (OS-surgery) until death differed significantly between the original and extended group; OS-nCRT with a median survival of 45.9 months (95% CI 38.4-53.4) versus 30.3 months (95% CI 27.2-33.5) (P<0.001) and OS-surgery with a median survival of 56.8 months (95% CI 46.6-67.0) versus 33.6 months (95% CI 26.6-40.7). Independent prognostic factors for OS were age (P=0.021), WHO performance status (P<0.001), pathologic differentiation (P<0.001), ypN-stage (P<0.001), tumour regression grade (P=0.037) and post-operative complications (P=0.008). No significant difference was found in pCR, post-operative morbidity and mortality, and DFS (both measured after nCRT or surgery until recurrent disease).
Conclusion: Extending the original eligibility CROSS criteria in locally advanced EC patients was associated with a poorer OS, but had no impact on pCR, post-operative morbidity and mortality, and DFS. The CROSS regimen can be implemented safely in a 'real-world' setting, but individual factors that may contribute to OS should be considered in decision making.

PS-24-043
Prognostic significance of tumour budding and desmoplastic reaction in patients with pancreaticobiliary subtype ampullary adenocarcinoma: a preliminary study
A. Yavuz*, K. Karaca, M.Y. Çelik, C.İ. Başsorgun, G.O. Elpek
*Akdeniz University Hospital, Turkey

Background & objectives: Ampullary adenocarcinoma (AAC) is a malignancy originating from the ampulla of Vater, often detected at early stages due to biliary obstruction. This study investigates the prognostic impacts of desmoplastic reaction (DR) and tumour budding (TB) in the pancreaticobiliary (PB) subtype.
Methods: In this retrospective study of 42 patients with PB subtype AAC, we examined demographic data, TNM stage, histological grade, lymphovascular invasion, and perineural invasion. TB was evaluated according to the International Tumour Budding Consensus Conference (ITBCC), and the DR was classified into three groups based on the maturation of the stroma. Statistical analyses utilized SPSS version 27.
Results: In our study of 42 patients with pancreaticobiliary subtype ampullary adenocarcinoma, TB exhibited a strong correlation with DR ($p < 0.001$). Additionally, TB was significantly associated with lymphovascular invasion ($p = 0.011$). DR, when classified into three groups, displayed marked associations with perineural invasion and histological grade ($p = 0.046$ and $p = 0.022$, respectively). Survival analyses demonstrated significant differences in survival rates across the DR and TB categories (Log Rank $p = 0.036$ and Log Rank $p = 0.044$, respectively), emphasizing the predictive role of TB in determining patient outcomes and indicating DR as a potential prognostic parameter.
Conclusion: Our findings suggest that evaluating TB according to the International ITBCC criteria effectively stratifies patients with pancreaticobiliary subtype AAC for treatment and prognosis. Additionally, the relationship between TB and DR confirms the role of the microenvironment on tumour behaviour in AAC. The presence of these associations necessitates further research with larger patient series to clarify the impact of DR in the prediction of the prognosis of pancreaticobiliary subtype AAC more accurately.

PS-25Poster Session Infectious Diseases Pathology

PS-25-001
Utility of PCR-hybridization based technique in the detection and typing of Mycobacteria species in pathology biopsies
R.I. Alvarado Cuenca*, L. Ortega Comunian, L. Aguirrezabal Marcotegui, I. Fernandez de la Prieta, I. Menendez Lora, M.T. Perez Vilanova, M.C. Etxezarraga Zuluaga, C. Valenti Ponsa, A. Gaafar Eleraky
*Pathology Department- Basurto University Hospital, Spain

Background & objectives: The VisionArray® MYCO-ZYTOVISION is a PCR based technique that allows identification of tuberculous and nontuberculous Mycobacteria in pathology biopsies. The objective of this study is to evaluate the efficacy of the technique in daily practice.
Methods: Retrospective study, revising all cases diagnosed as granulomatous inflammation during 2022 y 2023. These cases have been studied by the VisionArray MYCO-ZYTOVISION, and results have been compared against the traditional Ziehl-Neelsen staining. In addition, clinical history microbiology studies have been revised.
Results: 29 cases of granulomatous inflammation have been included in the study, 55% of which showed necrotizing granulomas. Mycobacteria tuberculosis has been detected by VisionArray MYCO-ZYTOVISION in 8 cases "28%", while other Mycobacteria species have been detected in 1 case "3%". Ziehl-Neelsen staining was positive in only 4 cases "13%".
Conclusion: The VisionArray® MYCO-ZYTOVISION is a sensitive and rapid technique for detection of Mycobacteria species in suspicious pathology biopsies, with an excellent correlation to specific microbiologic studies.

PS-25-002
Cutaneous leishmaniasis: a Tunisian healthcare problem
L. Bouzidi*, S. Makni, M. Zghal, C. Chaari, T. Sellami Boudawara, S. Graja

*Department of Pathology, Habib Bourguiba University Hospital, Sfax, Tunisia

Background & objectives: Cutaneous leishmaniasis is on the rise in our country and still constitutes a public healthcare problem. The aim of our work is to describe the epidemiological, clinical and anatomopathological characteristics of this lesion.
Methods: This is a retrospective study of 29 cases of cutaneous leishmaniasis collected in our pathology department over a period of 14 years (2006-2019).
Results: There were 12 men and 17 women (sex ratio 0.7) from the South Tunisian. The average age was 53.41 years with extremes ranging from 16 to 90 years. All patients clinically presented a nodular ulcero-crusting lesion which was bifocal in four cases. The main location of the lesions was the cephalic region, affected in 21 cases. The upper limb was affected in 3 cases and the lower limb in 8 cases. One lesion was located next to the sternum. The pathological examination showed a dense dermal inflammatory infiltrate composed essentially of macrophages. Leishman bodies were noted inside the macrophages and were clearly objectified after the PAS colouring.
Conclusion: Cutaneous leishmaniasis is frequent in our country and continues to pose a real public healthcare problem in Tunisia. The emergence of severe and resistant forms must encourage the multiplication and strengthening of prophylactic measures.

PS-25-003

SARS-COV-2 in pets: an epidemiological, clinical, and laboratory study in veterinary clinics of a Northeastern region of Brazil

S. Samuel Feitosa Machado, F. Maria Soares de Sampaio, J. Ferreira de Andrade, I. Rodrigues de Lima Cruz, A. Alencar Coelho, A. Maria Araújo Silva, T. Ribeiro Morais, D. de Andrade Amorim, M. Maria Felipe Girão, W. Natalia Santos Maciel, E. Mares Ferreira Feitosa, H. Felipe Nogueira De Carvalho, M. do Socorro Vieira dos Santos, C. Gleidiston Lima da Silva, J. Carneiro Melo*
*University of Fortaleza, Brazil

Background & objectives: Coronaviruses infect a variety of mammalian vertebrate animals, causing several diseases with different degrees of clinical severity. The close contact of dogs and cats with humans allows us to question whether they may be involved in the COVID-19 transmission chain.
Methods: An observational, descriptive cross-sectional trial was carried out to evaluate the prevalence of SARS-CoV-2 infection in dogs and cats of Juazeiro do Norte, Crato and Barbalha, Brazil, for 2 years. Cats and dogs domiciled in the study area were randomly selected. Biological samples (sera and swabs) were collected from the animals and subjected to chemiluminescence and RT-PCR assays.
Results: The results showed 274 animals included in the study, of which 26 (9.5%) tested positive for SARS-CoV-2 antibodies, with 22 (12%) of them being dogs out of the 184, and 4 (4.4%) being cats out of the 90. Out of 51 swabs collected, none were detectable for SARS-CoV-2. Consequently, a serological prevalence of 9.5% and an indeterminate infectious prevalence were found.
Conclusion: The results allow us to infer that, possibly, domestic animals (dogs and cats) may be involved in the transmission chain or be reservoirs of the COVID-19 virus, a fact that leads to the expansion of the study, considering it is an emerging disease of notable importance in public health.

PS-25-005

Peripheral virus distribution in patients with fatal Borna encephalitis points possible alternative clinical presentations - a case report series

P. Grochowski*, N. Jungbäck, T. Schaller, F. Lippek, J. Schlegel, B. Märkl, F. Liesche-Starnecker
*Pathology, UKA Augsburg, Germany

Background & objectives: Borna disease virus 1 (BoDV-1) causes fatal encephalitis in endemic regions. There are reports on peripheral spread of this highly neurotropic virus. Nevertheless, there are no systematic analyses of the virus distribution aside from the central nervous system.
Methods: We analysed autopsy material from 4 deceased with BoDV-1 infection regarding the presence of BoDV-1 nucleoprotein in visceral organs (including e. g. heart, lung, liver, thyroid gland, pancreas, stomach) with immunohistochemistry. Additionally, we revaluated the tissue morphology considering local inflammatory reaction to presence of the virus, which is commonly observed in central nervous system and contributes to the fatal outcome.
Results: BoDV-1-presence could be shown in small peripheral nerves in thyroid gland, pancreas, adrenal glands, left side heart (in 2 cases respectively) and in stomach (1 case). One patient was a transplant recipient from earliest reported infection cluster and showed additional infiltration in peripheral spinal nerves, oesophagus, mediastinal and retroperitoneal adipose tissue, lungs, liver as well as in the implanted but not their own kidney. Neither inflammatory nor any other tissue reaction was observed. In one case, no peripheral spread could be shown (the patient also presented an atypical brain distribution of BoDV-1 due to a high-dose immunosuppression). No patient showed BoDV-1 positivity aside of the peripheral nerve tissue.
Conclusion: We confirm that BoDV-1 spreads to small peripheral nerves, pronouncing organs innervated by vagus nerve. Even though no specific (inflammatory) reaction and therefore no local damage was observed, consecutive autonomic nerve system dysregulation may occur in some patients. Investigations regarding such alternative clinical presentations apart from the typical encephalitis should be considered.

PS-25-006

Learning from loss: a four-year (2020-2024) analysis of COVID-19 mortality in a Romanian infectious diseases' hospital

M.M. Köteles*, D. Lay, G. Olteanu
*County Emergency Hospital Bihor, Romania

Background & objectives: The COVID-19 pandemic challenged Romania's Healthcare System in an unprecedented way. Our retrospective study investigated the deaths that occurred within the Clinical Hospital of Infectious Diseases and Pneumophysiology Dr. Victor Babes Timisoara, Romania between 2020 and 2024.
Methods: We evaluated the number of deaths that were recorded in the digital registry of the hospital's 11 departments over a period of 4 years. Only patients with COVID-19 positive tests were included in the study. Further, investigation of the data followed SARS-COV-2 related pathologies: pneumonia, acute respiratory distress syndrome (ARDS), aspergillosis, pulmonary embolism (PE), and sepsis.
Results: A total number of 2444 deaths were identified, of which 1174 (48.04%) had confirmed SARS-CoV-2 infection prior to death. Among the 1174, 545 (46.42) were female and 629 (53.58) males. The average age at death was 72.04, with the oldest patient being 98 years old and the youngest 28 years old. Multiple COVID-19 related pathologies were diagnosed at the time of death in the same individual, from these concurrent conditions, pneumonia was identified in 96.59% of deaths, sepsis in 41.4%, ARDS in 16.78%, and PE in 2.21%. No cases of COVID-19 associated pulmonary aspergillosis (CAPA) was reported.
Conclusion: This retrospective study revealed high mortality rates especially in frail, older patients. Surprisingly, the data showed very low rates of ARDS and PE diagnoses compared to existing literature, and unexpectedly no CAPA diagnoses. From these results several conclusions can be drawn even in pandemic circumstances, minimally invasive procedures should be continued such as computed tomography angiography for thromboembolic events and bronchial aspirations/lavages for diagnosing co-infections like CAPA. Furthermore, there's need for improved recognition and management of COVID-19 associated ARDS.

PS-25-007

The first wave of COVID-19 in Slovakia – clinicopathological correlation

L. Krivosikova*, M. Palkovic, P. Janega, P. Babal
*Institute of Pathological anatomy, Faculty of Medicine, Comenius University Bratislava, Slovakia

Background & objectives: The onset of the COVID-19 pandemic was exceptionally slow in Slovakia. This fact allowed us to analyse autopsy findings in the vast majority of patients with fatal COVID-19 during the first wave in Slovakia.
Methods: We analysed samples of lungs from 25 out of 28 patients who died from COVID-19 during the 1st wave. The presence of the virus was confirmed by immunohistochemistry using antibodies against nucleoprotein and S1 subunit of the spike protein. We evaluated signs of diffuse alveolar damage, other pathological changes, therapy, laboratory parameters, and comorbidities. The data were statistically analysed.
Results: The average age of the patients was 79, the majority were females (19/25). Everyone had at least one comorbidity. 22/25 presented with dyspnoea. CRP was increased in 19/21 patients. Leukocytosis was present in 14/21 patients, caused by increased neutrophil count. Decreased lymphocytes were present in 8/21 patients. Microthrombosis was found in 9/25 cases. There was a correlation between the neutrophil and leukocyte count, CRP, and long-term immobility. Surprisingly, we did not find any correlation between microthrombosis and anticoagulation therapy, or the level of D-dimer. Oxygen therapy correlated with perivascular inflammatory infiltrate. We found a correlation between hyaline membranes and monocyte count, therapy with antimalarials, and thrombocyte count.
Conclusion: The first wave in Slovakia was very specific. We autopsied 89% of cases of fatal COVID-19 with a detailed description of microscopic findings and clinicopathological correlation. The early introduction of strict anti-epidemic measures resulted in an exceptionally low number of fatalities during the first wave of COVID-19. The anticoagulation therapy showed only limited effect on microthrombosis development.

PS-25-008

Emerging trends in human pulmonary dirofilariasis: a case series from Hungary

L. Kuthi*, T. Zombori, L. Tiszlavicz, F. Hegedus, S. Almási, B. Baráth, M. Almakrami, M. Jamal EJ, N. Barta, Z. Ujfaludi, T. Pankotai, A. Hajdu, J. Furák, A. Sejben
*Department of Surgical and Molecular Pathology, National Institute of Oncology, Hungary

Background & objectives: Human pulmonary dirofilariasis (HPD) is a rare zoonotic infection mainly linked to Dirofilaria immitis. Although more prevalent in Mediterranean countries, sporadic cases occur in temperate regions. Radiologically, HPD often presents with nonspecific findings, mimicking pulmonary neoplasms.
Methods: This study reports a 12-year case series from Hungary, emphasizing a rise in incidence. Patient data and clinical presentations were gathered from medical records. Grossing data along with histological slides were. Special stains were employed to rule out other infectious agents, while DNA extraction from lesions facilitated polymerase chain reaction (PCR) analysis to confirm the helminth subtype.
Results: Among the patients studied (males: 3, females: 2), all were of middle age (median: 52 years; range: 37-69 years) and presented with tumour-like lesions primarily in the right lung, necessitating lobectomy or wedge resection. Dry cough and chest pain were the most commonly observed symptoms, with only one patient exhibiting blood eosinophilia. Grossly, the lesions had a median size of 18 mm (range: 6-22 mm) and were predominantly located in subpleural regions. Histological examination consistently revealed a necrotizing granulomatous reaction, characterized by remnants of helminths. Other potential infectious agents were excluded via specialized staining techniques. PCR analysis definitively confirmed the presence of Dirofilaria immitis in each case.
Conclusion: This case series sheds light on HPD as an emerging zoonosis, suggesting a likely increase in its incidence within temperate regions. Therefore, clinicians should maintain a heightened awareness of HPD in the differential diagnosis of pulmonary coin lesions. A thorough pathological examination can reliably establish the diagnosis of HPD, while PCR analysis identifies the helminth subtype.

Funding: The project was implemented with the support from the National Research, Development and Innovation Fund of the Ministry of Culture and Innovation under the National Laboratories Program (National Tumor Biology Laboratory (2022-2.1.1-NL-2022-00010))) Grant Agreement with the National Research, Development and Innovation Office, This research was funded by the University of Szeged, Faculty of Medicine Research Fund-Heténi Géza Grant (Grant No. 5S 340 A202) and the New National Excellence Program (Grant No. ÚNKP-23-4-SZTE-385).

PS-25-009

Assessment of toll-like receptor 9 expression in immune cells in lung tissue from patients with drug-resistant tuberculosis

P. Kuzyk*, S. Gychka, S. Nikolaienko
*Bogomolets National Medical University, Ukraine

Background & objectives: Ukraine has one of the highest incidences of drug-resistant tuberculosis (DR-TB). This study aims to evaluate the expression of Toll-like receptors (TLRs) in immune cells, which are crucial for both innate and adaptive immunity.
Methods: We examined lung tissue samples from 26 deceased DR-TB patients and 24 non-TB individuals. TLR 9 expression in immune cells was quantified using immunohistochemical methods with anti-CD289 (TLR 9) monoclonal antibodies. Expression intensity was qualitatively rated on a scale of 0 (absent), 1 (weak), 2 (moderate), or 3 (pronounced).
Results: An immunohistochemical study of the lung tissue of non-TB individuals demonstrated pronounced expression of TLR 9 by macrophages (2.72 ± 0.24) and low expression of TLR 9 by lymphoid cells of the lung tissue (1.28 ± 0.12). Conversely, in the tuberculosis lesions of the lung tissue of patients who died from progressive DR-TB, there was a low expression of TLR 9 by the macrophages of tuberculosis foci, lower than TLR 9 by the alveolar macrophages in non-TB areas (0.82 ± 0.12 versus 2.23 ± 0.22, $p < 0.05$).
Conclusion: The markedly reduced expression of TLR 9 in immune cells within DR-TB lesions suggests cellular exhaustion, potentially contributing to the progression and severity of the disease.

PS-25-010

Modified auramine-rhodamine stain contribution to identify mycobacterium tuberculosis

L. Ruivo*, M. Pinho Fialho, H. Silva Santos, J. Almeida Tavares, C. Ferreira
*Department of Pathology - Unidade Local de Saúde Santa Maria (ULSSM); Instituto Politécnico de Lisboa (ESTeSL), Portugal

Background & objectives: Mycobacterium tuberculosis (MT) infection often causes multiple organ granulomatous disease. Suspicious lesions are often biopsied in order to exclude malignancy. Ziehl-Neelsen (ZN) staining is the histological standard diagnostic tool for MT, although auramine-rhodamine (AR) appears to have better detection ratios.
Methods: We evaluated all biopsies with suspected clinical tuberculosis (combined or not with microbiological testing), from January

2022 to September 2023 in a tertiary hospital centre, with histological confirmation of granulomatous inflammation and tested with ZN staining. The biopsies were reevaluated using AR staining with a modified protocol in which phenol was replaced by trident for cell membrane permeabilization.
Results: The study comprised 53 cases, 27 females and 26 males. The most frequent biopsy sites were lymph nodes (38% - 20/53) and lung (36% - 19/53). Necrotizing granulomatous inflammation was found in 75% of cases (41/53), 32% of which (13/41) tested positive for ZN stain and were further confirmed with modified AR. From the remaining ZN-negative cases (68% - 28/41), 39% (11/28) tested positive in the microbiological study; from those, 73% (8/11) were positive using modified AR.
Conclusion: Although ZN is the histological gold standard method to assess the presence of MT, its evaluation is hampered by the fact that the number of mycobacteria is often below the technique's detection threshold. AR has greater sensitivity and easier fluorescence visualization, even at lower magnification and with fewer bacilli. Additionally, the proposed modification in the technical protocol for AR, makes it less harmful for the performer and does not compromise the quality of the technique.

PS-25-011
Effects of COVID-19 vaccine and/or infection on COVID-19 expression in skin biopsies
Y. Yuyucu Karabulut*, N.G. Bolatt
*Mersin University, Turkey

Background & objectives: SARS-CoV-2 infection, declared as a pandemic by the WHO, primarily spreads through droplets and contact transmission. It manifests with many system symptoms. Also, skin manifestations during the course of the disease have been identified, including urticaria, morbilliform rash, vesicular eruption.
Methods: we investigated the immunohistochemical expression of viral antigens in skin biopsy materials. A total of 79 patients who underwent skin biopsy for various reasons at our centre within a 2-month period after COVID-19 PCR positivity and/or vaccination were included in the study. Of the 79 patients, 63 had symptoms after vaccination, and 16 had symptoms during and after infection.
Results: COVID-19 expression was detected in 19 of the 79 patients. Of the 19 patients with expression, 14 had post-vaccination skin lesions, and 5 had skin lesions after infection. Among the cases with expression, 4 had psoriasis, 2 had vasculitis, 2 had drug eruption, and others were diagnosed with pemphigus vulgaris, mycosis fungoides, contact dermatitis, lichen planus, erythema multiforme, granuloma annulare, fibrotic dermatitis, pruritus gravidarum, pityriasis lichenoides chronica, Duhring, and bullous pemphigoid.
Conclusion: In conclusion, significant antigen expression in vascular endothelial cells was mainly evaluated in psoriasis cases.

PS-26Poster Session Ophthalmic Pathology
PS-26-002
Corneal dystrophies: twenty years' experience
M. De Uribe Viloria*, V. Macarrón, E.P. Sánchez López, S. Quinones, E. Ruiz-Bravo
*La Paz University Hospital, Spain

Background & objectives: Corneal dystrophies (CDs) are inherited disorders, usually bilateral, symmetric, slowly progressive, not related to environmental or systemic factors, characterised by slowly progressive corneal opacities that lead to visual impairment. Our study aims to shed light on an often-forgotten pathology.
Methods: We reviewed our files from 2004 to March 2024 and found 60 cases. We performed routine staining and histochemical studies in all 60 cases. The diagnosis was made according to the Second Edition of the IC3D Classification of Corneal Dystrophies (2015). Epidemiological data was obtained from clinical history.
Results: Our study included 58 patients (36 female (63.5%), 22 male (36.5%); median age 70). 1 patient (1.7%) was diagnosed with Epithelial Basement Membrane Dystrophy (EBMD), 1 (1,7%) with Central Cloudy Dystrophy of François (CCDF), 1 (1.7%) with Posterior Polymorphous Corneal Dystrophy (PPCD), 2 (3.4%) with Lattice Corneal Dystrophy (LCD), 3 (5.1%) with Granular Corneal Dystrophy, type 2 (GCD2) and 50 (86.2%) with Fuchs endothelial corneal dystrophy (FECD). Those diagnosed with EBMD, PPCD and LCD were male while the one diagnosed with CCDF was female, 2/3 diagnosed with GCD2 were male, 34/50 (68%) of patients diagnosed with FECD were female and 5/50 recidivated after corneal transplant (1 male and 4 females).
Conclusion: CDs are rare genetic disorders affecting approximately 0.09% of the population. FECD is the most frequent one. Current classification systems identified four main groups of CDs based on clinical, histologic, and genetic information. Management of CDs varies, sometimes they are medically treated but the majority of them will eventually require excising or ablate the abnormal corneal tissue (PK, DALK, DSAEK, DMEK). More studies are needed to address the challenges of these rare entities.

PS-26-003
Anatomopathological perspectives on ocular coloboma: unravelling associations with ocular and syndromic alterations
S. Quinones*, E.P. Sánchez López*, G. Escuer-Albero, I. Esteban-Rodríguez, R.M. Regojo, E. Ruiz-Bravo
*La Paz University Hospital, Spain

Background & objectives: Ocular coloboma results by defective closure of the embryonal fissure. Recent reviews include clinical, radiological, and genetics perspectives, without anatomopathological insights. The aim is to review our cases incorporating their association with ocular abnormalities and syndromic alterations.
Methods: After diagnosing the latest case in our centre, we reviewed our records of clinical autopsies perinatal and infants (from 1967 to 2023) and biopsies (1995 to 2023) and found 28 cases of coloboma. Clinical histories were available.
Results: Colobomas are classified according to the damaged structure, with the iris being the most frequently involved (11/28), followed by palpebral (8/28) and chorioretinal areas (5/28). Optic nerve involvement was demonstrated in 14% of cases. In retinal cases, neural retinal growth persists, leading to tissue rolling at the retinal pigment epithelium gap. Disorderly neuroblastic proliferation in adjacent retina form occasionally dysplastic rosettes.
Remarkably, 57% of cases showed other ocular anomalies, with microphthalmia (12/28) being the most prevalent, followed by retinal dysplasia (7/28). Furthermore, bilateral defects were observed in 15 patients, representing over half of our sample. A notable majority (75%) displayed syndromic or genetic associations, including Trisomy 13 and CHARGE syndrome.
Conclusion: Eye biopsy is extremely uncommon in embryological development defects, as diagnosis mainly relies on clinical-radiological evaluation. However, when performed, such biopsies provide valuable insights into the histopathological characteristics of these embryological defects. These results contribute to enrich our understanding from a clinicopathological perspective. Furthermore, it affords the opportunity to explore the associations between colobomas and rare syndromes or entities.

PS-27Poster Session Uropathology

PS-27-003
Multiparameter cell-cycle measurement enables a better assessment of cancer aggressiveness in urothelial bladder cancer than Ki67 LI alone

E. Bady*, J.H. Müller, L. Hornsteiner, S. Elezkurtaj, F. Roßner, S. Schallenberg, A.H. Marx, M. Fisch, M. Slojewski, S. Hallmann, S. Koch, N. Adamini, G. Sauter, H. Zecha, T. Schlomm
*Institute of Pathology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

Background & objectives: Immunohistochemical determination of the Ki67 labelling-index is a clinically well-established tool for assessing the proliferative activity of tumours. Other cell cycle proteins such as Minichromosome maintenance-3 (MCM3) have been evaluated for clinical utility much less intensively.
Methods: To study the difference and potential complementarity of Ki67 and MCM3 based proliferation measurement, both proteins were analysed by multiplex fluorescent immunohistochemistry in 1,994 urothelial bladder cancers in a tissue microarray format. Results were compared with clinico-pathological parameters (pT, grade, CK20, p16 and p63). A deep learning-based algorithm for automated cell and marker detection was used for image analysis.
Results: In our 1,994 urothelial bladder cancers, the average Ki67-LI was 16% and the average MCM3-LI was 39%. Of all panCK+ tumour cells, 14% were positive for both proteins, 20% were only positive for MCM3, 0.002% only for Ki67, and 67% were negative for both markers. Compartments of proliferating cells were defined: early (MCM3+/Ki67-), intermediate (MCM3+/Ki67+), late phase of the cell cycle (MCM3-/Ki67+) and full proliferation (MCM3+ or Ki67+). Comparison these compartments with clinico-pathological parameters revealed the best significance for the MCM3-LI for differences in pT (F=93.34), pN (F=1.25), grade (F=460.38), p16 (F=107.54) and p63 (F=56.76), each $p<0.0001$. The "full proliferation"-LI was most tightly linked to a CK20 expression (F=28.42, $p<0.0001$).
Conclusion: The combined analysis of MCM3 and Ki67 enables the distinction of cells in early, intermediate, and late phase of the cell cycle. In urothelial bladder cancer MCM3 quantification alone or in combination with Ki67 often resulted in stronger relationships with clinicopathological parameters than the Ki67 LI alone. These results suggest that a more subtle analysis of cell cycle proteins might enable a better evaluation of cancer aggressiveness than Ki67 measurement alone.

PS-27-004
Prognostic value of tumour-infiltrating lymphocytes in muscle-invasive urothelial bladder carcinomas
Y. Ben Romdhane*, Z. Lajmi, A. Bdioui, A. Mahmoudi, M. krifa, S. Mestiri, S. Hmissa
*University Hospital Sahloul, Tunisia

Background & objectives: Tumour-infiltrating lymphocytes (TILs) are an independent prognostic marker in a variety of tumours, including melanoma, colorectal and breast carcinoma. So far, there have been only a few studies investigating TILs and their prognostic value in muscle-invasive urothelial bladder carcinomas (MIUBC).
Methods: A retrospective study on MIUBC cases treated in our institution between 2019 and 2022. TILs were scored following the guidelines established by the International TILs Working Group. Analysis of TILs were performed on HE-stained sections by two pathologists. Two groups were defined: low and high TILs. Associations between TILs density and clinicopathological parameters were examined using the Chi square test.
Results: Our series included 72 patients with MIUBC. There were 65 males and 7 females. The mean age was 68.13 years. All patients underwent a radical cystectomy. According to the standardized International TILs Working Group method, 40 cases (55.6%) were classified as low TILs and 32 (44.4%) as high TILs. TILs density was significantly associated with vascular invasion ($p=0.014$), lymphovascular invasion ($p=0.001$) and perineural invasion ($p=0.023$). There were no significant associations between age, gender, tumour size, grade, histological variant, concomitant carcinoma in situ, budding, pT stage, pN stage and the degree of TILs.
Conclusion: In conclusion, our study confirm that TILs assessed by using the International TILs Working Group system are a strong independent positive prognostic factor in patients with MIUBC. TILs assessment should be incorporated into pathological reports and included in staging guidelines to provide a comprehensive prognostic information and aid in therapeutic decision making.

PS-27-005
The comparison of prevalence and location of positive surgical margin positivity in prostate cancer patients undergoing open, laparoscopic, and DaVinci robot-assisted radical prostatectomy
J. Borowczak*, M. Maniewski, Ł. Szylberg
*Clinical Department of Oncology, Oncology Center in Bydgoszcz; Center of Medical Sciences, University of Science and Technology in Bydgoszcz, Poland

Background & objectives: Positive surgical margins (PSM) influence the risk of biochemical recurrence and prognosis in patients with prostate cancer. This study investigated the location and prevalence of PSM among patients undergoing open, laparoscopic, and robot-assisted radical prostatectomy.
Methods: We conducted a retrospective analysis of histopathological reports and clinical data of 100, 91, and 243 patients undergoing open, laparoscopic, and DaVinci robot-assisted radical prostatectomy. Patients with T2/T3 tumours, no lymph node or distant metastasis, and no history of neoadjuvant or adjuvant therapy were included.
Results: PSM rates were 55%, 31.9%, and 35.8% for open, laparoscopy, and robot-assisted radical prostatectomy, respectively. PSM rate in the laparoscopic and robot-assisted groups was significantly lower than in the open surgery group; however, there were no differences in PSM rate between laparoscopic and robot-assisted groups. The apex was the most common location in the laparoscopy group, while lateral margins were the most prevalent in open and robot-assisted groups. The extensity of PSM was not associated with increased odds of biochemical recurrence, but patients with PSM had increased odds of early biochemical recurrence (OR 3,4 [95% CI, 1,6 to 7,1]).
Conclusion: Robot-assisted prostatectomy may achieve lower PSM rates and potentially reduce the risk of early biochemical recurrence. The location of PSM may be due to the used technique of surgery. While in our study PSM increased the odds of early biochemical recurrence, neither the extensity of PSM nor its location seemed to affect patient's prognosis.

PS-27-006
Insights into testicular tumours: a two-decade journey at a single-institution
A. Canastra*, C. Albuquerque, D. Gonçalves
*CUF Descobertas Hospital, Lisbon, Portugal

Background & objectives: Despite their low incidence, understanding the spectrum of testicular tumours is crucial for effective management and improvement of patient outcomes. This study aims to provide a detailed analysis of testicular tumour cases from a single healthcare institution in Lisbon.
Methods: A retrospective analysis was conducted on testicular tumour cases diagnosed in surgical specimens at our institution, from 2004 up to March 2024. Pathology reports were thoroughly reviewed to extract relevant data, including patient age, specimen laterality, histologic subtype, tumour size, extension, presence of lymphovascular invasion and germ cell neoplasia in situ. Patients with non-primary metastatic lesions were excluded.

Results: Out of a total of 270 testicular tumours reviewed, 89% were identified as germ cell tumours, 7% as sex cord-stromal tumours, while diffuse large B-cell lymphomas made up 3%. Of the germ cell tumours, 67% were pure, with seminoma comprising 85% of these cases. Mixed tumours predominantly consisted of embryonal carcinoma, yolk sac tumour, and teratoma, representing 82%, 65%, and 54% of cases, respectively. Lymphovascular invasion was detected in 39% of germ cell tumours, with invasion of the rete testis observed in 25%, epididymal invasion in 8%, and invasion of the spermatic cord in 4%. Regarding sex cord-stromal tumours, only one case met the criteria for malignancy.
Conclusion: Germ cell tumours constituted the majority of cases, with seminomas being the predominant histologic subtype. Sex cord-stromal tumours were relatively rare, with only one case meeting the criteria for malignancy, suggesting a generally favourable prognosis for this subtype. Lymphovascular invasion was a notable finding in a significant proportion of cases, especially in non-seminomatous tumours, underscoring the metastatic potential and emphasizing the importance of vigilant surveillance and treatment planning.

PS-27-008

A new technology for real-time intraoperative detection of tunica muscularis in transurethral resection of bladder tumour (TURBT): how to avoid second look for low grade urothelial carcinoma

M. Cieri*, S. Moretto, R. Contieri, G.M. Elefante, L. Terracciano, G. Lughezzani, R. Hurle, N. Buffi, P. Colombo
*Humanitas Research Hospital, Italy

Background & objectives: In non-muscle invasive bladder carcinoma, the assessment of tunica muscularis in TURBT samples is of relevance for staging and treatment, indeed its absence leads to a second resection. We evaluated the performance of Histolog® technique for assessing its presence intraoperatively.
Methods: From October 2023 until March 2024, 47 patients with a suspected diagnosis of bladder cancer have been selected. The study included: collection of patient data; acquisition of specimen images using Histolog® scanner (SamanTree Medical, Lausanne, Switzerland); annotation of the presence or absence of tunica muscularis by two uropathologists; comparison of the results with hematoxylin and eosin (H/E) stained slides.
Results: Median size of tumours was 0.7 cm; overall, the accuracy rate of Histolog® images and corresponding H/E images in detecting tunica muscularis was 74% (concordance reached in 32/47 samples). Four out of 47 were not evaluable and a total of 11 mismatches occurred. All cases misclassified as "absent" on the Histolog® images, showed the presence of tunica muscolaris on H/E slides, but two of them with only a limited amount of muscle bundles. Interestingly, when tunica muscularis was absent, none of the cases were mislabelled as "present" (positive predictive value = 100%).
Conclusion: This is the first study evaluating the use of Histolog® technology in TURBT specimens. The intraoperative device supports tunica muscularis assessment, avoiding unnecessary surgical treatment in patients with a low-grade neoplasm, with an accuracy rate of 74%, a positive predictive value of 100% and a negative predictive value of 47%. The technique is feasible and timesaving, but it requires to be improved with more training cases, to produce better quality images and to have an enhanced experience by pathologists.

PS-27-009

The role of epithelial-mesenchymal transition in venous invasion of clear cell renal cell carcinoma

T. Cugura*, E. Boštjančič, J. Jeruc
*Oncology Institute Ljubljana, Slovenia

Background & objectives: Epithelial-mesenchymal transition (EMT) is a dynamic process through which cells lose their epithelial features becoming spindled and motile. EMT is involved in the progression of many tumours. We explored EMT activation in vascular invasion of renal cell carcinoma (RCC).
Methods: We included tissue samples from 12 cases of clear cell RCC with renal vein invasion. The expression of main EMT markers (miR-200 family, miR-205, SNAI1/2, TWIST1/2, ZEB1/2, CDH1) was analysed by qPCR and compared between non-neoplastic kidney (N), the tumour centre (TC), tumour periphery (TP) and venous tumour thrombus (VTT). Expression of E-cadherin, N-cadherin and ZEB2 was analysed using immunohistochemistry.
Results: When comparing TC, TP and VTT to corresponding N, we observed miR-200 family and SNAI2 to be differentially expressed in all investigated tumour areas (TC, TP and VTT). We also observed CDH1 differential expression in TP and TWIST1 in VTT and TC when compared to N. However, when VTT was compared to either TP or TC, only miR-200c and miR-429 showed statistically significant differential expression in VTT compared to TC. We also observed change in expression of miR-200a in VTT when compared to TP, however the expression did not reach statistical significance.
Conclusion: Our current results clearly indicate that miR-200c and miR-429 play an important role in the vascular invasion of RCC. Therefore, it can be postulated that miR-200c is one of the key factors in the malignant progression of RCC, since our previous results also suggest its involvement in the sarcomatoid transformation of RCC.

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PS-27-010

Can pattern of invasion along with depth of invasion be predictors of lymph node metastasis in penile squamous cell carcinoma?

D. Das*, B.V. Rao, M.K. Pasam, S. Indulkar, S. Kodandapani, R. Sharma, S. Jain, S.R. Thammineedi
*India

Background & objectives: Inguinal lymph node metastasis (ILNM) is one of the important factors in determining the outcome of penile squamous cell carcinoma (PC). Hence, we attempt to study the pattern along with depth of invasion in predicting the likelihood of positive ILNM.
Methods: A retrospective observational study with ninety PC who underwent lymph node dissection during January 2020 to April 2022 was done. Pattern of invasion was classified as pushing or infiltrative. Depth of invasion was classified as superficial ($\leq$ 5 mm) or deep ($>$ 5 mm). Statistical analysis was done in SPSS version 20. A p value of <0.05 was considered significant.
Results: Lymph node metastasis was identified in 36 cases (40%) with all showing infiltration pattern and none showing pushing pattern. Infiltrative pattern showed statistically significant association with nodal positivity in different tumour stages (T1b, T2 and T3; p value= 0.005, <0.001, 0.006 respectively) and higher in combined T3 and T4 tumour group (p value= 0.005). In early tumour stages, the positive and negative predictive values of pattern of invasion were 100% and 77.8% respectively. Depth of invasion $>$ 5mm was seen in 66 (73.3%) and $\leq$ 5mm in 24 (26.7%). Among 66 cases, lymph nodal metastasis was seen in 31(46.97%) having significant association with lymph node metastasis (p value= 0.025).
Conclusion: A significant association of pattern of invasion (POI) and depth of invasion (DOI) with increased lymph node metastasis is noted. In the early stages, POI showed high positive predictive value and negative predictive value with good accuracy indicating that the POI can be used to predict inguinal lymph nodal invasion. Hence, we recommend that the POI along with DOI to be reported on a routine basis for better management of the patient.

PS-27-011

Programmed cell-death ligand 1 (PD-L1) expression and analysis of microsatellite instability/ DNA mismatch repair (MSI/MMR) status in penile squamous cell carcinoma (PC)

D. Das*, B.V. Rao, M.K. Pasam, S. Indulkar, S. Kodandapani, R. Sharma, S.R. Thammineedi
*India

Background & objectives: Immune checkpoint inhibitors with detection of MSI/MMR status are currently used in treatment of several tumours. This study attempts to evaluate the expression of PD-L1 in tumour cells and tumour-infiltrating lymphocytes with the analysis of MSI/MMR status in a PC.
Methods: A retrospective observational study was done on fifty cases of PC. Immunohistochemistry was performed by using anti-PD-L1 antibody and anti-MLH1, anti-PMS2, anti-MSH2 and anti-MSH6 antibodies to access MMR expression. The expression of PD-L1 was evaluated where <1% was considered as negative, ≥1% positive. The expression of MMR was evaluated with nuclear staining. Statistical analysis was done in SPSS version 20.
Results: 42/50 showed positive PD-L1 expression. 30/42 cases showed low positive expression for PD-L1 followed by 12 cases showed high PD-L1 expression. There was significant association of PD-L1 with grading (p value= 0.042), lymph node metastasis (p value= 0.015), lymphovascular invasion (p value= 0.015) and nodal stage (p value=0.007). The PD-L1 expression did not correlate with tumour stage and perineural invasion (p value >0.05). Of 42/50 cases showed pMMR, 7 cases showed lo-pa MMR and only one case showed dMMR. There was no significant association of expression of MMR with grading, tumour and nodal staging, lymphovascular invasion and perineural invasion. However, only 2% of dMMR cases showed high PD-L1 expression.
Conclusion: The expression of PD-L1 was associated with high grade tumours, lymph nodal metastasis, LVI and nodal stage. PD-L1 testing done for high grade tumours, propends for creating targeted treatment by using immune check point inhibitors. dMMR, however was noted only in 2% of cases with high PDL1 expression.

PS-27-012

Histological subtypes and divergent differentiation of urothelial carcinoma across molecular subtypes in bladder cancer: a study from the VESPER trial

J. Fontugne*, C. Krucker, C. Groeneveld, V. Harter, F. Radvanyi, S. Culine, C. Pfister, Y. Allory
*Institut Curie, France

Background & objectives: Associations between the consensus molecular classification of muscle-invasive bladder cancer and histological subtypes or divergent differentiation of urothelial carcinoma (UC) are partially known. Our aim was to assess these molecular and histopathological features in the prospective VESPER trial (NCT01812369).
Methods: This post-hoc study analysed NAC-treated patients with available diagnostic TURBT FFPE specimens. Pathological review identified the presence of histological subtypes or divergent differentiation. Areas with distinct morphology were macrodissected for RNA-seq, with multiple sampling in cases with heterogeneity. Consensus molecular classification was computed for each area. Association between molecular subtypes and conventional UC, histological subtypes and/or divergent differentiation were evaluated.
Results: We sequenced 424 areas from 303 tumours, comprising conventional UC (49.5%), squamous differentiation (14.4%), micropapillary (9.7%), sarcomatoid (6.1%) nested (4%), larged nested (3.5%), as well as samples of rare subtypes. Using the consensus classifier, samples were Basal/squamous (Ba/Sq) (35.8%), Luminal Unstable (LumU) (21.5%), Stroma-rich (STR) (21.7%), Luminal Papillary (LumP) (14.4%), Luminal Non-Specified (LumNS) (5,4%) and Neuroendocrine-like (NEL) (1.2%) subtypes. Preliminary analysis showed that conventional UC were composed of all molecular subtypes. In contrast, squamous differentiation, sarcomatoid and clear cell subtypes were associated with Bq/Sq subtype. Most micropapillary samples were LumU (73.2%). Nested areas were mainly STR (58.8%) whereas most large, nested areas split between LumP (33.3%) and STR (40%).
Conclusion: We report a large series of RNA-seq in selected areas of TURBT specimens after pathological review and macrodissection, with multisampling in a subset of heterogeneous cases. Matched molecular and histological subtypes confirmed that squamous differentiation and sarcomatoid subtype are mostly Ba/Sq. We discovered that micropapillary UC were associated with LumU. Distinct molecular subtypes between nested and large nested subtypes supported separate oncogenesis. Conventional UC harboured high molecular heterogeneity. Other rare subtypes will require specific cohorts for further molecular characterization.

PS-27-013

Molecular characterization and identification of molecular signatures that correlate with response to immunotherapy in metastatic renal cell carcinoma scenario

F. Galuppini*, S.E. Rebuzzi, G. Fornarini, G.D.L. Crudele, F. Schiavi, A. Caliò, G. Martignoni, A.P. Dei Tos, M. Brunelli
*Pathology Unit, Department of Medicine (DIMED), University of Padua, Padua, Italy

Background & objectives: Clear-cell renal cell carcinoma (ccRCC) is a treatment-resistant neoplasia that has abnormal angiogenic and immunosuppressive characteristics. Metastatic disease patients receive targeted treatments according on their clinical characteristics. Unfortunately, no biomarkers are available to guide therapy decisions for these individuals.
Methods: Patients were categorized as responders (progression-free survival ≥ 12 months) and non-responders (progression-free survival < 3 months) after receiving ≥ 2nd line nivolumab. The molecular analyses were conducted using the platform NanoString nCounter®, which analysed the expression of a panel of 66 microRNA from the gene signatures involved in angiogenesis; immunomodulation; tumour invasion and mechanisms of calcium channel flows.
Results: The mRNA of the FASLG gene was found to be significantly more expressed in the tissues of responder patients. ($p < 0.05$). A dichotomization of the signatures genes into two major pathways emerged: one consisting of the angiogenesis genes and a subclass of invasion genes (Angio-invasion pathway), the other consisting of the remaining invasion signature genes, T-effector response genes and calcium channel flows genes (Immuno-invasion pathway). Considering the correlation between signatures, pathways and clinic-pathological data, a statistically significant correlation emerged between Angiogenesis signature over-expression and responders ($p = 0.035$). While non-responders' patients showed significant over-expression of both Angio-Invasion and Immuno-Invasion pathways ($p = 0.02$).
Conclusion: Molecular characterization of mRCC will enable the design of a panel of genes to better identify patients of appropriate genotype, and to improve treatment decision-making.

PS-27-014

Regressed (burnt-out) germ cell tumour of the testis - a retrospective study of two hospitals for almost four decades

P. González-Peramato*, B. Popescu, V. Macarrón, E. García Fernandez
*La Paz University Hospital, Spain

Background & objectives: A regressed (burnt-out) germ cell tumour represents a complete or partial spontaneous regression of a germ cell

tumour, resulting in a testicular parenchymal vascularized scar. It was first described by Pryn in 1927.
Methods: A retrospective search was done in two university hospitals for the last 37 years. Of all orchidectomy specimens we identified 30 cases of regressed germ cell tumours, and we divided them into two categories: completely regressed tumours (21 cases) and partially regressed tumours (9 cases). We reviewed all the slides of the cases and evaluated the morphological features in the clinical-radiological context.
Results: Patients were aged between 20 and 74 years (mean 39,37), initial presentation was metastasis in 15 cases with retroperitoneal localization in 12 cases. Morphologically the scar area measured between 3 and 25 mm and, in most cases, it was related to the rete testis. It was composed of thick collagen associated with very mild and scattered inflammation with phantom tubules. The vessels were thin and thick, and some with arteriolar hyalinosis. The vast majority of cases did not have necrosis, macrophages with haemosiderin, calcifications or GCNIS. The most common tumour type was seminoma. Testicular parenchyma showed mixed atrophy in 55%. Most patients have been cured after excision, only two died.
Conclusion: Regressed germ cell tumours are very rare and are mainly related with germ cell tumours derived from GCNIS, although very rarely with spermatocytic tumour (one of our cases). Most patients are diagnosed in advanced stages with metastases, especially in retroperitoneum. It can be seen even in elder patients where there is a low frequency of germ cell tumours. Most of them are unifocal. Testicular parenchyma revealed normal spermatogenesis only in 2 out of 27 cases, although with infrequent presence of GCNIS.

PS-27-015
KDM6A expression loss is a common feature in low-grade non-invasive urothelial carcinomas of the urinary bladder
F. Viehweger, N. Gorbokon*, H. Plage, M. Lennartz, N. Schraps, T. Mandelkow, E. Bady, A.H. Marx, H. Samtleben, R. Simon, G. Sauter, T. Schlomm, H. Zecha, M. Kluth, S. Minner
*Institute of Pathology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

Background & objectives: KDM6A (syn. UTX) is an epigenetic regulator which is frequently mutated in urothelial carcinoma. Because KDM6A loss causes a dependency on EZH2, a potential therapeutic target, KDM6A analysis may have therapeutic importance.
Methods: To assess the suitability of immunohistochemistry (IHC) for analysis of KDM6A expression loss, more than 2,500 tumours were analysed by IHC in a tissue microarray format, and KDM6A mutations were determined by DNA sequencing. The cohort included 636 patients who underwent radical cystectomy for muscle-invasive disease (pT2-4).
Results: KDM6A expression loss occurred in 36.0% of 350 pTa G2 low-grade, 23.0% of 152 pTa G2 high-grade, and 18.5% of 92 pTa G3 tumours ($p=0.0002$). The frequency of KDM6A expression loss did not further decrease in pT2 (17.2%), pT3 (21.9%), and pT4 (18.2%) cancers. A KDM6A loss was more common in male (22.2%) than in female patients (15.4%; $p<0.0001$), and more frequent in (male) tumours with Y-chromosome loss (36.1%) than in cancers without Y-chromosome loss (16.3%; $p<0.0001$). Sequencing revealed truncating KDM6A mutations in all 15 male patients with KDM6A expression loss, but in only 4 patients (all female) out of 37 tumours with retained KDM6A expression.
Conclusion: Our data demonstrate that truncating KDM6A mutations occur in a significant subset of urothelial carcinomas which is linked to low-grade non-invasive cancer, male gender and loss of the Y chromosome. The predominance of KDM6A loss in low-grade tumours makes KDM6A IHC a promising new tool for the identification of low-grade dysplasia in biopsies and early bladder cancer detection in cytology.

PS-27-016
Loss of MTAP expression is highly homogeneous and linked to homozygous 9p21 deletion and unfavourable tumour phenotype in urothelial bladder cancer
N. Gorbokon*, N. Wößner, N. Schraps, M. Fisch, M. Slojewski, T. Ecke, S. Koch, S. Minner, R. Simon, J. Weischenfeldt, G. Sauter, T. Schlomm, D. Horst, L. Bubendorf, M. Kluth
*Institute of Pathology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

Background & objectives: Homozygous 9p21 deletions including the MTAP gene are common in urothelial carcinoma and result in a vulnerability towards drugs targeting pathways that depend on an intact MTAP function.
Methods: To determine the prevalence and clinical significance of MTAP deficiency as well as its intratumoural homogeneity in urothelial bladder carcinomas, >2,500 tumours were analysed by fluorescence in situ hybridization (FISH) and immunohistochemistry (IHC) in a tissue microarray format. An additional TMA containing 5 samples from 5 different tumour blocks from particularly large pT2-4 carcinomas was analysed by MTAP IHC.
Results: 9p21 deletion was homozygous in 364 (21.3%) and heterozygous in 334 (19.5%) of 1,711 analyzable tumours. The rate of 9p21 deletions increased from pTa G2 low (9.2% homozygous, 25.8% heterozygous) to pTa G2 high (32.6%, 20.9%; $p<0.0001$) but was slightly lower in pTa G3 (16.7% each). In pT2-pT4 carcinomas, 9p21 deletions were homozygous in 23.3% and heterozygous in 17.9% and were tied to advanced pT status ($p=0.0014$) and poor overall survival ($p=0.0461$). MTAP deletion was always homogeneous in 25 out of 83 tumours with ≥3 different analysed samples. Immunohistochemical MTAP expression loss was strongly linked to homozygous 9p21 deletions ($p<0.0001$), advanced pT status and poor overall survival ($p<0.05$ each).
Conclusion: A complete MTAP expression loss is common in urinary bladder cancer and strongly tied to homozygous 9p21 loss and aggressive disease. Given the high homogeneity of MTAP deficiency in our cohort, we anticipate that drugs targeting MTAP-deficiency may be highly useful in bladder cancer. MTAP IHC is a nearly perfect surrogate for the detection of MTAP deficiency in this tumour entity.

PS-27-017
HER2 and CDK12 expression in muscle invasive bladder cancer: correlation with grade, subtype and survival
B. Günay Gülen*, B. Sarsık Kumbaracı, I.R. Durusoy Onmuş, F. Kızılay, E. Güler, A. Gülen, S. Sen
*Ege University Faculty of Medicine, Department of Pathology, Turkey

Background & objectives: HER2 and CDK12 are localized in same locus of chromosome 17. There are a limited number of studies regarding prognostic role of them in bladder cancer. We analysed these antibodies on tumour subtype and prognosis in muscle-invasive urothelial carcinoma (MUIC).
Methods: In the study, 415 cases out of 457 who underwent radical cystectomy due to MIUC were included. In cases with no residual tumour at the cystectomy, slides of TUR materials were re-evaluated. Immunohistochemically HER2 and CDK12 expressions were analysed at tissue micro-array blocks at conventional urothelial carcinomas(cUC) as well as at UC with concomitant subtype at 474 tumours areas.
Results: The mean age was 63,8±9,6(22-93) years. Among tumour subtypes 248(52.3%) tumours were pure cUC, 97(20.5%) squamous, 41(8.6%) glandular, 23(4.9%) micropapillary. The number of other subtypes was quite low. The follow-up period was 88.03±5.5(1-253) months; 17(4%) cases had local recurrence, whereas 96(23.1%) had metastasis, and 232(64%) died of cancer. CDK12 and HER2 positivity were 8.2% and 5.7% in tumours. Co-expression was found in eight

tumours, 75% of which were pure cUC. HER2 was detected in 30.4% of micropapillary tumours, whereas CDK12 was negative in all of them. CDK12 expression was higher in squamous differentiation (11.3%) than in others. No correlation was found between CDK12 and HER2 expression and overall and disease-free survival.
Conclusion: Bladder cancer is one of the most common cancers of the urogenital system, and approximately 25% of patients have infiltrative urothelial carcinoma morphology. HER2 expression occurs commonly in many cancer types. Moreover, the prognostic role of CDK12 alterations is unknown in bladder cancer. Both genes are potential candidates for the management of targeted tumour therapies. In our study, HER2 and CDK12 expression in MIUC and its relationship with clinicopathological findings are investigated.

PS-27-018
Comparison of a modified staging system with 8th edition AJCC criteria in a North American cohort of pT2/pT3 HPV-negative penile squamous cell carcinoma
B. Tekin, A. Sali, S. Menon, J. Cheville, C. Smith, S. Jenkins, S. Dasari, A. Cubilla, R. Whaley, L. Herrera Hernandez, R. Jimenez, L. Pagliaro, L. Erickson, R. Guo, S. Gupta*
*Mayo Clinic, USA

Background & objectives: The staging for pT2/pT3 penile squamous cell carcinoma (pSCC) has undergone major changes. Some authors proposed criteria wherein the distinction between pT2/pT3 was made using the same histopathological variables that differentiate pT1a/pT1b.
Methods: We focused on the pT2/3 stages of HPV-negative pSCC (i.e., tumours invading corpus spongiosum [CS]/corpus carvernosum [CC]) and compared the prognostic ability of the following systems: (i) AJCC, 8th edition criteria; (ii) modified staging criteria proposed by Sali et al (Am J Surg Pathol. 2020; 44:1112-7). Disease-free survival (DFS) and progression-free survival (PFS) were assessed using Cox regression.
Results: In the proposed system, pT2 tumours were defined as those without lymphovascular invasion (LVI) or perineural invasion (PNI), and grade 1/2; whereas pT3 showed one or more of the following: LVI, PNI, and/or grade 3. Forty-eight pT2/pT3 cases were included (AJCC, pT2: 27 [12 upstaged to pT3 with proposed criteria] and pT3: 21 [7 downstage to pT2 with proposed criteria]; Proposed, pT2: 22 and pT3: 26). DFS and PFS did not differ between pT2 and pT3 using the current AJCC definitions (p=0.19 and p=0.10, respectively). However, a statistically significant difference was present for both DFS and PFS between pT2 and pT3 using the proposed definitions (p=0.004 and p=0.003, respectively).
Conclusion: This study is based on a single-institution, North American cohort of patients with HPV-negative pSCC. The proposed staging system incorporating grade, LVI, and PNI has the potential to improve the prognostication of pT2/pT3 HPV-negative pSCC. Each of these histopathologic variables has been shown to have a significant association with outcomes in pSCC. Further studies are needed to demonstrate the utility of this modified staging system in patient populations from varied geographic regions.

PS-27-019
Fluorescence confocal microscopy for the pathological evaluation of radical prostatectomy margins
M. Ivanova*, S. Luzzago, F. Mistretta, G.G. Vago, G. Pravettoni, O. Pala, D. Lepanto, D. Bottero, G. Marvaso, G. Petralia, B.A. Jereczek-Fossa, O. De Cobelli, G. Renne, N. Fusco, G. Musi
*Division of Pathology, European Institute of Oncology IRCCS Milan, Italy

Background & objectives: Positive surgical margins (PSMs) following prostatectomy are associated with increased local recurrences. Intraoperative frozen section (IFS) analysis can reduce final PSM but is time-consuming. Aim: to evaluate the ex-vivo fluorescence confocal microscopy (FCM) performance against IFS in PSM pathological assessment.
Methods: Two independent pathologists analysed 54 surgical margins from 45 patients who underwent robot-assisted radical prostatectomy, using FCM (Vivascope 2500M-G4) and IFS. The results were compared against the final pathology report (gold standard). The study measured inter-observer reproducibility and agreement between FCM and IFS (Cohen's k). Sensitivity, specificity, positive and negative predictive values (PPV and NPV) of FCM were also assessed.
Results: The inter-observer agreement for FCM varied from moderate (κ=0.74) to nearly perfect (κ=0.90), according to the positivity category (negative, probably negative, positive, probably positive). FCM achieved an optimal balance of sensitivity (70.5%) and specificity (91.8%), along with PPV (80.0%) and NPV (87.1%). In comparison, IFS demonstrated higher sensitivity (88.2%), specificity (100%), PPV (100%), and NPV (94.8%). The agreement between FCM and IFS analyses varied from moderate (κ=0.62) to strong (κ=0.86), across the four evaluated categories.
Conclusion: FCM can be consistently used among different pathologists with a high degree of concordance, but its diagnostic performance is not superior when compared to IFS analysis. The variable agreement between FCM and IFS underscores the potential complementary roles of these methods. While FCM provides a reliable alternative with certain advantages, such as potentially being less time-consuming than IFS, the latter's superior diagnostic performance makes it the more effective standard against which surgical margin assessments are evaluated.

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PS-27-020
NGS testing practices and molecular profiles of BRCA1/2 in prostate cancer: real-world insights from France, Italy, Spain, and Austria
A. Janiszewski*, D.B. Roche, X.B. Bustillo, A. Agarwal, D. Constantin, G. Morales, S. Lima, L. de Visser, F. Hodeib, R. Dowlati
*SOPHiA GENETICS, Switzerland

Background & objectives: BRCA1/2 testing can inform which prostate cancer patients might respond to PARP inhibitors (PARPi) (Shah, et al. IntJMolSci.2021;22:12628). To better understand those that could benefit from PARPi, we investigated NGS BRCA1/2 testing practices and results across France, Italy, Spain, and Austria.
Methods: The SOPHiA DDM™ Platform (SOPHiA GENETICS SA, Switzerland) was used to analyse pseudonymized real-world genomic profiles (Q1 2022 – Q4 2023) across 54 institutions. Aggregated anonymized statistical data were obtained from 27 somatic and 25 germline SOPHiA GENETICS NGS panels capable of detecting BRCA1 and BRCA2 alterations from RNA or DNA.
Results: Between 2022-2023, 88,991 individuals across France, Italy, Spain, and Austria were tested with SOPHiA GENETICS NGS panels capable of detecting BRCA1/2 alterations. 524 BRCA1 and 661 BRCA2 unique pathogenic variants were identified amongst 1,486 BRCA1/2 mutation-positive individuals tested with somatic panels and 3,876 tested with germline panels. Overall, 2,967 of those tested with somatic panels had a prostate cancer tag; 459 of these had a BRCA1/2 mutation (positivity rate ~15%). 52 of the individuals tested with germline panels had a prostate cancer tag; 5 of these had a BRCA1/2 mutation (positivity rate ~10%). The majority of the BRCA1/2 variants found in the mutation-positive cases (~90%) were nonsense or frameshift.

Conclusion: These data provide new insights into the occurrence of BRCA1/2 alterations in prostate cancer profiles, and NGS testing

practices across France, Italy, Spain, and Austria. The comprehensive characterization of the molecular epidemiology of BRCA1/2 variants and their prevalence are crucial to identify the metastatic castration-resistant prostate cancer patients that can benefit from PARP inhibitors.

PS-27-021

Application of an artificial intelligence algorithm fo prostate cancer detection and Gleason grading in prostate biopsies: experience of Rennes University Hospital in France

S. Kammerer-Jacquet*, G. Sebag, C. Despax, N. Rioux-Leclercq
*Rennes University Hospital, France

Background & objectives: Artificial intelligence tools can support prostate cancer detection and Gleason grading ensuring a rapid and reproducible diagnosis. We present our experience of using a first-read application in prostate cancer in the University Hospital of Rennes in France.
Methods: We report the deployment of the algorithm in our digital routine activity, the performance of the algorithm that we have been using for 9 months and compare the impact on our activity in terms of time to answer and numbers of immunohistochemistry (IHC).
Results: Cases are manually assigned in a cloud environment from the image management system. Experienced uropathologists (n=2) open the dedicated viewer using a contextual launch and use it as first or second read application and report in the laboratory information system. Over the 622 cases processed (7331 slides), 2814 slides were scored with 93,2% agreement in cancer detection (high-likelihood) and 100% agreement in the absence of cancer (low-likelihood, n=579), 43% (n=1210) were labelled "medium likelihood" with cancer observed in 4,7% (n=57). For Gleason grading, 415 slides were scored with 76.6% agreement. The time to answer decreased for the pathologist using the application for first read and the number of IHC remains constant.
Conclusion: The level of integration of the algorithm is crucial in assessing the time saved. We underline the reliability of the algorithm in the absence of cancer, but Gleason grading still needs to be improved.

PS-27-022

Risk stratification of urine cytology specimens using The Paris System (TPS2): an institutional experience from a tertiary care centre

S. Kaushal*, H. Jangir, A. Narwal, S.S. Adhikari, B. Nayak, A. Seth
*Department of Pathology, India

Background & objectives: The Paris System for Reporting Urinary Cytology (TPS) is designed to standardize the criteria and terminology used in urinary tract cytology reporting. This study aimed to assess the reproducibility of TPS 2 and to analyse the correlation with follow-up biopsies.
Methods: Urinary tract cytology specimens with follow-up biopsies over one year (n=116) were reviewed and reclassified according to TPS criteria. Surgical follow-up diagnoses were correlated with the initial cytology diagnoses and TPS interpretations, and the results were compared.
Results: By Applying TPS2.0, the distribution of cases was as follows: 16.7% were categorized as ND/U, 2.3% as NHGUC, 42.1% as AUCs, 50.0% as SHGUC, and 81.8% as HGUC.TPS 2 demonstrated a specificity of 82% and a sensitivity of 89% in identifying histologically confirmed HGUC. Applying TPS 2 in comparison to our previous reporting system resulted in fewer cases in the atypia category (12.2 % vs 25.3%) and higher specificity, accuracy, and predictive value.
Conclusion: TPS2 criteria showed a higher specificity, sensitivity and predictive value and decreased the rate of "atypia" reporting in comparison to our previous reporting system. TPS 2 is an important step towards standardizing the criteria and terminology for reporting urinary cytology.

PS-27-023

Unsupervised nuclei classification in non-muscle-invasive bladder cancer

M. Koeller*, L. Zikken, J. Klaeger, G. Wasinger, C. Kaltenecker, A. Oszwald, E. Compérat
*Department of Pathology, Medical University of Vienna, Austria

Background & objectives: Nuclei classification is mainly performed in a supervised manner, impeding the identification of previously unrecognized phenotypes. Hence, it was investigated if unsupervised learning is capable to identify distinct phenotypes in Non-Muscle-Invasive Bladder Cancer (NMIBC), and their relation to tumour grade.
Methods: Nuclei (n=220.800) within 140 images of NMIBCs (inconspicuous=49, pTaLG=47, pTaHG=44) were segmented, cropped, rescaled and stain normalized. A Vision Image Transformer with DINO framework was used to learn a nuclei representation (384 dim.), which was reduced by means of Principal Component Analysis (50 dim.). Leiden Clustering was used to identify phenotypes. Grade association was assessed using Logistic Regression Analysis.
Results: Nuclei were homogeneously distributed in the learned latent space, however, could be partitioned into six clusters. Review by two expert uro-pathologist independently found the clusters to be morphologically meaningful and consistent. Main differences between clusters could be attributed to shape, chromatin texture and the presence of nucleoli. Nuclei of all classes could be found at varying degrees, in all images within all grade groups. No cluster showed significant differences between grade groups ($p>0.05$). However, one cluster (showing presence of nucleoli) displayed an increase in mean frequency from inconspicuous to pTaHG, with pTaHG showing a p-value at the border of significance ($p=0.051$).
Conclusion: In this experiment the Vision Transformer with DINO framework displayed the capability to generate morphologically meaningful nuclei representations that seemed to capture histo-pathologically relevant concepts without the need of annotations. Phenotype frequencies appeared in a biologically consistent way, suggesting that the framework can be used to generate a nuclei foundation model comprehensible by pathologists. Hierarchical transformers might refine the search for relevant phenotypes in NMIBC and will be evaluated in future work by our group.

PS-27-025

High stromal CD39 expression is a strong prognostic factor for longer survival in ≥ pT2 urothelial bladder cancer

S. Ledderose*, S. Rodler, L. Eismann, F. Klauschen, M. Rudelius, A. Sendelhofert, C. Ledderose
*Institute of Pathology, Faculty of Medicine, LMU Munich, Germany

Background & objectives: Accurate prognostic assessment is critical in advanced bladder cancer (BC). The ectonucleotidase CD39 plays a crucial role in the regulation of purinergic signalling mechanisms that contribute to progression of BC. However, the prognostic value of CD39-expression in BC remains unclear.
Methods: CD39 expression was immunohistochemically analysed in tissue-microarrays containing tumour tissue from 180 BC-patients. Immunoreactivity of CD39 in tumour cells and tumour-associated stroma was scored using the histochemical scoring system (H-Score). Associations between high and low CD39 scores and clinicopathological variables, overall survival (OS), tumour-specific survival (TSS) and disease-free survival (DFS) were retrospectively analysed.
Results: Mean age at the time of surgery was 67.4 (±9.7) years with the majority of patients being male (73.3%). Mean follow-up was 3.0 years and 150 (83.3%) patients died during follow-up. None of the tumour samples exhibited high CD39 expression in tumour cells (0%). However, strong stromal CD39 expression was observed in 50% of tumour samples, correlating with a lower UICC stage ($p<0.001$).

Patients with high stromal CD39 expression demonstrated significantly longer median OS (p<0.001), TSS (p<0.001), and DFS (p=0.02) compared to those with low CD39 expression. Furthermore, high stromal CD39 expression proved to be an independent positive predictor of OS (p=0.02) and TSS (p=0.01) in multivariate analyses.
Conclusion: The prognosis of BC is poor and current therapies are often associated with severe side effects and significant costs. To avoid overtreatment, there is a high demand for new biomarkers that can accurately assess the prognosis of patients with BC. Our results indicate that high stromal expression of CD39 is a powerful prognostic factor for better survival in BC patients. Prospective studies with larger case numbers are warranted to confirm our findings.

PS-27-026
Analysis of MicroRNA-371-373 in low grade gliomatous tumours of germ cell tumour origin supports biological similarities to teratoma
J. Lobo*, N.T. Tavares, C. Jerónimo, R. Henrique, T.M. Ulbright, A.M. Acosta
*Liga Portuguesa Contra o Cancro, Portugal

Background & objectives: Glial tumours of germ cell origin are rare in men, occurring predominantly after chemotherapy. Most exhibit low-grade histologic features, and their spectrum is wide. Their origin and biologic relatedness to other histologic subtypes of germ cell tumours remains incompletely understood.
Methods: Glial tumours of germ cell origin arising in male patients were manually dissected (FFPE sections) to extract RNA for miR-371/miR-372/miR-373 RT-qPCR. TCam-2 cell line was used as positive control. No template controls were included. Results were classified as positive, negative, and in the grey zone.
Results: A total of 8 glial tumours of germ cell origin (low-grade histologic features) were assessed. The glial tumour was abundant/often predominant. In one case, the glial tumour was the only histologic component. In the remaining 7 cases, other components were also present (only teratoma in 3/7, both teratoma/non-teratoma in 2/7, only non-teratoma in 1/7, and ENET in 1/7). RT-qPCR for miR-371a-3p showed five cases were negative and three were in the grey zone, but none was positive. Results for miR-372-3p/miR-373-3p followed the same pattern. As expected, miR-371a-3p was highly positive in Seminomas (3), embryonal carcinomas (3), choriocarcinomas (2), yolk-sac tumours (4), and negative in mature teratomas (4), assessed for comparison.
Conclusion: Our results demonstrate that the miR-371-373 expression profile of low-grade glial tumours of germ cell origin is similar to that of teratoma, suggesting that they may exhibit shared biologic characteristics.

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PS-27-027
Validation of FGFR3 immunohistochemistry as a predictor of FGFR3 genetic alterations in urothelial carcinoma
R. López Del Campo*, C. Mercader, R. Calderon, J. Albaiges, L. Ferrer-Mileo, I. Ribera-Cortada, I. Trias, A. Vilaseca, L. Rodríguez-Carunchio

*Hospital Clínic Barcelona, Spain
Background & objectives: In the era of FGFR3-targeted therapies, FGFR3 status is crucial in urothelial carcinoma. Genetic testing is the gold standard, but limitations like cost and turnaround time exist. We aimed to validate FGFR3 immunohistochemistry (IHC) as a predictor of FGFR3 alterations.
Methods: In a retrospective study, we selected 41 patients with urothelial carcinoma for FGFR3 analysis. FGFR3 status was established through polymerase chain reaction (PCR) and we performed FGFR3 IHC which was evaluated by three observers. IHC results were dichotomised as positive or negative and FGFR3 status was the gold standard. Clinical data were reviewed, and diagnostic parameters were calculated.
Results: The study included 41 patients (31 males, 10 females; median age 71 years) with 37 bladder and 4 upper urinary tract urothelial carcinomas. Staging showed 3 Tx, 7 Ta, 6 Tis, 4 T1, 9 T2, 8 T3 and 4 T4, with 37 high-grade and 4 low-grade tumours. Among the muscle-invasive group, 11 cases were wild type and 11 had FGFR3 alteration; while in non-muscle-invasive tumours, there were 10 wild type and 9 altered cases.
FGFR3 IHC exhibited 80% sensitivity, 95% specificity, 94% positive predictive value (PPV) and 83% negative predictive value (NPV). We observed substantial agreement (Cohen's kappa = 0.755) between IHC and PCR.
Conclusion: In our study, FGFR3 IHC demonstrated high specificity and PPV as a surrogate marker for FGFR3 genetic alterations in urothelial carcinoma. Furthermore, substantial agreement between IHC and PCR was observed.

These results suggest that FGFR3 IHC could potentially obviate the need for FGFR3 genetic testing in patients with positive IHC results, thereby potentially alleviating the workload of molecular pathology labs. Further research into the efficacy of this proposed diagnostic algorithm is warranted.

PS-27-028
Glycoprotein non-metastatic B expression in renal cell carcinoma with leiomyomatous stroma
S. Marletta*, A. Caliò, M. Brunelli, L. Marcolini, L. Stefanizzi, G. Martignoni
*Division of Pathology, Humanitas Istituto Clinico Catanese, Catania, Italy

Background & objectives: Renal cell carcinomas (RCCs) with leiomyomatous stroma (RCCLMS) are characterized by CK7/CA9 expression and comprise several tumours with different molecular features, including TSC1-2/mTOR mutations. Recently, glycoprotein nonmetastatic B (GPNMB) expression has been described in RCC with TSC1-2/mTOR alterations.
Methods: In the present work, we sought to report the clinical-pathological features of a series of fourteen RCCs with an RCCLMS-looking morphology and to test them with a comprehensive immunohistochemical (ICH), including CK7, CA9, and GPNMB.
Results: Tumours were relatively small, ranging from 1 cm to 3.5 cm (median 1.9 cm), and, to date, all the patients are alive with no evidence of disease. Morphologically, the neoplasms showed branching tubule-papillary structures composed of bland-looking clear cells (G1-G2 by ISUP/WHO) intermixed with variable transecting fibromuscular stroma. As for IHC, strong and diffuse CK7 and CA9 labelling was detected in all the tumours. A noteworthy proportion of the cases (5/14, 37%) displayed significant GPNMB expression, ranging from 10% to 90% of neoplastic cells.

Conclusion: Our data provide novel insights into the molecular hallmarks of RCCLMS and support the adoption of GPMNB to the IHC panel of rare and challenging renal cell neoplasms to identify a subset of tumours potentially carrying TSC1-2/mTOR pathogenetic mutations distinguishing them from morphologically overlapping tumours harbouring different molecular alterations.

PS-27-030

Bright-field multiplex immunohistochemical analysis of tumour microenvironment (TME) in embryonal carcinoma

S. Melotti*, V. Tateo, F. Ambrosi, F. Giunchi, F. Vasuri, A. Grillini, E. Franchini, F. Massari, V. Mollica, F. Mineo Bianchi, M. Colecchia, A.M. Acosta, J. Lobo, M. Fiorentino, C. Ricci
*Pathology Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy

Background & objectives: Embryonal carcinoma (EC) is crucial for prognosis and reprogramming of germ cell tumours of the testis (GCTT). We adopted bright-field multiplex immunohistochemistry (BF-mIHC) to evaluate tumour microenvironment (TME) components [T-cells, B-cells, and tumour-associated macrophages (TAMs)] in EC.
Methods: We characterized TME of 49 ECs with our laboratory-developed BF-mIHC protocol [OCT4 (Yellow), CD20 (Purple), CD3 (Brown), and CD68 (Green)]. The results were dichotomized (-low and -high) as previously described and compared (Fisher's exact test) between the following population subgroups: a) clinical stage-I (CS-I)/metastatic disease (MTS) at diagnosis; b) relapse/no relapse; c) EC reprogramming phase-1 (ECphase-1)/EC reprogramming phase-2 (ECphase-2).
Results: The BF-mIHC analysis showed the following results: a) CD68high ($p<0.001$) and CD3high ($p=0.026$) were significantly associated with MTS at diagnosis; b) CD20high ($p=0.014$) and CD3high ($p=0.017$) were significantly associated with no relapse; c) CD68high ($p<0.001$) was significantly associated with ECphase-1. Using the cut-off values found for the subgroup relapse/no relapse, patients with CD20high ($p=0.003$) and CD3high ($p=0.048$) had significantly longer primary relapse-free survival (PRFS). No differences in PRFS were observed according to CD68 cut-off values.
Conclusion: Our results support a key role of TME in biology and prognosis of GCTT. Specifically, T- and B-cells influence prognostic features (clinical stage at diagnosis, relapse, and PRFS) but not reprogramming of GCTT. By contrast, TAMs may have a less relevant prognostic role (clinical stage at diagnosis) but may be involved in maintaining the stem-cell phenotype of EC (ECphase-1) preventing the differentiation/maturation towards teratoma, choriocarcinoma, and yolk sac tumour (ECphase-2).

PS-27-031

Effects of Brazilian berry (Myrciaria jaboticaba) peel extract in castration-resistant prostate cancer (CRPC): lobe-specific histopathological responses in the Transgenic Adenocarcinoma of the Mouse Prostate (TRAMP) model and in vitro evaluation of human tumour cell lines

F. Montico*, J. Souza Gianchetto, F.R. Schievano, P. Felix da Silva, F. Rabelo Santos, I. Lopes Lemos, M.R. Maróstica Júnior, V.H. Alves Cagnon
*Institute of Biology, University of Campinas, Brazil

Background & objectives: Castration-resistant prostate cancer (CRPC), which is refractory to androgen deprivation therapy (ADT), accounts for the majority of disease-associated deaths worldwide. The aim herewith was to investigate Brazilian berry (jaboticaba) peel extract (JPE) as an adjuvant therapy to ADT against CRPC.
Methods: TRAMP mice were surgically and chemically castrated (enzalutamide, 10 mg/Kg), with or without JPE administration (5,8 g/Kg). Controls were sham castrated and received JPE or vehicles. Prostatic lobes were harvested for histopathology and immunohistochemistry. Cell viability and protein expression of proliferative and apoptotic mediators were analysed in CRPC cells (PC-3 and 22Rv1) upon enzalutamide (40uM) treatment and/or several JPE concentrations.
Results: TRAMP prostate showed lobe-specific responses to JPE treatment and/or androgen ablation. Dorsolateral and anterior lobes were the most and less sensitive to ADT regarding cancer progression, respectively, whereas the ventral prostate presented unique chemo preventive effects of JPE in the CPRC setting. Such responses were paralleled by the PCNA expression patterns across the prostatic lobes. Moreover, in poorly differentiated CRPC, JPE contributed to maintain smooth muscle periacinal layer integrity. Both PC-3 and 22Rv1 cell viabilities were time and dose-dependently impaired by JPE treatment. Mechanistically, in the latter cell line, such an effect involved a shift towards a pro-apoptotic and antiproliferative status following JPE administration, either per se or associated to enzalutamide.
Conclusion: JPE chemo preventive actions on CRPC progression may be greatly related to the androgenic reliance of the initial lesions, thus explaining the remarkable effects in the ventral prostate, which is primarily dependent on androgen signalling. In vitro results pointed to JPE potential to interfere in canonical pathways of cell proliferation and apoptosis and thereby negatively impact human CRPC cell survival. Altogether, our findings suggest JPE as a promising adjuvant therapy to ADT and encourage future clinical studies with this natural extract.

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PS-27-032

FGFR alterations in a contemporary real-world cohort of advanced or metastatic urothelial carcinoma

N.-N. J. Nguyen*, E. Olkhov-Mitsel, K. Craddock, M.R. Downes
*Department of Laboratory Medicine and Pathobiology, University of Toronto, Canada

Background & objectives: Patients with advanced or metastatic bladder cancer (BC) harbouring FGFR mutation, amplification or fusion may clinically benefit from FGFR inhibition therapy. Herein, we described the frequency of FGFR alterations in a contemporary cohort of advanced/metastatic BCs that underwent reflex testing.
Methods: We sequenced primary and metastatic lesions of patients with advanced/metastatic BCs (2021-2024) as part of a provincial initiative. This included in-house and external specimens. The Oncomine Comprehensive Assay v3 (DNA) and Oncomine Comprehensive Assay Plus (RNA) were performed on the S5 Prime next-generation sequencer. FGFR1, FGFR2 and FGFR3 variants were analysed using Ion Reporter version 5.18 and following AMP/ASCO/CAP guidelines.
Results: 147 BCs (M:F=3.4:1) were included. Median age was 73 years (range 37-92). Half were external cases. Primary specimens (n=99) were: cystoprostatectomy-44, transurethral resection-39, cystectomy-8, ureterectomy-5, ureter biopsy-2, urethrectomy-1. Stage distribution of sequenced primary tumours was: pTa-3, pT1-6, pT2-35, pT3-48, pT4-25. Sites of sequenced metastases (n=48) were node-8, liver-7, lung-3, kidney-2, neuro-2, peritoneum-1, other-4. Histologic types were urothelial carcinomas (UCs)-139, squamous cell carcinoma-2, adenocarcinoma-1. Squamous, trophoblastic and glandular differentiation was present in 17, 1 and 3 UCs, respectively. Histologic subtypes were NOS-124, plasmacytoid-6, micropapillary-3, large nested-2, small nested-1, clear cell-1, microcystic-1, sarcomatoid-1, neuroendocrine-1. FGFR alterations were seen in 23 (16.5%) UCs: FGFR1 amplification-2, FGFR2 point mutation-2, FGFR3 point mutation-14, FGFR3 fusion-6.
Conclusion: Based on reflex molecular analysis performed on consecutive advanced/metastatic BCs, we found FGFR alterations to be present in approximately 17% of UCs, with FGFR3 being more frequently altered than FGFR1 and FGFR2 genes. These patients could gain clinical benefits from receiving a FGFR inhibitor such as erdafitinib which is an approved drug to treat FGFR-altered BCs lacking response to chemotherapy. Future studies will include a larger cohort to assess the correlation of FGFR alterations with histologic subtypes of invasive UC.

PS-27-034

Review of outcomes in patients with Gleason score 3+4 and ≤10% pattern 4 in prostate cancer biopsies at a tertiary care centre

N. Sah*, A. Haider, I. Cutforth, A. Freeman, L. Dickinson, F. Giganti, B. Lamb, A. Woernle, A. Mitra
*Cancer Institute, University College London, United Kingdom

Background & objectives: Gleason Score 7 (GS7) prostate cancer biopsies, with an increased percentage of Gleason Pattern 4 (%GP4), confer worse prognoses. We evaluated the outcomes of patients with minimal (≤ 5%) versus 10% GP4 in GS7 prostate biopsies (PB).
Methods: This is a retrospective study of 165 patients that underwent MRI-guided PB over a 12-month duration in 2019, at University College London Hospital (UCLH). Patients that scored Gleason 3+4, Grade Group 2, with a %GP4 ≤ 10%, were selected. They were further reviewed for adverse clinicopathological and radiological findings if they underwent radical prostatectomy (RP) at UCLH.
Results: From our cohort, 34 patients had ≤ 5% GP4, and 131 patients had 10% GP4 in their GS 3+4 PB specimens. The 10% GP4 group exhibited more adverse pathological features compared to the minimal %GP4 group, including higher mean percentage core involvement (38.8% vs 32.4%), greater mean cancer length (6.39mm vs 5.29mm), and greater presence of perineural invasion. Conversely, the ≤ 5% GP4 group showed higher pre-treatment radiological risk parameters. In RP outcomes, 10% GP4 cases displayed higher risk T-staging (>T2c) and more discordance in Gleason grading (11.1% vs 0%) and clinical T-staging (63.8% vs 30%), resulting in higher rates of upgrading and upstaging compared to the minimal %GP4 group.
Conclusion: Our study underlines the value in reporting %GP4, in accordance with ISUP Consensus recommendations, to guide patient management. Increasing amounts of %GP4 were associated with poorer pathological outcomes in both GS7 PBs and RPs and can be used as a surrogate marker for poorer clinical outcomes. Unlike previous studies, our data showed that minimal %GP4 cases were not often downgraded to Gleason Score 3+3=6 in RP specimens.

PS-27-035

Comprehensive genomic profiling and immunohistochemical analysis of prepubertal-type testicular neuroendocrine tumours in post pubertal patients reveal a possible relationship with small intestinal neuroendocrine tumours

L. Szalai*, M. Leiner, E. Tóth, K. Bíró, M. Gallai Rubovszkyné, Z. Melegh
*National Institute of Oncology, Hungary

Background & objectives: Prepubertal-type testicular neuroendocrine tumours are rare entities whose genetic background and immunohistochemical properties are poorly understood. Here, we present four cases in which immunohistochemical, and molecular studies were performed to better understand the characteristics of these lesions.
Methods: Between 2006 and 2023, we identified four cases of prepubertal-type testicular neuroendocrine tumours in post pubertal patients with no extragonadal disease. The 12p chromosomal status was assessed by fluorescence in situ hybridization (FISH). Immunohistochemical studies (synaptophysin, chromogranin, CDX2, TTF1, SATB2, OCT4, Ki67) were performed for all patients. Comprehensive genomic profiling (CGP) by Oncomine Comprehensive Assay Plus was performed on one patient.
Results: Immunohistochemical tests showed strong positive staining for synaptophysin and chromogranin in all four patients. TTF1 and OCT4 were negative. Strong CDX2 positivity was identified in 2 patients, and weak positivity was identified in the other two patients. SATB2 showed negative staining in two patients, focal positive staining in one patient and cytoplasmic staining in another patient. The proliferation activity was less than 5% with Ki67 antibody. No 12p chromosomal aberrations were identified by FISH. In one patient, CGP analysis was performed, and an 18q chromosomal deletion involving the SMAD4, SMAD2 and DSC3 genes was detected. SPEN gene mutation was also identified. Currently, all patients are alive with no disease recurrence.
Conclusion: Immunohistochemistry showed varying degrees of positivity for intestinal markers in our patients. In one patient, we identified a deletion involving chromosome 18q in a region previously described as characteristic of small intestinal neuroendocrine tumours. These findings indicate intestinal differentiation and a possible relationship between these tumours and small intestinal neuroendocrine tumours. This may also pose differential diagnostic problems. In such cases, investigation of the gastrointestinal system is recommended to exclude a metastatic lesion.

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PS-27-036

Spatial transcriptome analysis of intraductal carcinoma of prostate

T. Tsuzuki*, T. Takahara
*Aichi Medical University, Japan

Background & objectives: The presence of intraductal carcinoma of the prostate (IDC-P) is known as cancer cell retrograde proliferation into the preexisting gland and has been recognized as the worst prognostic factor. However, its biological features are still unrevealed.
Methods: We selected six patients who underwent radical prostatectomy with IDC-P components. We chose representative FFPE blocks containing IDC-P and performed spatial transcriptome analysis using Visium (10X Genomics) for each case. We examined 4,992 genes for IDC-P, conventional invasive adenocarcinoma, and non-tumoural glands by manually classifying spots into the following categories: “IDC-P,” “non-IDC,” “non-cancer,” “HGPIN,” and “stroma.”
Results: We have identified 13 spatial clusters, and out of those clusters, cluster 7 has the highest concentration of the IDC-P component, accounting for around 40% of its spots. Cluster 7 is characterized by high levels of folate hydrolase (FOLH1) and prostate stem cell antigen (PSCA), along with high expression of arachidonic acid pathway members PLA2G2A and PLA2G7. We then analysed differentially expressed genes between "IDC-P" and "non-IDC-P," representing the IDC-P component and usual prostate adenocarcinoma, respectively. The markers in cluster 7, FOLH1, PSCA, and PLA2G2A, known for their aggressive histology, advanced stages, and progression to androgen-independent status, are significantly enriched in "IDC-P."
Conclusion: IDC-P and conventional invasive adenocarcinoma share the same genes. However, IDC-P exhibits unique gene abnormalities that are associated with the progression of prostate cancer. Our findings suggest that IDC-P originates from invasive cancer and acquires a higher degree of malignancy through a retrograde progression into the preexisting glands.

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PS-27-037

Defining epigenetic biomarkers of aggressive prostate cancer

S. Logotheti, K. Mesiakaris, E. Kontogianni, M. Estecio, R. Soundararajan, P. Shepherd, K. Lazaros, A. Vrahatis, C. Logothetis, A. Aparicio, V. Tzelepi*
*Department of Pathology, School of Medicine, University of Patras, Greece

Background & objectives: Aggressive variants of prostate cancer (AVPCs) share the virulent characteristics of androgen-indifferent disease and have limited therapeutic options. We have hypothesized that epigenetic alterations represent potential mediators of these aggressive phenotypes and may serve as diagnostic biomarkers and therapeutic targets.
Methods: DNA methylation analysis was performed on the AVPC patient-derived xenografts (PDXs) MDA PCa-177-B and 189-1, that are clonally related while displaying distinct morphologic and molecular profiles. Publicly available datasets (GSE123111) of normal prostate and BPH samples were also retrieved. Differential methylation and enrichment analysis was performed to provide insights on candidate epigenetic biomarkers and pathways associated with AVPCs.
Results: In total, 42 genes that encode known proteins (i.e. GSTP1, KRT5, ESM1, PHB, UPK3A) were hypermethylated in both PDXs and hypomethylated in non-neoplastic tissues, while 53 genes (i.e. B4GALT1, GDF15, KLF8, LY75, PM20D1, SLC4A10, TSPAN1) were hypomethylated in the two PDXs and hypermethylated in non-neoplastic tissues. Among these were genes that have been previously linked to prostate cancer progression. Genes involved in chromatin remodelling (SLFN11) were also identified. Enrichment analysis showed that both hypo- and hypermethylated genes are significantly involved in the Cadherin ($p<0.001$) and Wnt ($p<0.001$) signalling pathways and hypomethylated genes were also involved in mannose metabolism ($p<0.001$).
Conclusion: The methylome analysis of two clonally related, lineage-drifting prostate tumours identified a number of candidate epigenetic biomarkers that are associated with the AVPC phenotype. Future studies in clinical samples are currently under way to validate their utility as diagnostic and prognostic biomarkers. The WNT and Cadherin signalling pathways were highlighted as integral pathways of plastic cells that may explain their capacity to adapt to new sites and evade therapy.

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PS-27-038
Primary neuroendocrine carcinoma of the prostate: a case series
E. Panopoulou, E. Kontogianni, K. Mesiakaris, S. Kontogiannis, V. Zolota, S. Logotheti, V. Tzelepi*
*Department of Pathology, School of Medicine, University of Patras, Greece

Background & objectives: Neuroendocrine carcinomas (NECa) (small-cell carcinoma-SCC and large-cell NECa-LCNEC) of the prostate usually develop after disease progression, under the pressure of therapy; de novo presentation is an extremely rare entity and its clinical and pathologic characteristics have not been adequately described.
Methods: The electronic files of the Department of Pathology of the University Hospital of Patras from 2009 to 2023 were searched and 1150 prostatectomies, 76 transurethral resections and 1737 needle biopsies with a diagnosis of prostate carcinoma were identified. Cases with a primary diagnosis of neuroendocrine carcinoma of the prostate were retrieved and their histologic slides were reviewed.
Results: Six cases of primary NECa, representing 0.002% of the cases, were identified. Mean age was 68 years old and mean PSA levels were 3ngr/ml. One case was a pure SCC, one a LCNEC and the rest were NECas mixed with adenocarcinoma. Mean % of NECa in the mixed cases was 55% and showed features of both SCC and LCNEC. Intraductal spread of the NECa was present in three of the cases. P53 showed a mutated pattern of expression in one case and was concordant between the adenocarcinoma and the NECa in all cases. AR and PSA showed variable staining and proliferation index was extremely high in NECa.
Conclusion: Primary NECa of the prostate, albeit being an extremely rare entity, can be seen in routine practice, either mixed with adenocarcinoma or in a pure form and is associated with low PSA levels, which may mislead the clinicians. Both NECa components are seen in the mixed cases and may show intraductal spread similarly to their adenocarcinoma counterparts. In contrast to therapy-related NECa, p53 frequently shows a wild-type pattern of expression and AR and PSA may be positive.

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PS-27-039
Expression patterns of TIGIT and LAG-3 immune regulation receptors across molecular subtypes of muscle-invasive bladder cancer
S. Sujitwanit, M. Knežević, S. Mašić, I. Tomaskovic, B. Kruslin, M. Ulamec*
*Medical Faculty University of Zagreb, Croatia

Background & objectives: Muscle-invasive Bladder cancer (MIBC) is an aggressive disease which requires early detection and multimodal treatment. Immune checkpoint inhibitors (ICIs) showed to be very effective. In our research we asses expression of possible ICI targets, TIGIT and LAG-3 in MIBC.
Methods: 63 FFPE samples of MIBC (33 luminal and 30 basal molecular subtypes), were analysed for tumour histology, muscle invasion, and molecular subtype by immunohistochemistry (gata-3, CK20, CK5/6, p16). Immunohistochemical expression of immune checkpoints, T-cell immunoglobulin with ITIM domain (TIGIT) and lymphocyte activation gene 3 (LAG-3) was assessed as percentage of positive tumour cells and inflammatory cells in the tumoural/peritumour stroma.
Results: TIGIT showed heterogeneous expression, membranous epithelial expression and cytoplasmic expression in inflammatory cells. Epithelial expression of TIGIT was found in 39 patients, percentage of positive cells ranged from 1% to 50%. In luminal/basal subtype it was found in 18/21 cases. In inflammatory cells it was expressed in all samples, ranging from 1 to 70%. Most of the cases showed more than 5% positivity, in luminal/basal subtype it was found in 31/26 cases. LAG- 3 showed lower proportion of positive cells, epithelial cells were entirely negative. Inflammatory cells showed expression in 39 samples, percentage of positive cells ranged from 1 to 10%. In luminal/basal subtype it was found in 15/24 cases.
Conclusion: Our study showed differences in expression of TIGIT and LAG-3, immune regulation receptors across MIBC, without statistical differences in molecular subtypes for TIGIT. TIGIT showed high percentage of positivity in subset of MIBC patients, mostly in inflammatory cells of intra/peritumoural stroma. LAG-3 showed very limited expression, only in inflammatory cells, with higher expression in basal subtype. Our results can contribute to the design and correlative study of therapeutic response in clinical trials targeting TIGIT and LAG-3.

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PS-27-040
Clinical impact and implications of next generation sequencing for identification of BRCA mutations in Metastatic Prostate Cancer (mPCa)
S. Vatrano*, N. Vella, C. Alario, A. Chiarandà, C. Taranto, R. Scillieri, C. Mauceri, P. Pepe, F. Fraggetta
*Gravina Hospital Pathology Unit Via Portosalvo 9 95041 Caltagirone Italy

Background & objectives: To determine the therapeutic and clinical impact of genetic testing for BRCA mutation analysis to identify both

somatic and germline mutations using formalin-fixed paraffin-embedded (FFPE) tissue and its implications for patients and their families.
Methods: Targeted next generation sequencing (T-NGS) analysis of all coding and flanking intronic regions of BRAC1/2 genes was performed in 52 patients with mPCa collected at Gravina Hospital (Caltagirone, Italy). The MiSeq NGS system (Myriapod-NGS BRCA1-2 panel, Diatech Pharmacogenetics) was used, and the results were compared with germline analyses from corresponding blood samples within 20 working days.
Results: All FFPE cases were successfully genotyped, with the exception of two cases with low tumour content, but both libraries and sequencing CQ metrics were good. Seven (13%) germline mutations previously identified in tumour tissue were confirmed in blood analysis, and three (6%) additional somatic alterations were detected, demonstrating loss of function of BRCA genes in these patients with therapeutic implications. Of the seven cases with germline variants, four (57%) had a family history of PCa or other disease, while the remaining three (43%) patients had no hereditary predisposition. All identified genetic variants had been previously described in the major mutation databases, and most of them involved the BRCA2 gene.
Conclusion: T-NGS analysis for BRCA genetic testing using FFPE tissue in the clinical setting of mPCA patients appears to be a valuable tool, not only for therapeutic purposes, but also to identify families with genetic predisposition that may be underdiagnosed according to canonical criteria. Furthermore, the present study emphasises the need to evaluate BRCA mutations at the metastatic stage prior to castration resistance status, given the complexity of molecular analysis, thus increasing the number of patients suitable for targeted therapy.

PS-27-041
Evaluation of radical prostatectomy margins with surface imaging nonlinear microscopy
T. Weber*, A. Estevez, T. St Jacques, R. Dsouza, J. Sun, G. Nieto Blanco, S. Duncan, H. Cui, M. Andreana, B. Gershman, P. Chang, A. Wagner, S. Rosen, J. Fujimoto, Y. Sun
*Massachusetts Institute of Technology, USA

Background & objectives: Comprehensive frozen section analysis of radical prostatectomy margins can increase nerve-sparing rates (NeuroSAFE); however, it is time-intensive. Nonlinear microscopy can accurately detect prostate cancer in fresh specimens and has potential to be a higher-throughput alternative to frozen section analysis.
Methods: Fresh radical prostatectomies were rapidly stained in fluorescent analogs of H&E. The entire unsliced prostate was placed on a glass imaging window mounted on a motorized XY stage. The prostate was secured and compressed with an adjustable elastic cover. Large area, surface (en face) images were acquired by tiled acquisition. Following imaging, specimens were submitted for standard histopathological evaluation.
Results: In this IRB-approved preliminary investigation, five radical prostatectomies were evaluated. To image a larger area than could be flattened at one time, the prostate was rotated before additional image acquisitions. Four images per specimen were acquired: left posterior, posterior medial, right posterior, and apex. The user could adjust the acquisition area to span the surface of interest. The average image area was 12 square-cm amounting to 1.2 gigapixels sampled at 1 μm/pixel (10× WSI-equivalent). Two uropathologists reviewed the images in QuPath. Adipocytes, vessels, nerves, ganglia, and muscle were readily apparent, as were areas of cauterization. In one case, benign prostate glands were present at the surface near the apex.
Conclusion: Nonlinear microscopy enables the generation of large-area, H&E-like digital images of radical prostatectomy surfaces. Compared to frozen section analysis, the elimination of inking, slicing, and freezing steps streamlines workflow and potentially reduces on-site skill requirements. Furthermore, the surface imaging configuration overcomes challenges associated with imaging freshly cut whole mount slices, particularly tissue expansion and margin retraction, as encountered in a preceding 53-subject study. Additional experience is needed to assess the accuracy of cancer detection on surface images.

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PS-27-042
Malignant penile resections in a specialist referral centre - a case series and review of the literature
L. Williams*, A. Vargiamidou
*University College Hospital, United Kingdom

Background & objectives: Penile cancer is a rare disease, with treatment centred in specialist centres. Few larger patient case series have been undertaken. Our study analyses the existing literature in this topic and compares histological findings from our centre to previously published data.
Methods: All patients undergoing penile surgery for invasive malignancy over a 15-month period (January 2023-March 2024) were included in this study. Cases of PeIN alone were excluded. Recorded data included surgical management, tumour subtype, grade, pathological stage, perineural or lymphovascular invasion and nodal status. We also examined margin involvement, a criterion on which there is little existing literature.
Results: The histology of 90 patients undergoing surgical management was included, including external referral cases. Procedures included glansectomy (32%), circumcision (24%) and partial penectomy (14%), glans resurfacing (10%), penectomy (6%) and wide local excision (13%). Disease stage was most often pT1b (n=31), and pT2 (n=22). Nodal involvement was seen in 11% of cases. High tumour grade was predictive of nodal involvement (p=0.015), and all patients with nodal disease had a tumour of at least grade 3. Grade was not predictive of margin involvement (p>0.05). Perineural invasion was identified in 26% of cases and was strongly predictive of nodal involvement (p=0.0002). The margin most often involved by invasive disease was deep.
Conclusion: Interestingly, our findings suggest invasive disease involvement of the deep margin and peripheral soft tissue margins to be most often encountered, whereas previous literature found penile fascia surrounding the urethra to be most often involved. Our data did, however, find several factors predicting nodal involvement to align with previous literature. Further studies comparing overall survival and recurrence- free survival to margin status will add to the existing scanty literature on this valuable topic.

ePosters

E-PS-01E-Poster Session Autopsy Pathology

E-PS-01-001
Digital forensic histopathology whole-slide images library value in cardiomyopathies spectrum education
C. Amalinei*, A.D. Timofte, I. Caruntu, S.E. Giuşcă, R.A. Balan, E. Avădănei, L. Lozneanu, A. Rusu, M.B. Chifu, A. Grigoras
*"Grigore T. Popa" University of Medicine and Pharmacy, Romania

Background & objectives: Whole-slide-based imaging techniques or digital microscopy provide useful tools in microscopy education, including cardiomyopathies histopathological diagnosis. The development of a whole-slide-based imaging library is a current priority in our university.
Methods: An European project consortium is currently developing a cardiomyopathies histopathology training section, supported

by whole-slide-based imaging techniques. The slides selected from our archives have been scanned, collected in a library, followed by annotations and measurements for students, including: myocardium and endocardium thickness, cardiomyocytes diameters, myocytes necrosis areas, fibrosis percent, capillaries density, and inflammatory infiltrate.
Results: By dedicated software tools, the following features were demonstrated: increased length and/or width of cardiomyocytes, cytoplasmic miofibrillary loss and vacuolization, nuclei enlargement, individual myocytes death, interstitial fibrosis with an increased number of lymphocytes and macrophages, variable capillaries density, along with arterial walls thickening. Areas of interest delimitations and measurements tools applied in the assessment of these criteria of diagnosis led to the discrimination between different types of cardiomyopathies. Additionally, the availability of self-training modules within the software platform provides a valuable educational resource to Medicine undergraduate and postgraduate students, according to their training curricula.
Conclusion: The merger between digital histopathology and interactive diagnostic software represents a pivotal progress in the understanding of cardiomyopathies, as added-value of our digital library. We may consider that the innovative whole-slide imaging techniques provides modern educational tools in cardiac pathology, facilitating comprehensive learning experiences for both undergraduate and postgraduate Medicine students. The digital interactive learning opportunities facilitate skills development in histopathological diagnosis, including cardiomyopathies spectrum, contributing to improved competences that may be further applied in clinical practice and patient care.

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E-PS-01-002
Microscopic findings in incidental calcified tumour-like lesions in forensic pathology
C. Amalinei*, L.A. Riscanu, B.G. Ioan, A. Grigoras
*"Grigore T. Popa" University of Medicine and Pharmacy, Romania

Background & objectives: Calcifications may have different significance in forensic pathology. The aim of this study was to evaluate the various microscopic findings of incidental calcified nodules identified in autopsy, along with their diagnosis and differentials.
Methods: The autopsy files of the last five years of our Department have been reviewed, followed by selection of nine cases of incidental partial or completely calcified nodular lesions, with cases age distribution between 43 to 84 years old, eight men and one woman. These cases have been investigated by routine paraffin-embedding sections, followed by hematoxylin-eosin (H&E) and Masson trichrome stainings.
Results: The gross findings showed partial or completely calcified nodular lesions, 30 up to 90mm diameter. The lesions displayed a variable disposition in liver parenchyma in seven cases, in the spleen subcapsular area, in a case, and a multifocal lesion within the first-third anterior right ribs in another case. Variable cystic areas, associated with laminated membranes, necrosis, surrounded by fibrosis, with a mononuclear inflammatory infiltrate, containing rare eosinophils have been detected in seven cases, diagnosed as late stage echinococcal lesions. Solid areas, containing spindle cells embedded in a hyalinized stroma with variable chronic inflammation observed in two cases led to the diagnosis of calcifying fibrous tumours.
Conclusion: The incidence of nodular calcifications and their significance in forensic pathology is challenging. The corroboration of gross and microscopic features may discriminate between late stage calcified echinococcosis and calcifying fibrous tumours.

E-PS-01-003
Significance of solid and cystic benign renal lesions incidentally discovered in autopsy
C. Amalinei*, L.A. Riscanu, T.A. Balan, S.E. Giuşcă, I. Caruntu, A. Grigoras
*"Grigore T. Popa" University of Medicine and Pharmacy, Romania

Background & objectives: The incidence of benign renal tumours is low, most of them being incidentally detected in clinical practice or at autopsy. The aim of our study was to demonstrate the morphological variability of benign renal lesions incidentally discovered by necroptic examination.
Methods: The autopsy reports of our Department, from the last five years, have been reviewed, and 40 cases of incidental benign renal tumours have been selected. The collected specimens have been investigated by routine paraffin-embedding, followed by haematoxylin-eosin (H&E) and Masson trichrome stainings, and immunohistochemistry technique using CK AE1/AE3, CK7, Desmin, HMB45, MelanA, SMA, S100, and Vimentin markers.
Results: The study group comprised 28 men and 12 women, ages ranging between 28 to 95 years old. Gross findings were variable, from well-delimited white-yellowish or red-brownish small masses, up to 2cm diameter, to multiple well-circumscribed, multilocular cystic lesions, ranging between 4-7.5mm diameter. The microscopic examination added to immunohistochemistry, in selected cases, revealed characteristic features of renomedullary interstitial cell tumour in 21 cases, of angiomyolipoma, the classic variant, in 10 cases, of multilocular cystic nephroma in eight cases, and of renal corticomedullary junction capillary hemangioma in a case, respectively.
Conclusion: Despite their rarity, benign renal lesions should be considered in the differential diagnosis of other renal tumour masses. Their significance is variable, highlighting their possible involvement in thanatogenesis. The microscopic examination associated with the immunohistochemistry method is important in diagnosis certification.

E-PS-01-004
Air embolism due to atrio-oesophageal fistula following catheter ablation: a case report
J. Amaral*, J. Pimentel, R. Almeida, M.A. Cipriano
*ULS Coimbra, Portugal

Background & objectives: Atrio-oesophageal fistula (AEF) is a rare event following percutaneous catheter radiofrequency ablation for atrial fibrillation, with a prevalence of 0.1-0.25%. It usually presents with chest pain, fever, neurological or gastrointestinal symptoms, with an overall mortality rate of 65%.
Methods: We present a case of a 77 year old woman who had a long standing history of atrial fibrillation and heart failure, with multiple episodes of emergency department admission.
Results: The patient underwent percutaneous catheter radiofrequency ablation and presented to the emergency department 6 days later with a right pleuritic chest pain with posterior irradiation that began the day after the procedure. A thoracic CT angiography failed to reveal any signs of an AEF. Five days later the patient enters a comatose status with seizures. On the cerebral CT there was evidence of cerebral infarcts and intravascular gas, suggestive of air embolism. On the following day, the patient was pronounced dead. Post-mortem findings include an AEF with 2 mm diameter and evidence of multiple cerebral infarcts. There was release of air on a submerged section of the brain.
Conclusion: Despite being a rare occurrence, clinicians should be aware of this possible complication in order to quickly detect and institute treatment. In autopsy, AEF is easily detected while employing the en bloc method of evisceration, but can be overlooked with the

Virchow method. Therefore, in the proper context, this condition must be kept in mind, and a method that preserves the relationship between organs must be favoured for the post-mortem examination.

E-PS-01-005

Novel use of simulation in autopsy training for pathologists

R. Farrell*, A. Stanley, K. Culligan, R. Cooney, D. Byrne, L. Aalto, S. Phelan
*Division of Anatomic Pathology, Galway University Hospital, Ireland

Background & objectives: Autopsy is an essential medico-legal tool and a requirement for pathology education and training. However autopsy training is limited by a lack of appropriate cases.
Our objective was to develop a simulated autopsy workshop for early-stage histopathology trainees.
Methods: The workshop was co-designed and delivered by an expert faculty of prosectors, forensic pathologist, neuropathologist and a general pathologist. A donor cadaver was used. The trainees' learning was supported by a prosected cadaveric model of the vertebral artery anatomy and 3-D printed models of hearts to demonstrate normal cardiac dissection, and a simulated external examination was carried out with trainees.
Results: Trainee and faculty feedback was positive. All trainees (n = 8) indicated that they felt more confident in autopsy practice after the simulation, and all felt that this was a program that should be repeated. Specific feedback from both faculty and prosectors noted that the process of evisceration was slower and tissues firmer than at a real autopsy. Trainees also expressed a preference for longer sessions to facilitate more in-depth dissection of each autopsy block.
Feedback on the 3-D organs revealed that they were useful in demonstrating normal anatomy but the texture was too firm allow for easy dissection.
Conclusion: Simulation using cadavers and 3-D printing, offers a valuable autopsy experience. Modifications, to include prosected specimens and more time, are required. Continued advancements in 3-D printing and cadaveric fixation techniques will enhance the learner experience. This novel simulated autopsy workshop is valuable but it does not completely remove the need for invasive adult autopsies for training. However, it is a promising educational experience that addresses a gap and we plan to continue this workshop as part of pathology education.

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E-PS-01-006

Clinico-morphological peculiarities in cases of deaths induced by methadone toxicity

D. Gorelova*, O. Reshetnikova, A. Ermakov, A. Mokhova
*Immanuel Kant Baltic Federal University, Russia

Background & objectives: There has been a steady growth of mortality parameters caused by methadone overdose worldwide. The study focuses on medical records data, autopsy results and histopathological changes with an emphasis on the mechanisms of thanatogenesis connected with methadone toxicity.
Methods: Post-mortem examination records in 116 cases of deaths induced by methadone toxicity were reviewed. The data from the autopsy protocols were analysed taking into account the age and gender of the patients. Biochemistry and toxicology were performed in all cases. Demographic characteristics and clinical peculiarities were noted. Naked eye pictures and microscopic features of brain and internal organs were studied.
Results: The study showed an increase of autopsies connected with methadone toxicity among other poisoning. The majority of deaths were registered in the 26-35 age group (39.7%). Male dead bodies were more commonly seen at an autopsy bed than female ones (correspondingly 39 to 7). The other age group ranged 36-45 years (37,1% of cases). Thirty-nine men and four women were in latter group. Four female deaths were in the age' group under 17. 13,8% of cases (15 men and 1 woman) presented the 18-25 age group. The oldest group included 7 males over 45 y.o. (6,0%). Postmortem investigation revealed pathological changes in the patient's brain, heart, lungs, kidneys and liver.
Conclusion: The data of the above studies have shown that methadone abuse significantly increased during recent years. A major growth in dependence was recorded among male patients aged 26-45 years. Pathomorphological changes in internal organs are discussed in the aspect of thanatogenesis of the identified injuries. Further study is needed to support the effective therapies for opioid users and prevent the fatal outcomes in case of methadone maintenance therapy programs.

E-PS-01-007

Histopathologic peculiarities of kidneys in cases of methadone-mediated fatalities

D. Gorelova*, O. Reshetnikova, E. Romanova, A. Ermakov
*Immanuel Kant Baltic Federal University, Russia

Background & objectives: Methadone-replacement therapy of opioid addict patients is accompanied with the morbidity growth due to toxicity of this drug. A negative impact of a methadone on a renal functions prompted us to study.
Methods: Autopsies of 100 dead bodies of men and 16 women aged from 17 to over 45 years were carried out, followed by histological examination of tissue samples from brain and internal organs, with special attention to signs of kidney damage. Pathomorphological data were compared with the results of toxicological studies, as well as with materials from patient medical histories.
Results: Acute kidney damage was presented with a tissues' swelling, congestion of blood vessels and capillary loops of glomeruli with commonly seen stasis of erythrocytes. Protein dystrophy in the hyaline-droplet and vacuolar pattern often registered in convoluted tubules' epithelial cells. Twenty percent of cases showed signs of a lymphoplasmacytic infiltrates presence. Few cases had stromal neutrophilic infiltration due to concomitant infection. Focal tubular atrophy, segmental glomerulosclerosis with fibrotic periglomerular interstitium were revealed in seven male's bodies over 45 years old.
Conclusion: Addiction to opioids followed by the methadone-replacement therapy may cause a nephrotoxic impact on a drug- abused patient. Post- mortem examination revealed various kidney injuries, such as blood circulation disorders and convoluted tubule epithelium damage of varying severity. Patchy interstitium inflammatory infiltrates with some sclerotic features were mainly discovered in elder group of patients. Morphologically based recommendations that take into account the characteristics of the nephrotoxic effects of methadone can promote better therapeutic algorithms for opioid addict patients.

E-PS-01-008

Histopathological features of a liver damage caused by methadone toxicity

D. Gorelova*, O. Reshetnikova, E. Romanova, A. Ermakov
*Immanuel Kant Baltic Federal University, Russia

Background & objectives: Methadone substitution therapy of opioid dependence is accompanied by an increase in deaths due to methadone toxicity worldwide. The aim of present study was to determine the nature of structural liver's changes in the thanatogenesis of such deaths.
Methods: Eighty-nine standardized autopsies in cases of deaths related to methadone toxicity were performed. The study group included 78 males' and 11 female's bodies. The investigation reviewed clinical data,

autopsy protocols, postmortem toxicological analyses. Histological slides stained with hematoxylin and eosin were studied at magnifications x 5; x20; x40. The findings were analysed together with clinical data from the medical records.
Results: Present study has found that 87,6% were male patients included into the group. Their ages varied within 26-45 y.o. Postmortem examination revealed pathological changes in a liver, which included acute hemodynamic changes on the background of chronic inflammatory processes. Microscopic features revealed congestion, stasis and focal stromal edema. Various types of protein dystrophy were found in hepatocytes. Some liver cells were swollen had rarified cytoplasmic alterations. The majority of cases have shown the portal hepatitis patterns (from persistent to active with 1-4 degrees of activity). Portal tracts were enlarged with areas of stellate-like periportal sclerosis. Inflammatory mononuclear infiltrates were common findings within the portal tracts as well as lymphoid aggregates.
Conclusion: The investigation of a liver tissue injury suggests that hepatocytes damages with inflammatory response and blood circulation disturbances an important link in thanatogenesis of methadone- related deaths. Further investigations are needed for devising successful methadone substitution therapy algorithms.

E-PS-01-009
Clinically unrecognized tuberculosis sepsis – autopsy case report
R. Jankovic*, I. Filipović, M. Jovanović, M. Đuknić, J. Jevtić, N. Boričić, S. Glumac, N. Šimšić, M. Zivotic
*University of Belgrade, Faculty of Medicine, Institute of Pathology, Serbia

Background & objectives: Tuberculous sepsis represents a serious complication of tuberculosis, characterized by the characteristic spread of bacteria through the bloodstream, triggering a systemic inflammatory response, which can lead to rapid deterioration of the condition and a fatal outcome.
Methods: A 70-year-old man presented to the hospital with weakness and watery stools occurring 3 days prior. He had a chronic cough with whitish sputum, a history of hypertension, a myocardial infarction 5 years ago, and was a long-term smoker.
Results: Lung examination revealed diffuse crackles and diminished breath sounds, with an oxygen saturation of 70%. Chest X-ray showed diffuse opacification of both lungs. Laboratory tests indicated elevated INR, anemia, leukopenia, elevated CRP, fibrinogen, and severe hypoalbuminemia. Symptomatic, supportive, and antibiotic therapy was started. Despite treatment, the patient passed away. A clinical autopsy revealed lung and intestinal abnormalities: rubbery lungs with multiple consolidations, and multiple intestinal ulcers. Histopathological analysis revealed granulomas in various organs composed of Langhans giant cells, epithelioid cells, and lymphocytes, with necrosis in some. Ziehl-Neelsen stain revealed acid-fast bacilli in organs with granulomas. The lungs also exhibited fibrinopurulent bronchopneumonia with diffuse alveolar damage and occasional hyaline membrane formation.
Conclusion: Histological findings correlated with clinical data indicate tuberculous sepsis as the most likely cause of the patient's death. This serious complication of tuberculosis often leads to rapid deterioration of health and a fatal outcome, especially in older patients with comorbidities.

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E-PS-01-011
A case of diffuse pulmonary ossification as a rare finding at autopsy
Y. Kuzyk*, A. Arefyeva, V. Bobrenok
*Danylo Halitsky Lviv State Medical University, Ukraine

Background & objectives: Diffuse pulmonary ossification (DPO) is a rare condition of unknown origin defined by widespread heterotopic bone production within the pulmonary tissue. DPO is usually associated with preexisting chronic pulmonary and/or heart disorders, although in some cases may be idiopathic.
Methods: An analysis of the clinical and instrumental data of the medical history of the case of DPO in 46-year-old woman was carried out. Fragments of lung tissue removed during autopsy are stained with hematoxylin-eosin, Masson's trichrome, Hart's resorcin-fuchsin.
Results: A 46-year-old woman was hospitalized for acute necrotizing and haemorrhagic pancreatitis. A laparotomy operation with drainage of the abdominal cavity was performed. Severe intoxication due to acute pancreatitis led to the death of the patient on the 5th day of her stay in the hospital.
During the autopsy, in addition to signs of acute pancreatitis, an undiagnosed lung disease was found. Lungs of gross examination were increased in size, diffusely compacted, gray in color, with little air, crisp on section. Histologically, bundles of collagen fibers and bone structures were observed, which form a wide-loop mesh tissue with the involvement of lung tissue.
Conclusion: The presented case of the racemose subtype DPO is an example of rare, underecognized pulmonary disease. According to literature review, applying the HRCT scan, clinicians have a sensitive tool to detect DPO in earlier stage, which will enable a better understanding this entity and its relation to preexisting diseases.

The pathogenesis of DPO is remains open, the connection with pneumoconiosis is discussed, at the same time, the metaplastic bone formation such a responce to inflammation is not excluded.

E-PS-01-012
Minimally invasive treatment complications in congenital hepatic hemangioma: autopsy findings and review of 56 years cases
V. Macarrón*, S. Quinones, G. Barrios Millán, M.I. Esteban-Rodríguez, R.M. Regojo
*La Paz University Hospital, Spain

Background & objectives: Traditional treatment for congenital hepatic hemangioma (CHH) has been based on surgery. However, new minimally invasive treatments, which are not risk-free, have been emerging. Our study aims to assess the pathological complications associated with these newer approaches.
Methods: We report two cases of prenatally diagnosed neonates with an hepatic vascular lesion sonographically consistent with CHH. Postnatally, these patients underwent minimally invasive treatments with curative intention, but they experienced complications that ultimately led to their death. Furthermore, we conducted a retrospective search for CHH autopsy cases within autopsies performed at a tertiary centre from 1967 to 2024.
Results: The first patient is a female full-term neonate presenting heart failure attributed to an arteriovenous shunt at CHH. Endovascular embolization employing coils and polyvinyl alcohol particles is carried out after conservative treatment. However, embolizing material disseminated seeding occurs. The subsequent case involves a preterm male neonate exhibiting similar symptoms. Diagnosed CHH has a nutrient hepatic artery, which is embolized with coils. Other arterial vessels are embolized with cyanoacrylates, which cause respiratory distress due to lung intravascular dissemination. In addition, among the autopsies performed in the last 56 years, another nine cases of foetuses and neonates diagnosed with CHH are identified, with only one additional diagnosis in the past two decades.
Conclusion: The implementation of minimally invasive treatments for CHH has notably enhanced patient survival rates in recent years. This can be demonstrated due to the limited diagnosis of this pathology in autopsies conducted in the last 20 years at our hospital. However, these

treatments are not devoid of complications, so their execution requires experience and multidisciplinary consensus in which the risk-benefit balance of the medical procedures should be decided.

E-PS-01-013

A paediatric case of autoimmune polyglandular syndrome type 1

P. Madžar*, K. Lah Tomulić, A. Milardović, A. Verbić, G. Đorđević
*Department of Pathology and Cytology, Clinical Hospital Center Rijeka, Croatia

Background & objectives: Authors present the clinical and autopsy findings in the case of a paediatric patient with type I autoimmune polyendocrinopathy syndrome.
Methods: Autoimmune polyglandular (polyendocrinopathy) syndrome type 1 (APS 1) is due to mutations in the autoimmune regulatory gene (AIRE), with about 60 different mutations described so far. Pathogenic gene variants lead to multiorgan autoimmunity characterised by multiple endocrine glands' functional impairment due to loss of immune tolerance.
Results: A two-year-old girl initially presented with high body temperature, vomiting, positive meningeal signs and elevated inflammatory laboratory parameters. On admission, she was somnolent with a GCS of 14. Lumbar puncture indicated a bacterial infection. Brain MSCT showed extensive brain oedema with the absence of grey and white matter differentiation bilaterally temporally and frontobasally. Cerebrospinal fluid culture was positive for Streptococcus pneumoniae, even though she had been vaccinated. Despite intensive treatment measures, the patient died 11 days after admission. Autopsy verified acute suppurative meningoencephalitis, nonspecific interstitial pneumonitis and chronic pancreatitis with extensive fibrosis and steatonecrosis. The results of genetic testing proved the presence of a pathogenic variant of the AIRE gene.
Conclusion: APS-1 is a potentially underdiagnosed condition due to the rarity and enormous variability in its presentation. Patients with APS-1 have an increased risk of mortality due to abnormal autoimmune response, particularly hepatitis, nephritis and pneumonitis. Although APS-1 is characterised by multiorgan autoimmunity, patients may have a clinically significant immune deficiency in response to infection before any autoimmunity symptoms, as seen in the presented case.

E-PS-01-014

Comparison of the final clinical and autopsy detected diagnoses in sepsis

B. Magrupov*, V. Sharipova, V. Ubaydullaeva, T. Verevkina
*Center for Professional Development of Medical Workers, Republican Research Center of Emergency Medicine, Uzbekistan

Background & objectives: With sepsis, more than a third of patients die, while the immediate causes of death may remain unknown. Autopsy largely helps to establish them.
Methods: 107 cases (56% autopsy was performed within 24 hours after the death was pronounced) of patients with sepsis who died in the Department of Surgical Resuscitation of the Republican research Centre of Emergency Medicine in 2020-2021 were studied. The final clinical and pathoanatomic diagnoses were compared in accordance with the International Goldman System of categories of diagnosis discrepancies.
Results: As a result of autopsies, 3 (5%) of the deceased had a discrepancy in the diagnoses of class I and 14 (23%) — class II according to the International Goldman System. During his lifetime, diseases or their complications were not recognized in 17 (28%) cases, mainly acute myocardial infarction of type 2 (3 cases) and liver abscesses (3 cases).
Conclusion: A pathoanatomic autopsy is a modern and important diagnostic tool that can clarify the causes of death.

E-PS-01-015

Insights into hereditary multiple osteochondromas: a case report in foetus

J.P. Maldonado*, C. Cerdeira, A.C. Lai, R. Pina
*ULS Coimbra, Portugal

Background & objectives: Hereditary Multiple Osteochondromas (HMO), an autosomal dominant disease originating from EXT1 and EXT2 gene mutations with high penetrance, manifests as benign bone tumours, causing skeletal deformities and growth reduction. Approximately 10% of affected individuals result from de novo pathogenic variants.
Methods: A 34-year-old woman, with a history of spontaneous abortion at 7 weeks, presented with premature membrane rupture at 20 weeks of pregnancy. The foetus, with proper weight for gestational age, showed craniofacial dysmorphisms and retrognathia. Combined screening in the first trimester indicated low pregnancy risk. Due to foetal inviability, a termination of pregnancy followed by foetal autopsy was conducted.
Results: After conducting the foetal autopsy, several prominent nodular lesions were identified on the ribs bilaterally. The largest ones, measuring 1.8cm in diameter on the right, at the 7th and 8th ribs, and 1.3cm on the left, between the 8th and 9th ribs, were particularly noteworthy. In section, these nodular lesions were found to be composed by a cap of cartilaginous tissue. Histological examination revealed osteochondromas. Subsequent to this, a skeletal X-ray was performed, which apparently did not reveal any other lesions besides these. Additionally, it was observed that the nodular lesions were causing compression of the lower lobe of each lung, further highlighting their significant impact on the foetal condition.
Conclusion: While HMO was incidentally discovered and not the cause of the premature rupture of membranes, this case emphasizes the importance of genetic awareness. In scenarios like this, screening parents for mutations in the EXT1 and EXT2 genes can provide valuable information for future pregnancies, enabling proactive measures to address potential complications associated with the disease, mainly progression towards chondrosarcoma. Accidental findings like HMO underscore the significance of thorough genetic evaluation, facilitating preventive interventions and improved outcomes in potentially affected families.

E-PS-01-016

Pathologic examination of myocardial infarction using ape/ref-1 for postmortem application

J. Na*
*Department of Forensic Medicine, Republic of Korea

Background & objectives: Apurinic/apyrimidinic endonuclease 1 (APE1) is a multifunctional enzyme involved in the base excision repair pathway. APE1 acts as a reductive activator of many transcription factors and has also been named redox effector factor 1, Ref-1.
Methods: Immunohistochemical staining for APE1/Ref-1 was performed in the hearts of individuals who died from 10 myocardial infarction (MI) cases and 15 control cases with other causes of death (trauma, asphyxia, natural death except MI). Furthermore, we quantitatively analysed APE1/Ref-1 expression by western blot in two opposite sites of the myocardium of MI group.
Results: Immunohistochemical positivity for APE1/Ref-1 was observed in the hearts of individuals who died from MI, while immunohistochemical positivity was not observed in the control group, despite the presence of lesions associated with chronic heart disease. Furthermore, immunohistochemical positivity for APE1/Ref-1 was identified in the cardiomyocytes and microvascular endothelium of the myocardium supplied by the culprit artery in the same heart affected by MI. Among the MI group, APE1/Ref-1 was only expressed in myocardial endothelial cells in cases with early MI.

Conclusion: In conclusion, these results suggest that detection of expression of APE1/Ref-1 could potentially be used for postmortem diagnosis of MI. Additionally, our findings indicate that APE1/Ref-1 may be involved in microvascular dysfunction in the early MI. Furthermore, we think this analysis could help in understanding the pathophysiology of MI about novel causes such as microvasculature dysfunction. Further studies with a larger number of autopsy cases are needed to confirm a postmortem usefulness of APE1/Ref-1.

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E-PS-01-019

Sudden death due to mitrogynine (Katrom) toxicity: an unusual case report and review of the literature

J.P. Olano*, J. Nickels
*University of Texas Medical Branch, USA

Background & objectives: We, hereby, report an unusual case of sudden death due to mitrogynine (Katrom) toxicity in a young 30-year male with history of systemic hypertension. He was found unresponsive at work on a boat with successful resuscitative efforts after 40 minutes.
Methods: The patient arrived to the ER and imaging indicated severe cerebral edema consistent with anoxic brain injury. He was pronounced dead 48 hours after admission. A complete autopsy was performed and post-mortem toxicology was done on post-mortem blood using Gas Chromatography/Mass Spectrometry (GC/MS). Full neuropathologic examination was also conducted. The spouse reported that he was a habitual consumer of Katrom.
Results: The main autopsy finding was severe cardiomegaly with left ventricular concentric hypertrophy (heart weight: 650 gm; LV thickness: 2.0 cm). This condition led to the development of a fatal ventricular arrhythmia with sudden cardiac arrest and anoxic encephalopathy resulting in cerebral edema and cerebellar tonsillar herniation. Microscopic examination of the brain revealed hyaline arteriolosclerosis most likely due to systemic hypertension. There was no evidence of lesions responsible for secondary systemic hypertension such as catecholamine-producing tumours, adrenal cortical tumours, etc. GC/MS revealed mitragynine at a level of 400 ng/mL. Pre-mortem levels were most likely higher since the patient was hospitalized for 2 days before his demise.
Conclusion: Mitragynine is a natural alkaloid derived from the Kratom tree (Mitragyna speciosa). It is found in Southeast Asia and is an agonist of the mu, delta and kappa opioid receptors. In 127 fatalities, 10 had mitrogynine as the sole intoxicant. Three cases had levels of 260-1,900ng/mL. In another 3 cases, levels ranged from 1,590-3,420. Chronic toxicity has been described and effects on the cardiovascular system include hypertension and potential for lethal ventricular arrhythmias due to prolongation of the QT interval.

E-PS-01-020

Foetal postmortem study: correlation between echocardiography and postmortem study in foetuses with a heart abnormality diagnose. Termination of pregnancy protocol in our center

E. Oliva Domínguez*, K. Gonçalves Villarreal, I. Orbegozo Arrizabalaga, I. García Miranda, J.I. Iparraguirre Santiago, M.L. Ramírez Feliz, A. del Campo Real, I. Llano Rivas, L. Zaldumbide Dueñas, L. González Mosteiro
*Hospital Universitario Cruces, Basque Country, Spain

Background & objectives: To stablish the correlation between the echocardiography and the postmorten study in foetuses with a heart abnormality diagnose in a termination of pregnancy and to show the protocol followed in these cases at our centre.
Methods: We reviewed the foetal postmorten study reports from the last three years (2021-2023) at our centre. Cases of foetuses with a heart abnormality diagnose were extracted. Echocardiography and postmorten study were compared to find out the value of the postmorten study. A total of 129 postmorten reports were recorded, 20 of them had a echocardiography heart abnormality diagnose.
Results: 20 postmorten studies verified a previous echocardiography heart abnormality diagnose (100%): compared to the echocardiography, 12 showed the same abnormalities (60%), 5 showed more abnormalities (25%) and only 3 showed fewer abnormalities (15%). Regarding the protocol, at 12th week of gestational age, a score is obtained combining ultrasound morphological indicators and biochemical markers of chromosomopathy. If the risk of a heart abnormality is high, an echocardiography and a genetic study are performed. If a malformation is detected and progenitors decide to terminate the pregnancy, a postmorten study is recommended to confirm these ultrasound findings. Subsequently, all the test results are assessed to stablish a recurrence risk in future pregnancies.
Conclusion: Postmorten study is a key element in a heart abnormality diagnose in foetuses from a termination of pregnancy. Not only it confirms the presence of a heart abnormality but also, in some cases, detects other subtle malformations undetectable by ultrasound. These findings can guide the genetic tests and have important implications in future pregnancies. Furthermore, the confirmation of the ultrasound findings relieves parents since the tough decision to terminate the pregnancy is, in general, based on these findings.

E-PS-01-021

A case of Miller-Diecker syndrome – integrated imaging and genetic diagnosis

C. Cerdeira, R. Oliveira*
*CAPGS, Portugal

Background & objectives: Miller-Dieker syndrome (MDS) is a rare genetic condition characterized by lissencephaly, distinctive facial features and severe neurologic. MDS is caused by a deletion on the short arm of chromosome 17 (17p). Most cases are not inherited and occur randomly.
Methods: Female 41 years old, pregnant of 26 weeks, submitted to pregnancy termination due to brain and renal ecographic changes. A genetic study showed a deletion on the short arm of chromosome 17 (17p), thus compatible with MDS.
Results: Foetus examination showed a large mouth and forehead, with small nostrils. Internal examination exhibits a right kidney larger than the left, with a double ureter; there is an incomplete bowel rotation with an appendix located in the umbilical region. The brain had an external smooth surface – lissencephaly with a mild subarachnoid haemorrhage. Histological examination of the brain showed an immature brain, translating into a delay in development, with an immature and less cellular cortex. The Purkinje cells and hippocampus are also poorly developed.
Conclusion: MDS is incurable. Suspicion for this syndrome should be raised by imaging findings of lissencephaly, with diagnosis supported by molecular findings.

E-PS-01-022

Foetal autopsy in a private laboratory – the experience from Centro de Anatomia Patológica

C. Cerdeira, A. Pereira, J. Germano Rego de Sousa, M.J. Germano de Sousa, R. Oliveira*
*CAPGS, Portugal

Background & objectives: Foetal autopsy is a complex procedure. The integration of molecular and radiological data is fundamental for a

precise diagnosis. Usually, this procedure is performed in public institutions but the increase in demand has prompted evaluation in private laboratories.
Methods: A total of 65 foetal autopsies were performed in the last 18 months. All foetal autopsies were performed by an experienced assistant, with the post-graduated formation and, when necessary, supervised by a pathologist. The method of choice was the one described by the Portuguese College of Pathology. Genetic testing was performed whenever possible.
Results: The major findings were genetic: trisomy 21 (n=13), trisomy 18 (n=4), trisomy X (n=2) trisomy 13 and 19 (n=1, each) and 1 case of chromosome 9 structural mutation. 19 cases had vascular/hypoxia causes, one due to mutation in Leiden factor V and, in 7 cases the foetus was unremarkable. A polymalformative condition (including complex cardiopaties) was present in 7 cases and 3 had central nervous system defects. Corioamniotitis was the demise cause in 3 cases. One case had an abdominal wall defect, one had a diaphragm hernia and one had a congenital volvulus. A syndrome was identified in three cases (Potter syndrome, Miller-Dieker syndrome and Hadju-Cheney syndrome).
Conclusion: Foetal autopsy is a possible scenario in a clinical laboratory in Portugal, especially when executed by a trained staff and in conjugated with specific genetic testing. In cases of complex malformation and "normal" genetic array, an exome sequence should be considered to assess genetic alterations.

E-PS-01-023
Tubulinopaties – morphology may not be enough! Genetics is fundamental
C. Cerdeira, R. Oliveira*
*CAPGS, Portugal

Background & objectives: Tubulinopathies (or tubulin-related cortical dysgenesis) are rare and comprise a wide and overlapping range of brain malformations, due to mutation in the tubulin (TUB) gene. We describe a case, raising the awareness of this entity.
Methods: 23-week pregnant with image detection of brain malformation, with ventriculomegaly, cerebellum hypoplasia and thin callosum body. TUB mutation was detected by NGS.
Results: Male foetus with rather unremarkable external surface. Brain with 94.3g, edematous, without lissencephaly, with biventricular hydrocephaly and a thin callosum body – 0.2cm thick, and subarachnoid haemorrhagic foci. Cerebelum with normal diameter (2.6cm). There was no choroid plexus cysts.
On histological examination, there was a poor definition of the cortical layer, with only individualization of 4 layers, associated with mild voluminous germinal zones. No glomerular cortical structures or axonal bundles were evident.
Conclusion: TUB mutations can induce a wide variety of changes, from lissencephaly, dysgiria, dysmorphic basal ganglia and cerebellum dysplasia, among others. Due to the necessity of distinguishing tubulinopathies from other clinical entities with similar brain malformations, a wide genetic study should be employed in these cases.

E-PS-01-024
Thymic hypoplasia: lessons of an infant autopsy findings
J. Ortega-Balderas*, M. Ponce-Camacho, O. Barboza Quintana
*Hospital Universitario Jose Eleuterio Gonzalez, Mexico

Background & objectives: The thymus in innate immunodeficiencies is composed of epithelial cells with minimal fatty infiltration. Infants with postnatal hypoplasia exhibit abundant adipose tissue dissecting collections of epithelial cells. We present the autopsy findings of a non-suspected thymus hypoplasia.
Methods: A 3-month-old male, with desquamative erythroderma at 2 weeks of life with poor response to steroids and calcineurin inhibitors treatments, was admitted due to fever and generalized tonic-clonic seizures. Despite admission to the intensive care unit, he developed severe acute respiratory distress syndrome, septic shock, and bacteremia. After hemodynamic deterioration and three cardiorespiratory arrest events, he unfortunately died.
Results: An autopsy revealed no malformations, damage to the skin basement membrane with pigment incontinence and extravasation of erythrocytes, acute haemorrhagic pneumonia, absence of white pulp in the spleen, bone marrow maturation arrest, thymic hypoplasia with fatty infiltration with absent Hassall's corpuscles, and absent lymphoid tissue in the respiratory and gastrointestinal tract. Immunohistochemistry markers resulted in negative TDT, CD3, CD20, OSCAR, and focal CD5 positivity. The final diagnosis encompassed thymus hypoplasia, necrotizing haemorrhagic pneumonia, necrosis of the adrenal medulla, bone marrow maturation arrest, and cerebral hypoxia-related changes.
Conclusion: This autopsy exposed the possible reason for the patient's early onset of multiple gastrointestinal and skin conditions, and the poor response to multiple topical and systemic treatments, as well as a rapid deterioration during his stay at our hospital.

E-PS-01-025
Pulmonary and renal histopathological findings of patients treated with immune ckeckpoint inhibitors: a report of two autopsy cases
M.M. Petrino*, V. Macarrón, S. Quinones, E. Miraval Wong, M.d.C. González García
*La Paz University Hospital, Spain

Background & objectives: Immune checkpoint inhibitors (ICPIs) are targeted therapy drugs that improve T cell response against cancer, but have also been associated with autoimmune adverse events. Our objective is to describe some renal and pulmonary histopathological features related to ICPIs.
Methods: We studied the renal and pulmonary autopsy histopathological findings of two patients who had been treated with ICPIs for a metastatic oncologic disease. The medical history of both patients was available.
Results: The first patient was treated with nivolumab-ipilimumab for stage IV melanoma. The autopsy revealed disseminated cancer; histologic findings of acute lung injury such as edema, hyaline membranes, reactive type II pneumonocytes, lymphocytes, eosinophils, siderophages and vacuolated macrophages; and renal injury in the form of focal glomerular fibrinoid necrosis, focal tubulitis, acute tubulointerstitial nephritis and venulitis, with deposits of C3 along vessel walls, glomerular mesangium and tubular walls. The second patient was treated with cisplatin-gemcitabine-atezolizumab for stage IV urothelial carcinoma. The autopsy revealed a complete tumour pathological response, an intense chronic tubulo-interstitial nephritis with focal acute tubular necrosis and a chronic peribronchial inflammatory infiltrate. No microorganisms were found.
Conclusion: Of the two cases described, the first patient showed no significant tumour response to ICPIs while the second presented with complete pathological response. Both of them developed renal histopathological injuries, and the first patient pulmonary histopathological findings, that although inespecific, have been described as possible autoimmune adverse events of the therapy with ICPIs.

E-PS-01-026
Acardius foetus: a multi-case pathological study and comprehensive literature review
S. Quinones, M. De Uribe Viloria*, E. Tornay, M. Parrón, I. Esteban-Rodríguez, R.M. Regojo
*La Paz University Hospital, Spain

Background & objectives: Twin reversed arterial perfusion sequence (TRAP) is a rare and exclusive complication of monochorionic multiple

gestations, based on the presence of arterio-arterial anatomosis in the placenta. There is a great variability of anomalies related to the acardiac foetuses.
Methods: After following a unique case, we reviewed our records and found the anatomopathological and clinical reports from our centre were reviewed (1967-2023), finding 6 cases of TRAP sequence. These included an autopsy and placenta examination and a radiological postmortem analysis. In terms of placental diagnoses, the Amsterdam Consensus classification was used. Our results were compared with previously published studies.
Results: Regarding the classical classification of Das (1902), out of our 6 cases, the most frequent was anceps (3/6) which shows a partial development of craniofacial structures with cerebral tissues, extremities and body. One case was an acardius acephalus which is the most frequent type regarding the bibliography, being characterized by the absence of head structures, upper limbs and thoracic organs with an acceptable development of lower limbs and pelvis. Another case was acardius amorphous, represented by a tissue mass without recognizable organs and another one was unclassifiable type due to being papyraceous.
Furthermore, placental anastomosis were recognizable, except one case probably due to the intrafoetal laser treatment.
Conclusion: This study provides valuable insights into acardius foetus, emphasizing the importance of early detection and comprehensive management. It is important to highlight that the placenta and its anastomosis has a fundamental role in terms of pathophysiology and new treatments, as ntrafoetal laser, can change the placental findings observed

All these findings contribute to a better understanding of this rare condition and may guide future research and clinical practice for improved pump twins outcomes.

E-PS-01-027
Non-immune hydrops fetalis associated with MYBBP1A gene
S. Quinones, M.A. Abad*, M. De Uribe Viloria, M. Parrón, J.A. Tenorio, P. Lapunzina, I. Esteban-Rodríguez, R.M. Regojo
*La Paz University Hospital, Spain

Background & objectives: Non-immune hydrops fetalis (NIHF) is a rare entity characterized by excessive fluid accumulation within the foetal extravascular compartments, which increases the risk of prenatal/intrauterine death. Although the introduction of massively parallel sequencing, approximately 30% of cases remained unsolved etiology.
Methods: We present a stillbirth case with severe NIHF in which a complete autopsy study was performed, including postmortem radiological study, placental examination and trio exome sequencing (foetus and parents). The capture kit was Nextera exome and samples were sequenced in NovaSeq6000 (Illumina). Quality analysis, alignment and variant calling were performed with an in-house and variant prioritization with VarSeq-software (Golden Helix).
Results: We presented the case of a female stillbirth at 27+3 weeks of pregnancy with severe NIHF including generalized subcutaneous edema with laterocervical cystic higroma, moderate serohematic ascitis and pleural effusion. We observed data suggestive of severe intrauterine growth restriction related with weight (
In addition, radiological study showed small punctate calcifications on tarsi, without other punctae in other locations.
In terms of genetic analysis, the trio exome sequencing resulted in the identification of two heterozygous variants in the MYBBP1A gene each inherited from an asymptomatic parent.
In the bibliography consulted, there were only two cases that related NIHF to this genetic variant.
Conclusion: In recent years, the implementation of whole sequencing has resulted in the diagnosis of new genetic variants associated with NIHF. However, there are still many cases without known etiology. New variants appear, sometimes being difficult their interpretation and suggesting a challenge from a clinical and therapeutic point of view. Knowledge of these genetic alterations, as heterozygous variants of MYBBP1A gene, could help clinicians in the interpretation, severity and classification of NIHF.

E-PS-01-031
Analysis of maternal mortality: obstetric direct and indirect causes in Kazakhstan, 2023
A. Sapargaliyeva*, N. Cherepkova, V. Grinberg
*Kazakh National University, Faculty of Fundamental Medicine, Kazakhstan

Background & objectives: In 2023, out of 40 registered cases of maternal mortality in Kazakhstan, our study examined 22 cases. Our objective was twofold: to understand the patterns of maternal mortality and to delineate the interplay between direct obstetric causes and indirect factors.
Methods: The Research Center for Obstetrics, Gynecology, and Perinatology, Department of Pathology conducted a thorough analysis of autopsy reports spanning from January 1st, 2023, to December 31st, 2023 from different regions of Kazakhstan. We divided all cases into direct (12) and indirect maternal deaths (7).
Results: Direct cases included sepsis, cases characterized by abnormal uterine bleeding, preeclampsia, with one of bilateral pneumothorax and 2 cases of massive intracerebral haemorrhages, amniotic fluid embolism, and massive hepatic necrosis
Indirect causes of undiagnosed somatic and oncological diseases included:
Additionally, three cases of maternal deaths at home were documented, where the precise cause remained undetermined due to the low quality of forensic examination.
Conclusion: Analysis of maternal mortality, particularly in the category of "Obstetric Pathology" (direct maternal death), underscores missed opportunities in all cases. Conversely, in the "Indirect maternal death" category, delayed diagnosis of somatic and oncological diseases emerged as a significant concern. Moreover, this analysis shows the predominance of direct maternal mortality.

E-PS-01-032
Metastatic tumour of ovarian sex cord stroma on the anterior abdominal wall: a case report in an elderly woman
A. Sapargaliyeva*, N. Nurgaliyev, S. Serikov
*Kazakh National University, Faculty of Fundamental Medicine, Kazakhstan

Background & objectives: We present a rare case of metastasic tumour of a sex cord originating from the ovary (10x6 cm). Fifteen years prior, the patient underwent supravaginal amputation of the uterus and appendages due to ruptured right ovarian cyst and intrapelvic bleeding.
Methods: Histological examination, including Hematoxylin and Eosin staining, and immunohistochemical analysis (Inhibin-alpha, Calretinin, Caldesmon, CD34, CD99) were used to confirm the tumour's origin.
Results: Hematoxylin and Eosin staining revealed a biphasic tumour comprising areas of spindle cells and nests of round epithelial-like polymorphic cells in the skin and underlying tissue. Immunohistochemical analysis showed positivity for inhibin-alpha and calretinin in epithelioid areas, while caldesmon was positive, and CD34 and CD99 were negative in spindle-ovoid areas. The morphological and immunophenotypic profile suggests a nonspecific tumour of the sex cord stroma arising in endometriosis.
Conclusion: Our case highlights the rare occurrence of ovarian tumour metastasis to an unusual site on the anterior abdominal wall, possibly

attributed to the implantation route of metastasis during the prior surgery of supravaginal amputation of the uterus. The biphasic nature of the tumour suggests its origin from foci of endometriosis.

E-PS-01-033

Retrospective analysis of iatrogenic disorders in obstetric practice: implications for maternal mortality in Kazakhstan

A. Sapargaliyeva*, N. Cherepkova, V. Grinberg
*Kazakh National University, Faculty of Fundamental Medicine, Kazakhstan

Background & objectives: In our study conducted at the Research Center, Department of Pathology, we analysed 22 cases of maternal mortality, focusing on identifying iatrogenic disorders. Our objective was to discern the significance of iatrogenic pathology in understanding thanatogenesis in each case.
Methods: Following the guidelines set by the Ministry of Public Health of the Republic of Kazakhstan, we categorized the identified cases into two groups: Category I, representing erroneous medical influences directly leading to death (4 cases), and Category II, where pathology arose during medical procedures with no direct link to the cause of death (3 cases).
Results: Category I iatrogenic pathology cases included:
- massive tracheal necrosis associated with endotracheal intubation;
- uterine rupture during cesarean section;
- bilateral pneumothorax associated with mechanical ventilation.
- amniotic embolism resulting from cervical laceration due to prolonged induction with oxytocin.
These cases were classified as "iatrogenic medical trauma" and deemed the primary cause of death.
Category II iatrogenic pathology cases:
- 2 cases of unilateral pulmonary contusion after cardiopulmonary resuscitation;
- rib fracture without displacement during cardiopulmonary resuscitation;
These cases were also categorized as "medical trauma" but were unrelated to the cause of death.
Conclusion: Our analysis revealed a notable incidence of medical injuries in obstetric practice, primarily stemming from errors during labor and delivery in intensive care units. While both Category I and Category II iatrogenic pathology were observed, only Category I cases were directly linked to the cause of death. It is imperative to address these medical errors to enhance maternal healthcare outcomes, particularly in intensive care settings.

E-PS-01-034

Unveiling granulomatous arteritis: autopsy findings

A. Sapargaliyeva*, S. Koibakov, R. Kuanyshbekova
*Kazakh National University, Faculty of Fundamental Medicine, Kazakhstan

Background & objectives: Granulomatous arteritis is an infrequent discovery in pathology, often encountered incidentally during autopsies of cases involving aortic dissection. The etiology of granulomatous arteritis typically remains elusive.
Methods: We report the postmortem findings of a 50-year-old Caucasian woman B. admitted to the cardiology centre in critical condition (BP=92/57; heartrate=78 bpm) with a diagnosis of "repeated infarction of the anterior myocardial wall, aortic dissection." The patient succumbed to her condition 7 hours after admission.
Results: An autopsy revealed a dissected aorta extending from the arch to the abdominal aorta, with intraluminal hematoma and luminal obstruction. Microscopic examination of the aorta demonstrated lymphoid cell nonnecrotizing granulomas and extensive aortic sclerosis. Additionally, granulomas were observed within intramyocardial arteries, accompanied by obliteration of the lumen of blood vessels. Histopathological analysis confirmed the diagnosis of non-necrotizing granulomatous arteritis.
Conclusion: The patient's death was attributed to aortic arch dissection and intraluminal hematoma formation leading to luminal obliteration. Nonnecrotizing granulomatous inflammation and partial obliteration of the lumen of blood vessels suggest a cyclical nature of granulomatous arteritis, providing insight into the clinical manifestation of recurrent acute myocardial infarction.

E-PS-01-035

The challenging diagnosis of tetrasomy 12p mosaicism: a case report

S. Ben Tekaya*, T. Tlili, I. Bahri, W. Mokni, N. Ouini, A. Ben Abdelkader, B. Sriha, M. Mokni
*Tunisia

Background & objectives: Pallister-Killian syndrome (PKS) is a rare genetic disorder characterized by mosaic tetrasomy of the short arm of chromosome 12 (12p). We aim to highlight the crucial contribution of autopsy in the diagnosis of this rare condition.
Methods: We are reporting the case of a male newborn of unrelated, apparently healthy
couple. The pregnancy was uneventful. The newborn presented severe respiratory distress and was admitted to the neonatal intensive care unit. He died on day 2 of life and was referred to the pathology department for an autopsy.
Results: On external examination, facial dysmorphism was noted, with orbital hypertelorism, anteverted nostrils, a long philtrum, a thin upper lip, sparse eyelashes and eyebrows, and marked frontotemporal baldness. The feet were small with nail hypoplasia. Internal examination revealed the presence of a major bilateral pulmonary hypoplasia, alongside a large congenital diaphragmatic hernia of abdominal viscera (small intestine, stomach, and transverse colon) into the thoracic cavity. A skin biopsy was performed and submitted for cytogenetic evaluation. Karyotype analysis of skin fibroblasts revealed the presence of a supernumerary isochromosome12p, confirming the diagnosis of PKS.
Conclusion: Prenatal diagnosis of PKS remains challenging. The cytogenetic diagnosis is also difficult due to the tissue-limited mosaicism of tetrasomy 12p. Karyotype from cultured blood lymphocytes is often normal. Cytogenetic analysis from skin biopsies is indicated to confirm the diagnosis. Pathologists and neonatologists should be aware of the suggestive dysmorphic features and malformations associated with this syndrome so that appropriate sampling can be made for cytogenetic confirmation. Genetic counseling is reassuring as PKS is sporadic.

E-PS-01-036

Postmortem imaging for pathologists: imaging findings of chronic diseases with pathologic correlation

N. Solomon*, J. Elifritz, N. Adolphi, H. Sanchez, A. Sailer, J. Kroll, B. Daly, D. Gascho, M. Thali, B. Vermillion, S. Thorn, M. Revzin, A. Sinusas
*Department of Radiology, Yale School of Medicine, USA

Background & objectives: Imaging is increasingly used in postmortem (PM) investigations. In addition to identifying cause of death, it can demonstrate findings reflecting various chronical medical conditions, including those related to consequences of events, habits, or lifestyle choices that bore the ultimate cost.
Methods: This presentation will focus on PM computed tomography (CT) findings, although select PM magnetic resonance imaging (MRI) studies will be included. Imaging findings related to various common medical conditions will be discussed and demonstrated in case examples. A few less common examples will also be included.

Healthy comparison cases will be provided to help emphasize the relevant imaging findings.
Results: Although the scope of nonenhanced PM CT has acknowledged limitations, its capacity to reveal a wide variety of pathologies is similar to that of nonenhanced clinical CT. This presentation will review a variety of chronic medical conditions and their associated imaging findings on non-enhanced PM CT, including pulmonary emphysema, hepatic steatosis, alcoholic cirrhosis, medical renal disease, atherosclerotic cardiovascular disease, heart failure, cerebrovascular disease, diabetes mellitus, and more. Comparisons of imaging findings to depictions of gross pathology for various disease entities is anticipated to aid pathologists' in learning PM CT interpretation.
Conclusion: In the absence of a bullet or a smoking gun, the identification of PMCT findings related to various medical diseases—especially in the presence of potentially associated acute findings—can provide confirmation that death occurred secondary to natural causes and increase confidence in the diagnosis of a medical cause of death.

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E-PS-01-037
High grade diffuse large B-cell lymphoma diagnosed at autopsy - case report and 10-year retrospective review
C. Stacey*, M. Staunton
*Beaumont Hospital, Ireland

Background & objectives: Diffuse Large B-cell Lymphoma (DLBCL) is the most common type of Non-Hodgkin's Lymphoma, accounting for 28-31% of adult lymphomas. The disease is aggressive and patients usually present with rapidly enlarging lymphadenopathy and constitutional symptoms, some however, present with extranodal disease.
Methods: We present the case of a 74 year old gentleman, who died following a sudden cardiac arrest in hospital. At autopsy, a large bilateral perinephric mass was found, encasing both the ureters, as well as surface deposits on the kidneys. Samples of this perinephric mass, as well as all other organs, were taken for analysis.
Results: Histologically, the perinephric mass showed a sheet-like infiltration of malignant atypical cells with vesicular chromatin and prominent nucleoli, most consistent with atypical B lymphoid cells. A panel of immunohistochemistry was performed to confirm lymphoma and identify the subtype. The tumour cells stained positive for CD20, CD79a and BCL2, weakly positive for BCL6 & MUM1 and negative for pan-cytokeratin CD3, CD10, CD15 & CD30. cMYC also showed weak focal staining, 5-10%. This staining diagnosed a diffuse large B-cell lymphoma (DLBCL), with an activated, post-germinal centre phenotype. Other than myocardium, all other organs sampled, including kidney, liver, spleen, lungs and gastrointestinal tract were infiltrated by lymphoma, despite looking grossly uninvolved.
Conclusion: The case described, is an unusual presentation of DLBCL, discovered at autopsy. To evaluate the rarity of this presentation, a retrospective review of autopsies from 2014 to 2024 was carried out to discover other cases of lymphoma discovered at autopsy. 10 cases were found of lymphoma discovered at autopsy and not previously known. In 4 of the 10 cases, the lymphoma was a either the direct cause of death or a significant contributing factor to the cause of death.

E-PS-01-038
Comparative analysis of pre-mortem and post-mortem diagnoses in deceased patients in clinical centre of Vojvodina over a three-year period
M. Šunjević*, A. Ilić, I. Stanišić, V. Trivunović, Ž. Panić, M. Panjković
*Clinical centre of Vojvodina, Serbia

Background & objectives: Autopsy represents a significant medical tool that serves to prove the time and cause of death, as well as the diseases that led to it. The study aimed to perform a comparative analysis of clinical and post-mortem pathohistological diagnoses.
Methods: The retrospective study included autopsy reports of deceased patients in the university hospital over three years. The sample consisted of a group of 355 adult patients analysed by gender, age, autopsy years, and clinics at which patients were treated. The Goldman classification was used for discrepancies between clinical and post-mortem diagnoses.
Results: Among deceased patients, most of them were men, according to an analysis of autopsy records. The majority of patients died at the Emergency Center, Clinic for Abdominal and Endocrine Surgery and Clinic for Anesthesia, Intensive Care and Pain Therapy. The dominant age category was 71-80 years (27%). The class marking the divergency of diagnoses, that is class I, was the most represented in the analysis of 2018 and 2019 (33.8% - 2018 and 31.1% - 2019), while the class marking minor divergency of diagnoses (class IV) had the highest percentage in the 2017 analysis (28.6%), and the class I was defined in 27.4% of cases.
Conclusion: The differences in clinical and pathohistological diagnoses should be expected on various levels, due to the circumstances during diagnostic procedures and treatment of patients.

E-PS-01-039
Influence of maternal age on extremely preterm birth and causes of death of extremely preterm infants
V. Trivunović*, S. Ivić, I. Stanišić, Ž. Panić, T. Lakić, M. Panjković
*University clinical centre of Vojvodina, Novi Sad, Serbia
Background & objectives: Extremely preterm infants (EPI) (< 28 weeks gestation) are at high risk for death and disability. As maternal age at pregnancy increased over the years, we investigated its influence on EPI as well as the most common causes of death.
Methods: A retrospective study was conducted at the Center for Pathology and Histology of the University clinical centre of Vojvodina. Querying patients' histories and autopsy findings, we identified 51 autopsies of extremely preterm infants at our institution in three years (2021-2023). Influence among the collected parameters (gestational age, maternal age, medical conditions, and cause of death) were statistically analysed.
Results: Maternal's average age was 31,32±5,87 years. The average gestational week at birth was 25 2/7±1 3/7 while the average time of survival was 6,37±9,12. 4 women had a history of hypertension and 2 had a history of diabetes. Linear regression showed statistical significance ($p<0,05$) of age influence on gestational week. With every year of the maternal's age, gestational week at birth increased for 0,08 days. Intraventricular hemorrhage and neonatal respiratory distress syndrome were the main causes of death in almost all of the cases (90,19%) dominantly as a combination of two (74,5%). Necrotizing enterocolitis was established as the main diagnosis in 5 newborns, all between the 25th and 28th week.
Conclusion: Despite technological development and improvement in neonatal care, extremely preterm birth remains a challenge and is a significant cause of infant and child morbidity and mortality. Maternal age is a risk factor for the unfavourable outcome of pregnancy. The use of glucocorticoids, surfactants, and ventilation contributed to higher overall survival and a decrease in pulmonary-related deaths, making necrotizing enterocolitis more common as a cause of death, especially in later gestational weeks.

E-PS-01-040
Case report of a foetal ARCN1 - related syndrome and literature review
P.I. Voinescu*, M.A. Abad, G. Barrios Millán, R.M. Regojo
*La Paz University Hospital, Spain

Background & objectives: ARCN1-related syndrome, described by Izumi in 2016, is characterized by facial dysmorphisms, micrognathia, short stature and developmental delay. With only 18 cases reported in the literature (5 foetus), our aim is to report an additional foetal case of this syndrome.
Methods: Our findings have been obtained from the necropsy of a 28+1 weeks stillborn interrupted due to foetal malformation and intrauterine growth restriction diagnosed in 20 weeks with genetic confirmation of ARCN1 mutation. We also performed postmortem radiographs and placental study. Furthermore, we performed a review of the literature.
Results: The 28+1 weeks stillborn, weighing 1000 g (p25-50) with phenotypical alteration: micrognathia, broad nasal bridge and low set ears . Postmortem radiological study reported absence of nasal bone, rhizomelicshortening of large bones, ribs shortening y brachymesophalangia of 5th fingers. Regarding the central nervous system, we identified the presence of cerebellar dysplasia. The histological study of the placenta revealed the presence of high-grade chronic villitis and abnormal villous maturation.
Conclusion: The present report highlights a rare case of foetal ARCN1-related syndrome, characterized by facial dysmorphisms, micrognathia and rhizomelic shortening, underscoring the importance of multidisciplinary work with the prenatal echography, the genetic study and a complete postmortem examination. Thesefindings emphasize the syndrome's multisystem involvement and potential implications for foetal development specially the cerebellar dysplasia related with developmental delay, autism and seizures.

E-PS-01-041
HIV- infection in forensic medicine practice
V. Zinserling*, E. Esaulenko, V. Isakov, G. Pavlova, D. Slatina
*VA Almazov Research Center, Saint-Petersburg, Russia

Background & objectives: At the end of 2022, 461,879 patients with HIV infection died in Russia, a significant part were autopsied in forensic medical service units. There is no description of the results of such studies in the literature.
Methods: Analysis of deaths with HIV infection at the Bureau of Forensic Medicine of St. Petersburg. Retrospective study for 2018-2022. 268 cases - 2% of the total number of corpses examined. During, blood was taken for ELISA. In 2018 there were 91 such deaths, in 2019 – 55, in 2020 – 56, in 2021 – 34 and in 2022 – 32.
Results: Women - 21.3%, and men - 78.7%. Average age 40.6 y. Increase in the age of deaths: 2018 - 38.3, and in 2022 - 43.1. Corpses were delivered from home - 48.5%, in 41.0% - from various hospitals, in 10.5% of cases from the street. Violent death in 33.0%. Death due to poisoning with methadone, alcohol and other substances in 29.5%. Causes of death with concomitant HIV infection: diseases of the cardiovascular system - 10.8%; alcoholic cardiomyopathy – 8.6%; new coronavirus infection – 3.7%; toxic nephropathy – 0.7%, oncopathology - 4.1%, pneumonia - 6.3% of cases. Liver diseases - in 4 cases, one case each of pancreatitis and peritonitis.
Conclusion: 29.5% of patients died from complications of HIV infection: tuberculosis in 14 (5.2%) patients, cytomegaly in 4 cases, pneumocystis in 3. Meningitis and encephalitis - three times.Over the past 5 years, among the deceased admitted for forensic medical examination, has been a decrease of HIV-infected. In non-violent deaths, respiratory diseases prevailed. In 13.0%, HIV infection was combined with tuberculosis with generalized lesions of the lymph nodes. Cytomegaly and pneumocystosis were noted. Among concomitant diseases, liver damage predominated.

E-PS-02E-Poster Session Breast Pathology

E-PS-02-001
Increased Stromal ENPP1 expression in malignant phyllodes tumour correlates with poor prognosis
S.S. Ahmed*, J. Iqbal, V.C.Y. Koh, J.X. Seow, D.M.N. Nur, R. Shi, J.Y.S. Chan, P.H. Tan
*Singapore General Hospital, Singapore

Background & objectives: ENPP1 degrades extracellular 2'3'-cyclic GMP-AMP (cGAMP) and negatively impact immune stimulator Interferon gene (STING). Mutation in ENPP1 leads to loss of its degradation ability and increases susceptibility to immunotherapy. We analysed ENPP1 expression in malignant phyllodes tumour (mPTs).
Methods: Utilizing tissue microarrays, immunohistochemistry was performed on formalin-fixed, paraffin-embedded tissue. ENPP1 expression in the stromal cells of the mPts was analysed. The comparison of the clinicopathological data was done using Chi-square test. Disease free survival (DFS), disease specific survival (DSS) & metastasis free survival (MFS) were estimated with Kaplan-Meier analysis. The two-sided statistical significance level was set at 0.05.
Results: ENPP1 expression in the stromal cells of mPTs was analysed in relation to patient age and ethnicity, tumour features such as size, stromal cell hypercellularity, overgrowth, atypia & mitosis, tumour borders (circumscribed and permeative) and malignant heterologous elements and disease outcomes. ENPP1 expression significantly correlated with permeative borders (p=0.011). ENPP1 expression was associated with poor DFS (p=0.011), DSS (p=0.047) and MFS (p=0.032).
Conclusion: ENPP1 expression is associated with poor survival in mPTs, Point mutation in ENPP1 render it susceptible to immunotherapy and could be targeted as part of an immunotherapy regimen.

E-PS-02-002
HER-2 equivocal invasive breast carcinomas: morphological and molecular correlation
O. Ait Ouhssain*, C. Dabaj, H. Rais
*Morocco

Background & objectives: The molecular classification of invasive breast carcinomas has allowed to distinguish five molecular groups: luminal A, luminal B, Her2/neu, basal-like and unclassified. Our objective is to achieve a morphological and molecular correlation of equivocal HER 2 infiltrating breast carcinomas.
Methods: This retrospective study is spread over 45 months, comprising 111 patients collected at the Mohammed VI University Hospital for diagnosis and monitoring. The equivocal Her2-infiltrating breast carcinomas are analysed morphologically and molecularly and classified as amplified and non-amplified.
Results: Eighty-point two percent of equivocal infiltrating breast carcinomas received are non-amplified and 19.8% are amplified. The non-amplified group contains the lowest rate of associated CIS, grade III, vascular emboli as well as associated metastases and mitoses; while the amplified group represents a high rate of grade III, a significant proportion of vascular emboli, and a positive percentage of progesterone and estrogen as well as a positive Ki67.
Conclusion: Amplified equivocal infiltrating breast carcinomas are different from non-amplified ones and have a pejorative prognosis. The clinicopathologic features are consistent with the molecular profile so it should be considered as prognostic factors.

E-PS-02-003
Molecular alterations of breast carcinoma: a single-centre experience
M.H. Toper, K.E. Akar*, H. Kaya
*Department of Pathology, Marmara University, Turkey

Background & objectives: Breast carcinomas are the most commonly seen and molecularly heterogeneous tumours in women. Our study

aims to share preliminary results regarding molecular tests conducted at our centre.
Methods: We conducted targeted genome sequencing of 34 samples from female patients with breast carcinoma using The Archer® VariantPlex® Solid Tumour kit, additionally analysed 8 samples from breast carcinoma patients using the BRCA MASTR Plus Dx kit on the Illumina NextSeq/Novaseq device, between 2021 and 2024.
Results: The median age of the 39 patients in our study was 47 (range: 28-83). The most frequently mutated gene was TP53 (n = 12, 35.3%), followed by PIK3CA (n = 8, 23.5%), KRAS (n = 2, 5.9%), PTEN (n = 2, 5.9%), AKT1 (n = 1, 2.9%), ESR1 (n = 1, 2.9%), CDH1 (n = 1, 2.9%), and IDH1 (n = 1, 2.9%). Among cases with TP53 mutation, PIK3CA mutation was observed in 2 cases, KRAS mutation in 2 cases, and PTEN/CDH1 mutations in 1 case. Microsatellite instability was not detected in the cases. BRCA1 mutation was detected in one tumour (n = 1, 12.5%) among 8 patients.
Conclusion: Due to the majority of cases in our study being constituted of triple-negative cases, TP53 mutation, which is reported to be more common in these cases in the literature, was observed frequently. Most of the mutations we detected in our study have been reported to be associated with prognostic, predictive, and drug resistance implications, making their identification in breast tumours significant.

E-PS-02-005
A comparative analysis of WHO and MD Anderson classification of phyllodes tumours: impact on patient outcomes
C. Albarracin*, Y. Wu, L. Goetz, Q. Ye, N. Sneige, S. Pasyar, R. Bassett, H. Chen, I. Bedrosian
*UT MD Anderson Cancer C, USA

Background & objectives: In 1992, MD Anderson (MDA) initiated a categorical diagnostic schema for phyllodes, incorporating stromal overgrowth, infiltrating margins, mitosis >10/10 hpf and stromal nuclear pleomorphism. We assess concordance between, and impact on outcomes, of World Health Organization criteria and MDA criteria.
Methods: A retrospective study was conducted on 118 cases diagnosed as phyllodes tumour from 2008-2019 at our institution. Criteria used by MDA and the WHO were applied to classify these tumours. Clinical data, pathologic findings and patient outcomes were collected using the patients' electronic medical records.
Results: Local recurrence is significantly associated with stromal overgrowth (p 0.06) and extent of stromal cellularity (p 0.08). Metastasis significantly associated with stromal overgrowth (p<0.001), atypia (p 0.002), extent of stromal cellularity (p 0.003) and mitosis (p 0.03). In univariate analysis stromal overgrowth, >10 mitosis and infiltrative borders were significantly associated with overall survival There were 51 benign and 35 borderline cases by MDA and WHO criteria. Of 32 malignant PT (MPT) by MDA, 19 were reclassified as borderline by WHO due to absence of some of the criteria. Metastasis in these reclassified borderline PT occurred in 4/19 (21%) compared to 2/32 (5.7%) in borderline PT diagnosed by both MDA/WHO criteria.
Conclusion: Stromal overgrowth is significantly associated with worse local recurrence, distant metastasis and overall survival. While MDA and WHO criteria demonstrate good concordance in diagnosing benign and borderline PT, a significant number of MPT by MDA criteria were reclassified to borderline PT by WHO criteria; with several of the reclassified tumours demonstrating aggressive tumour behaviour. The median survival is similar between groups whether classified by WHO or MDA criteria. Additional validation is required with larger cohort.

E-PS-02-006
Immunohistochemistry in the evaluation of cauterized margins in breast surgery specimens
S. Almási*, G. Cserni
*Department of Pathology, Albert Szent-Györgyi Medical School, University of Szeged, Hungary

Background & objectives: In daily breast pathology practice, interpretation of cauterized margins of breast conservative surgery specimens might be challenging. Our aim was to find a combination of immunostains, which could be helpful in categorizing cautery damaged neoplastic and non-neoplastic tissues.
Methods: We analysed the value of estrogen receptor (ER), progesterone receptor (PR) and keratins 5&14 (CK5, CK14) immunohistochemistry (IHC) retrospectively to determine the nature of cauterized tissues at the margins, in 34 lesions from 23 patients.
Results: With the examination of HE stains 27 cases were of uncertain nature. The majority (18/27) could be classified as non-neoplastic or neoplastic and 6/27 of the remaining lesions could be favoured as neoplastic or non-neoplastic, with only 3/27 remaining uncertain. All four IHC reactions proved to be helpful in the differentiation of these lesions in almost half of the cases. In 19/27 lesions, three or four IHC stains were helpful in the classification process. The keratins (CK5 and CK14) were the most helpful. With the combination of this quadruple IHC staining we could categorize 23 of the 27 lesions.
Conclusion: Based on our results, CK5, CK14, PR and ER IHC reactions can help in distinguishing between cautery damaged neoplastic and non-neoplastic tissues. Despite the fact that keratins were the most advantageous, and CK5 and/or CK14 may be sufficient in their own, all four IHC may yield the best support for decision making. The essential approach is that the results must be interpreted with caution, in the context of the given patient's disease.

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E-PS-02-007
Invasive lobular carcinoma of the breast: clinicopathological insights into long-term prognosis
M. Alzamora*, J. Castro, N. Coimbra, C. Leal, J. Silva
*Department of Pathology, Portuguese Oncology Institute of Porto (IPO-Porto), Portugal

Background & objectives: Invasive lobular carcinoma (ILC) reportedly has a favourable short-term prognosis, yet studies indicate similar or worse long-term outcomes than invasive breast carcinoma (IBC)-NST. Despite distinct clinical, pathological, and molecular profiles, management and follow-up strategies for ILC and IBC-NST remain similar.
Methods: With recent advancements, it's crucial to comprehend which factors determine worse long-term prognosis, aiding in distinguishing patients who might benefit from additional therapy. Our study aimed to identify clinicopathological factors associated with long-term outcomes in ILC. We collected data of all patients diagnosed with ILC, from 2010-2013, who underwent primary resection, without neoadjuvant therapy, at our institution.
Results: A total of 154 patients were included, with a median age at diagnosis of 55.5 years. Median tumour size was 22.0mm, with 33% showing multiple tumours, mostly of the same type. The majority (85.7%) were histological grade 2, 7.8% grade 1, and 6.4% grade 3. Most cases were hormone receptor (ER and PR) positive and HER-2 negative, with 32% presenting negative/low (<20%) PR expression. Lymphovascular invasion (LVI) was observed in 16% of cases. Lymph node metastasis (LNM) was present in 41%.
Overall survival (OS) rates were 89.6% at 5 years and 85.1% at 10 years follow-up. Histologic and nuclear grade, as well as LVI and LNM, significantly correlated with OS.
Conclusion: Despite favourable prognostic features, there is still ongoing debate regarding ILC outcome. Risk stratification and

therapeutic decision pose challenges, particularly in early-stage cases with intermediate-risk characteristics.
We focused on ILC patients with long-term follow-up (10+ years post-diagnosis), correlating several clinicopathological features, such as size, histologic pattern, grade, and receptor status, with OS and disease-free survival.

Improved understanding of ILC behaviour and prognosis could improve management strategies, identifying candidates that benefit from additional therapies, while avoiding overtreatment in low-risk patients.

E-PS-02-008
Granulomatous mastitis: a rare benign entity mimicking carcinomatosis
R. Ayadi*, E. Braham, K. Mekni, K. Belaid, R. Yaiche, I. Mallek, O. Ismail, C. El Fekih, A. Ayadi
*Department of Pathology, Abderrahmen Mami Hospital, Tunisia

Background & objectives: Granulomatous mastitis (GM) is an uncommon chronic inflammatory disease of the breast, which is often difficult to differentiate both clinically and radiologically from malignancy, thus posing a diagnostic dilemma.
This study discusses the causes and clinocopathological characteristics of GM.
Methods: We retrospectively reviewed a pathology database covering 2004 to 2023. We identified patients who fit the histologic criteria of GM. The diagnosis was confirmed by either core needle biopsy (CNB) or excisional biopsy. All slides were examined with hematoxylin-eosin. All of the cases were reviewed by a pathologist.
Results: There were 43 female patients, aged between 32 and 673 years with a mean of 49,69. 32 patients had breast-fed in the last 5 years, but none were lactating at the presenting time.4 patients had a bilateral lesion. 27 patients presenting with mastitis had inflamed skin and pain. A histopathologic examination was performed on the specimens from CNB (n=37) or excisional biopsy (n=6). Microscopically, granulomatous reaction was composed of epithelioid cells and multinucleated giant cells with lymphocytes and neutrophil polymorphs around the breast lobules. Caseous necrosis was observed (n=2) and microabscess formation also observed (n=20). idiopathic with undetermined causes was the most common etiology (95,34%), followed by tuberculosis (4,65 %).
Conclusion: Diagnosis of GM is challenging due to its nonspecific clinical presentation and the similarities of radiographic evaluation to other inflammatory breast diseases or malignancy and which may be misdiagnosed as carcinoma. The diagnosis of this entity must be based on a multidisciplinary approach.

E-PS-02-009
Unusual phyllodes tumour presenting in two adolescent girls
A. Arnout*, E. Bamac, L. Alarcon, C. Kaur
*St Georges Hospital, United Kingdom

Background & objectives: Phyllodes tumours are rare in adolescent girls and only a few cases have been reported.
Methods: We present two excised phyllodes tumour cases after a B3 fibroepithelial lesion diagnosis on breast core biopsies. One is a 15-year-old presented with bilateral breast masses and the other is a 17-year-old presented with three masses in the left breast.
Results: Macroscopically, the phyllodes lesion for the first case was described as cream, fibrofatty tissue measuring 80mm in maximum diameter and shows homogenous cream, whorled, and mucinous cut surface, while the second tumour was a classical well-circumscribed fibroadenoma. On the other hand, in the second case, the phyllodes lesion was macroscopically described as an encapsulated cream breast lump measuring 32mm in maximum diameter showing a tan, multi-lobulated and glistening cut surface. The other two masses were well-circumscribed fibroadenomas. Microscopic examination reveals, in both lumps features of a phyllodes tumour, with borderline features in the second. Both cases were reviewed by the Nottingham team who concurred with the diagnoses.
Conclusion: It is important to recognise these tumours at this age because they tend to grow rapidly and recur if not fully excised.

E-PS-02-010
Factors predicting complete pathological response to neoadjuvant chemotherapy in breast carcinoma
O. Belhadj*, O. Boudaouara, W. Ben Makhlouf, M. Triki, M. Zghal, L. Ayadi, T. Sellami Boudawara, W. Ben Kridis
*Department of Pathology, Habib Bourguiba University Hospital, Sfax, Tunisia

Background & objectives: Neoadjuvant chemotherapy (NAC) improves outcomes of patients with non-metastatic breast cancer once a complete pathological response (pCR) to chemotherapy is achieved.
We aim through this study to identify clinico-pathological factors predictive of a pCR after NAC in breast carcinoma.
Methods: Our study included 97 patients with breast carcinomas treated by NAC followed by surgery, between 2013 and 2023. The pCR, defined according to the RCB score, corresponds to the absence of residual invasive carcinoma in both breast and lymph nodes. Chi-square test was used to investigate associations between pathological response and various clinico-pathological parameters. A p-value <0.05 was statistically significant.
Results: The mean age of patients was 48 years. Oestrogen or progesterone receptors were positive in 73.2% of cases. About half of cases (50.5%) overexpressed HER2. Luminal B breast cancer was the most frequent molecular subtype (46.4%) followed by HER2-positive molecular subtype (14.4%). A sequential NAC regimen based on anthracyclines and taxanes was used in 81.4% of cases. A pCR was achieved in 11 cases (11.3%). In univariate analysis, pCR was associated with the negativity of oestrogen and progesterone receptors ($p<0.005$ and $p=0.019$ respectively), a HER2-positive molecular subtype ($p < 0.001$) and a sequential NAC regimen ($p = 0.039$).
Conclusion: The occurrence of pCR is usually a rare in breast cancers treated by NAC. Indeed, according to the available data, pCR rates vary between 10 and 30%. Our study suggested that negative hormone receptor status as well as HER2-positive molecular subtype are significantly associated with pCR. Furthermore, the use of a sequential NAC regimen was predictive of pCR in our series.

E-PS-02-011
Mucinous cystadenocarcinoma of the breast: a case report
K. Ben Lazreg*, L. Njim, A. Bellalah, S. Ben Hammouda, A. Zakhama, M. Njima
*Fattouma Bourguiba University Hospital, Monastir, Tunisia

Background & objectives: Mucinous cystadenocarcinoma(MCA) is a rare and recently described primary breast cancer with strikingly similar histomorphology to ovarian, pancreatic, and gastrointestinal counterparts. Less than 30 cases were reported in English literature. Herein, we report another rare case.
Methods: A 70-year-old woman presented with a lump in the right breast. Mammography revealed a Mass of 8x10 cm involving the union of the right external quadrants. The patient underwent a needle biopsy showing intermediate nuclear-grade carcinoma in situ(CIS) with necrosis. Therefore, a right mastectomy was indicated.
Results: The grossing examination showed a cystic mass measured 7.5cm with mucoid content and a focally thickened wall with

endoluminal tumour buds. Histopathology revealed variably sized interconnected mucin-filled cysts lined by cubic epithelium showing long and branched papillae. Small clusters were seen floating in the mucin. Intracellular and extracellular mucin was stained with bleu alcian. Tumour cells showed moderate atypia and low mitotic activity. There were foci of intermediate nuclear grade CIS with necrosis. Tumour cells were negative for neuroendocrine markers. Our case was estrogen and progesterone receptors positive, and human epidermal growth factor receptor-2 negative with a low proliferative index. There were no metastases in the 13 axillary lymph nodes.
Conclusion: unlike its histological counterparts of the ovary and pancreas, the MCA is a very rare entity. It occurs after menopause with a mean age of 61 years. It's composed of cysts lined by cells with secretion of mucus. MCA of the breast needs to be differentiated from mucinous carcinoma. The latter does not form cystic structures. MCA is frequently associated with CIS. MCA is usually triple negative. In addition to our observation, only two hormonal receptor-positive cases were reported.

E-PS-02-012
Molecular profile of breast cancer experience of pathology department university hospital of Marrakech between 2010 and 2022
C. Benallal*, I. Es-Saoudy, H. Asmouki, H. Rais
*Department of pathology UHC Mohamed VI Marrakech, Morocco

Background & objectives: Breast cancer is the most frequent malignancy among women in Morocco. In this study, we provide an approach on the molecular invasive breast carcinoma subtypes in the region of Marrakesh.
Methods: We analysed 2040 breast invasive carcinoma cases diagnosed at the pathology department of the Mohamed VI University hospital, Marrakesh between January 2010 and June 2022. Molecular subtypes were determined and their associations with the clinicopathological characteristics of the tumours and prognostic factors were examined.
Results: The mean age at diagnosis was 50,1 years. Invasive ductal carcinoma was the predominant histological type (81,96%), followed by lobular invasive carcinoma (6,57%). Histological grade II tumours were the most frequent (69.46%), followed by advanced histological grade (22,7%). Lymph node positive tumours were observed in 61.55% of cases. Most tumours were hormone receptor positive (72,25%) and 22,65% were HER2 positive.Unlike most international molecular profiles Luminal B was the most common molecular subtype (36.39%) followed by Luminal A (18,95%), Triple Negatif (12,38%) and HER2 (19,65%).Luminal B subtype had a poorer prognosis than Luminal A. Compared with Triple Negative subtype, HER2 subtype tend to spread more aggressively and had a poorer prognosis.
Conclusion: Unlike Western countries, breast cancer occurs at an earlier age and is diagnosed at a more advanced stage in Marrakesh. In this region, hormone receptor-positive tumours are predominant and so the majority of breast cancer patients should benefit from hormone therapy. HER2 subtype presents an aggressive tendency, suggesting the importance of anti-HER2 therapy. This study will contribute in developing appropriate screening and cancer management strategies in Morocco.

E-PS-02-013
Refining the pathologic features of invasive pleomorphic lobular carcinoma: a comprehensive study
I. Blazquez*, J. Bosch, J. Azcarate, A. Petit, E. Guerra, A. Gumà, S. Pernas, M.A. Garcia Tejedor, M.T. Soler
*Hospital Universitari de Bellvitge, Spain

Background & objectives: Invasive pleomorphic lobular carcinoma (IPLC) is a variant of lobular carcinoma. Traditionally considered to have an aggressive clinical course, there is no consensus on diagnostic criteria. Our work intends to characteritze the pathologic features of this variant.
Methods: Cases diagnosed as IPLC on surgical specimen within the past three years at our centre were systematically collected. Information regarding previous core needle biopsy (CNB), as well as pathological data, e-cadherin and p53 imexpression were recorded.
Results: We obtained 22 cases, 21 women and one man. On CNB, 72 %(n=16) were histologic G2 and 18%(n=4) were G3. Only 4 cases (18%) were diagnosed as IPLC on CNB. 68%(n=15) were Luminal and 32%(n=7) triple negative. Mean Ki67: 29.3%. E-cadherin: complete loss in 65% and aberrant expression in 35%. P53: moderate-weak expression in 15%. Tumour-infiltrating lymphocytes (TILs): 68% (mean TILs:17.2%). On surgical specimen, 40%(n=9) were upgraded to G3. Most IPLC were diagnosed at advanced stages, exceeding pT2. Nine patients underwent neoadjuvant treatment resulting in partial response with a mean fibrosis of 45%.
Conclusion: IPLCs are high grade tumours that are often undergraded and underdiagnosed on CNB, hinting that CNBs may underrepresent the heterogeneity of this variant. P53 and E-cadherin are of limited usefulness for diagnosing this histological subtype. None of the patients receiving neoadjuvant chemotherapy had complete response.

E-PS-02-014
Complete pathological response to neoadjuvant chemotherapy and its impact on breast cancer outcomes
O. Boudaouara*, W. Ben Makhlouf, M. Bouhamed, S. Graja, S. Charfi, T. Sellami Boudawara, W. Ben Kridis
*Tunisia

Background & objectives: Several studies supported the prognostic value of a complete pathological response (pCR) to neoadjuvant chemotherapy (NAC) in breast cancer. This study attempted to investigate the impact of pCR on overall survival (OS) and progression-free survival (PFS).
Methods: Our study included 97 patients with breast carcinomas treated by NAC followed by surgery, between 2013 and 2023. Data were retrieved from each patient's medical record. Mean OS and PFS were calculated using the Kaplan-Meier method. A univariate analysis using log-rank test was then performed to identify prognostic factors associated with a better survival. A p-value <0.05 was statistically significant.
Results: The mean age of patients was 48 years with a mean tumour size of 59 mm. According to molecular classification, luminal B and A breast cancer were the most frequent molecular subtypes (72.1%) followed by HER2-positive subtype (14.4%). Mean OS and PFS were 84.25 months and 56 months respectively. A pCR was achieved in 11 cases (11.3%). On univariate analysis, pCR achievement was significantly associated with a longer PFS in both whole cohort and HER2-positive breast cancer patients ($p=0.03$ and $p=0.02$, respectively). As such, pCR was implicated in a better OS, but relationship was statistically significant in only HER2-positive breast cancer group ($p=0.02$).
Conclusion: Our findings confirm that achieving pCR after NAC was notably related to the improvement of PFS and OS, especially for patients with HER2-positive breast cancer. Thus, pathologist's role seems to be crucial in predicting long-term outcomes through assessing the quality of pathological response to NAC. Further researches should focus on optimizing treatment regimens to increase pCR rates and improve outcomes.

E-PS-02-015
Predictors of complete pathological response to neoadjuvant chemotherapy in patients with HER2 overexpressing breast cancer
O. Boudaouara*, W. Ben Makhlouf, S. Makni, M. Mellouli, W. Ben Kridis, T. Sellami Boudawara, C. Chaari
*Tunisia

Background & objectives: Several studies agreed that Her2-overexpression in breast carcinoma was predictive of a complete-pathological-response (pCR) to neoadjuvant-chemotherapy (NAC), particularly when anti-Her2 therapy (e.g. trastuzumab) was incorporated into the NAC-regimen. This study investigates clinico-pathological factors predictive of pCR after NAC in HER2-overexpressing-breast-carcinomas.
Methods: Our study included 34 patients HER2-overexpressing-breast-carcinomas treated by NAC (± trastuzumab) followed by surgery, between 2013 and 2023. The pCR, defined according to the RCB score, corresponds to the absence of residual invasive carcinoma in both breast and lymph nodes. Chi-square test was used to investigate associations between pathological response and various clinico-pathological parameters. A p-value <0.05 was statistically significant.
Results: The mean age of patients was 49 years. Oestrogen or progesterone receptors positivity was noticed in 73.5% of cases. Luminal-B breast carcinomas accounted for 70.5% of cases followed by HER2-positive breast carcinomas (29.5%). A sequential chemotherapy regimen based on anthracyclines and taxanes was used in all cases. Targeted anti-Her2-therapy (trastuzumab in all cases) was added to NAC regimen in 47% of cases. Seven patients (20,6%) reached pCR. In univariate analysis, negative oestrogen and progesterone receptor status was significantly associated with pCR ($p<0.024$ and $p=0.012$ respectively). The pCR rate was three-times higher in patients receiving combined NAC with anti-HER2-therapy than in those with NAC alone (12% versus 4% ; $p=0.03$).
Conclusion: The present study showed that hormone-receptors-negative-breast cancers respond better to NAC than their hormone receptor-positive counterparts. Moreover, the use of neoadjuvant anti-Her2-therapy combined with NAC leaded to higher pCR rates among HER2-overexpressing breast carcinomas. Yet, factors influencing the quality of response to NAC remain still unclearly established.

E-PS-02-016
Comparison of pathological parameters, hormone receptor, Cerbb2 and Ki67 profile before and after neoadjuvant chemotherapy in breast cancer
G.H. Cavus*, T. Ozturk, C. Turker Saricoban
*Istanbul University-Cerrahpasa, Cerrahpasa Medical School, Turkey

Background & objectives: Neoadjuvant chemotherapy (NAC) is increasingly preferred treatment method. In our study, pathological parameters, hormone receptor, CerbB2 and Ki67 profiles compared before and after NAC, and aimed to determine an additional parameter that can help the prediction of the patient's prognosis.
Methods: In the Department of Medical Pathology, Cerrahpaşa Faculty of Medicine, between 2016 and 2023, cases reporting breast biopsy before chemotherapy and surgery material after chemotherapy were screened. 174 patients diagnosed with primary breast cancer, whose histological grade, immunohistochemical estrogen receptor (ER), progesteron receptor (PR), CerbB2 and Ki67 data were available before and after chemotherapy, were included in the study.
Results: It was seen that cases with a higher histological grade before NAC had a higher response rate to NAC. In the comparison before and after NAC, it was observed that PR showed a significant decrease. In addition, when the cases with a CerbB2 score of 3+ before NAC and those with a score of 2+ and HER2 amplification detected by SISH were compared with each other, it was determined that patients with a score of 3+ at the beginning responded better to NAC.
Conclusion: When deciding on NAC, detailed examination of histopathological parameters and molecular subgroups at the stage when the patient is first diagnosed contains important information in terms of predicting the NAC decision, treatment dose and prognosis of the patient at the first diagnosis stage and will contribute greatly to planning personal treatment. has been considered.

E-PS-02-017
A comparative analysis of E-cadherin expression in invasive lobular carcinoma, in situ carcinoma and normal breast epithelium
A. Cernat-Stefan*, L. Djerroudi, A. Vincent-Salomon
*Institut Curie, France

Background & objectives: Lobular carcinoma in situ (LCIS) and invasive lobular carcinoma (ILC), as opposed to ductal carcinoma in situ (DCIS) are characterized by loss of tumour cell cohesion. LCIS and ILC lack E-cadherin immunostaining, although patterns of aberrant expression have been described.
Methods: In a series of 245 ILC from our institution, the E-cadherin expression (clone NCH38) was retrospectively assessed in LCIS, DCIS and normal mammary glands associated with invasive carcinoma. E-cadherin percentage, H-Score and pattern of expression were evaluated, as well as myoepithelial cells displacement with LCIS pagetoid spreading.
Results: LCIS was present in 152 out of 245 ILCs (62%). In 120 (78.94%) LCIS cases, myoepithelial cells displacement with pagetoid spreading was observed. Out of the 152 LCIS, 84 (55.23%) had an aberrant E-cadherin expression and the predominant pattern was membranous incomplete (90.5%). E-cadherin staining was stronger in 51 (33.55) LCIS than the surrounding ILC and 7 LCIS (4.6%) demonstrated a weaker immunostaining.
DCIS was a concomitant finding in 35 out of 245 ILCs (14.3%). One case displayed a cytoplasmic staining for E-cadherin and 11 (31.5%) cases showed a decreased expression.
In 23 cases (9.2%), the normal breast glands demonstrated a decreased E-cadherin expression, with an H-Score less than 200.
Conclusion: In situ carcinomas of the breast may show an aberrant staining for E-cadherin. In the case of LCIS, a pitfall in evaluating E-cadherin expression is the common occurrence of myoepithelial cells displacement. In one third of cases, the LCIS component showed a higher expression of E-cadherin than the invasive component. The molecular mechanism underlying this aberrant E-cadherin staining in LCIS component remains to be determined.

E-PS-02-018
Periductal stromal tumour: a case report of the 22nd case in the literature
D. Chiba*, O. Bado, H. Hamchi, I. Bahri, W. Mokni, S. Bentekaya, B. Sriha, M. Mokni
*Department of Pathology, Tunisia

Background & objectives: Periductal stromal tumours(PTS) are rare biphasic tumours of the breast that exhibit low-grade malignancy.Only 21cases have been reported in the literature.Since the characteristics of this entity haven't been well defined,we thought it would be interesting to present this case.
Methods: We report the observation of a postmenopausal 61-years-old woman, who presented with a left breast mass, without ipsilateral lymphadenopathy. The patient underwent a mastectomy and was diagnosed with periductal stromal tumour after morphological and immunohistochemical analysis in our Department of Pathology at Farhat Hached Hospital in Sousse-Tunisia.
Results: On macroscopy, we found a firm mass measuring 16 cm long axis, occupying all quadrants,poorly limited in places,yellowish in appearance with myxoid and cystic changes.
Histologically, it was a biphasic tumour with predominant stromal component composed of moderate cellularity,made up of several cell types of which myofibroblastic spindle cells were predominant.This stromal component surrounded benign ducts in the absence of clear "leaf-like".Tumoural cells showed positive stainings for CD34, Ckit (CD117) and AML (actin smooth muscle). The staining was negative for β-cathenin and we conclude to periductal stromal tumour, and

more precisely and based on criteria of the Armed Forces Institute of Pathology to a periductal stromal hyperplasia of the breast.
Conclusion: Periductal stromal hyperplasia is an exceedingly rare biphasic breast tumour with benign ductal elements and spindle-cell stromal proliferation lacking a phyllodes architecture. There are few case reports published in the English and the French literature.The prognosis is generally favourable when the excision is complete. They affect middle-aged women. They were considered for long time a rare subtype of phyllode tumours but recently some studies showed the absence of genetic that suggests the existence of two independent entities.

E-PS-02-019
Invasive breast carcinoma with osteoclast-like stromal giant cells: a case report on a rare breast tumour type
N. Chiote*, S. Neves, A.P. Rodrigues, J.R. Vizcaíno, N. Jorge Lamas
*Portugal

Background & objectives: Breast carcinoma with osteoclast-like giant cells (OGCs) is a rare breast carcinoma variant characterized by the infiltration of OGCs into the tumour. Prognosis remains to be firmly established, but the presence of OGCs is unlikely to impact on patient outcome.
Methods: We report the case of a 67-year-old woman with a previous history of right breast carcinoma who presented with a novel 12 mm nodule on her left breast. A biopsy was performed and the histopathological analysis suggested the presence of an invasive breast carcinoma of no special type (NST) with osteoclast-like stromal giant cells. The patient underwent breast-conserving surgery (BCS).
Results: A 8x5x4cm breast lumpectomy surgical specimen was received. It had irregular external surface and no skin represented. Upon sectioning, an extensive poorly defined whitish area was found, and medially to it was an indurated whitish area of 9x8x7mm. Histopathological analysis confirmed the presence of invasive breast NST carcinoma with osteoclast-like stromal giant cells (OGCs), grade II [ER>90%, PR:30%, HER-2: negative (Score 2+ on immunohistochemistry, with negative FISH analysis), Ki-67: 10%-14]. CD68 immunohistochemistry highlighted the presence of OGCs. The surgical margins were clear of neoplastic cells.
Conclusion: Breast carcinoma with OGCs is a rare variant representing less than 2% of all breast cancers, with nearly 200 cases reported in the 40 years following its discovery. The features of the carcinoma component of the lesion are fundamental to define the patient prognosis, being more frequently of well-differentiated to moderately differentiated invasive breast carcinoma. Our patient was submitted to radiotherapy and adjuvant hormonal therapy. Eight months have elapsed since surgery and no signs of disease relapse have been identified.

E-PS-02-020
Can sentinel lymph node (SLN) total tumour load (TTL) assessment by one-step nucleic acid amplification (OSNA) assay assist in the decision for additional axillary surgery in breast cancer patients after primary systemic treatment (PST)?
A.R. Coelho*, P. Pontes, A. Marques, B. Peleteiro, I. Amendoeira
*Pathology Department, São João Local Health Unit, Porto, Portugal

Background & objectives: TTL can accurately predict non-SLN status in treatment-naive breast cancer patients. However, its role after PST is still not well defined. Our aim was to determine the predictive ability of TTL to identify positive non-SLN in patients submitted to PST.
Methods: A cohort of breast cancer patients submitted to PST, with assessment of SLN status by OSNA and subsequent axillary lymph node dissection (ALND), was selected (2016-2023). Clinico-pathological features were collected. Receiver operating characteristic (ROC) curve was used to quantify TTL predictive ability and most suitable cutpoint. Logistic regression models were performed to identify who might benefit from ALND.
Results: Our series included 44 female patients with a median age of 51 years (range: 35-93). Invasive carcinoma of no special type was the most common histological subtype (n=34/44, 77.3%), and histological grades 2 and 3 the most frequent (34.1% and 63.6%, respectively). 37 patients received PST with chemotherapy and 7 with hormonal therapy. Most cases (84.1%) had a partial pathological response on surgical specimen (Pinder classification). Non-SLN involvement was not significantly associated with clinico-pathological features. A TTL value of > 90000 copies was able to predict the presence of non-SLN metastasis, even after adjustment to other clinico-pathological features (OR=11.10, 95%CI:1.39-88.72, p=0.023).
Conclusion: It is well documented that, in treatment-naive breast cancer patients, TTL accurately predicts non-SLN status, thus discriminating patients who may benefit from ALND. In patients submitted to PST, these observations are still not well established. In this cohort, using TTL as a predictor, only a cut-off of 90000 copies was found to maximize sensitivity and specificity to predict non-SLN positivity. No clinico-pathological associations were found. Although these results are encouraging, a larger sample size is needed to support ALND waiving.

E-PS-02-023
A new case of tall cell carcinoma with reversed polarity
A. Córdoba*, L. Ruiz, R. Beloqui, I. Amat, D. Guerrero
*Hospital Universitario de Navarra, Spain

Background & objectives: Tall cell carcinoma with reversed polarity is a rare subtype of breast carcinoma, described in 2003 as a carcinoma similar to the tall papillary thyroid carcinoma. It has been recognised as a new entity in the WHO classification.
Methods: We present a new case of a 48-year-old female patient with a personal history of Schöenlein Henoch purpura, bilateral ovarian cystectomy for teratoma, left oophorectomy for cystadenoma. She had retromuscular breast prostheses.
Mammography was performed and a 6 mm dense nodule was detected in the left breast. After needle core biopsy, segmentectomy and sentinel lymph node biopsy were performed.
Results: Breast parenchyma showing a circumscribed nodule with a diameter of 6.6 mm, consisting of a group of closely arranged nodules formed by papillary structures, leaving space and lumina visible. In other areas, the papillary structures are stacked in a solid papillary pattern. The neoplastic papillary structures are composed of tall cylindrical cells with eosinophilic cytoplasm and nuclei located at the apical pole, giving the impression of reverse nuclear polarity.
The immunohistochemical profile was triple negative. In addition, Ki-67 was 5% and CK 19 negative. An NGS study detected the following alterations: IDH2 mutation (p.Arg132Ser) in exon 4 of the gene, and PIK3CA mutation (p.His1047Arg) in exon 21 of the gene.
Conclusion: It is characterised by mutations in the IDH2 gene.
It is noteworthy that it has a triple negative phenotype; however, it shows an indolent clinical course.
It is important to recognise this tumour to avoid diagnostic errors and to differentiate it from carcinoma in situ, solid papillary carcinoma, encapsulated papillary carcinoma and metastatic thyroid carcinoma.

In this case, we have observed that it is negative for cytokeratin 19, which may be a peculiar feature of this type of breast carcinoma.

E-PS-02-024
Pleomorphic adenoma of the breast
A. Diez Fernández*, M. Martinez Lopez
*Hospital 12 de Octubre, Spain

Background & objectives: 62-year-old woman of Asian origin consults for presenting with a nodule in her right breast, which has increased in size. She reports no gynaecological symptoms. Ultrasound and mammography showed a hypoechoic nodular image with a lobulated border measuring 16mm.
Methods: All slides were stained with H&E and immunohistochemistry techniques were performed to manifest epithelial and myoepithelial cells. An exhaustive bibliographic search has been carried out.
Results: There is a proliferation of epithelial and myoepithelial cells with a chondromyxoid stromal component with cartilaginous differentiation in the background. The lesion appears to be delimited. The glandular epithelial component of benign appearance predominates, which is lined by myoepithelial cells. The inner layer is cuboidal-columnar and abundant apocrine metaplasia is observed; while the outer layer has a polygonal, spindle-shaped appearance. The architecture is heterogeneous with rounded ducts, some angulated, cords or trabeculae and are arranged very tightly. The lack of nuclear atypia, absence of myoepithelial cells, high mitotic activity and necrosis would rule out the possibility of metaplastic carcinoma.
Conclusion: Pleomorphic adenoma of the breast, also called benign mixed tumour. This is a low-grade indolent mixed epithelial-myoepithelial neoplasm that most frequently occurs in the parotid gland and is rare in the breast. The importance lies in the difficulty of its diagnosis in core needle biopsies as it could be misdiagnosed as metaplastic carcinoma due to atypia, architectural distortion or mesenchymal material that can be observed and lead the patient to undergo aggressive surgery.

E-PS-02-025
The comparative analysis of metaplastic breast carcinoma and triple negative breast carcinoma for prognosis and survival outcomes
O.F. Dilbaz*, R. Ucak, C. Tanik, F. Kabukcuoglu
*Health Sciences University Sisli Hamidiye Etfal Health Application and Research Center, Turkey

Background & objectives: Metaplastic breast carcinoma (MBC) and triple negative breast carcinoma (TNBC) exhibit an aggressive clinical course. In this study, we investigated clinicopathological parameters, recurrence rates, and survival relationships by performing a comparative analysis between these two groups.
Methods: Clinically followed-up 51 TNBC cases and 24 MBC cases were selected. All data were obtained, and pathological parameters were re-evaluated by a specialist pathologist experienced in breast pathology. All groups and parameters (age, histological grade, pT stage, lymphovascular invasion, perineural invasion (PNI), clinical stage, tumour-infiltrating lymphocytes (TILs), ER, PR, and HER-2 immunohistochemistry, Ki67 index) were determined. Comparative analysis was performed.
Results: The mean age,tumour grade, and pT stages of the MBC group were statistically significantly higher than TNBC group. pN stage, PNI and Ki67 rates were found to be statistically significant in patients with recurrence. However, no statistically significant differences were detected in the disease-free survival and overall survival(OS) rates between groups. In univariate analysis, pN stage and PNI were recurrence risk factors[Hazard ratios(HR): 4.265, 5.477]. For multivariate survival cox regression analysis, tumour size and the triple negative subtype were found to be significant(HR: 1.4 and 3.95) for mortality alone. As the pT stage increased, OS decreased in all groups statistically significantly. No significant differences were observed in the remaining parameters.
Conclusion: Lymph node involvement, perineural invasion, high Ki67 index and pathologic T stage were the parameters confirmed as recurrence risk factors and associated with a negative prognosis for all groups. These features were already expected for these tumour types. Survival differences were not statistically significant between MBC and TNBC. However, the overall tendency was for MBC to have a worse clinical course. On this matter, we predict that precise results could be achieved by developing detailed molecular analysis methods.

E-PS-02-029
Cancer to cancer metastasis: a rare case of occult breast cancer metastasis into lung adenocarcinoma
A. Elhag*, O. Busari, E. Khalifa, A. Rahman
*Hull University Hospitals NHS Trust, United Kingdom
Background & objectives: Tumour to tumour metastasis is rare. Occult breast cancer, the presence of histologically confirmed breast cancer in a metastatic site without radiological or histological evidence of breast disease. We present a case of occult breast cancer metastatic to lung adenocarcinoma
Methods: A 64 year old woman presented to the chest physician with symptoms of venous entrapment. CT scan revealed suspicious ground glass opacity in the upper right lobe. She had no previous history of breast cancer history but had bilateral breast augmentation. She subsequently had a right upper lobectomy. Mammography 2 years later detected a right breast lesion which was resected.
Results: The histology of the resected right upper lobe confirmed a well differentiated lung adenocarcinoma containing solid clusters of cells which proved to be of breast origin on immunohistochemistry, being positive for ER, and GATA3 and negative for TTF-1, CD56 and CDX2.; metastatic to the right hilar lymph node The resected breast specimen showed ER positive invasive ductal carcinoma.
Conclusion: We describe a very rare phenomenon stressing the importance of careful workup of unusual tumour morphology for optimum patient's management.

E-PS-02-030
Optimizing breast screening reporting: insight from a hospital audit
A. Elmahs*
*University Hospital Crosshouse, United Kingdom

Background & objectives: The Royal College of Pathologists recommends that 80% of breast screening cores be reported within 7 days. Our study aimed to assess our compliance with national guidelines and identify methods to improve turnaround time (TAT).
Methods: A first audit at Bradford Teaching Hospital compared TAT of breast screening reporting with national guidelines. Subsequent audits evaluated BIRAD 4/5 lesion concordance with histological results. Starting in October 2023, we pre-requested hormonal receptors based on the BIRAD code. A re-audit assessed TAT improvements.
Results: The first audit, spanning from December 2022 to October 2023, on 218 cases, showed that 68% were reported within 7 days, mainly due to requests for hormonal receptors post-histological evaluation. A second audit on 268 cases demonstrated 97% radiological/histological concordance. A trial pre-requesting hormonal receptors based on radiological BIRAD followed, resulting in 97% of cases being reported within 7 days in a subsequent re-audit on 63 cases (November 2023 to January 2024).
Conclusion: Pre-requesting hormonal receptors based on radiological BIRAD can enhance breast screening TAT, providing significant radiological/histological concordance, particularly in BIRAD 4/5 cases.

E-PS-02-031
The relationship between HER2 immunohistochemical staining patterns and treatment response in breast cancer
M. Erdal Cesur*, F. Aker
*Department of Pathology, Haydarpaşa Numune Training and Research Hospital, Turkey

Background & objectives: Treatment response and survival rates in HER2-positive breast cancer have been discovered to be lower in cases

with heterogeneity. The present study aimed to investigate the effect of heterogeneous HER2 staining determined by immunohistochemistry (IHC) on treatment responses.
Methods: HER2 staining patterns from 72 pretreatment core biopsies diagnosed with HER2-positive breast carcinoma, were categorized as focal (<30%), heterogeneous (30-79%), or homogeneous (≥80%) based on the total percentage of cells with complete membranous staining, and their impact on treatment response to neoadjuvant HER2-targeted therapy was examined. Additionally, various clinicopathologic factors were analysed to assess their potential effects on treatment response.
Results: Pathological complete response (pCR) was achieved in 53 cases (73.6%). Eight (11.1%) cases were classified as focal, 22 (30.6%) as heterogeneous, and 42 (58.3%) as homogeneous. Overall, cases with nonhomogeneous staining comprised 41.7%. In the univariate analysis, factors such as age ≥ 45, absence of lymphovascular invasion, TIL score, TIL ≥ 10%, ER and PR negativity, HER2-enriched molecular subtype, and homogeneous staining were significantly associated with better treatment responses. Furthermore, in the multivariate analysis, lymphovascular invasion, PR status, and HER2 staining patterns were identified as independent factors affecting treatment response.
Conclusion: The coexistence of HER2-positive and negative cells renders targeted therapy ineffective against all cells. Reporting the percentages of staining alongside positive or negative results when reporting HER2 status is crucial, as it may impact treatment decisions and the clinical follow-up process. Such cases may be candidates for novel treatment strategies or escalation approaches.

E-PS-02-033
Breast metachronous primary angiosarcoma
S. García-Fuertes*, N. Franco Rubio, E. Ponce Casas, R. Vilorio, E. Mejia, C. del Agua Arias-Camisón, M.J. Cardiel García
*Hospital Clínico Universitario Lozano Blesa, Spain

Background & objectives: Breast angiosarcoma, first described by Borrman in 1907, constitutes an infrequent vascular neoplasm with an incidence of about 0,05% among malignant breast tumours. Presence of bilateral neoplasms suggests a metastatic disease over the possibility of a second primary tumour.
Methods: We describe the case of a 57-year-old female patient, with no history of radiation, who presents a circumscribed and fast-growing mass on her left breast and developing of a new contralateral lesion after the next six months. Grossly, both specimens showed evident nodular neoplasms of well defined borders and haemorrhagic surfaces. Neither of the tumours had skin involvement.
Results: Microscopically, breast parenchyma was extensively infiltrated by a neoplastic proliferation, with vascular structures connected with each other, conforming wide and enlarged vascular spaces. These were covered by pleomorphic endotelial cells with hyperchromatic nuclei and scarce citoplasm. There were no mitotic figures nor necrosis. In the immunohystochemical study, these atypical cells were positive for nuclear and cytoplasmic vascular markers (FLI-1, ERG, CD31 and CD34). Given the time of developing of the second neoplasm, she was diagnosed as metastatic primary breast angiosarcoma, without adyuvant therapy. Two years later, she underwent a vertebral biopsy with histological findings consistent with spinal angiosarcoma spreading. Despite of the use of chemotherapy, she was finally exitus.
Conclusion: Primary angiosarcoma is the most frequent breast sarcoma, representing a minority of all breast malignancies. It has an unknown etiology, rapid growth and poor prognosis. They are classified into two main forms: idiopathic angiosarcoma, in younger patients, and treatment-related angiosarcoma, both of them with different genomic changes. Regarding metastatic disease, most common sites are lung, liver, bone and contralateral breast, with regional lymph nodes rarely affected.

E-PS-02-034
Enhancing HER2 evaluation: correlation between APIS breast cancer subtyping kit and IHC/ISH for accurate HER2 quantification
A. Gasior*, J. Gorniak, K. Howard, M. Harrison, L. Gough, S. Rollinson, Z. Pounce, A. Wegscheider, A. Niendorf
*APIS Assay Technologies Ltd., United Kingdom

Background & objectives: HER2 is a breast cancer (BC) prognostic marker. Detecting HER2-low expression is crucial to identify patients who could benefit from novel anti-HER2 therapies. Here, HER2 mRNA expression detected by APIS Breast Cancer Subtyping Kit is correlated with IHC scoring.
Methods: Formalin-fixed, paraffin-embedded BC sections (N=642) from core needle biopsy or resection, underwent histological assessment (IHC) and testing with the APIS kit. HER2 2+ IHC score specimens were resolved via ISH amplification. Diagnostic accuracy of the kit was evaluated by reporting concordance between IHC/ISH and APIS kit mRNA expression in terms of overall, negative and positive percent agreement (OPA/NPA/PPA).
Results: A strong correlation was found between IHC/ISH results and HER2/ERBB2 expression detected by the APIS kit, demonstrating high percent agreement (OPA of 94.2%, PPA of 89.2% and NPA of 94.9%). The APIS kit detected ERBB2 mRNA expression in a subset of patients considered HER2-negative, with an IHC score of 0 or 1+, demonstrating the higher sensitivity of RT-qPCR-based detection methodologies and highlighting the continuous nature of ERBB2 expression.
Conclusion: The APIS Breast Cancer Subtyping Kit accurately detects HER2/ERBB2 expression. The findings suggest that relying solely on IHC categorisation may not suffice for predicting response to novel anti-HER2 treatments. Utilising additional cut-offs could enhance the stratification of ERBB2 mRNA expression, distinguishing a 'HER2-low' group. Further investigations correlating expression levels with responses to anti-HER2 therapies are necessary to validate this approach.

E-PS-02-035
Prognostic value of SOX-2 nuclear expression in triple-negative breast cancer
I. Guzelis*, B. Bolat Kucukzeybek, M. Gursoy, Y. Yilmaz, Y. Kucukzeybek
*Izmir Katip Celebi University Ataturk Training and Research Hospital Pathology Department, Turkey

Background & objectives: Triple-negative breast cancer is an aggressive subtype of breast cancer. SOX-2 is a cancer stem cell marker that plays a role in tumourigenesis. Study goal: Association of SOX-2 expression with clinical outcomes and histopathological parameters in triple-negative breast cancer patients.
Methods: The study included 95 triple-negative breast cancer cases diagnosed between 2008 and 2020. An in-vitro diagnostic SOX-2 antibody was applied to the tumoural slides in a validated automated stainer. The expression of SOX-2 was defined as a SOX-2 H score ≥1.
Results: The expression of SOX-2 was observed in 29 cases (30.5%). Tumour multifocality was significantly associated with the absence of SOX-2 expression (p=0.013). SOX-2 expression was weakly correlated with perinodal infiltration (p=0.074). Absence of SOX-2 expression was weakly associated with containing a special histological type (p=0.086). At a median follow-up of 76 months, SOX-2 expression was not associated with overall or disease-free survival. R-based statistical analysis determined a SOX-2 H score 2 cut-off. The overall and disease-free survival of cases with an H score ≥3 was lower than others. However, there was no statistical significance between an H score ≥3 and the survival data (p=0.567, p=0.978).

Conclusion: The percentage of SOX-2 staining is typically low, as only 1% of tumour cells exhibit cancer stem cell characteristics. In conclusion, the prognostic significance of SOX-2 could become clear in a larger group of triple-negative breast cancer patients using approved methodologies.

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E-PS-02-038

Clinicopathological features and prognostic significance of HER2-low status in breast carcinoma

N. Ilieva-Shipchanova*, D. Tashkova, E. Bangieva, N. Miteva
*Medical University- Plovdiv, Complex Oncology Center Plovdiv, Bulgaria

Background & objectives: After the clinical trial Destiny Breast 04, the classification for HER2 evaluation expanded by the recognition of the novel diagnostic category HER2-low. This study aims to evaluate the prognostic significance of HER2-low among HR-positive and triple-negative breast cancer.
Methods: A cohort comprisin 487 newly diagnosed patients with breast carcinoma for the period January-December 2023 were selected. Data about the age, pathological stage, histological subtype, grade, nodal involvment, HR status and molecular subtype were collected. Subsequently, statistical analysis was conducted using IBM SPSS 19 software. Then we further evaluated if there is any correlation between HER2-low immunohistochemistry and prognostic features.
Results: Among the 487 patients, 109 (23%) had low HER2 expression, 85 (13,7%) had HER2 positive expression and 300 (63,3%) had negative HER2 expression. The average age was 62.5 $\pm$ 13.2 years. The distribution of HER2-low cases among molecular subtypes was as follows: 20,2% - Luminal A-like, 68,8% - Luminal B-like and 11% - Basal-like. Among the HR-positive cases HER2-low status was more commonly associated with higher stage, higher grade, lymph node metastasis, decreased PR immunohistochemical expression and high Ki-67 proliferative index. All these correlations were more pronounced in the setting of Luminal A-like carcinomas. Regarding Basal-like tumours, HER2-low expression was linked to lower stage, lower grade and lower Ki-67 index.
Conclusion: HER2-low breast tumours represent a newly identified diagnostic category with promising implications for therapeutic intervention. The prevalence of HER2-low status exhibits variability across different tumour types and displays a tendency to increase with disease progression. Our study findings indicate a correlation between HER2-low status and unfavourable patient prognosis within the hormone receptor-positive subgroups. Conversely, HER2-low status appears to be associated with a more favourable prognosis among patients diagnosed with triple-negative breast cancer.

E-PS-02-039

How a giant phyllodes tumour defied diagnosis - a case study

P. Ioana-Alexandra*, C. Suciu, G. Prilipceanu, A. Dema
*ANAPATMOL Research Center, Victor Babes University of Medicine and Pharmacy, Romania

Background & objectives: Phyllodes tumour (PT) is a rare fibroepithelial neoplasm of the breast, classified into three categories: benign, borderline, and malignant. Benign and borderline tumours are more common, whereas malignant ones are less frequent.
Methods: We present the case of a giant malignant Phyllodes tumour in a 46-year-old woman presented to the Plastic and Reconstructive Surgery Department with an ulcerated tumour encompassing the entire left breast. The core-needle biopsy revealed a spindle cell proliferation devoid of epithelial elements. Mastectomy was performed. The following antibodies were used for the IHC study: anti-p63, anti-CD34, anti-Ki67.
Results: Gross examination revealed a mastectomy specimen measuring 25cm/19cm/17cm, entirely replaced by a multinodular brown-white tumour with black, gray, and yellow areas. Several cystic areas containing serous-citrine fluid were also identified. Histological analysis showed a fibroepithelial tumour with a predominance of mesenchymal component. Stromal cellularity was increased with numerous nuclear overlapping, moderate atypia, and evident nucleoli, intense mitotic activity (15 mitoses/10 HPF; Ki-67- 40%).The tumour was diagnosed as malignant Phyllodes tumour.
Conclusion: This case underscores the challenges encountered in establishing a definitive diagnosis od phyllodes tumour, both in core-needle biopsy samples and mastectomy specimens. Due to their rapid growth, extensive tissue involvement, and potential for ulceration and hemorrhage, timely diagnosis and appropriate management are crucial factors to improve outcomes for patients with this rare breast neoplasm.

E-PS-02-040

Invasive breast carcinoma with signet ring cell differentiation and extracellular mucin production: a case report

S. Işıksoy*, I. Bağcı, E. Yılmaz, N.S. Şeker
*Eskişehir Osmangazi University, Turkey

Background & objectives: Invasive breast carcinomas with extracellular mucin and signet ring cell morphology show heterogeneity as regarding the amount of both components and nuclear grading. Herein we present a case of high grade invasive breast carcinoma with these histopathologic features.
Methods: The biopsy specimen was processed for routine paraffin embedding, and 4 mm paraffin sections were stained with H&E stain and used for immunohistochemical analysis with appropriate retrieval techniques, antibody dilutions and controls.
Results: Paraffin blocks of the segmental breast biopsy material of a 63-year-old female were consulted to our department. On H&E sections, the 17 mm diameter tumour consisted of clusters of mitotically active neoplastic cells with abundant nuclear pleomorphism within extracellular mucin pools. Many cells had intracellular mucin causing signet ring cell morphology. Ductal carcinoma in situ was found adjacent to the invasive tumour. Immunohistochemically, ER and PR were negative, and CerbB2 was equivocal. Ki-67 proliferation index was 45%. FISH analysis showed Her2 amplification. No metastatic focus was detected in the examination of sentinel lymph node biopsy.
Conclusion: Carcinomas with abundant extracellular mucin rarely have signet ring cell morphology. Presented case has widespread extracellular mucin, differs from classical pure mucinous carcinomas with its high-grade morphology and signet ring cell differentiation. In other hand, the molecular subtype of the case was in her2 enriched. Our case is presented due to these unusual features.

E-PS-02-041

Metaplastic differentiation at the metastatic site in mammary carcinoma - histopathological diagnostic pitfalls

T. Kawasaki*, T. Umesaki, H. Shimada, N. Fujiuchi, Y. Ichiki, R. Taguchi, A. Fujimoto, H. Kodama, S. Ichihara, M. Suzuki, R. Kawamura, S. Takemi, J. Ichikawa, A. Mouri, K. Kaira
*Saitama Medical University, Japan

Background & objectives: Herein, we report an extremely rare case in which the primary lesion was an invasive breast carcinoma of no special type (IBC-NST), while the associated distant metastasis was consistent with "metaplastic" carcinoma.
Methods: A 59-year-old Japanese woman who had undergone partial resection for right mammary cancer at the age of 47. The pathological diagnosis, which we also reviewed in detail, was IBC-NST, measuring

27 mm (pT2), histological grade 3, luminal B-like (HER2-negative). Fat invasion and lymphovascular infiltration were observed. The sentinel lymph node biopsied was intact. Adjuvant chemo- and hormonal therapies were administered.
Results: At the 12-year follow-up after surgery, chest X-ray, CT, and PET-CT revealed a 16 mm mass suspected to be lung cancer in the left upper lobe. Transbronchial lung biopsy was inconclusive and resection was performed. Histopathologically, the tumour was composed of a solid and glandular invasive growth of carcinoma cells with irregular and hyperchromatic nuclei. The carcinoma exhibited distinct squamous differentiation with keratinization at some sites. Although primary adenosquamous carcinoma was initially considered, based on morphology, biomarker immuno-results were: ER (positive), PgR (low positive), HER2 (score 2+), and Ki67/MIB-1 (75%). Furthermore, the carcinoma cells showed GATA3+, mammaglobin+, GCDFP15+, CK7+/CK20-, p40+, CK5/6+, and TTF-1-. FISH analysis revealed no HER2 gene amplification.
Conclusion: Based on these pathological findings, we regarded the pulmonary lesion as corresponding to breast cancer metastasis. It is noteworthy, from the diagnostic and therapeutic perspectives, that, although exceptionally rare, even if the primary lesion is an IBC-NST, pronounced metaplastic changes might be present at the metastatic site. Under such circumstances, immunohistochemistry is a powerful tool for determining whether the neoplasm is primary or metastatic.

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E-PS-02-042
Clinicopathological study of primary breast lymphoma - a South African experience
M. Khaba*, K. Ngobese, T.
*Sefako Makgatho Health Sciences University

Background & objectives: Primary breast lymphoma is a rare form of non-Hodgkin lymphoma. Their clinicoradiological features lack specificity and can be similar to those of breast cancer. This study aimed to report on the clinicopathological features of primary breast lymphoma from our centre.
Methods: This was a retrospective cross-sectional study of cases diagnosed with primary breast lymphoma from 2012 to 2022. The clinicopathological characteristic data was retrieved from the laboratory information system. Haematoxylin and Eosin stained and immunohistochemically stained slides were reviewed according to the 5th edition of the WHO classification of haematolymphoid tumours. Stata-14 was used to analyse the data.
Results: The study consisted of 38 cases with female predominance and average age of 39 years. Of the 38 cases, 68.4% (n=26) were HIV positive and 62% (n=16/26) were on antiretroviral therapy. The patients presented with painless mass in 58% (n=22) and painful mass in 42%(n=16) of the cases. Of the painful mass, 19% (n=3) had fungating lesions while 25% (n=4) had ulcerated skin. Majority of the cases involved the right breast (34%) followed by left (29%), bilateral (18%) and not specified (18%). Histopathologically, diffuse large B-cell lymphoma was the common diagnosis (n=28, 63%) followed by plasmablastic lymphoma (n=8, 21%), Burkitt's lymphoma (n=4, 11%) and B-Cell lymphoblastic lymphoma (n=2, 5%).
Conclusion: Primary breast lymphoma is a rare form of breast malignancy. While not frequently encountered, it is important for pathologists and clinicians to be aware of the potential occurrence of primary breast lymphoma when patients present with a breast mass. Accurate diagnosis is essential to avoid unnecessary mastectomies.

E-PS-02-043
Alterations in surrogate molecular signatures, androgen receptor and Ki67 index in pre and post neoadjuvant chemotherapy in primary invasive breast carcinoma
A.A. Khan*, S. Zaheer
*Vardhman Mahavir Medical College, India

Background & objectives: Change in receptor status post neoadjuvant chemotherapy calls for evaluation as it might warrant change in the treatment plan. Through this study, we intend to evaluate the alterations in receptor status and Ki67 index post neoadjuvant chemotherapy in breast cancer.
Methods: It is a retrospective study which includes 100 patients diagnosed with invasive breast carcinoma, NST. All the patients received neoadjuvant chemotherapy followed by modified radical mastectomy as final treatment. The ER, PR, Her2neu, AR and Ki67 index of pre and post chemotherapy specimens were evaluated using immunohistochemistry. Mathematical parameters including IHC4 were also derived to evaluate Ki67 proliferation index.
Results: We observed a decrease in modified bloom Richardson scoring(BR) in 31.4% of the patients whereas 14.2% of the resection specimens showed an increased BR score post NACT. A significant discordance in expression of ER, PR, Her2neu and AR were seen ($p<0.005$). A significant variation in Ki67 proliferation index was also observed in pre and post chemotherapy biopsies.Among the molecular subtypes highest discordance was seen in Luminal B subtype, followed by Luminal A. No discordance was seen in Her2neu enriched tumours. As per the MAGEE recurrence score a significant discordance was observed between biopsy and surgical resected specimens ($p=0.03$).
Conclusion: We observed a significant discordance in hormone receptor status and androgen receptor expression in patients receiving neoadjuvant chemotherapy. The study emphasizes to re-evaluation of biomarkers and prognostic scores on surgical resected specimens for better management and prognostication. The another aspect which requires further investigation is biological effects of chemotherapeutic agents on cancer cells which can play an important role in deciding adjuvant therapy and follow up.

E-PS-02-044
Estrogen receptor and progesterone receptor expression changes in breast cancer local metastases compared with primary tumour
K. Konyshev*, S. Sazonov
*Institute of medical cell technologies; Ural state medical university, Russia

Background & objectives: Reasons and clinical significance of hormonal receptors expression discordance in primary tumour and metastasis of breast cancer stay unclear. Objective: to assess discordance rate of estrogen receptor and progesterone receptor expression in breast cancer local metastasis compared with primary tumour.
Methods: Surgical specimens of the primary tumour and local metastases of 104 patients with breast cancer were studied. Immunohistochemistry (antibodies to ER, PR) was used to determine expression level of corresponding biomarkers in primary tumour and metastases. Allred score was used. Frequency of receptor expression changes in metastases was analysed depending on primary tumour expression level using Fisher exact probability test.
Results: Biomarker expression level of primary tumour and metastasis was correspondently totally discordant, increased, decreased: Estrogen receptor – whole sample 67/104 (64,4%), 49/104 (47,1%), 18/104 (17,3%) ($p<0,05$); in cases with expression level of primary tumour: 0/2 – 8/31 (25,8%), 7/31 (22,6%), 1/31 (3,2%); 3-6 – 42/43

(97,7%), 35/43 (81,4%), 7/43 (16,3%) (p<0,05); 7-8 – 17/30 (56,7%), 7/30 (23,3%), 10/30 (33,3%). Progesterone receptor – whole sample 64/104 (61,5%), 44/104 (42,3%), 20/104 (19,2%) (p<0,05); in cases with expression level of primary tumour: 0/2 – 14/46 (30,4%), 12/46 (26,1%), 2/46 (4,4%) (p<0,05); 3-6 – 41/42 (97,6%), 29/42 (69,1%), 12/42 (28,6%) (p<0,05); 7-8 – 9/16 (56,3%), 3/16 (18,8%), 6/16 (37,5%).
Conclusion: Expression level change in metastases of breast cancer was found in 64,4% cases for estrogen receptors, 61,5% cases for progesterone receptors in the sample. Among cases with such kind of tumour heterogeneity, frequency of cases with increase of biomarker expression level was significantly higher than frequency with decreased one for both estrogen and progesterone receptors in the whole sample as well as in the groups with 3-6 expression level in primary tumour.

E-PS-02-045
Case report of a mammary myofibroblastoma with epithelioid morphology – a potential diagnostic pitfall
O. Kouroukli*, E. Spiteri, P. Vlachou, P. Dolkiras, C. Vourlakou
*Evaggelismos General Hospital, Athens, Greece

Background & objectives: Myofibroblastomas of the breast are rare benign mesenchymal tumours arising from the mammary stroma. We present a case of mammary myofibroblastoma with epithelioid features in order to highlight the challenges in this diagnosis.
Methods: We received an FNB biopsy from a 2 cm mass in the right breast of a 69-year-old man. On H&E the diagnosis was not straightforward, so we proceeded to immunohistochemical studies with the following markers: AE1/AE3, GATA-3, TRPS-1, AR, ER, RGR, Desmin, a-SMA, Calponin, BCL2, CD10, CD34, CD99, RB1, SOX-10, STAT-6 and Ki-67.
Results: Microscopic examination showed a tumour composed of epithelioid or plump spindle cells in bundles. Despite the partly epithelioid appearance, immunohistochemical studies excluded the diagnosis of an invasive carcinoma. The characteristic immunophenotypic findings of CD34 and desmin expression together with loss of RB-1 expression confirmed the diagnosis of myofibroblastoma.
Conclusion: The diagnosis of myofibroblastoma, especially on small samples, can be challenging. Pathologists should be aware of this rare entity and its morphologic spectrum. The knowledge of the potentially deceiving epithelioid appearance of myofibroblastomas should prompt pathologists to request the proper immunohistochemical markers when this diagnosis is suspected. Given the benign nature of myofibroblastomas, it is crucial to avoid a misdiagnosis of an invasive carcinoma.

E-PS-02-047
TRPS1 expression in breast angiosarcoma
L. Kuthi*, T. Pancsa, B. Pósfai, A. Schubert, S. Almási, E. Papp, Y.C. Chien, E. Kálmán, A. Kovács, J. Kulka, L. Varga, G. Cserni
*Department of Surgical and Molecular Pathology, National Institute of Oncology, Hungary

Background & objectives: Angiosarcoma (AS) of the breast exhibits distinct forms based on etiological and genetic features. Typical morphology allows a straightforward diagnosis which becomes challenging when histological features overlap with other tumours.
Methods: AS cases and clinical parameters were collected from participating institutes, and slides were reviewed and studied using CD31, ERG, MYC, and TRPS1 immunostainings.
Results: One primary AS (age: 33 years; tumour size: 210 mm) and 34 radiation-associated-ASs (median age: 73.5 years, range: 45-89 years; median size: 44 mm, range: 5-130 mm) were studied. ERG and CD31 were diffusely positive in all cases, while MYC labeled each radiation-associated-AS; 60% of ASs displayed TRPS1 labeling. Consensus scoring by four independent readers identified 12 out of 35 AS cases as unequivocally TRPS1-positive. However, uncertainty surrounded 9 additional cases due to a lack of reader agreement (substantial; with a Fleiss kappa value of 0.76).
Conclusion: Our study establishes that a notable proportion of breast AS expresses TRPS1, challenging the previously asserted high specificity of TRPS1 for breast carcinomas. This discovery broadens the spectrum of entities expressing TRPS1, impacting the differential diagnosis. Notably, in our investigation, both CD31 and ERG proved equally effective as markers in confirming the endothelial origin of the tumours. Also, MYC protein was expressed in all radiation-associated AS cases indicating the pathognomonic genetic alteration of these tumours.

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E-PS-02-048
Biphasic metaplastic carcinoma with a spindle cell component and mixed invasive carcinoma: an intriguing case
Z. Lajmi*, Y. Sarra, F. Vosra, S. Mestiri, M. Mokni
*University Hospital Sahloul, Tunisia

Background & objectives: Metaplastic breast carcinoma (MBC) is a rare and aggressive subtype of breast cancer, comprising 1% of all breast tumours. It is defined histologically as tumours with squamous epithelial differentiation and/or mesenchymal components. Multiple components often co-exist in the same tumour.
Methods: We report a case of 49-year-old female who presented with a retro-areolar mass of the right breast. with skin induration, diagnosed as an invasive breast carcinoma of no special type on fine needle biopsy. The tumour was staged as T4b. the patient underwent a neoadjuvant chemotherapy. Radical mastectomy was than performed.
Results: On gross examination, serial sectioning showed a greyish, poorly-circumscribed lesion measuring 8×6.5 cm. Microscopically, the lesion consisted on biphasic metaplastic carcinoma composed of an admixture of spindle cells carcinoma (20%) and mixed invasive carcinoma (80%). The latter component was formed by lobular carcinoma with pleomorphic features (50%) and invasive carcinoma of no special type (30%). Spindle cell component was made of short fascicules encompassing large atypical gland. The presence of lobular component was confirmed by loss of E-cadherin stain that was also partially and weakly expressed by the non-invasive specific component suggesting an epithelial mesenchymal transition.
Conclusion: Biphasic MBC is a rare entity. The concurrent mixed invasive carcinoma is an even more unusual event. This entity represents a great therapeutic challenge because it is weakly responded to systemic therapy. Large Molecular investigations of MBC are fundamental to identify targeted therapies.

E-PS-02-049
High-grade metaplastic carcinoma of the breast with heterologous mesenchymal differentiation - a difficult case
A. Lapa*, P. Rodrigues Veiga, R. Rocha, C. Leal, J. Fraga
*Department of Pathology, Portuguese Oncology Institute of Porto (IPO-Porto), Portugal

Background & objectives: Metaplastic carcinomas with mesenchymal elements are frequently composed of different areas (mesenchymatous

and carcinomatous), varying from mild atypia to malignant characteristics and in which carcinomatous areas may be scarce. Differentiation between soft tissue sarcomas and breast carcinomas is often challenging.
Methods: A 46-year-old woman underwent breast echography that showed a 2,9cm lesion and an adenopathy. A biopsy of the breast lesion was performed, with a result of a no special type, grade 3, triple negative breast carcinoma. The patient was transferred to our institute, where the adenopathy was biopsied, and a second observation of the breast biopsy was performed.
Results: Histologically, the lymph-node showed a small group of cells with rhabdoid morphology, immunonegativity for cytokeratins, GATA-3 and p63 and immunopositivity for desmin, myogenin and MyoD1. The pathology report stated involvement by a neoplasia with rabdomyoblastic differentiation/ rhabdomyosarcoma.
This strange presentation in the lymph node imposed a revision of the external breast biopsy, which showed a poorly differentiated neoplasia, with solid pattern and some giant cells with ample and eosinophilic cytoplasm. Immunohistochemistry revealed positivity for CKAE1/3, p63, GATA-3, desmin, myogenin and myoD1. The final diagnosis was a grade 3, metaplastic carcinoma with rabdomyosarcomatous differentiation.
Patient is currently under neo-adjuvant treatment due to locally advanced disease.
Conclusion: This was a very interesting case, due to its presentations as a possible lymph node sarcomatous metastatic element. The distinction between non-special type carcinomas, metaplastic carcinomas and soft tissues tumours harbours great importance, resulting in different response to treatment and outcomes. Among metaplastic carcinomas, specific subtypes may also result in distinct outcomes. In metaplastic carcinomas with mesenchymal differentiation which lack conventional breast carcinoma areas, it is essential to prove the presence of epithelial differentiation through immunoexpression of cytokeratins and/or p63.

E-PS-02-050
Association between immunohistochemical markers and response after neoadjuvant chemotherapy in advanced breast cancer
H. Lee*, O. Lee, S. Son, C.G. Woo
*Chungbuk National University, Chungbuk National University Hospital, Republic of Korea

Background & objectives: Neoadjuvant chemotherapy (NACT) is an effective therapeutic plan in advanced breast cancer (ABC). Determination of molecular or immunohistochemical (IHC) subtype of ABC before NACT is an essence procedure when selecting regimen and expecting response.
Methods: One hundred and sixty-one patients of ABC were obtained between January 2018 and July 2023. Pathologic diagnosis and IHC assays of hormone receptors, HER2, ki-67, and p53 were performed in the needle biopsy specimen of every patient. Every resected specimen after NACT was pathologically examined including stages and NACT response which was divided into better and worse response groups.
Results: The percentage of good response to NACT was 27.5% for luminal type, 78.4% for HER2 type, and 44.4% for triple-negative (TN) type. On the resection specimen, HER2 type showed lower ypT stage and better NACT responses. Luminal type was highly related to positive ypN stages. TN type showed significantly higher p53 mutation status. Cases with higher (≥50%) ki-67 index were associated with better NACT responses in luminal type (p=0.011) but with worse NACT responses in HER2 type (p=0.039). Association between p53 mutation status and NACT response was not statistically significant in any types, but all four cases of p53-wild TN type were poorly responded to NACT.
Conclusion: Association between IHC Markers and NACT response is different among molecular subtypes in ABC. Therefore, assays of p53 and ki-67 as well as hormone receptors and HER2 on the biopsy specimen may be helpful when considering NACT in ABC.

E-PS-02-051
A study focusing on the relationship between tumour regression patterns and prognosis after neoadjuvant chemotherapy for breast cancer
Y. Liu*, J. Shang, Y. Ding, J. Li
*The Fourth Hospital of Hebei Medical University, China

Background & objectives: Residual tumour load is a key factor in evaluating breast neoadjuvant therapy, and this study investigates the histological changes in tumour bed regression patterns of invasive ductal carcinoma tumours of the breast after neoadjuvant chemotherapy to predict patient prognosis.
Methods: 494 cases of primary invasive ductal carcinoma treated with preoperative neoadjuvant chemotherapy in our hospital were included. The HE sections were histologically typed under the microscope and classified into 9 regression patterns according to the histological features, and the effects of regression patterns on the prognostic results were analysed.
Results: There were 494 cases included, and 234 cases were histologically classified as centripetal regression, including: type A centripetal regression without surrounding smaller foci, type B circling regression, type C massy regression, type F striated regression, type G isolated remnants, and type H pathologically fully reactive. 130 cases of centripetal regression were categorized as type E solid with essentially no regression; Type D sieve-like regression, and Type I mixed regression. Tumour regression pattern was closely related to overall survival, and tumours with centripetal regression had longer disease-free survival ($P<0.01$) and overall survival time ($P<0.05$).
Conclusion: The results showed that centripetal regression pattern was more likely to recur and had shorter overall survival. Histologic changes in the tumour bed after neoadjuvant chemotherapy determine tumour recurrence and metastasis to a certain extent, and postoperative assessment of histologic changes in the tumour bed of breast macroscopic specimens is feasible and can provide a basis for clinical treatment decisions and surgical approaches.

E-PS-02-052
Sensitivity analysis of different HER2 clone numbers for detecting HER2 low and ultra-low expression in invasive breast cancer
Y. Liu*, J. Shang, J. He, Y. Ding, J. Li
*The Fourth Hospital of Hebei Medical University, China

Background & objectives: With the clinical development of novel anti-HER2 agents targeting HER2 breast cancers, the detection of HER2-low and ultra-low expression is a hotspot of interest.It is necessary to explore the results of different HER2 antibody clone numbers.
Methods: Forty cases of invasive breast cancer treated surgically between January and April 2023 were screened. HER2 immunohistochemical staining of the remaining five sections was performed on the Ventana Bench Mark ULTRA Fully Automated Immunohistochemical Staining Platform using five antibodies, 4B5, MXR001, CB11, EP3 and SP3. FISH was performed on cases with a 2+ HER2 immunohistochemical reading for either antibody.
Results: The staining accuracy of the different antibody assays was analysed using 4B5 as the gold standard, and the results showed that CB11 was more accurate with a KAPPA value of 0.902, while MXR001 had a lower interpretation accuracy. Cases were further categorized into HER2-positive, HER2 low-expression and HER2-negative cases, and the lowest concordance among the five antibody interpretations was found in HER2 low-expression cases, with an ICC value of 0.658.4B5 had a higher detection rate (55%) for HER2 low-expression cases.HER2-negative cases were further categorized into HER 0 and HER2-ultra-low cases, and the results showed that MXR001 detected more HER2 0 cases, with little difference between 4B5 and MXR001.
Conclusion: The overall consistency of HER2 expression between antibodies of different clone numbers was high, but the consistency of

detecting HER2 low and ultra-low expression cases was poor, and there were differences in the detection rates, which still need to be validated by more subsequent studies.

E-PS-02-053

The influence of CEACAM1 on tumour cell proliferative activity

M. Lyndin*, I. Kube-Golovin, A. Romaniuk
*Academic and Research Medical Institute, Department of Pathology, Sumy State University, Ukraine

Background & objectives: The leading oncopathology in women is breast carcinoma. Proliferative cell activity, influenced by tumour histological features and synthesis of tumour-specific proteins serve as key prognostic markers. CEACAM1 may serve as a selective indicator of malignant breast cancer progression.
Methods: Mouse anti-CEACAM1 monoclonal antibody was employed in immunohistochemical investigation to detect CEACAM1 in breast cancer tissue. Proliferative cell activity was assessed using rabbit anti-Ki-67 monoclonal antibody . To confirm the regulatory function of CEACAM1 in cell proliferation, we utilized MCF7 breast cancer cells lacking CEACAM1 expression (CEACAM1–) and those transfected with human CEACAM1 (CEACAM1+).
Results: During our investigations, we found that CEACAM1-positive foci of invasive ductal carcinoma of the breast (irrespective of their expression pattern) exhibited significantly lower proliferative activity compared to CEACAM1-negative tumour areas. Among all CEACAM1-positive cases, the lowest proliferative activity was observed when CEACAM1 was apically localized in neoplastic cells and showed a stronger staining. Increased cell proliferation associated with membranous and cytoplasmic localization of CEACAM1 can be explained by the progressive functional inertness of these proteins. Additionally, MCF7 CEACAM1- cells demonstrated significantly higher proliferation rates compared to MCF7 CEACAM1+ cells.
Conclusion: Analyzing the relationship between cell proliferative activity and their CEACAM1 profile, we confidently assert that CEACAM1 exhibits a suppressive effect on cell division, as evidenced by immunohistochemical and immunofluorescent co-expression studies of Ki-67 and CEACAM1 in breast cancer tissues. Furthermore, our in vitro experiments confirmed the inhibitory effect of CEACAM1 on breast cancer cell proliferation.

E-PS-02-054

Comparison between unresected and resected b3 lesions after long term follow up

M.E. Maracci*, G. Randazzo, A. Marcatelli, L. Santilli, M.C. Cucchi, V. Galluzzo, A. Baldissera, E. D'Angelo, S. Ciabatti, A. Mura, A. Maestri, A. Tafà, M.P. Foschini
*Department of Biomedical and Neuromotor Sciences, University of Bologna, Unit of Anatomic Pathology, Bellaria Hospital, Bologna, Italy

Background & objectives: The B3-category encompasses a group of lesions with low potential of malignant transformation. Aim of the present study is to evaluate long term follow up of B3-lesions, comparing cases treated with open surgery and by vacuum-assisted biopsy (VAB) only.
Methods: 246 B3 lesions including FEA, ADH and LIN, diagnosed between January 2008 and December 2015, by VAB were retrieved. Core needle biopsies were excluded. Cases were subdivided as follows: Open surgery (OS, 166 cases) when surgical excision followed the B3 diagnosis and VAB only (80 cases) when no further surgery was performed after the diagnosis of B3.
Results: Open Surgery: 16.2% (27 of 166) were upgraded to in situ and/or invasive carcinoma. Additional 30 (18.07%) cases developed in situ or invasive carcinoma at 1 to 14 years after the B3 diagnosis (mean 7.6). VAB only: No further events were recorded in the 80 cases included in the group.
Conclusion: The present series compares B3 lesions surgically treated when the mammographic finding had not completely removed by VAB and B3 lesions completely removed by VAB procedure. The data here obtained show that the VAB only is a safe procedure in cases of B3 lesions of limited extent. On the contrary when the mammographically detected alterations cannot be completely removed by VAB only, OS is important to reduce the risk of malignant transformation.

E-PS-02-055

Bland-looking spindle cell lesions of the breast on core-needle biopsy: a morphological and immunohistochemical approach

S. Marletta*, L. Salvatorelli, G.M. Vecchio, G. Broggi, G. Angelico, A. Rizzo, G. Magro
*Division of Pathology, Humanitas Istituto Clinico Catanese, Catania, Italy

Background & objectives: Bland-looking spindle cell lesions of the breast (BLSCLB) encompass a wide pathological spectrum, ranging from indolent to rarer life-threatening diseases. Their recognition could be challenging, especially on core-needle biopsies (CNBs), with most being labeled as "B3" regardless of their nature.
Methods: Herein, we sought to investigate the feasibility of proper classification of the most frequent BLSCLBs on CNBs by matching them with the corresponding surgical specimens. Thirteen cases were retrieved, including five mammary-type myofibroblastomas (MFBs), six primitive desmoid fibromatoses (DFs), and two bland-looking fibromatosis-like metaplastic carcinomas (FLMCs). The collected samples were then thoroughly studied for their morphological and immunohistochemical (IHC) findings.
Results: Histological features favouring the diagnosis of MFBs both on CNBs and surgical resections were the presence of short fascicles of spindle cells intermingling with thick keloid-like collagen fibers with no evidence of enclosed normal breast parenchyma. Conversely, on pre- and postoperative DFs and FLMCs were morphologically similar, showing longer perpendicular bundles of spindle cells, some of which with slender "perineural-like" morphology, embedded in a fibromyxoid stroma, infiltrating ductal-lobular structures. According to IHC, MFBs could be differentiated from the other lesions by their diffuse ER and desmin positive staining. Moreover, pan-cytokeratins and p63 immunoreactivity are helpful clues in distinguishing DFs from FLMCs.
Conclusion: Our data suggest that a correct diagnosis of the most common BLSCLB can be confidently obtained on CNBs based on morphological and IHC features. Diffuse ER and desmin expression support the diagnosis of MBF, avoiding the abuse of the "B3" category for this benign tumour.

E-PS-02-057

Metaplastic breast carcinoma: clinical and pathological perspectives from a tertiary oncology institution

A. Milićević*, O. Živković, I. Jovanić, I. Petrovic, A. Lazarević, K. Obradović
*Institute for Oncology and Radiology of Serbia

Background & objectives: Metaplastic breast carcinoma (MpBC) is an uncommon histologic type of invasive breast cancer. The aim of this study is to explore histopathological and clinical features of metaplastic breast cancer to enhance understanding of its diagnosis, prognosis, and treatment strategies.
Methods: The retrospective study included all patients with the pathohistological diagnosis of MpBC diagnosed between January 2022 and December 2023 at the Institute for Oncology and Radiology of Serbia. We reviewed age, tumour size, localization, histological grade, axillary nodal status, presence of lymphovascular invasion, receptor status (ER,

PR, Her2-neu), Ki67 prognostic index, and MpBC subtype using the institute's database.
Results: A total of 3650 patients with invasive breast cancers, 16 of them were female patients histopathologically diagnosed with MpBC and were included in the research. The mean age of the patients was 60.68 ± 15.14 years. The tumour was predominantly in the right breast. The most common histological type in our study was mixed MpBC, with 7 (43.75%) cases. Most tumours (43.75%) were pT2, and 12 cases (75%) had high-grade histological gradus. Four patients (25%) had positive axillary lymph node metastasies. Lymphovascular invasion was identified in one patient (6.25%). The tumours in 9 (56.25%) patients were triple negative, and the Ki-67 proliferation index ranged between 10% and 80%.
Conclusion: MpBC is a rare entity characterized by triple-negative phenotype breast cancer. Most of the patients in the series showed no axillary lymph node involvement, lymphovascular invasion, or hormone receptor negativity. MpBC encompasses a broad spectrum of benign and malignant entities, making diagnosis challenging. Since pathohistological and immunohistochemical examinations are the primary means of diagnosing, it is essential to manage patients appropriately to lower the disease's high risk of both local and distant recurrence.

E-PS-02-058
Myofibroblastoma of the breast – report of four cases and review of literature
A. Milićević*, O. Živković, I. Jovanić, I. Petrovic, A. Lazarević, K. Obradović
*Institute for Oncology and Radiology of Serbia

Background & objectives: Myofibroblastoma of the breast is an uncommon benign stromal neoplasm composed of fibroblasts and myofibroblasts, primarily diagnosed in older men and postmenopausal women. Myofibroblastomas have various histopathological variants: collagenous, cellular, infiltrative, myxoid, lipomatous, epithelioid, and deciduoid types.
Methods: In the present study, we report four cases of patients with confirmed myofibroblastoma of the breast in one year at the Institute for Oncology and Radiology of Serbia. We reviewed age, tumour size, localization, histological type, and immunohistochemical characteristics using the institute's database. All tumours were treated with wide surgical excision after core needle biopsy.
Results: Four cases of breast myofibroblastoma were identified, including three females and one male patient. The mean age was 59,75 ± 8.77 years. All female patients were in postmenopause. The tumours were palpable and mammographically detectable. Three patients had a tumour in the left breast, and the average diameter was 42.25 mm. All the tumours were surgically excised. Histological examination of excised specimens confirmed the diagnosis of myofibroblastoma of the breast, showing different morphological types. Immunohistochemically, the tumours were positive for Vimentin, CD34, estrogen, progesterone, and androgen receptors and negative for cytokeratins, p63, and S100.
Conclusion: Since the clinical and radiological features of myofibroblastoma are nonspecific and differential diagnoses encompass a wide spectrum of breast conditions, histopathological and immunohistochemical verification after core biopsy and/or excision is crucial for establishing the diagnosis of this rare entity.

E-PS-02-059
Two breast malignancies in a young patient leading to detection of p53 mutation
J. Morris*, C. Quinn, R. Prichard, A. Maguire
*St Vincent's University Hospital and BreastCheck, Irish National Breast Screening Programme, Dublin, Ireland

Background & objectives: Detection of breast malignancy at an early age may prompt genetic testing to identify an underlying predisposition to malignancy and determine risk of future malignancies.
Methods: A 26 year old woman presented with an enlarging right breast mass. Imaging demonstrated a circumscribed 45mm mass with cystic areas. Needle core biopsy (NCB) was performed and diagnostic excision was recommended following discussion of the findings at multidisciplinary team meeting (MDM).
Results: NCB showed a markedly pleomorphic malignancy with spindled and epithelioid cells, negative for cytokeratins, ER, PR, HER2, GATA3, S100, SOX10, p63, ERG, CD30, CD45, desmin. Excision contained a 48mm tumour, well-circumscribed, with fleshy cut surface, solid with cystic areas. Microscopically, leaf-like architecture and fibroadenoma-like morphology were identified focally. There was marked stromal cellularity, nuclear atypia and overgrowth, frequent mitoses and infiltrative edge despite macroscopic impression of circumscription. Appearances were interpreted as malignant phyllodes tumour. A 2mm focus of high-grade DCIS was seen in a separate margin specimen. Following MDM review, a treatment plan was formulated. The patient was referred to clinical genetics service. A pathogenic germline TP53 variant was identified.
Conclusion: This patient was diagnosed with malignant phyllodes tumour and high-grade DCIS, two relatively unusual breast pathologies at her young age. This led to genetic testing and identification of a TP53 pathogenic variant which informs management of her current malignancy and optimal approach to follow-up and surveillance.

E-PS-02-060
Rare case report of diffuse pseudoangiomatous stromal hyperplasia associated with breast enlargement in a 24-year-old
F. Muresan*, G. Simion, A. Iliesiu
*Bucharest University Emergency Hospital, Romania

Background & objectives: Pseudoangiomatous stromal hyperplasia (PASH) is a rare benign mesenchymal breast tumour first described in 1986. The condition is typically asymptomatic and affects women aged 14-67 years-old. Symptomatic forms are usually focal and manifest as unilateral, circumscribed or irregular, slow-growing nodules.
Methods: This paper presents an extremely rare case of PASH associated with gigantomastia in a 24-year-old patient. The patient is diagnosed with bilateral diffuse breast enlargement and decided bilateral mastectomy.
Results: Gross examination of the post-fixation mastectomy specimens revealed a 2800 gr. left breast and a 2500 gr. right breast. Both breasts were white-gray and firm, with a relatively uniform cut-section surface interspersed by gelatinous regions. The microscopic aspects were suggestive of PASH, characterized by numerous interconnected slit-like spaces lined by flattened spindle cells (myofibroblasts) resembling endothelial cells. The pseudoangiomatous spaces were separated by hyalinized collagen bundles. We performed immunohistochemical markers to demonstrate the fibroblastic origin of the endothelium-like cells. The pathological process displayed a diffuse pattern, involving both breasts entirely. Additionally, micronodular regions featuring dilated ducts surrounded by fibroblastic stroma and sparse inflammatory infiltrates were observed, suggestive of fibroadenoma.
Conclusion: PASH is usually associated with the presence of a unilateral, well-circumscribed, and slow-growing breast mass. This lesion may be associated with other benign or malignant lesions. To date, only 19 cases of diffuse PASH associated with bilateral breast enlargement have been described in scientific literature. Even considering its rarity, recognizing this unusual PASH presentation is important for the correct management of patients, both from diagnostic and therapeutic points of view.

E-PS-02-061
Male breast carcinoma: a 10-year institutional review
R. Nikfar*, F.E. Kombak, N. Zeizafoun, L. Kowtha, S. Hiya, M. Harigopal

* Icahn School of Medicine at Mount Sinai, USA

Background & objectives: Male breast cancer (MBC) is rare, accounting for less than 1% of all breast cancers in men. In this 10-year retrospective study, we investigated the clinicopathologic features with the aim of improving the recognition of breast cancer in male patients.
Methods: 78 out of 100 male breast cancer patients met the criteria needed to be included in this study. During the last ten years (2014–2024), they had either a mastectomy or a lumpectomy.
Results: The median age of diagnosis was 66.5 years. Infiltrative ductal carcinoma (88%), followed by ductal carcinoma in situ (8%), was the most frequent final diagnosis. Patients presented with lump (21%) or nipple discharge (2%). The stages of breast cancer were stage I (46%), II (20%), and III (2%). Lymph node metastasis was seen in 32% of cases. 25% of cases had a family history of breast cancer. Breast cancer susceptibility gene 2 (BRCA2) was associated with 15% of MBC cases. The majority of invasive MBC were ER and PR positive and HER2 negative (74%); Her2 positivity was seen in 10% of MBC cases, with only one triple negative case (1%).
Conclusion: The diagnosis and prognostic markers in our male patient population mirror those of the general female population worldwide. A strong association has been observed between the BRCA2 mutation and family history in our cohort study of MBC. While breast cancers in women continue to be the primary source of data for treatment algorithms, further research is needed to enhance management and guide therapeutic decisions for men with breast cancers.

E-PS-02-062
Benign breast lesion clinically mimicking malignancy: nipple adenoma
M. Ozsen*, Y. Çakır
*Departmentof Medical Pathology, BursaUludağ University Faculty of Medicine, Bursa, Turkey

Background & objectives: Nipple adenoma is a rare benign breast tumour. The aim of this study was to evaluate the clinicopathologic features of this rare entity which can be clinically confused with malignancy and to emphasize its differentiation from other lesions.
Methods: The study included cases diagnosed as nipple adenoma by examining the breast materials evaluated in our centre between January 2010 and April 2024. The cases were retrospectively reviewed for age, gender and clinicopathological features (lateralization, clinical presentation, radiological findings, time to histopathological evaluation, preliminary diagnosis and follow-up period).
Results: All 10 patients included in the study were female. The age distribution of the patients ranged between 26-67 years and the mean age was 43+12.54 years. In 3 (30%) of 10 cases, the nipple adenoma was located in the right nipple, while in 7 (70%) cases it was located in the left nipple. The most common clinical presentation was nipple crusting. Paget's disease and/or malignancy were among the clinical prediagnoses in all but 1 case. The diagnosis was made from a mastectomy specimen in our only case, whereas all other cases were diagnosed from punch biopsy material.
Conclusion: Adenoma of the nipple, which may be clinically confused with Paget's disease and histopathologically with invasive breast carcinoma, is a rare neoplasm that poses diagnostic difficulties due to its various histomorphologic features. Unlike malignant lesions in the differential diagnosis, the fact that simple excision is sufficient in treatment makes it essential to make an accurate diagnosis, especially in biopsy material.

E-PS-02-063
Quantitative data generated by digital image analysis shows high levels of correlation with manual scores produced at external quality assessment of triple negative breast cancer for PD-L1 expression
S. Parry*, A. Dodson
*UK NEQAS ICC & ISH, United Kingdom

Background & objectives: UK NEQAS ICC & ISH conducts external quality assessment (EQA) for PD-L1 in triple-negative breast cancer (TNBC) to benchmark participants' results. Manual assessment is used. We generated digital image analysis (DIA) scores on the same materials for comparison and validation
Methods: Distributed materials comprising tonsil, positive and negative TNBC samples, and cell-lines (x4) from 9 EQA runs conducted between 2022 and 2024 were analysed for PD-L1 expression by DIA using a Visiopharm app. These data were compared with agreed consensus manual scores from four experts assessing concurrently. For each sample the t-test was used to test for significant differences between groups
Results: Overall, 298 slides were assessed. The SP142 clone (Ventana) was used to stain 243 (81.6%); 37 (12.4%) were stained with 22C3 (Dako); for 18 (6.0%) the primary was unknown.
When manual scores were used to group sample types according to correct or incorrect levels of PD-L1 expression, the tonsil showed no significant difference, and the negative tumour and two of the cell-lines were not informative because all specimens fell into the correct-level groups. For the positive tumour and the remaining two cell-lines the mean QS for each correct-level group was significantly different from those of the incorrect-level groups (significant at $P<001$ for the tumour, and at $P<0.0001$ for the cell-lines).
Conclusion: We have demonstrated statistically significant associations between manually assessed results and their matched DIA-derived quantitative scores.
These results validate the manual assessment process and raise the possibility of supplementing the information fed-back to participants with fully quantitative data.

The lack of associative evidence for the tonsil brings into question its usefulness as a control in this setting. Similarly, the lack of sensitivity shown by two of the cell-lines indicates that they may serve no useful purpose in the EQA process.

E-PS-02-064
A rare case of pleomorphic adenoma of the breast: a reminder of malignancy overdiagnosis
J.P. Pereira De Castro*, J. Azevedo, G. Miranda, J. Silva, Â. Rodrigues
*IPO-Porto, Portugal

Background & objectives: Epithelial-myoepithelial tumours of the breast are relatively uncommon neoplasms that can present diagnostic difficulties, especially in biopsies. Pleomorphic adenoma is an example that deserves special recognition despite being a rare and benign entity.
Methods: A 76-year-old woman was referred to our institution due to a 28 mm retroareolar mass in the right breast with a diagnosis of invasive carcinoma of no special type, grade 1. Immunohistochemistry performed on the biopsy showed negative expression of estrogen and progesterone receptors and HER-2 1+. After multidisciplinary discussion, the patient underwent a total mastectomy.
Results: Histology revealed a well-circumscribed tumour, composed of epithelial and myoepithelial cells, forming bilayered glands and anastomosing irregular structures in a rich chondromyxoid stroma. There was no atypia, mitotic figures or necrosis. These findings were compatible with pleomorphic adenoma, morphologically similar to its salivary gland counterpart.
The main differential diagnoses are mucinous carcinoma and matrix-producing carcinoma. However, the presence of a low-grade tumour with triple-negative profile should lead to consideration of alternative entities beyond invasive carcinomas, namely the epithelial-myoepithelial tumours. Additional immunohistochemistry and molecular studies were conducted to support the diagnosis.
Conclusion: We encountered a benign tumour initially suspected to be an invasive carcinoma on biopsy. The lack of concordance between

tumour grade and immunohistochemistry results, the biphasic pattern of the neoplasm and the prominent chondromyxoid stroma suggest the diagnosis of a pleomorphic adenoma, which is a typical tumour in the salivary glands but uncommon in the breast.

E-PS-02-065

The role of fascin expression in triple-negative breast cancer: immunohistochemical study in a retrospective cohort

D. Pérez Parra*, F. Postigo Corrales, L. Barona García, D.R. da Cruz Ribeiro, M.A. Beltrán Videla, A. Albadalejo González, M.I. Ortuño Moreno, D. Torres Moreno, A. Sánchez Espinosa, J.M. Acosta Ortega, A.B. Arroyo Rodríguez, A.M. Hurtado López, G. Luengo Gil, J. García Solano, P. Conesa Zamora
*Pathology Department. Hospital Santa Lucía, Spain

Background & objectives: Triple-negative breast cancer (TNBC), with a poor prognosis, often relies on chemotherapy despite limited efficacy. Fascin protein, linked to invasion, metastasis, and chemotherapy resistance, is a promising therapeutic target. This study aims to identify potential candidates for anti-fascin drugs.
Methods: We conducted an observational study on TNBC cases diagnosed between 2010 and 2022, with follow-up until December 2023, in Cartagena (Murcia, Spain), evaluating biological, oncological, and prognostic variables. Clinical data were collected from medical records. Histological parameters were obtained using PAT-Win Pathology software, and fascin levels were assessed via immunohistochemistry on paraffin-embedded tissue microarrays.
Results: In this study of 146 TNBC patients, the predominant subtypes were 'not otherwise specified' (115 cases) and medullary carcinomas (18 cases). Among surgically intervened patients, 98 had infiltrating tumours, while 33 did not. Of these, 61 received neoadjuvant chemotherapy, with 28 showing infiltrating carcinoma and 33 showing complete response. Regarding oncological stage, 31 were stage II, 94 stage III, and 14 stage IV.
The expression of fascin in tumour cells significantly correlated with HER2 values ($p<0.001$) and showed no significant correlations with overall survival/disease-free survival. Conversely, fascin in peritumoural fibroblasts related to the medullary subtype ($p<0.05$), and associated with better overall survival ($p=0.018$) and progression-free or disease-free survival ($p=0.022$).
Conclusion: The results regarding staining with fascin in tumour cells suggest the need for further research to elucidate its relationship with TNBC and prognostic factors. On the other hand, staining with fascin in peritumoural fibroblasts, particularly in surgically treated patients receiving neoadjuvant chemotherapy, is promising as a prognostic indicator and potentially guides personalized chemotherapy for patients with incomplete histological response. Further studies are needed to validate these findings.

E-PS-02-066

Metaplastic carcinoma of the breast - case series of a single centre

M. Pinho Fialho*, L. Gonçalves, L. Ruivo, A. Gradil, L. Correia
*Department of Pathology - Unidade Local de Saude Santa Maria (ULSSM); Instituto Politécnico de Lisboa (ESTeSL), Portugal

Background & objectives: Metaplastic carcinoma breast cancer (MpBC) is a rare and heterogeneous group of invasive breast carcinomas. Despite some studies and case reports data are currently limited. Our work aims to evaluate the clinicopathological features and the prognosis of MpBC patients.
Methods: Retrospective unicentric study of MpBC diagnosed from January 2000 to February 2024. Pathological reports were accessed for specific patterns of MpBC, grouped as monophasic/biphasic tumours and TNM stratified according to WHO Breast Tumours 5th edition and AJCC 8th edition. Time-to-event outcomes were calculated using the Kaplan-Meier method and the log-rank test.
Results: We identified 44 patients, 1 male, median age 59 years-old (33-98), 9 metastatic ad-initio. Biphasic-MpBC corresponded to 77%; heterologous-mesenchymal-differentiation was found in 34%, spindle-cell carcinoma in 6.8%. Ki67 ranged from 20 to 95%. Twenty-seven were triple-negative, eight luminal-B, six HER2-positive tumours. Median follow-up time was 82.1 months and median overall survival (mOS) 32.1 months. Subgroup analysis showed no statistically significant differences between monophasic/biphasic MpBC or histological patterns. Metastatic patients and patients over 60 years had a poorer prognosis (25.1 vs 115.5 months $p=0.053$; 20.0 months vs mOS not reached $p=0.001$, respectively). In luminal-B patients, mOS was not reached (vs 32.1 months -triple-negative and 10.6 months -HER2).
Conclusion: MpBC is rare, reported only in up to 2% of all invasive breast cancers. Given its uncommon nature, pathology reports lack uniformity. Establishing protocols is crucial to accurately identifying and reporting patterns to better determine treatment strategies. Our data suggests better outcomes regarding Luminal-B, non-metastatic patients. However, the limited number of patients prevented a statistically significant evaluation of differences between histological subtypes. Multicentric studies are needed to correlate demographic, histological or immunohistochemistry factors with patients' outcomes.

E-PS-02-067

The significance of histopathological parameters in female patients after breast implant placement: a retrospective study

M. Prvanovic*, D. Dundjerovic, S. Tatic, M. Zivotic, N. LIlic, J. Jeremic
*Institute of Pathology, University of Belgrade, Serbia

Background & objectives: Mammoplasty, involving breast implants, is common for aesthetic enhancement or post-mastectomy reconstruction. Complications such as capsule contractures and anaplastic large cell lymphoma may arise, displaying histopathological variations. This study examines patient demographics, time intervals, and complications post-mammoplasty, including cancer history.
Methods: A study of 27 patients with breast implants at the Institute of Pathology, Faculty of Medicine, University of Belgrade, from January 2019 to December 2023, analysed patient age, indications for mammoplasty, and time intervals to complication onset. Descriptive statistics and Fisher's exact probability test were applied to archived histopathological specimens for analysis.
Results: Patients experiencing complications post-mammoplasty had an average age of 50.1 years, with a mean time interval of 16.7 years from implant placement to complication onset. Histopathological analysis revealed prevalent synovial metaplasia (100%), chronic inflammation (76%), foreign material deposition (52%), and granuloma formation (32%). Remarkably, 22% of patients had a history of breast cancer, while 88% opted for mammoplasty primarily for aesthetic enhancement purposes.
Conclusion: This retrospective study highlights older patient age and a prolonged interval between implant placement and complication onset compared to existing literature. A majority of patients sought mammoplasty for aesthetic enhancement, with fewer than expected having a history of breast cancer. These findings underscore the importance of histopathological evaluation and clinical vigilance in managing complications associated with breast implants.

E-PS-02-068

Tumour-associated neutrophils facilitate stemness of breast cancer cells

Q. Wu, S. Wang*, Z. Feng
*Department of Pathology, Anhui Medical University and The Second Affiliated Hospital of Anhui Medical University, Hefei, Anhui, China

Background & objectives: Eliminating cancer stem cells and enhancing antitumour immunity remain challenges in cancer therapy. Tumour-associated neutrophils (TANs) remarkably correlate with poor outcomes in breast cancer patients, but their impact on cancer stemness traits is unclear.
Methods: The relationship of neutrophils with breast cancer stemness was analysed using both TIMER database and immunohistochemistry, in which CD66b was used to mark neutrophils and CD133 and SOX9 to cancer cell stemness. To detect the stemness traits of breast cancer cell lines, the cultured supernatant of TANs was used to stimulate cancer cells for sphere formation, RT-qPCR and WB assay.
Results: The TIMER database analysis demonstrated positive correlations between neutrophils and breast cancer stemness markers CD133, SOX9, and CD44, and a negative correlation with CD24 in breast cancer. Immunohistochemistry showed a correlation between CD66b+ neutrophils infiltrating in breast cancer tissues and CD133 ($r=0.347$, $P<0.05$) and SOX9 ($r=0.410$, $P<0.05$) expression of cancer cells. In vitro, TANs supernatant facilitated spheroid formation of breast cancer cells compared to the supernatant of quiescent neutrophils. RT-qPCR showed significantly higher mRNA levels of CD133, SOX9, and CD44, with a lower CD24 level in TANs group ($P<0.05$). WB confirmed elevated protein expression of SOX2 and SOX9 in TANs group versus quiescent neutrophils group ($P<0.05$).
Conclusion: The infiltrating neutrophils correlating with stem-like features of breast cancer cells suggests their potentially role in promoting cancer cells stemness. This paves the way for therapeutics targeting neutrophils treatment and immunotherapy in breast cancer.

E-PS-02-069
Histological features in triple negative breast cancer: predictors of response and progression in relation to HER2 expression
E.R. Quintero Barbon*, C.E. Haro Haro, J.T. Zúñiga Gaitán, S. Ramon y Cajal Agüeras, V. Peg Cámara
*Vall d'Hebron University Hospital, Barcelona, Spain, Colombia

Background & objectives: Triple-negative breast cancer (TNBC) tends to be clinically aggressive but often demonstrates complete response (pCR) to neoadjuvant systemic chemotherapy (NST). To analyse histological characteristics of low HER2 (1+/2+) in comparison to HER2 (0), and their compartmentalization or response to NST.
Methods: 155 cases diagnosed with TNBC between 2014 and 2022 were collected. They were grouped according to HER2 (0 vs Low) analysed by immunohistochemistry +/- ISH, compared by tumour size, histological grade, proliferation index before TNBC, and their correlation with pCR.
Results: We analysed 155 cases with a mean age of 57.5 years and a mean tumour size of 24.45 mm. Most cases were invasive breast cancer without special type (91%), with histological grade 3 (78%). Regarding treatment, a significant difference was observed in lower response to NST in HER2 2+ cases ($p=0.033$) and a trend towards pCR in HER2 0 cases ($p=0.053$). A significant association was observed between a high proliferation index (Ki 67 of 69.18%) and higher histological grade with pCR ($p=0.001$). In addition, histological grade 3 showed a correlation with HER2 0 status ($p=0.001$), compared to cases with lower histological grades (Grades 1 and 2) with low HER2 expression.
Conclusion: In our series, Statistical significance was observed between histological grade 3 and elevated Ki 67 proliferation index with pCR. In addition, a significant association was observed between TNBC histological grade 3 and HER2 0 expression. Although no significant correlation was found between pCR and HER2 status, a trend towards pCR was observed in HER2 0 cases, suggesting a hypothetical role of HER2 low expression in response to neoadjuvant systemic therapy in TNBC. Larger series are needed to confirm those findings.

E-PS-02-070
Lymph node status as a predictor of pathologic response post neoadjuvant chemotherapy in breast cancer patients
Z. Radicevic*, M. Petričević, N. Kurtovic, L. Klobučarić, I. Zagorac, M. Bakula, R. Alaghehbandan, J. Rajc
*Department of Pathology and Forensic medicine, Osijek University Hospital, Osijek, Croatia, Faculty of Medicine, University of Osijek,Osijek, Croatia

Background & objectives: Pathologic response to neoadjuvant chemotherapy remains unpredictable for some breast cancers. In this study, we assessed a corelation between advanced stage of disease with lymph node metastasis and pathologic response post neoadjuvant chemotherapy in different subtypes of breast cancers.
Methods: We reviewed 180 breast cancer patients treated with neoadjuvant chemotherapy at University Hospital Osijek. Four categories of lymph node metastasis (N0, N1, N2, N3) were assessed in five subtypes of breast cancers (Luminal A, Luminal B HER2+, Luminal B HER2-, HER2+,and triple-negative), and compared with residual tumour burden (scored as RCB 0, RCB 1, RCB 2, RCB 3).
Results: Of 180 patients, 55,6% were N0, 28,3% N1, 14,4% N2, and 1,7% were N3. The best pathologic response post neoadjuvant chemotherapy was in HER2 negative tumours, with a complete pathological response rate of 35%. We found that positive axillary lymph node status was positively correlated with poorer outcome and more extensive residual tumour in all breast cancer subtypes. Further, luminal B Her2 negative and triple-negative subtypes with N3 were significantly associated with extensive residual tumour burden (RCB 3) (Fisher exact test, $p<0,001$).
Conclusion: Our findings show that the number of positive axillary lymph nodes is positively correlated with extended residual disease, especially in Luminal B HER2 negative and triple-negative tumours. Therefore, these patients may be candidates for different or a rather more aggressive neoadjuvant treatment.

E-PS-02-071
Profile changing of ER, PR, HER2 between primary tumour and locoregional metastases in breast cancer
A. Rais*, Y. Houcine, S. Kamoun, M. ALAYA, M. Driss
*Pathology department, Salah Azaiez Institute, Tunisia

Background & objectives: The expression status of estrogen receptors(ER), progesterone receptors(PR) and human epidermal growth factor receptor 2(HER2) in breast cancer(BC) is an important indicator of treatment and prognosis. Herein we analyse changes in expression of these biomarkers between primary tumours and locoregional metastasis.
Methods: This retrospective study included 89 patients with invasive breast carcinoma and ymph node metastasis between 2008 and 2022. Cases receiving neoadjuvant chemotherapy were excluded. Immunohistochemical evaluation determined ER, PR, and HER2 expression in both primary tumours and lymph node metastases.
Results: All patients were female, with a median age of 50 years (range: 28-84 years). The percentage of positive staining for ER, PR, and HER2 in primary lesions was 64%, 57 %, and 15 %, respectively, While in metastatic lymph nodes, it was 59%, 41%, and 11%, respectively. Equivocal HER2/neu expression level (2+) was found in 12 cases in primary tumours and in 8 cases in lymph nodes. ER expression levels differed between locoregional metastasis and primary tumours in 18 of 89 cases (20%), PR expression differed in 24 cases (26%), and HER2 showed a difference of 49%.
Conclusion: Significant variation exists in the expression of ER, PR, and HER2 receptors between primary lesions and locoregional metastases. This difference may be attributed to the presence of polyclonal tumour cells, nature of the fixed tissue, subjective judgment of staining

positivity by pathologists, and previous treatment. Reassessment of marker expression throughout the disease course is crucial for follow-up, treatment planning, and prognosis evaluation.

E-PS-02-072

Pathological and molecular features of breast cancer

A. Rais*, Y. Houcine, M. Alaya, A, S. Kamoun, M. Driss
*Pathology department, Salah Azaiez Institute, Tunisia

Background & objectives: Breast cancer(BC) is the most frequent cancer among tunisian women and worldwide. Its anatomopathological and molecular features must be studied on an ongoing basis to assess its changes over the years.Herein we aimed to determine (BC) features in Tunisian women.
Methods: We conducted a retrospective descriptive study of 99 patients who were diagnosed with invasive breast cancers in our laboratory over a 14-year period, from 2008 to 2022. The molecular typing was based on immunohistochemical markers: estrogen receptor (ER),progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2), and cell proliferation index (Ki-67).
Results: The average age was 52 years (range: 28-84 years). Specimens included in the study were mastectomies in 47% of cases , lumpectomies in 18% and the rest were microbiopsies . Ten patients had received a neoadjuvant chemotherapy. Nonspecific invasive cancer was the most frequent histological type. SBR grade II was most prevalent. Hormone receptors were positive in 63% of cases. Her2-Neu receptors were overexpressed in 14 % of cases. The ki67 was ≥ 20% in 48 % of cases. Luminal B was the most common molecular subtype and presents 46% of cases .
Conclusion: Breast carcinoma in Tunisian women is characterized by its high frequency. Our results reinforce the need to develop programs for the prevention and early diagnosis of this cancer.

E-PS-02-073

Oesophageal adenocarcinoma that metastasized to breast was misinterpreted as primary breast adenocarcinoma (NOS): a rare case report

G. Richter*, K. Hilgers, P. Richter
*Institute of Pathology, Germany

Background & objectives: A breast tumour is more likely to be a primary breast carcinoma than a metastasis of the breast. It is crucial that metastases of the breast are identified for correct patient management. Metastases of the breast occur in both genders
Methods: We present a case of a 55-year-old Caucasian female with solid tumour of the breast. The specimens were routinely stained with hematoxylin and eosin. Also, they there immunohistochemically stained with primary antibodies Pan-cytokeratin, cytokeratin 5/6, cytokeratin 7, cytokeratin 20, TTF-1 and KI-67 were performed. In addition, immunohistochemically staining with primary antibodies estrogen and progesterone receptor and HER2 were performed.
Results: Histological examination shows cuboidal and less often columnar cells, containing enlarged nuclei with coarse and partially vesicular chromatin. Using Immunohistochemistry, we detected a positive reaction for Pan-cytokeratin, cytokeratin 7 and a negative reaction for cytokeratin 5/6, cytokeratin 20, TTF-1, estrogen and progesterone receptor in the tumour cells. We detected a HER2 score 0 (negative). A liver metastasis was found during the staging and an CDX2 positive / GATA3-negative adenocarcinoma was diagnosed. On further investigation an oesophageal primary tumour was found. In addition, we investigated the specimen of the breast and found a positive CDX2 reaction and a negative result for GATA3. We favour a breast metastasis of an oesophageal adenocarcinoma.
Conclusion: We present a case of breast metastasis of oesophageal adenocarcinoma in a female. It is not always necessary to use immunohistochemistry to confirm primary breast origin of a tumour in the breast. In our case, the morphology and triple-negative biology, the absence of a carcinoma in situ, and the clinical presentation suggest a different primary tumour. A correspondingly extensive panel of clinically and immunohistochemically investigations is needed for correct classification for this very rare breast metastasis of an oesophageal adenocarcinoma.

E-PS-02-074

A clinicopathological study of invasive apocrine carcinoma of the breast: a single centre experience

V. Risteski*, M. Kochoska, T. Angelovska, A. Jovcheva-Trajkovska, A. Eftimov, R. Jovanovic, S. Kostadinova-Kunovska, M. Bogdanovska-Todorovska
*Institute of Pathology, Faculty of Medicine, University Ss. Cyril and Methodius, Skopje, Republic of North Macedonia

Background & objectives: Breast cancer is a divergent and multiplex disease encompassing distinct histologic and molecular genetic types. The aim of the study was to analyse clinicopathologic characteristics of patients with apocrine breast carcinoma using integrated state of art technologies.
Methods: We performed a study that included 17 cases that met the criteria for apocrine breast carcinoma diagnosed between 2015 and 2023 at the Institute of Pathology in Skopje. We used TruSight Tumour 15 Gene Panel (Illumina) to analyse gene mutations in nine patients. Furthermore, protein expression of α-methylacyl-CoA racemase (AMACR) was analysed.
Results: The median age of the patients was 61,9 years. All the patients were diagnosed with histological grade three. The average tumour size was 3,46cm and positive lymph nodes were detected in 70,5% of the patients. Most of the patients presented at stage II and III (III 35, 3%; II: 47,0%; and I: 17,7%), and the mean Ki67 index was 30%. Majority of the cases (58,8%) were triple negative while HER-2 overexpression and/or amplification was detected in 41,2%. AMACR expression was detected in 73,3% of the cases. Clinically relevant genomic alterations were detected in of 66,7% of the patients. Most frequent altered genes were TP53 (66,7%), PIK3CA (11,1%) and ERBB2 (11,1%).
Conclusion: Our study revealed that most of the cases were triple-negative with clinically relevant genomic alterations in more than 60% of the cases. These neoplastic lesions also have AMACR overexpression. The current evidence states that AR-positive breast carcinomas may have limited clinical benefit from adjuvant chemotherapy. Cancer genomic profiling of apocrine carcinomas emerges to be an optimistic approach that could reveal possible targets for individualized treatment.

E-PS-02-075

Invasive lobular carcinoma with papillary features mimicking papillary carcinoma - clinicopathologic and molecular characterization of this new variant with a systematic review of the literature

R. Rocha*, P. Rodrigues Veiga, A. Lapa, C. Leal, N. Coimbra, C. Santos, A. Barbosa, J. Costa
*Department of Pathology, Portuguese Oncology Institute of Porto, Portugal

Background & objectives: A new variant of invasive lobular carcinoma (ILC) mimicking a papillary carcinoma has been recently reported by several authors, characterized by a well circumscribed mass, with a fibrous pseudocapsule and papillary architecture.
Methods: We report the case of a 68-year-old woman diagnosed with two lesions of ILC with papillary features, with a prior history of breast cancer. Molecular characterization by NGS using the TruSight Hereditary Cancer panel is ongoing. We conducted a systematic literature review using PubMed without language or date restrictions: of 272 initial papers, 6 were selected, containing 8 additional cases.

Results: Among the 9 cases, the median age at diagnosis was 72(minimum:61;maximum:86) years and all patients were female. The median size was 28mm(12;45). No known genetic predisposition syndromes were reported. Eight(89%) cases were submitted to core-needle biopsy: 3(33%) were classified as encapsulated/solid papillary carcinoma, 2(22%) as ILC, 2(22%) as invasive carcinoma, NST and 1(11%) as lobular carcinoma in situ. None were admixed with additional histologic subtypes in the surgical specimen. Six(67%) cases were classified as histologic grade II. All cases were ER+/HER2- and presented loss of E-cadherin. One case presented a lymph node metastasis. None of the cases presented locoregional recurrences, distant metastasis or deaths from disease.
Conclusion: We report a comprehensive systematic review in literature of ILC with papillary features, with molecular characterization of our case ongoing. Awareness of this variant is critical to avoid misdiagnosis with papillary carcinomas and to ensure appropriate management for patients. Useful diagnostic clues include the presence of discohesive, monotonous carcinomatous cells associated with fibrovascular cores and/or adjacent foci of classic ILC/LCIS, which should prompt staining for E-cadherin/beta-catenin/p120. Further studies are necessary to understand the clinical behaviour and prognosis of this variant.

E-PS-02-076

Morphological changes following cryoablation in breast cancer

L. Rodriguez Ariza*, A. Hidalgo Romero, V. Peg Cámara
*Vall d'Hebron University Hospital, Spain

Background & objectives: Cryoablation, a minimally invasive therapeutic percutaneous thermal ablation technique using freezing, can be used for early-stage breast cancer treatment. To validate cryoablation for invasive breast cancer treatment, we propose surgical resection of the lesion followed by histopathological assessment.
Methods: First four cases treated with cryotherapy and subsequently operated in our institution were selected. Age ranged between 71 and 93 years old, three of whom had non-special type invasive carcinoma (75%), with tumour sizes ranging from 0.6 to 1.6 cm in maximum diameter, none of the cases had an in situ carcinoma component, and all presented with T1N0 tumour stage.
Results: The cases involved women aged between 71 and 93 years, three of whom had non-special type invasive carcinoma (Luminal A, Luminal B HER2-, and Luminal B HER2+) and one had tubular invasive carcinoma (Luminal B HER2-). In the histopathological study of the tumour resection specimens, reactive fibrosis was found in all cases in the area treated with cryotherapy. Additionally, haemorrhagic changes were observed in two cases, and steatonecrosis was also observed in two cases. In none of the cases studied was residual invasive or in situ neoplastic cellularity observed.
Conclusion: Cryoablation is a therapeutic process that, in 100% of early-stage invasive breast cancer cases treated with this technique at our hospital, has demonstrated complete tumour elimination, without evidence of residual invasive or in situ neoplastic cellularity in subsequent histopathological studies of resection specimens. It thus emerges as an effective, less invasive, and safer treatment alternative compared to conventional breast cancer surgery, especially for patients with surgical contraindications.

E-PS-02-077

Prognostic significance of integrated computational pathology and gene expression analysis of triple negative breast cancer tumour microenvironment

I. Roxanis*, K. Zormpas-Petridis, S. Haider, D. Kolarevic, P. Gazinska, R. Salgado, A. Tutt
*Institute of Cancer Research, United Kingdom

Background & objectives: Triple negative breast cancer (TNBC) is characterised by poor outcome. Aiming to reveal biologically and prognostically significant features of the tumour microenvironment (TME) with potential clinical relevance, we integrated quantitative visual and artificial intelligence (AI)-based pathological assessment with gene expression.
Methods: In digital images from 118 cases with pathology and clinical data, we quantified visually and with the SuperHistopath tumour region classification algorithm, relative proportions of viable/necrotic tumour, post-necrotic changes, tumour stroma and immune infiltrates. Derived data were analysed for prognostic value and differentially expressed genes. mRNA was measured with NanoString (nCounter platform) using the Pan-Breast panel with 757 spike-in genes.
Results: Tumour necrosis was associated with distant (but not regional) metastasis and decreased survival (HR=0.3, p=0.005), independent of grade, stage, and proliferative activity. Combining necrosis with post-necrotic changes increased the prognostic power (HR=4.76, p=8.4x10-4). Extent of AI-quantified clustered immune infiltrates was also prognostic (HR=0.16, p=0.001), unlike standard visual assessment of infiltrating lymphocytes.
Along with genes denoting cell proliferation, chromosomal instability (CIN)-associated genes were up-regulated in necrotic tumours. Furthermore, genes related to increased neo-antigen presentation, and genes expressed by cytotoxic T lymphocytes and NK cells with increased cytolytic activity, were up-regulated in cases with increased immune infiltrates.
In analysis restricted to gene expression, up-regulation of DNA damage repair-related genes conferred decreased survival.
Conclusion: Quantification of TME constituents in TNBC is prognostic of distant metastasis and survival. Necrotic tumours appear more prone to distant but not regional metastasis, implying presence of clones intravasating directly into blood vessels. Based on our gene expression data, we will discuss how clones in necrotic tumours may undergo CIN-associated adaptation with upregulation of DNA damage repair genes. AI-assessed extent of immune infiltrates may be clinically valuable as immunotherapy biomarker. Associated genes could explain mechanisms of tumour immunogenicity and immunoediting.

E-PS-02-079

A rare case of amyloidosis limited to the breast: case report

S.M. Sabo*, A. Evsei, A. Birceanu, N. Copcă, C. Costras, M. Matanie, T. Turcu, R.G. Grigore

*Colentina Clinical Hospital, Romania

Background & objectives: Localized breast amyloidosis is a very rare pathologic entity, that must be confirmed by exclusion of systemic disease or hematologic malignancy. We report a recent case of localized breast amyloidosis (amyloid tumour) in a 64 years old woman.
Methods: A 64 years old female patient had a mammographically detected mass, located in the upper-outer quadrant of the left breast, which was surgically resected at an outside hospital. First differential diagnosis included fibromatosis, fibromatosis-like metaplastic invasive carcinoma (FLMC) and amyloid tumour.
Further extensive clinical and paraclinical workup revealed no hematological malignancy or any evidence of systemic disease.
Results: Histological examination showed a paucicellular, dense nodule, with slightly irregular margins, bordered by lymphoid aggregates, consisting of bundles and fascicles of bland spindle cells growing between eosinophilic or hyalinzed deposits of amorphous material, confirmed to be amyloid deposits on Congo red stain, by exhibiting apple-green birefringence when viewed under polarized light.
Immunohistochemical markers were used to exclude breast fibromatosis or FLMC. Beta-catenin showed only weak expression in the cytoplasm of the spindle cells and CD34, ER, PR, panCK were all negative.
A diagnosis of localized breast amyloidosis or amyloid tumour was established. No further treatment is necessary as prognosis is good, with a low chance of recurrence.

Conclusion: In systemic amyloidosis, usually immunoglobulin light-chain amyloid (AL) is deposited in a variety of tissues, while AA amyloidosis may complicate neoplasias or chronic inflammatory diseases. Breast involvement can be of primary localization, almost only AL type, or secondary due to systemic or hematologic disease. Secondary amylodiosis must be ruled out, because of the worse prognosis, compared to localized disease. Main treatment of primary amyloidosis of the breast is surgical removal with negative margins. Long-term hematologic follow-up might not be necessary.

E-PS-02-080

Unusual localisation of plasmacytoma: presented in breast

B.M. Polat, Z. Sagnak Yilmaz*, I. Saygin
*Dokuz Eylül University Institute of Health Sciences, Department of Molecular Pathology, Izmir, Turkey

Background & objectives: Plasmacytomas are solitary tumours that consist of neoplastic plasma cells. They may be a primary solitary mass without involvement of bone marrow, or they may accompany multiple myeloma. Solitary plasmacytomas are rare. Their presentation in breast tissue is much rarer.
Methods: A true-cut biopsy of the lesion was performed. The specimen was formalin-fixed and paraffin-embedded. The sections were stained with routine H&E. Immunohistochemistry was performed.
Results: A 51-year-old female presented with a palpable mass in the left breast. Ultrasound imaging showed a BIRADS-4A lesion at the periareolar site. Atypical plasma cells, which have an eccentrically located nucleus, were seen in histopathological examination. Neoplastic cells were immunoreactive for CD38, CD138, and CD45 and immunonegative for PANCK, GATA3, synaptophysin, and chromogranin.
Conclusion: Extramedullary plasma cell tumours are rare, mostly found in the upper respiratory tract, and involvement of the breast is even rarer. Histopathologically, primary breast carcinoma and plasma cell neoplasms can mimic each other. Immunohistochemical analysis is critical for differentiation. Even though this diagnosis is rare, it is important for the pathologist to suspect a plasma cell neoplasm histopathologically.

E-PS-02-081

Primary breast osteosarcoma with chondroid differentiation and lung metastasis misdiagnosed as an invasive carcinoma

M. Samaila*, C. Ofunne, N. Kwapmi, H. Dahir, O. Essien, C. Chikezie
*Nigeria

Background & objectives: Background: Primary extra-skeletal osteosarcoma of the breast is uncommon and less than 200 cases have been documented in literature since the first case in 1957. It is may misdiagnosed as an epithelial tumour due to inadequate tissue sampling.
Methods: Mastectomy specimen was formalin fixed and paraffin processed, stained with Haematoxylin & Eosin and Immunohistochemical antibodies
Results: Result /Case summary: A 45year old female with a trucut biopsy diagnosis of triple negative invasive ductal carcinoma, grade 2 (SBR 6/9) had six cycles of chemotherapy with intravenous Docetaxel 120mg twice weekly. She had mastectomy on completion of the 6th cycle. Mastectomy revealed sheets of malignant spindle cells, extensive osteoid and bone formation with focal chondroid matrix differentiation and numerous osteoclast giant cells. No malignant epithelial component or lymph nodes involvement was seen. IHC done was negative for ER, PR, HER-2, Desmin and Pancytokeratin. Focal positivity for SMA was seen. CT scan showed cannon ball metastasis in the lung fields.
Conclusion: Conclusion: The diagnosis requires supportive comprehensive use of epithelial IHC markers. We could not identify any epithelial malignancy in this thoroughly sampled mastectomy specimen. There was an initial misdiagnosis of an epithelial tumour rather than a metaplastic transformation. The optimal treatment modality is wide excision with free margins or mastectomy. Prognostic outcome is poor due to local recurrences and haematogenous spread to the lungs as seen in this patient. This report seeks to create heightened awareness amongst pathologists and clinicians.

E-PS-02-082

Outcomes of breast B3 lesions between 2019 and 2022 – a single centre study

D. Saseendran*
*St. Georges NHS hospital, United Kingdom

Background & objectives: B3 breast lesions represent a heterogeneous group with uncertain malignant potential. The primary objective of this audit is to assess and compare the national audit data with our departmental data and aim to identify contributing factors of B3 rates.
Methods: A retrospective analysis of our pathology database from March 2019 to April 2022 was performed to identify all B3 lesions diagnosis. Cases were stratified into B3 with and without atypia. Subsequent excisions related to each biopsy were evaluated, and the positive predictive value was computed. These findings were juxtaposed with published data by National Breast Screening Programme Pathology Audit (2019-2022).
Results: Our department's audit data closely aligned with national figures, yet our B3 rate and positive predictive value (PPV) stood as high outliers. We identified more B3 cases (326 vs. 391) and achieved a higher PPV for B3 with atypia lesions (29.5% vs. 36%) compared to the National Breast Screening Programme Pathology Audit. Several factors potentially contribute to these discrepancies, including our department's elevated case volume and possible differences in categorization thresholds. Variations in biopsy techniques and sampling quantity at SGH may also play a role. Furthermore, the disparity between NBSPA and our audit could be due to differing data availability during the national audit.
Conclusion: In summary, our audit provides insight into the intricate nature of B3 breast lesions, revealing both similarities and differences between our departmental data and national statistics. Although our figures closely align with national trends in B3 rates and positive predictive values, our department exhibits distinct features, including increased identification of B3 cases and higher PPV for lesions with atypia. Factors such as case volume, biopsy criteria, and data availability likely influence these discrepancies

E-PS-02-083

Prevalence of HER2-low and ultralow expression in breast cancer: a comprehensive review from real world data in a German University Hospital

U. Sommer*, C. Scheffold, A. Forberger, G. Baretton
*Institute of Pathology, University Hospital Carl Gustav Carus, Medical Faculty, Technical University of Dresden, Dresden, Germany

Background & objectives: Understanding HER2-low and ultralow breast cancer subtypes is crucial, particularly for targeting these groups with antibody drug conjugates (ADCs), such as Trastuzumab deruxtecan, to optimize therapeutic approaches.
Methods: We conducted a retrospective immunohistochemistry analysis on 1,000 breast cancer samples from 2018-2021 at a German university hospital, categorizing HER2 status into null, ultralow (IHC>0< 1+), low (IHC 1+ or IHC 2+ without amplification), and positive (IHC 3+ or IHC 2+ with amplification). Sample types, tumour characteristics (primary/metastatic, TNM, grading), and biomarkers (ER, PR, Ki67) were assessed.
Results: Preliminary analyses show notable instances of HER2-low and ultralow expressions, suggesting significant variability linked to

histological subtypes, grading, and hormonal receptor statuses. These variations highlight the potential of these subtypes as biomarkers for ADC therapies, including Trastuzumab deruxtecan. Presence of HER2-low and ultralow categories may influence therapeutic outcomes and guide treatment strategies. Detailed prevalence rates and additional statistical analyses are in progress to thoroughly evaluate the implications of HER2 expression levels on treatment efficacy and to explore potential correlations with clinical outcomes.
Conclusion: The identification of HER2-low and ultralow expressions is vital for tailoring ADC therapies like Trastuzumab deruxtecan, potentially broadening treatment applicability and improving patient outcomes. These preliminary results support the strategic expansion of ADC usage across various HER2-expressing tumours, emphasizing the need for continuous research to substantiate these findings and optimize treatment protocols.

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Funding: This study was financed by Daichii Sankyo and AstraZeneca

E-PS-02-084
A 5-year retrospective audit of the reporting of neoadjuvant breast cases against the ICCR reporting guidelines
C. Stacey*, L. McKenna, A. Hennessy
*Beaumont Hospital, Ireland

Background & objectives: There is an increasing role for neoadjuvant therapy in the treatment of breast cancer. In 2023, the International Collaboration on Cancer Reporting (ICCR) published a dataset for standardised reporting of breast cancer resection specimens following neoadjuvant therapy.
Methods: With the requirement for a new local reporting template, it was important to audit our reporting of these cases and compare to the new international guidelines prior to implementation of such a template. A database search for excision breast specimens following neoadjuvant chemotherapy was performed for the years 2018-2023 and 166 cases were identified.
Results: 129 cases matched the search criteria and were analysed – composed of a mixture of HER2 positive cases & triple negative breast cancers. There was excellent reporting of tumour type, presence/absence of DCIS and laterality. However, reporting of the residual cancer burden score & repeat hormone receptors (where appropriate) was lacking as well as variability in the description of tumour bed. Looking at treatment response, 37.8% of cases had a (pathological complete response), which is higher than reported pCR rates published in the literature.
Conclusion: There is an ever increasing number of neoadjuvant breast excisions and with the introduction of the ICCR dataset, an audit of reported highlighted some deficiencies in reporting. A local reporting template based on the ICCR dataset was introduced and a re-audit is planned, to close the audit cycle.

E-PS-02-085
The analytical and clinical validity of the Nottingham histological grading system in neoadjuvant setting
S. Steen*, E. Karlsson, X. Chen, B. Acs, J. Hartman
*Karolinska Institutet, Sweden

Background & objectives: The Nottingham histological grading (NHG) system has shown robust prognostic implication in breast cancer. However, the analytical and clinical validity of the NHG system in neoadjuvant treated (NT) patients has not been demonstrated yet.
Methods: 507 NT patients with available grades for core needle biopsy (CNB) and subsequent resection specimen (RS) were evaluated. To adjust for pre-analytical/analytical bias between CNB and RS, the grades were compared with a control cohort (CC) of 297 primary operated patients. The change of grade between CNB and RS was compared. Survival analysis was performed in the NT cohort.
Results: We found a significant difference in grades between CNB and subsequent RS in both cohorts (Wilcoxon signed rank tests p-value<0.001). The agreement between paired CB and RS for grade was lower in the NT cohort (Quadratic weighted kappa=0,43) than in the CC (0,66). Grades in the NT cohort more often decreased from CNB to RS compared to the CC (Mann-Whitney U test p-value<0.001). Mitotic count and gland formation scores more often decreased in the NT cohort compared to the CC (p<0.001 respectively p<0.025). NHG performed on both CNB and RS were prognostic in the NT cohort (HR:2.03, CI:1.43-2.94, p<0.001 respectively HR:2.75, CI: 1.93-3.85, p<0.001).
Conclusion: Neoadjuvant treatment affects NHG with a significant decrease in grade from core biopsy sample to resection specimen. In neoadjuvant setting, grades in both core biopsy sample and resection specimen are strongly prognostic. Therefore, we recommend performing NHG both before and after neoadjuvant therapy.

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E-PS-02-087
A very rare cause of male breast lump: idiopathic granulomatous mastitis
L. Tekin*, F. Dinç, C. Yazkan
*Turkey

Background & objectives: Idiopathic granulomatous mastitis (IGM) is a rare, resistant, and recurrent benign disease of the breast. IGM can be clinically and radiologically confused with breast carcinoma, and core needle biopsy is needed to diagnose.
Methods: A 64-year-old man was presented with a retroareolar painful lump in his right breast of 2-week duration. The examination revealed a sub-areolar nonmobile, tender lump, and thickening in the areola and retraction of the nipple.The lesion was sampled with needle biopsy and evaluated microscopically.
Results: IGM's pathological findings are perilobular granulomatous inflammation, accompanied by infiltration centred on lobules with lymphocytes, plasma cells, epithelioid histiocytes, multinucleated giant cells, and neutrophils without intralobular micro abscess formation. Immunohistochemistry showed CD68 positive and PanCK negative staining in epithelioid histiocytes. The mycobacterial evaluation was negative.

Conclusion: IGM is a rare breast lesion and is presented because it is much rarer in men.
E-PS-02-088
Comparison of mast cell accumulation in the tumour microenvironment with prognostic parameters in breast cancer
l. Tekin*, M. Ünçel
*Turkey

Background & objectives: The tumour microenvironment in the cancer, influencing host defenses against the tumour. When the mast cell is active, mediators secreted from cytoplasmic granules .Mast cells can both suppress and promote tumour growth in the tumour
Methods: 84 cases were diagnosed with 77 Invasive Ductal Carcinoma and 8 Invasive Lobular Carcinoma, aged between 31 and 85 (average 54.9%).We retrospectively evaluated the presence of mast cells with CD117 immunohistochemically in the tumour microenvironment in mastectomy material and compared it with other prognostic parameters. Positively stained cells were counted as the sum of 3 high-power fields (400×).

Results: The tumour size of the cases was 0.7-10 cm (average 2.5cm). 34 cases (40%) Luminal A, 28 cases (32.9%) Luminal B, 14 cases (16.4%) triple negative, 7 cases (8.2%) triple (ER;PR;cerbB2) positive, 2 cases (2.3%) were cerbB2 positive. Mast cells stained with CD117 were detected in all cases. A minimum of 12 and a maximum of 202 (average 63.77) mast cells were counted in 3 HPF . In cases with peritumoural mast cell counts below the average; There was a significant correlation between ER negativity and pN(2-3).There was an inverse relationship between lobular carcinoma and intratumoural mast cell density.
Conclusion: The relationship between mast cells and prognosis in breast cancers is controversial. Although high mast cell density in the tumour microenvironment seems to correlate with positive prognostic parameters as an indicator of defense against the tumour, no significant difference was observed in molecular subtypes. More studies are needed in larger patient series to use mast cell density in the tumour microenvironment as a marker to determine breast cancer prognosis.

E-PS-02-089
Adenoid cystic carcinoma of breast: 13 years of experience in a single centre
M.F. Tekin*, M.H. Toper, H. Kaya
*Marmara University, Turkey

Background & objectives: Adenoid cystic carcinoma (ACC) is a rare breast tumour with classic, solid-basaloid, and high-grade transformation subtypes.
With this report, sharing our experience with four ACC cases, including one male, aims to contribute to literature on diagnosing and treating this tumour.
Methods: Between 2011 and 2023, four cases of ACC, comprising 0.2% of the total 1883 cases of primary breast carcinoma were diagnosed in the Medical Pathology Department at Marmara University. One case was male (25%), three cases were female (75%). Median age was 59 (range 41-71). All cases exhibited a single lesion, radiologically.
Results: The median tumour size was 2.3 cm (range 1,5-4). Histomorphological examination revealed pure classic subtype in one case, while 30% and 10% solid-basaloid subtype features were observed in two cases. In male patient who had not undergone resection, tru-cut biopsy showed 20% solid-basaloid and 80% classic morphology. CD117 and p63 were positive in all cases; SOX10 was positive in three cases. PR and cerbB2 were negative, with one case showing 10% weak ER positivity. Cases with high solid-basaloid morphology (30%-20%) had Ki-67 proliferation index of 30% and 40%. MYB gene rearrangement was detected in all cases. The median follow-up for resected cases was 43 months (range 4-132), with no recurrence observed.
Conclusion: ACC constitutes 0.1% of all breast carcinomas; our finding of 0.2% aligns with this. In males, ACC is exceptionally rare, with 18 cases reported in the literature; having a median age of 39 (range 13-82), younger than females, as seen our case.

This report, sharing our experience with ACC and our rare male case aims to contribute to the literature on ACC, a tumour uncommon in males, providing valuable insights.

E-PS-02-090
Assessment of specificity of TiLs subpopulations in HER2-low breast cancer
I. Telezhnikova*, E. Eremeeva, G. Setdikova
*Loginov Moscow Clinical Research Center, Russia

Background & objectives: HER2-low expressing tumours representing a distinct clinical entity. The objective of this study is to assess the specificity of tumour-infiltrating lymphocytes (TiLs) subpopulations in HER2-low breast cancer, which may contribute to the development of targeted immunotherapies and improve patient outcomes.
Methods: Conducted a comparative analysis of 60 tumour samples. These samples were divided into two groups: Group 1 consisted of samples from patients who did not receive NAT, and Group 2 from patients post-NAT. IHC performed to identify TiLs using markers CD163, CD4, CD8, and CD68. The staining was evaluated both at the invasive margin and within intratumoural regions.
Results: Was found that CD163 expression was the highest both at the invasive margin and within intratumoural regions, with CD163inv showing 20 [10; 40]% and CD163tum presenting 15 [7; 30]% respectively. The expression levels of CD4tum (5 [5; 7]%), CD8tum (2 [2; 5]%), CD68tum (5 [2; 7]%), CD4inv (5 [5; 10]%), CD8inv (5 [2; 5]%) and CD68inv (5 [2; 10]%) were significantly lower and did not differ substantially from each other. The administration of NAT did not have a significant impact on the infiltration of breast cancer tissue. However, within the analysis of TiLs subpopulations, a trend ($p=0.066$) towards increased CD8tum following NAT was noted.
Conclusion: The study revealed that CD163+ macrophages are the predominant subpopulation of TiLs in both invasive and intratumoural regions of HER2-low breast cancer. NAT did not significantly affect the overall infiltration of TiLs, although there was a trend towards increased CD8+ T-cell expression post-treatment. These findings suggest that CD163+ macrophages may play a pivotal role in the immune landscape of HER2-low breast cancer and could be a potential target for immunomodulatory strategies.

E-PS-02-091
Breast carcinoma with metaplastic and neuroendocrine differentiation
C. Roumbas, M. Sassi, N. Tepelenis*, D. Kapnias, C. Aggeli, T. Choreftaki
*Department of Pathology, General Hospital of Athens "Georgios Gennimatas", Athens, Greece

Background & objectives: Metaplastic carcinomas and neuroendocrine carcinomas (NECs) of the breast are rare malignancies with characteristic morphological and immunophenotypical features. Coexistence of metaplastic and neuroendocrine differentiation in invasive breast carcinoma has only rarely been reported in the literature.
Methods: We present a case of mixed small cell (NEC) and metaplastic carcinoma of the breast. A 58-year-old female, with no previous history of malignancy, presented with a lump in her right breast. Imaging indicated a mass suspicious for malignancy, confirmed by positive findings on fine-needle aspiration (FNA). Subsequently, she underwent modified radical mastectomy.
Results: Gross examination of the specimen revealed a tan-white, circumscribed, elastic, hard, and lobulated tumour in the upper outer quadrant, measuring 7cm in its largest dimension, along with a lymph node block in the axillary fat. Histologically, the tumour consisted mostly of small round blue cells with finely dispersed chromatin and scant cytoplasm that were positive for neuroendocrine markers Synaptophysin, Chromogranin-A (focally) and CD56 (small cell component). Additionally, intermingled foci of frankly malignant mesenchymal and squamous/adenosquamous differentiation, characteristic of metaplastic carcinoma, were observed. Both components were represented in lymph node metastases. Immunohistochemical studies were negative for TTF1, CDX2, ER, PR and HER2 (1+).
Conclusion: Small cell neuroendocrine, mesenchymal and squamous differentiation within the same breast carcinoma suggests a potential common precursor cell for both metaplastic carcinomas and NECs. Correct diagnosis of small cell breast carcinoma is crucial for treatment purposes, as it has shown responsiveness to chemotherapy regimens appropriate for small cell lung carcinoma. Our case underscores the importance of thoroughly sampling and examining carcinomas of the breast, as they can be mixed with other types that may benefit from different treatment modalities.

E-PS-02-092

Porocarcinoma nestled in the mammary gland - a rarity within a rarity

A.C. Tinca*, B.A. Lazar, A. Ungureanu, O.S. Cotoi
*Pathology Department of Mures County Clinical Hospital, Romania

Background & objectives: Porocarcinoma is an exceptionally uncommon malignant tumour originating from the skin's adnexal appendages, particularly the ducts of sweat glands. Although the exact pathophysiology remains somewhat elusive, there is a suspicion that this tumour evolves from an underlying poroma.
Methods: We report the case of a 51-year-old female patient presenting with a cutaneous tumour located on the left breast. The patient underwent surgical excision, and the excised tissue sample was subsequently submitted to our Pathology department. Paraffin-embedded sections were prepared and the specimen was examined using hematoxylin and eosin staining, followed by pertinent immunohistochemistry reactions.
Results: Under standard staining, we noted an ulcerated cutaneous epithelium. Subadjacent we observed a nodular tumour proliferation predominantly arranged in nest-like structures within the dermis, with continuity to the surface epithelium. Occasionally, lumina formation was noted, and focal palisading of nuclei was identified at the periphery. Tumour cells exhibited varied sizes, some smaller with reduced cytoplasm and hyperchromic nuclei, while others presented medium size, moderate amounts of pale eosinophilic cytoplasm, and enlarged nuclei with eosinophilic nucleoli. We detected 80/10 HPF. Peritumoural, chronic inflammatory infiltrate and melanophages are observed. Tumours cells were positive for CD117, CTK AE1/AE3, focally for SOX10 and ki67 index was 70%. The tumour extended to the mid-dermis.
Conclusion: Porocarcinoma is an exquisite rarity among cutaneous neoplasms, boasting distinctive morphological features, enigmatic pathophysiology, and therapeutic complexities awaiting further exploration. Primarily manifesting in the head, neck and lower limb regions, its occurrence is a marvelously infrequent phenomenon, with its presence within the mammary region being exceptional. This case shows the most important aspects of this tumour and provides potential diagnosis clues useful in daily practice.

E-PS-02-093

Analytical verification of the PATHWAY anti-HER2 (4B5) assay to assess HER2-ultralow status in breast cancer

P. Toro*, M. Dumas, M. Manoogian, S. Lucas, A. Baker, Q. Fang, X. Liu, M.T. Olson
*Roche Diagnostics International, Switzerland

Background & objectives: Robustness of the PATHWAY anti-HER2 (4B5) assay has been established for HER2-positive and HER2-low to evaluate HER2 status in breast cancer (BC) samples. We provide analytical data supporting a medical decision point of HER2-ultralow (HER2 IHC 0 with membrane staining).
Methods: Formalin-fixed, paraffin-embedded (FFPE) BC specimens were scored according to the 2018 ASCO-CAP guidelines. The "0" category was subdivided into: "0 with no membrane staining observed in tumour cells" (TC), ("Null"), and "0 with faint, partial staining of the membrane in 10% or less of the TC", ("HER2-ultralow").
Results: For analysis purposes, cases were distributed in two groups: 1. All "Null" and IHC 3+ cases and 2. HER2-ultralow, IHC 1+ and IHC 2+ cases. All IHC 2+ cases regardless of ISH status were grouped for this study. Using 24 unique BC cases, within-run repeatability, and between antibody lot, detection kit lot, instrument, and day intermediate precision assessments demonstrated an overall percent agreement (OPA) of 100%. Using 100 unique BC cases, between-reader and within-reader precision assessments demonstrated an OPA > 95%. Overall OPA across all evaluable observations in the interlaboratory reproducibility study was 99.2%. Within-block heterogeneity was evaluated in 15 cases, with 14 maintaining concordant HER2-ultralow status throughout the block.
Conclusion: HER2 IHC interpretation has a history of controversy due to competing scoring schema. Additionally, before 2022 no HER2 targeted treatment was available for the lower expression profiles (0, 1+, and 2+/ISH negative) and thus did not command the same level of interest as they do now. Here we demonstrate that the PATHWAY HER2 (4B5) assay is robust and reproducible in identifying HER2-ultralow tumours. The clinical utility of this cutoff is currently being explored in DESTINYBreast-06 (NCT04494425).

E-PS-02-094

The elusive differential diagnosis of sweat gland carcinoma of the skin from breast carcinoma metastatic to the skin or apocrine carcinoma arising in ectopic breast tissue in the axilla. An extraordinary case report

H. Trihia*, A. Mavrogiorgis, E. Kouskos, G. Stanc
*Metaxas Cancer Hospital, Greece

Background & objectives: Primary cutaneous apocrine/eccrine carcinoma is a rare adnexal tumour, with histology and staining, mirroring those seen in mammary ductal carcinoma. We describe a case of a skin adnexal carcinoma and describe the differential diagnostic challenges with metastatic breast carcinoma.
Methods: Histological slides and paraffin block from a diagnosed 'breast ductal carcinoma', were received for further immunostaining (IHC) from a 83-year old woman, with a skin ulcerated mass in the border between left breast and axilla. The histological appearances prompt for further meticulous clinical correlation, which resulted in the information that this lesion was present since 10 years and grew larger.
Results: The appearances were of a relatively bland looking infiltrative carcinoma in the reticular dermis and subcutaneous tissue, with 1mm distance from the surgical margin, with no emboli, which posed a d.d between a carcinoma with neuroendocrine differentiation and apocrine carcinoma. IHC was positive for CAM5.2, EMA, GATA-3, AR, ER, PR and CEA (rare), MIB-1 (10-15%) and negative for CK7, CK20, GCDFP15, chromogranin, synaptophysin, mammaglobin, c-erb-B2, CK5/6, p63, D2-40, S-100. The monotony of cellular appearance, lack of tumour emboli, CK7-, the anatomic location of the mass, the presence of microsatellite skin nodule, the clinical history of originally skin nodule of 10 years duration, were more in favour of primary adnexal carcinoma.
Conclusion: Primary cutaneous adnexal carcinoma is an extremely rare malignant sweat gland tumour, presenting as a slow-growing firm solitary cutaneous or subcutaneous nodule. It affects older individuals, mainly in the seventh decade and presents in areas with high apocrine glands density, such as the axilla. It is histologically and IHC indistinguishable from apocrine breast carcinoma metastatic to the skin or apocrine carcinoma arising in ectopic breast tissue in the axilla and can be diagnosed only by meticulous pathologic-clinical correlation.

E-PS-02-095

A rare case of primary breast chondrosarcoma clinically diagnosed as phyllodes tumour and metaplastic carcinoma with mesenchymal differentiation: a case report

T. Turcu*, A. Evsei, A. Birceanu, N. Copcă, S. Sabo, M. Cerbu
*University Emergency Hospital Bucharest, Romania

Background & objectives: Primary breast chondrosarcoma is exceptionally rare, with very few cases documented in medical literature, which complicates its diagnosis and management. This report emphasizes the role of histopathological and immunohistochemical evaluation, along with comprehensive macroscopic examination in diagnosing this rare entity.

Methods: Initially suspected as a phyllodes tumour based on clinical diagnosis, subsequent biopsy findings suggested a metaplastic carcinoma with mesenchymal differentiation. The resected specimen underwent rigorous tissue sampling to facilitate accurate histopathological and immunohistochemical analyses to differentiate this rare entity from more common breast tumours.
Results: Macroscopic examination revealed a 6.2 x 5 cm cystic, well-demarcated, lobulated tumour. Microscopic analysis displayed uni- and binucleated pleomorphic cells with visible nucleoli and atypical mitotic figures within a myxoid and cartilaginous stroma, and areas of necrosis. Immunohistochemical staining was negative for cytokeratin (AE1/ae3, CK8/18), estrogen receptor, and P63, but positive for S100, with a high Ki67 index of 60%. Radiological assessment excluded a metastasis from an extramammary site and therefore the diagnosis of primary breast chondrosarcoma G2 was made.
Conclusion: This case is a rare instance of primary breast chondrosarcoma, a diagnosis that was initially overlooked due to its histological overlap with other breast malignancies. The findings highlight the indispensable role of thorough macroscopic assessment and targeted immunohistochemical testing in confirming chondrosarcomatous differentiation, contributing valuable insight into the histopathological spectrum of rare breast tumours and reinforcing the need for vigilance in diagnostic processes.

E-PS-02-096
Epithelioid leiomyoma of the breast: a case report of rare entity
R. Veidemanis*, T. Balamurugan, S.E. Pinder, A. Gamage
*Department of Cellular Pathology, Royal Surrey County Hospital, United Kingdom

Background & objectives: Leiomyomas of the breast are very rare, with less than 30 cases reported in the literature. Even more, the diagnosis of epithelioid leiomyoma has been reported only once in the literature.
Methods: Case summary: A 60-year-old female was diagnosed with a new lesion on screening mammogram in the upper outer quadrant of the right breast. A core biopsy showed a nodular, non-encapsulated lesion of predominantly epithelioid, closely-packed nests of cells admixed with some more spindled forms.
Results: The lesional cells had relatively abundant eosinophilic cytoplasm with occasional vacuoles. The nuclei showed variation in size with occasional large nuclei with prominent nucleoli. There was no necrosis and mitoses were very sparse. There were fine hyalinised bands of fibrous tissue present between nests of lesional cells. On immunohistochemistry (IHC), the epithelioid cells showed focal reactivity for smooth muscle myosin heavy chain (SMMHC) with strong focal expression of SMA and caldesmon. Desmin, Bcl-2, ER and PR showed strong widespread positivity. The lesional cells were negative for CD34, CD10, S100, Melan A, SOX10, AE1/AE3, Cam5.2, CK5/6, p63, E-cadherin and HER2. MIB1 was low (< 10%).
Conclusion: The differential diagnoses of epithelioid leiomyoma include epithelioid myofibroblastoma, leiomyomatous variant of myofibroblastoma, CD34-deficient myofibroblastoma, invasive lobular carcinoma and low-grade fibromatosis like metaplastic breast carcinoma. The constellation of histological features of the lesion, supported by CD34 negative and smooth muscle positive IHC, the diagnosis of epithelioid leiomyoma was made. In view of the variation in nuclear size of the lesional cells and the lack of a well-defined margin, excision with a margin of normal surrounding tissue was recommended.

E-PS-02-098
Association between IDO1 expression and pCR rate in triple-negative breast cancer
S. Vtorushin*, S. Naumov, M. Taranenko, N. Krakhmal
*Cancer Research Institute, Tomsk National Research Medical Center of the Russian Academy of Sciences, Russia

Background & objectives: Subtypes of triple-negative breast cancer (TNBC), despite their common basal-like profile, have certain features that differ in the course and prognosis of the disease. Therefore, it is necessary to study molecular markers that may have potential predictive value.
Methods: 42 specimens from patients with T1-4dN0-3M0 TNBC were studied. All patients received neoadjuvant therapy. Immunohistochemical assessment of CK5/6 and IDO1 expression was carried out on sections of core biopsies before neoadjuvant therapy. The obtained data were compared with clinical and pathological characteristics, as indicators of tumour response to neoadjuvant therapy.
Results: Immunoactivated subtype was determined in CK5/6+/IDO1+ carcinomas. Such tumours were dominant and accounted for 81.25% (n=26/32). In these cases (CK5/6+/IDO1+), the presence of metastatic lesions in axillary lymph nodes was rarer and the rate of pathomorphological complete response (pCR rate) was higher than in carcinomas, whose molecular profile corresponds to the immunosuppressive subtype (CK5/6+/IDO1-).
Conclusion: The results of this study have shown the possibility of evaluating CK5/6 and IDO1 expression as markers that allow immunohistochemical differentiation of basal-like TNBC types: immune-activated or immunosuppressive. Breast carcinomas with triple negative molecular profile and immunohistochemically confirmed CK5/6+/IDO1+ tumour status are associated with higher rates of achieving complete pCR after neoadjuvant therapy. The obtained results demonstrate that evaluating IDO1 expression may have predictive value for the course of TNBC.

E-PS-02-099
PD-L1-positive cancer stem cells in primary tumour associated with progression of breast cancer
S. Vtorushin*, A. Kalinchuk, N. Popova, L. Tashireva
*Cancer Research Institute, Tomsk National Research Medical Center of the Russian Academy of Sciences, Russian Federation

Background & objectives: The lack of prognostic value of PD-L1 in patients with HR-positive breast cancer may be due to the unexpected stimulation of progression caused by PD-L1 expression on cancer stem cells. We evaluated prognostic significance of PD-L1 expression in tumour cells.
Methods: The study was enrolled 52 breast cancer patients (HR-positive, I-IIIA, T1-3N1-0M0). PD-L1 status was determinates by immunohistochemistry Assay. Multiplexed immunohistochemistry was used for evaluation stemness marker on cancer cells as well as PD-L1 expression. During the follow-up period, distant metastases free survival (DMFS) was assessed as the time from treatment initiation to the development of distant metastasis or death.
Results: The findings showed that PD-L1-positive tumour cells predominantly exhibit stem-like properties, which can also be combined with EMT features and show the prognostic potential in breast cancer. The patients were separated into two groups based on the percentage of PD-L1-positive CD44+CD24–N-cadherin– cells in order to assess DMFS. In the group of patients with less than 94.4% PD-L1-positive CD44+CD24–N-cadherin– cells, the DMFS was 75%, while in patients with more than 94.4% of these cells, it was 23.3% (HR (95%CI) 14.57 (1.72-122.90), p=0.0014).
Conclusion: The identification of a link between distant metastasis risk and the proportion of PD-L1-positive cancer stem cells in HR-positive breast cancer may serve as a valuable starting point for further research into biomarkers for immune checkpoint inhibitors treatments.

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E-PS-02-100
Breast Her-2 IHC assessment: pathologist concordance is excellent using the binary system (negative/positive) but poor using the

three-tier system (negative/low/positive) - a study of 612 practitioners from 62 countries

S. Wedden*, A. Chefani, A. Baltan, S. Costache, E. Andersson, A. Waydelich, T. Thomas, H. Kuzmenko, C. D'Arrigo
*CADQAS CIC, United Kingdom

Background & objectives: The approval of the antibody drug conjugate, Enhertu, necessitates refinement of the previously-binary breast Her-2 IHC classification system. It is now crucial to recognize the 1+ category using a three-tier classification. We evaluate concordance in our proficiency test participants.
Methods: We used data from the CADQAS Digital Interpretive Proficiency Test (DIPT) scheme to evaluate the following:

- Concordance in Her-2 IHC scores between DIPT participants & original clinical diagnoses.
- Comparison of clinical error rate for two-tier v. three-tier classification (using IHC + ISH).
- Impact of pathologist experience.
- Potential impact of DIPT participant errors on routine clinical practice.

Results: Since 2021, we have collected Her-2 DIPT data consisting of 5607 individual reads (49 cases) from 612 participants practising in 62 countries. There is good concordance in the binary classification system [negative (IHC 0/1+/2+ISH-)/positive (IHC 2+ISH+/3+)], with most clinical error occurring in the IHC2+/ISH– cases (10.56%). Using the three-tier classification system (negative, 1+ (low), positive), we see significant errors in the IHC0 category (43.54%) Participants are more concordant scoring Null/Zero than IHC0 ≤10% (Ultra-low). Frequently-reporting pathologists and trainees make fewest clinical errors, closely followed by trainees. Extrapolating DIPT data into routine clinical practice suggests a clinical error rate of over 16% for infrequently-reporting pathologists.
Conclusion: Pathologists have been using binary classification for >20 years and perform well. Indeterminate (2+) scoring can be resolved by ISH. There is poor concordance in the new three-tier system and there is no additional test to discriminate at the IHC0/1+ boundary. Our data provides evidence that worldwide implementation of the new classification requires significant support. Training targeted to 0/1+ and continuing provision of proficiency testing is essential to provide education, feedback and a benchmarking tool to pathologists and industry.

E-PS-02-101

Clinicopathological analysis of breast metaplastic carcinoma with epithelial mesenchymal transition characteristics

H. Wu*, Y. Gao, L. Wu, M. Duan, Z. Yu, M. Liu
*The Sixth Medical Center of PLA General Hospital, China

Background & objectives: Breast metaplastic carcinoma (MC) is a group of morphologically heterogeneous invasive breast cancer, accounting for less than 1% of all breast carcinomas. We report the clinicopathological characteristics of breast MC with extensive sarcoma differentiation and recurrence into non-specific invasive carcinoma.
Methods: Clinical and imaging data were collected, and paraffin section, HE staining, immunohistochemistry were used to examine morphology and immunophenotype. Next-Generation Sequencing technology (NGS) was performed to analyse the molecular signature.
Results: A 38-year-old female patient discovered a lump in her right breast accidentally in 2017. Ultrasound examination showed a hypoechoic mass, and a gross examination revealed a tumour with the size of 2×2×1.4cm. The tumour cells were spindle shaped, sarcoma like, a few high-grade ductal carcinomas in situ were seen around the tumour. Vimentin and S-100 were strongly positive, all epithelial markers and ER, PR, Her-2 were negative, Ki-67 index was 60%. MC with extensive sarcoma differentiation was diagnosed. Five years later, a right breast mass was discovered again, pathological diagnosis was invasive ductal carcinoma, grade 3. The NGS analysis of both tumours showed the same mutations in PIK3CA and TP53.
Conclusion: Breast MC is relatively rare, the correct diagnosis of this disease is crucial. In our case, the tumour has a wide range of sarcoma features and needs to be differentiated from primary breast sarcoma. The presence of ductal carcinoma in situ supports the diagnosis of MC. It is speculated that during the invasive process of tumours, the lineage characteristics of invasive cancers are weakened by the lineage characteristics of sarcomas, leading to epithelial mesenchymal transition. Further investigation is worth exploring.

E-PS-02-102

Characterization of HER2 positive breast cancer in Tunisia

R. Yaiche*, Y. Houcine, E. Saidi, F. Saadallah, S. Kamoun, K. Meddeb, M. Driss
*Abderrahmane Mami Hospital, Tunisia

Background & objectives: Breast cancer (BC) is the most common cancer among women in Tunisia and worldwide. Several molecular subtypes were identified. However, few studies characterized HER2-positive BC, specifically in Tunisia. We aim to report clinical, pathological, and prognostic features of this disease.
Methods: A descriptive, retrospective, cross-sectional study carried out over a 5-year period from 2018 to 2022, involving 58 patients operated on and confirmed at the Salah Azaiez Institute (SAI) for HER2-positive BC. Data were collected from pathology and medical reports taken from the SAI archives. HER2 status was interpreted by immunohistochemistry in first-line and CISH.
Results: 58 cases of HER2-positive primary BC treated with neoadjuvant chemotherapy were included. The mean age was 49 years. Average tumour size was 74 mm. Non-specific infiltrating ductal carcinomas were predominant (98%), mostly of grade III (62%). Most tumours were classified as pT2 (47%). HER2 status was mostly 3+ (91%). The predominant molecular profile was luminal B HER2-positive (78%). RCB classification showed chemoresistance in 21 cases (RCBIII), 19 cases displaying complete response and 18 partial responses. RCB
Conclusion: The characterization of HER2-positive BC in Tunisia is essential for informing clinical practice, research, and healthcare policies in the region. The findings of this study may contribute to a better understanding of the disease burden and help optimize the management of HER2-positive breast cancer patients in Tunisia.

E-PS-02-103

Comparison of Her2 status in primary and recurrent breast cancer as a therapeutic side effect and treatment factor

S. Zeneli*, M. Ikonomi, M. Shyti, I. Rrugeja
*UHC "Mother Teresa", Albania

Background & objectives: NAT are selected according to the molecular subtype of breast cancer.A considerable number with early breast cancer will eventually relapse.Treatment decisions are still based on the biological features of primary tumour without taking in consideration therapy effects on tumour expression
Methods: We took in examination all patients with breast cancer who were diagnosed between year 2022 - 2023 in UHC "Mother Teresa". Patients were examined by immunohistochemistry and silver in situ hybridization for Her2 status. 45 out of 350 patients had a metastatic breast cancer and were reevaluated for hormonal status changes after chemo and radio therapy were applied.
Results: This study revealed a clear discordance between primary tumours and its metastases for Her2 status. HER2 expression between

primary diagnosis and completion of treatment are relatively common in up to 30% of cases who were reevaluated.
Conclusion: Changes in HER2 expression post therapy may be prognostic in HER2-positive tumours becoming HER2-negative. Tissue sampling and Her2 re-analyzing of metastatic sites should be considered. Re-biopsy should be performed for patients with recurrent and metastatic breast cancer every time the disease progresses to assess the changes in molecular phenotype for individualized and precise treatment for patients.

E-PS-02-104
Metaplastic breast carcinoma with osteoclast-like giant cells: a rare case report
O. Živković*, I. Petrovic, A. Milićević
*Institute for Oncology and Radiology of Serbia

Background & objectives: Metaplastic breast carcinoma (MpBC) is a rare and aggressive malignancy that accounts for 0.2–5% of all breast cancers. It is characterised by the histological presence of at least two cellular types, typically epithelial and mesenchymal components
Methods: A 61-year-old postmenopausal female presented with a right breast lesion in the upper inner quadrant identified by mammography screening. Mammography revealed a lobulated tumour shadow measuring 20 x 20 mm at the indicated location. The lesion was surgically excised after a core needle biopsy, and the patient underwent radiation.
Results: A gross examination of the excised specimen revealed a firm, greyish tumour measuring 25 x 25 x 22 mm. The histopathological analysis showed a tumour composed of spindle cells in a fascicular and storiform arrangement. The tumour was infiltrated with lymphocytes, histiocytes, and numerous multinuclear osteoclast-like giant cells. Immunohistochemical staining revealed diffuse positivity in the spindle cells for CK AE1/AE3, CK7, and Vimentin, rare positivity for p63 and EMA, and negativity for S-100, E-cadherin, and GATA3. The Ki-67 proliferative index was 30%. The multinuclear giant cells were positive for CD68, leading to the diagnosis of MpBC with osteoclast-like giant cells.
Conclusion: Although rare and associated with aggressive clinical behaviour, MpBC represents a significant clinical entity with distinctive histological features and usually a triple-negative phenotype. Their clinical characteristics are nonspecific, making the diagnosis more challenging. As a result, histopathological evaluation and immunohistochemistry analysis are critical for diagnosing this rare MpBC entity.

E-PS-03E-Poster Session Dermatopathology

E-PS-03-001
Cutaneous synovial sarcoma - a case report and review of the literature
M.A. Abad Vintimilla*, E.P. Sánchez López, V. Diaz, A. Berjón, M.J. Beato
*La Paz University Hospital, Spain

Background & objectives: Synovial sarcomas are uncommon soft tissue malignant tumours of young people, favouring lower extremities. They are rare in skin, with few reported cases. Here, we present an unusual case of a 72-year-old woman that presented it on the scalp.
Methods: Definitive diagnosis was made using routine staining, molecular studies and immunohistochemical techniques, including CKAE1/3, EMA, MelanA, S100, CD34, CD10 and AML. We also reviewed the medical record to obtain data such as age, site, and clinical suspicion. Furthermore, we performed a review of the literature.
Results: Our case is a 72-year old female patient with a painful tumour in the scalp of 9x9mm, with a clinical suspicion of trichilemmal cyst. Histological examination revealed a distinctive spindle cell proliferation pattern, organized in fascicles with numerous mitotic figures, indicative of aggressive growth. Immunohistochemical analysis demonstrated positive expression of CKAE1/3, while EMA, MelanA, S100, CD34, CD10, and AML showed negative results, additionally, fluorescence in situ hybridization (FISH) revealed SS18 translocation in 100% of the cells, providing molecular evidence of synovial sarcoma.
Conclusion: General synovial sarcomas usually occur in soft tissues surrounding the joints, in limbs, feet, and hands. Those situated in the skin are exceptionally uncommon. There are fewer than ten documented cases. In this poster, we review all the cases published so far, and describe their characteristics. As in soft tissue sarcomas, prognosis depends upon various factors including tumour size, location, metastases, and response to treatment. Given their propensity for local aggressiveness and metastatic dissemination, timely identification is imperative.

E-PS-03-002
Special site nevus: melanocytic nevus on the labia majora
M.M. Agu*, B.A. Lazar, A.C. Tinca, O.S. Cotoi
*Mureș County Clinical Hospital, Romania

Background & objectives: Melanocytic nevi in certain areas, such as the genital area and the scalp, may resemble melanomas microscopically, but often behave benignly, not requiring surgery. Accurate differentiation by dermatologists and pathologists is crucial to avoid unnecessary treatments.
Methods: We present the case of a 24-year-old female with a pigmented labial lesion showing no size or color changes. The patient had no personal or family history of melanoma or skin cancer. The lesion was excised after clinical evaluation, followed by preparing paraffin-embedded sections for examination with hematoxylin and eosin staining and immunohistochemistry reactions.
Results: Microscopic examination revealed a proliferation of melanocytic cells, characterized by a junctional component of single cells and round or fusiform nests. These nests were irregularly distributed along the epidermal rete ridges and aligned parallel to the epidermal surface. Focal pagetoid growth was observed, confined to the centre of the lesion. Multinucleated melanocytes and macrophages were present toward the lesion's surface, while a minor lymphocytic inflammatory response was noted at the lesion's base. Immunohistochemical staining showed positivity for SOX-10, marking the melanocytes present at the junction of epidermis-dermis and intradermal.
Conclusion: Melanocytic nevi in the genital region represent less than 5% of pigmented lesions in this area of the body. Accurate diagnosis is challenging due to histological similarities between special site nevi and malignant melanoma. Precise assessment is essential to distinguish between these lesions, as misdiagnosis could lead to unnecessary wide excision or sentinel lymph node biopsy for melanoma. Increased awareness and recognition of this category of melanocytic lesions are vital to prevent overdiagnosis and overtreatment.

E-PS-03-003
Histiocytoid sweet syndrome in an infant
E. Aguilar Navarro*, A. Ortiz González, S. Blasco Muñoz, C. Capozzi, D. Pérez Parra, L. González Lorca, A. Sánchez Espinosa, D. Sánchez Gutiérrez, A. Buendía Alcaraz
*Pathology Department. Hospital Santa Lucía, Spain

Background & objectives: Description of an unusual histopathologic variant of Sweet Syndrome (SS) in a one year old girl presented with a history of skin lesions of one month duration characterized by violaceus cutaneous plaques and nodules previously blistered on face,buttocks and hands.

Methods: Histologically, edema of papillary dermis and mixed inflammatory infiltrate mainly composed of neutrophils within the reticular dermis was observed. Distribution was perivascular, perieccrine and typically interstitial associated with marked leukocytoclasis and ingestion of nuclear dust by histiocytes.The key feature was the presence of abundant mononuclear histiocyte-like cells. Immunohistochemical panel of antibodies was performed to characterize the origin of this cells.
Results: Due to the mixed infiltrate, immunohistochemical stain pattern can be challenging to interpret.Problematic histiocytoid mononuclear cells showed immunoreactivity for CD68, lysozyme and myeloperoxidase and were negative for CD45, TdT, CD20, CD1a, CD34, CD117. Myeloperoxidase positivity demonstrated that these cells are in fact immature myeloid cells rather than true histiocytes. Lysozyme positivity is also observed in mature neutrophils and normal histiocytes.A study of peripheral blood was performed. Fortunately, no dysplasic myeloid cells were seen in cytologic examination.Clinico-pathological correlation was done and the diagnosis was Histiocytoid Sweet Syndrome.Some histiocytoid cells rich cases have been described and it has been postulated that could represent a variant of SS or a stage of evolution.
Conclusion: SS or acute febrile neutrophilic dermatosis is a rare disease of unknown etiology. Extremely uncommon in children, it is associated more frecuently with infections or idiopathic cause rather than malignancies.Histiocytoid mononuclear cells in Histiocitoid Sweet Syndrome represent immature granulocytes. Lesions have a benign course and respond to treatment.Knowledge of this variant is important to avoid misdiagnosis as interstitial granulomatous dermatitis. Furthermore, it remains crucial to exclude leukemia cutis and a peripheral blood study and follow-up of the patients are mandatory.

E-PS-03-004
An integrative differential diagnosis between well-differentiated squamous cell carcinoma and keratoacanthoma
A.V. Alexe*, R.M. Bușcă, S. Niculae, V. Pascu, O. Ștefan, A.D. Brotoiu, S. Duțulescu, S. Zurac
*Department of Pathology, Colentina University Hospital, Bucharest, Romania

Background & objectives: The differential diagnosis between invasive well-differentiated squamous cell carcinoma (SCC) and its mimicker, the keratoacanthoma (KA), represents to this date a significant challenge in dermatopathology. Consequently, a comprehensive approach to distinguishing these two squamous proliferations is warranted.
Methods: This paper is a comparative-retrospective study that integrates clinical, histopathological and further immunohistochemical hallmarks of 34 cases, 20 SCC and 14 KA, diagnosed over a seven-year period at Colentina Clinical Hospital, in order to highlight a subservient differentiation. Thirteen multi-tissue paraffin blocks were constructed separately per diagnostic category. The p53, p63, p16, Ki-67 immunophenotype was determined using Leica bond kit.
Results: Upon clinical evaluation, neither anatomical location, age, nor sex demonstrated statistically significant correlations with the presentation. Histopathological examination revealed extensive overlap in the features of these two entities. However, immunohistochemical analysis identified p16 as a potential differentiating marker. Keratoacanthomas exhibited strong nuclear and cytoplasmic p16 expression, particularly at the advancing front, with additional cytoplasmic pattern in superficial regions. Conversely, well-differentiated squamous cell carcinomas displayed minimal p16 expression with similar characteristics. These findings challenge the prevailing theory suggesting a diffusely positive pattern for p53 and Ki-67 in well-differentiated squamous cell carcinoma compared to keratoacanthoma.
Conclusion: These findings suggest that the role of p16 expression in differentiating well-differentiated squamous cell carcinoma (SCC) from keratoacanthoma (KA) demands further investigation. However, the utility of p53 and Ki-67 in this context appears inconclusive based on this study. The differential diagnosis between these lesions remains a complex challenge, requiring integration of clinical, histopathological, and immunohistochemical data. Furthermore, achieving high interobserver agreement can be problematic.

E-PS-03-005
IgA pemphigus pustular dermatosis subcorneal type: a case report
C.T. Alfaro Cazon*, F.N. Figueroa, C.d.R. Pavon, P. Della Giovana
*Department of Anatomic Pathology, Hospital Nacional Prof. Alejandro Posadas. Anatomic Pathology, Argentina

Background & objectives: IgA pemphigus is a rare subtype characterized by painful, pruritic, vesicular pustular eruptions. It is defined by the presence of IgA antibodies that target transmembrane adhesion proteins in the epidermis. Subdivided into intraepidermal neutrophilic dermatosis and subcorneal pustular dermatosis.
Methods: We present a clinical case IgA pemphigus pustular dermatosis subcorneal type, with unfavourable clinical evolution. She was previously treated with cephalexin and oral corticosteroids without improvement. The patient evolves unfavourably as a result of sepsis due to infection of decubitus ulcers leading to death.To summarize this entity, we summarize the histomorphological and immunofluorescence direct.
Results: A 84-year old female patient with dermatosis of one month of evolution, which compromise skin folds and in the last days becomes generalized. Examination revealed generalized dermatosis with involvement of skin folds trunk and limbs, characterized by multiple annular erythematous plaques with pustular vesicular blistering lesions on the periphery. The largest ones are located on the trunk and show adherent meliceric crusts. Epidermis with subcorneal pustule formation and acantholysis associated with a dense inflammatory infiltrate of neutrophils and isolated acantholytic cells at the base. In dermis inflammatory infiltrate with predominance of neutrophils in perivascular and interstitial arrangement. Direct immunofluorescence shows IgA immunocomplex deposition in the cell membranes of epidermal keratinocytes.
Conclusion: The clinical phenotype of IgA pemphigus is much milder than classic pemphigus; however, as IgA pemphigus is a recently proposed entity, clinical data for its prognosis are still limited. Interdisciplinary study is essential to establish a timely diagnosis and treatment. Dapsone is considered the drug of choice.

E-PS-03-006
Blue nevi in uncommon locations
D. Almeida*, O.M. Da Rocha Moreira Pedro, R. Machado-Neves, M. Honavar, T. Amaro
*Portugal

Background & objectives: Blue nevus is a benign melanocytic lesion of pigmented fusiform melanocytes. The most common location is skin of the head and distal extremities, presenting as a dark macule, papule or nodule. Extracutaneous blue nevi occur unfrequently.
Methods: A retrospective analysis of the clinical files and pathology reports of blue nevi was performed from January 2002 to December 2023 at Hospital Pedro Hispano, Matosinhos, Portugal. Histological slides were reviewed.
Results: There were 351 diagnoses of blue nevi; 342 (97.4%) in the skin and 9 (2.6%) found in uncommon locations. We diagnosed 6 in the cervix, 1 in the prostate, 1 in a lymph node and 1 in the sclera. Almost all (8/9) diagnoses of blue nevus in uncommon locations were found

in surgical specimens were due to benign conditions (hysterectomy due to ovarian cyst, prolapse and fibroadenomas, cervical core biopsy, benign prostatic hyperplasia and a biopsy of pigmented scleral lesion. The lymph node blue nevus was found in a surgical specimen of cystectomy and bilateral ileo-obliterator lymphadenectomy for a urothelial bladder carcinoma.
Conclusion: The overall incidence of blue nevi is ~1%, most commonly in the skin and associated with a malignancy risk of 5.2-6.3%. They may be found in uncommon locations; most frequently in cervix (0.12-1.9%) and prostate (0.05-0.6%). Our clinical findings are consistent with published data. Pathologists should be aware of these diagnosis and their differential diagnosis.

E-PS-03-007
Sweat-gland carcinoma with neuroendocrine differentiation - case report and literature review
S. Alvarez Alonso*, R. Mazorra, Y. Guzmán Gómez, E. Montano Lumbreras, N. Fontanil Vior, J.J. Jiménez Velasco, C. Durán Vian, M.C. González Vela
*Hospital Universitario Marqués de Valdecilla, Spain

Background & objectives: Sweat-gland carcinoma with neuroendocrine differentiation (SCAND) is a new entity of cutaneous adnexal neoplasm proposed in 2022. This was previously labeled as low-grade neuroendocrine carcinoma of the skin (LGNECS) but renamed SCAND due to ductoglandular differentiation and its aggresive behaviour.
Methods: A 66 year-old male patient with a medical history of hypertension and smoker with no surgical history. He presented a 3 year history of a nodule in the anterior chest that had grown in last 6 months. Physical examination showed a 26x24 mm painless reddish lobulated nodule, with no other masses or lymphadenopathy detected.
Results: An excisional biopsy was performed and revealed a lesion located in the dermis and subcutis with no connection with the overlying epidermis and invasive margins. The tumour cells arranged in nested, trabecular and tubular pattern. The tumour cells were medium size, with round to oval nuclei with coarse granular chromatin. Few mitotic figures were observed. Immunohistochemical staining of the tumour cells was positive for estrogen receptor, progesterone receptor, synaptophysin, CD56, chromogranin A, cytokeratin 7 and GATA3. The tumour cells were negative for CK20, TTF1, CDX2 and SOX10. Inmunoexpression of p63 highlighted focal scattered myoepithelial cells, but tumour cells were negative. Consequently, the diagnosis was SCAND.
Conclusion: SCAND usually arises close to milk-lines and is more common in males. Histopathologically resembles breast cancer, but shows no relationship with breast parenchyma; endocrine mucin-producing sweat gland carcinoma can be ruled out based on location and abscence of extracelular mucin. A metastatic well-differentiated neuroendocrine tumour should also be considered, but TTF1 and CDX2 are negative. Immunoexpression for p63 by myoepithelial cells in our case could represent an in situ component, and it has not been described in other series.

E-PS-03-008
Cutaneous metastases - a rare finding in rectal carcinoma
C. Amalinei*, D.L. Pricope, A. Grigoras, R.A. Balan, M.V. Marinca
*"Grigore T. Popa" University of Medicine and Pharmacy, Romania

Background & objectives: The liver, lungs, and bones are the most common sites for colorectal cancer metastases, while cutaneous metastases are uncommon, with a reported incidence between 2.3- 6%. In this context, we present a rectal carcinoma with cutaneous metastases from our files.
Methods: We report the case of a 65-years old-men with stage III (cT3N2M0) rectal moderately differentiated adenocarcinoma who had neoadjuvant chemoradiotherapy and surgery. In evolution, he developed disseminated bilateral parenchymal lung metastases of up to 15 mm diameter, followed by cutaneous lesions associated with massive edema and ulceration. Both rectal and cutaneous specimens have been evaluated by routine histology and immunohistochemistry.
Results: The rectal surgical specimen displayed minimal tumour regression (Dworak 1) and the diagnosis was rectal carcinoma ypT3N1 LG-L1V1Pn1. Cutaneous lesions appeared after approximately three years from the first diagnosis and consisted in extensive violaceous skin papules of up to 0.8cm diameter, exhibiting ulceration and confluent areas, involving inferior limbs and genital region. The surgical skin samples showed completely excised dermis infiltration of intestinal-type adenocarcinoma. Tumour cells exhibited a strong, diffuse SATB2 positivity, supporting the diagnosis of cutaneous metastases of rectal carcinoma. The patient had deceased after six months of follow up from the time of cutaneous metastases diagnosis.
Conclusion: Although rectal carcinoma cutaneous metastases are rare, they should be considered in patients follow up, mainly in the setting of an already diagnosed metastatic disease. The histopathological examination of the suspected cutaneous metastatic lesions, along with SATB2 immunohistochemical exam can be a valuable tool for certification of metastatic lesions of rectal carcinoma.

E-PS-03-009
Leukocytoclastic vasculitis as an early cutaneous presentation of COVID-19 infection
E. Athanasiou*, C. Kouvidou, A. Therapontos, O. Kouroukli, E. Spiteri, C. Vourlakou
*Department of Pathology, Evangelismos General Hospital, Athens, Greece

Background & objectives: Cutaneous manifestations of COVID-19 are rare, with unknown etiology. Leukocytoclastic vasculitis (LCV) is idiopathic or secondary to autoimmune diseases, malignancies, drugs and chronic infections. The aim of this study is to present a case of LCV related to COVID-19 infection.
Methods: A 58-year-old female patient presented to the emergency department of our hospital with fatigue, fever (37,6 0 C) palpable purpura, multiple petechiae without ulceration in lower and upper extremities, sparing her face and scalp. No mucosal lesions, abdominal pain or arthralgia were found. Two weeks later, during her hospitalization, the patient developed dyspnea, cough and the COVID test was positive.
Results: The 4 mm biopsy of the lesion was done and the histological examination showed mild hyperkeratosis and acanthosis without epidermal ulceration, serum crusts, intraepidermal vesicle, or ischemic necrosis. The underlying dermis revealed features of vasculitis, involving superficial and mid dermal small-sized vessels, showing severe neutrophilic infiltrate with leykocytoclasia and nuclear dust, red cell extravasation. Fibrin necrosis of the vessels wall was not observed. A frozen biopsy for direct immunofluorescence was done. It showed IgA and C3 complement deposits in the small vessels wall. No deposits of IgG, IgM, C1q, C4 and fibrinogen were found. The morphological findings in correlation with immunofluorescence results were consistent with the diagnosis of IgA vasculitis.
Conclusion: Cutaneous lesions may be primary or secondary to respiratory infection. Pathogenic mechanisms are not fully understood, although the roles of a hyperactive immune response, complement activation and microvascular injury have been hypothesized. Circulating immune complexes could act as triggers for complement pathway activation, thus promoting neutrophil recruitment, vascular leakage and subsequent vessel wall injury and inflammation. COVID-19 causes a cytokine storm linked with a rise in IL6 levels and immune-complex mediated damage that can result in inflammation of small vessels.

E-PS-03-011

Coeliac disease unusual presentation by chronic skin ulcerations

P. Babal*, P. Durikova, L. Krivosikova, P. Janega
*Institute of Pathological Anatomy, Faculty of Medicine, Comenius University Bratislava, Slovakia

Background & objectives: Coeliac disease represents a significant public health problem worldwide. Its association with a broad range of cutaneous manifestations is well established. Dermatitis herpetiformis is the most common extra-intestinal manifestation of coeliac disease. Direct immunofluorescence remains the principal diagnostic confirmation.
Methods: We describe a case with multiple chronic skin ulcers arising in a 37-year-old woman, without other dermatological findings, without signs of herpetiform dermatitis manifestation. Suspected vasculitis was the reason for indication of histological evaluation with direct immunofluorescence of skin from the border of the defect.
Results: Although a variety of dermatological manifestations and co-occurring diseases may present with coeliac disease, primary skin ulcers have not previously been reported as a clinical feature. The patient denied any gastrointestinal symptoms. Direct immunofluorescence of the skin specimen identified IgA, IgM and C3 granular positivity along the basement membrane and IgA- and C3-positive walls of some small blood vessels. Suggested diagnosis of coeliac disease was confirmed by subsequent laboratory testing and duodenal biopsy. The patient was initiated on a gluten-free diet and prednisone, which resulted in rapid, complete, and persistent clearance of skin lesions, as well as the correction of chronic iron deficiency anemia.
Conclusion: The presented case report indicates the necessity to include chronic skin ulcers as another possible dermatological manifestation of unrecognized and/or untreated coeliac disease.

E-PS-03-013

Giant acne keloidalis nuchae

O. Belhadj*, C. Chaari, K. Turki, O. Boudaouara, S. Makni, K. Sellami, M.A. Fouad, H. Turki, T. Sellami Boudawara
*Department of Pathology, Habib Bourguiba University Hospital, Sfax, Tunisia

Background & objectives: Acne-keloidalis-nuchae (AKN) is an inflammatory disease that is characterized by the formation of nuchal fibrotic papules and plaques. This report aims to illustrate clinicopathological features of a giant form of AKN trying to elucidate its histopathogenesis.
Methods: We present a case of a AKN in a 29-year-old man diagnosed in pathology and dermatology departments of Sfax University Hospital.
Results: A 29-year-old-man, obese, having a history of hidradenitis suppurativa (HS) and a presumed nuchal keloid scar (KS). Despite multiple local treatments of his presumed KS, the lesions increased in size extending to the back, impeding neck mobility. Thus, a wide local surgical excision was performed.
Gross examination found a 50 cm-subcutaneous-heterogenous-greyish-mass. Histopathologic findings showed dermal keloidal scar like changes associated with agranulomatous foreign body inflammatory reaction surrounding hair shafts. Furthermore, chronic and acute suppurative folliculitis were evidenced.
A diagnosis of a tumour-stage-AKN was made. A delayed corticosteroid intra-lesional injection was performed postoperatively within 21 days. No recurrences were observed within one-month-follow-up.
Conclusion: Local excision is usually proposed for advanced refractory cases of AKN. Histpathologically, AKN is characterized by an inflammation of hair follicles with progression to keloidal papules, plaques, and scarring alopecia occurring mostly on the nape. In rare cases, it may grow to form real tumour-masses. Recent studies suggested a relationship between AKN and metabolic syndrome (e.g.morbid obesity observed in our patient).

E-PS-03-014

Inguinal extramammary Paget's disease in a male: a case report

K. Ben Lazreg*, S. Ben Hammouda, A. Ben Mabrouk, D. Beltaifa, M.M. Hamzaoui, L. Njim, A. Zakhama
*Fattouma Bourguiba University Hospital, Monastir, Tunisia

Background & objectives: Extramammary Paget's disease (EMPD) is a rare intra-epithelial malignancy, affecting primarily apocrine gland-bearing skin. It is more common in women and affect less frequently males. Herein we report a rare case of this misleading diagnosis in a male.
Methods: A 75-year-old man with no medical history presented to the dermatology department with a cutaneous purple lesion in the inguinal region. The clinically suspected diagnoses were pemphigus vegetans and fungoid mycosis. The patient underwent a cutaneous biopsy.
Results: Histologically, the epidermis showed acanthosis with hyperkeratosis and parakeratosis. There was an infiltration of the epidermal layers by large cells with a pagetoid arrangement. These cells had abundant clear or weakly eosinophilic cytoplasm and nuclei with moderate atypia and showing some mitoses. There was no image of dermal invasion. Bowen's disease or melanoma were ruled out thanks to the negativity respectively of P63, CK5/6 and PS100. Paget cells were positive for CK7. Thus, the diagnosis of EMPD was retained.
Conclusion: EMPD is an uncommon condition occurring in the sixth to eighth decades. Unlike our case, this entity shows female predominance and affects usually vulva. Principal differential diagnoses are Bowen's disease and superficial spreading melanoma. Immunohistochemistry is useful to distinguish EMPD form other entities. EMPD can be primary or represent an epidermotropic metastasis from a distant malignant neoplasm (colon, prostate or bladder). Early biopsy is crucial to establish a correct diagnosis for an early surgical excision of the lesion.

E-PS-03-015

COL5A1 and COL5A2 regulated by miRNA 21 and 199, modulate collagen V fibrillogenesis in keloid

V. Berton Liguori Zacchi*, A. Sousa Santos, L.H. Gomes Matheus, T. de Matos Lobo, Z.A. de Jesus Queiroz, C. Machado Baldavira, A.P. Pereira Velosa, V.L. Capelozzi, W. Paganelli Rosolia Teodoro
*Division of Rheumatology, Faculdade de Medicina da Universidade de São Paulo, Brazil

Background & objectives: We hypothesized that coding genes COL5A1 and COL5A2 and miRNA regulated the collagen fibrillogenesis in keloid cutaneous fibrosis. Thus, the present study investigated the effects of COL5A1 and COL5A2 and miRNA 21 and 199 on keloid scars.
Methods: Skin biopsies from 14 patients and 6 healthy controls were evaluated using histological scoring for severity and expression of COL5A1 and COL5A2 genes, by RT-qPCR. These data were correlated with patients' clinical characteristics and collagen V (ColV), miR21 and miR199.
Results: The expression of COL5A1 and COL5A2 genes was higher in keloid patients compared to controls (P=0.0208, P=0.0002, respectively). Regarding clinical characteristics, only for the sex variable there was a significant statistical difference for the expression of COL5A2 (P=0.03). In relation to the expression of the COL5A1 and COL5A2 chains with the established histological score, there was a difference in the expression of COL5A1 (P=0.007), and in the expression of COL5A2 (P=0.003). Very strong correlation was observed between miR21 and COL5A2 (ρ=0.854, P<0.001) and COL5A1 and COL5A2 (ρ=0.880, P<0.001) and strong correlation between papillary ColV and COL5A2 (ρ=0.615, P=0.004); miR21 and COL5A1 (ρ=0.640, P=0.002) and miR199 and COL5A2 (ρ=0.788, P<0.001).

Conclusion: In the current study, our results demonstrated that COL5A1 and COL5A2 regulated by miRNA 21 and 199, can modulate ColV cutaneous fibrillogenesis, defined as a sufficient cause for keloid; rather, the way that fibrillar collagen are present determines the potential of injury.

E-PS-03-018

Fibrosarcomatous dermatofibrosarcoma: a challenging diagnosis

O. Boudaouara*, W. Ben Makhlouf, M. Triki, M. Mellouli, L. Bouzidi, T. Sellami Boudawara, S. Makni
*Tunisia

Background & objectives: Fibrosarcomatous dermatofibrosarcoma (F-DFSP) is a rare variant of dermatofibrosarcoma, displaying distinctive high-risk histologic features and poor outcomes. This report aims to illustrate clinico-pathological features of this variant and emphasizes the pathologist's role in establishing the right diagnosis.
Methods: We present a case of a F-DFSP in a 44-year-old man diagnosed in our pathology department and treated in surgical department of Sfax hospital.
Results: A 44-year-old man presented with a-large-abdominal-wall-swelling. The patient reported the history of a-previously-quiescent-flat-lesion that recently grew rapidly, with erosion of the overlying skin. Computed-tomography showed a 10cm-well circumscribed-subcutaneous-mass. A core-needle-biopsy evidenced a-high grade-spindle cell-sarcoma suggesting a leiomyosarcoma or a fibrosarcoma. Standard wide surgical excision of the mass was then performed. Gross-examination found a 10cm-subcutaneous-whitish-multinodular-mass. Histological findings revealed areas of herringbone and fascicular sarcomatous-growth-pattern, with increased cellularity, marked atypia, and brisk mitotic activity admixed within an otherwise classic dermatofibrosarcoma (C-DFSP). Transition between the two components was abrupt. Both components stained for CD34 and were negative for smooth-muscle-markers. Surgical margins were focally involved. The diagnosis of an incompletely excised F-DFSP was made.
Conclusion: F-DFSP is the only variant of dermatofibrosarcoma that harbours a particularly aggressive clinico-biological behaviour in terms of local recurrences and distant metastases. Establishing an appropriate diagnosis may be challenging since fibrosarcomatous areas may be predominant as well as negative for usual immunohistochemical markers of C-DFSP (i.e. CD34). Thus, molecular testing of COL1A1-PDGFB gene fusion could be needed to affirm the diagnosis, as it is characteristic of all dermatofibrosarcoma variants.

E-PS-03-019

Pleomorphic dermal sarcoma: diagnostic difficulties in a case with lymph node metastasis

A. Brotoiu*, R. Andrei, A.V. Alexe, M. Bușcă, V. Marin, S. Zurac, C. Socoliuc
*Department of Pathology, Colentina University Hospital, Bucharest, Romania

Background & objectives: Pleomorphic Dermal Sarcoma is an unusual mesenchymal tumour typically occurring on sun-exposed skin of elderly adults, in the head and neck region, having a relatively high risk of recurrences and metastases. Given the aggressive behaviour, an accurate diagnosis is essential.
Methods: We present the case of an 87-year-old woman with a history of multiple squamous cell carcinomas and an excised forearm skin tumour followed two years later by an ipsilateral axillary lymph node metastasis. All the paraffin blocks from the skin tumour and two paraffin from the lymph node metastasis were received in consultation. Several immunohistochemistry tests were performed.
Results: Microscopic examination of the skin tumour revealed an ulcerated, fascicular, spindle cell malignancy, involving the dermis and subcutis, with epidermal contact and adjacent actinic keratosis. The lymph node metastasis presented similar fascicular areas and other diffuse, epithelioid areas. The lesional cells from both specimens were positive for vimentin, CD10, PDGFR-beta and focally positive for EMA. P63 was focally positive in the lymph node tumour, in the epithelioid areas. P40, CK5/6 and CK34BE12 were negative on all the paraffin blocks. Melanocytic markers were also negative. Based on the lack of any specific morphological squamous differentiation, the final diagnosis of pleomorphic dermal sarcoma with lymph node metastasis was rendered.
Conclusion: Pleomorphic dermal sarcoma is a rare tumour with diverse morphology which can be similar with that of spindle cell squamous cell carcinoma, melanoma or other sarcomas. These aspects, together with the possibility of lymph node involvement and the lack of any specific diagnostic markers, make this diagnosis one of exclusion. The case presented emphasizes the diagnostic difficulties encountered in evaluating aggressive dermal-based spindle cell lesions, especially in patients with a history of carcinoma, in the presence of lymph node metastasis.

E-PS-03-020

CDKN2A deletion in melanomas and its association with clinicopathological and immunological parameters: a TCGA-based study

Y. Cakir*, B. Lebe
*Dokuz Eylül University, Institute of Health Sciences, Department of Molecular Pathology, Turkey

Background & objectives: We aimed to compare clinicopathological parameters and survival between melanomas with and without CDKN2A deletion using the TCGA dataset. In addition, we investigated the relationship between CDKN2A deletion and immune cell infiltrations.
Methods: We used the 'TCGA, Firehose Legacy' data set via the Cbioportal website (www.cbioportal.org) for clinicopathological and survival comparison for two groups. The immunological analyses were done with the TIMER database (http://timer.comp-genomics.org/timer/). Cbioportal and TIMER are open-access, interactive bioinformatics tools providing an opportunity for genomic data analysis. $p<0.05$ value was considered statistically significant.
Results: Disease-free survival (DFS) was shorter in patients with CDKN2A deletion (median: 56.83 and 49.21 months, $p=0.01$), but there was no significant difference between two groups in terms of overall survival. Patients with CDKN2A deletion had an earlier age at diagnosis, lower Breslow thickness and T stage, and a lower rate of ulceration ($p<0.05$).
In the analysis performed on the TIMER database, a negative correlation was found between the presence of CDKN2A deletion and CD4+ T cells, B cells, and dendritic cell infiltration, while a positive correlation was found with macrophage infiltration ($p<0.05$).
Conclusion: We conclude that CDKN2A deletion seems to be associated with DFS and parameters related to the stage of the disease. Also, findings showing the relationship between CDKN2A deletion and the amount of immune cell infiltration may shed light on future studies.

E-PS-03-021

Concurrent eosinophilic angiocentric fibrosis and granuloma faciale: a case report highlighting histomorphological and immunohistochemical findings

Z. Canturk*, M. Celik, S. Ozturk Sari
*Medical Faculty of Istanbul, Department of Pathology, Istanbul, Turkey

Background & objectives: Eosinophilic angiocentric fibrosis (EAF) is a rare, chronic, benign fibroinflammatory lesion with an unknown etiology, primarily affecting the sinonasal mucosa and upper respiratory

system. Recent studies have suggested an association between EAF and IgG4-related diseases.
Methods: Here we present clinical, histopathological and immunohistochemical findings of a patient with EAF and granuloma faciale (GF).
Results: In our case, a 55-year-old woman presented with a nasal septum protrusion, leading to an incisional biopsy. Histopathological examination revealed angiocentric fibrosis concentrated around small-diameter vessels, exhibiting an onion skin-like appearance, within a fibrotic stroma. A dense inflammatory infiltrate rich in eosinophils accompanied the fibrosis, along with CD3(+) T lymphocytes and CD20(+) B lymphocytes, as demonstrated by immunohistochemistry. Further evaluation for IgG4-related disease association revealed a ratio of IgG4/IgG plasma cells around 15-20%, indicative of suspicion but not diagnostic. Additionally, the patient reported a previous diagnosis of GF in 2006, highlighting a potential association between EAF and GF.
Conclusion: EAF, often associated with GF and potentially IgG4-related diseases, manifests histomorphologically as angiocentric fibrosis surrounded by an eosinophil-rich inflammatory infiltrate. Patient history, including previous diagnoses such as GF, plays a crucial role in establishing potential associations. However, histomorphological and immunohistochemical findings alone may not be sufficient for diagnosing IgG4-related disease, emphasizing the need for further clinical and laboratory investigation.

E-PS-03-023
A rare tumour with unusual clinical presentation: a glomuvenous malformation of the forearm
L. Charfi*, A. Khemir, w. ben makhlouf, G. Sahraoui, I. Nasri, N. Boujelbene, I. Abbes, R. Doghri, K. Mrad
*Pathology department Salah Azaiez institute Tunisia / Precision Medicine and Oncology Investigation Laboratory (LR21SP01), Tunisia

Background & objectives: Glomuvenous malformation (GVM) are rare perivascular tumours counting for <1% of soft tissue tumours and 20% of glomus tumours (GT). GT develop preferentially in distal extremities. We report by the present study a case of GVM of unusual clinical presentation.
Methods: A case of GVM in the forearm was diagnosed in the pathology department of Salah Azaiez institute in Tunisia
Results: A 50-year-old man presented with a bluish unpainful tumour mass of in the forearm. Clinicians thought it would be a hemangioma. The tumour mass was surgically removed. Macroscopic examination showed an 18mm in diameter well circumscribed reddish nodule. Histopathologic examination revealed dilated vascular cavities with regular endothelium surrounded by clusters of small round cells provided with centrally located nuclei and eosinophilic cytoplasm. Those cells stained positively for SMA antibody and negatively for HMB45 and CD34 antibodies on histochemical staining. The diagnosis of GVM with complete surgical resection was retained.
Conclusion: GT present typically as solitary painful tumour masses developing especially in fingers and toes in young adults. Our patient was a 50-year-old male who presented with an unpainful mass of the foreman diagnosed clinically as a hemangioma. In the present case, despite the atypical clinical presentation morphologic aspects were typical for the diagnosis of GVM. Besides, immunohistochemical staining was of great help to exclude differential diagnoses such as paraganglioma and dermal nevus.

E-PS-03-024
Malignant proliferating trichilemmal tumour: a challenge for the diagnosis
M. Conde Ferreirós*, M. Carillo Cobarro, I. Bernal Simón, D.X. Ugás Burranca, A. Ordoñez Arrillaga, S. De Burgos González, A. Val-Carreres Castellote, I. Ruiz Díaz
*Spain

Background & objectives: Malignant proliferating trichilemmal tumours (MPTTs) are uncommon neoplasms which arises from the outer root sheath of the hair. MPTTs are primarily thought to develop de novo or can arise from a preexisting trichilemmal cyst (TC) or proliferating trichilemmal tumour (PTT).
Methods: A 59-year-old woman with no history of skin cancer, presented an8 cm scalp mass which was clinically diagnosed of epidermal cyst. A punch biopsy was made and informed to as squamous cell carcinoma. After that, the lesion was excised. The specimen was fixed in formaldehyde and embedded in paraffin. Haematoxylin-eosin and Immunohistochemical staining with p53 and ki67 were performed.
Results: The histological study of the specimen shows a multilobulated mass involving dermal and subcutaneous tissue. The tumour was composed by large nests with well circumscribed margins and focal infiltrative behaviour with invasion into the surrounding tissue, and desmoplastic stroma. Cytologically, the nests are composed by an atypical squamous cell with trichilemmal differentiation. They had atypical mitoses with high mitotic rate (15/mm2), nuclear pleomorphism, abundant eosinophilic cytoplasmandapoptotic keratinocytes. Immunohistochemical staining with p53 was patched (wild type) and ki67 proliferative index was 50% in hot spots.
Conclusion: MPTTs are very rare tumours which present a diagnoses challenge. They are frequently confused with squamous cell carcinomas, especially in small biopsies o samples as occurred in our case. Trichilemmal keratinization is the most important clue to distinguish both neoplasms. Other differential diagnosis includes PTTs and TCs. These two doesn't show cytologic atypia and mitotic activity, without infiltrative features.

E-PS-03-025
Cutaneous melanoma in children, adolescents and young adults: clinicopathological characterization of 44 cases
V. Cristóbal Redondo*, P. Cristóbal Redondo, J. Bañuls Roca, M. Niveiro De Jaime
*Dr.Balmis General Universitary Hospital of Alicante. Department of Pathology. Institute for Health and Biomedical Research, Alicante., Spain

Background & objectives: While paediatrics melanomas are extremely infrequent, accounting for the 1-4% of malignant children tumours, it has greater incidence in adolescence and young adulthood. Our study aimed to determine its prevalence in our population, clinical features and histopathological profile.
Methods: We conducted a retrospective observational study, selecting patients younger than 40 years with diagnosis of cutaneous malignant melanoma, treated and followed-up at our Institute between 2000-2024. Cases of choroidal and mucosal melanoma and those with inadequate samples for review were excluded. Medical records were examined to extract clinical data. Biopsy slides (H&E and immunohistochemistry) were retrieved to assess histopathological characteristics.
Results: Our casuistic encompassed 1 child, 3 adolescents and 40 young adults. Median follow-up time was 121 months. A slight predominance in women (53.2%) was observed, with a mean age at diagnosis of 29 years (9-39). The most common location was the trunk (32 cases; 72.8%) Mean longest diameter tumour was 10.23 mm (4-30). Histologic subtypes included: 2 nodular melanomas (4.5%), 4 spitzoid melanomas (9%) and 38 superficial spreading melanomas (86.5%). Almost half (46.4%) were associated with a melanocytic nevus. None of them showed lymphovascular or perineural invasion and there were only 4 demises, all of them with disseminated disease at diagnosis and a median survival time of 33 months.
Conclusion: Overall, melanoma is an aggressive malignancy with high morbidity and mortality, Nevertheless, this study corroborated that it has a favourable prognosis in this age group. As a result of its rarity,

it is still essential to accumulate experience and further investigations are needed.

E-PS-03-026

From rarity to recognition: hereditary progressive mucinous histiocytosis case report

D. Curto Aguilera*, J. Montero Menárguez, J.L. Rodríguez Peralto, M.C. Garrido
*Hospital Universitario 12 de Octubre, Madrid, Spain

Background & objectives: The hereditary progressive mucinous histiocytosis (HPMH) is a rare histiocytosis characterized by the development of cutaneous lesions caused by non-Langerhans cells and the deposition of mucin in dermis. Despite its rarity, identifying its histopathological characteristics is crucial for accurate diagnosis.
Methods: We present the clinical case of a 45-year-old male who presented to the Dermatology Department with erythematous papular cutaneous lesions distributed diffusely, predominantly on the head and extremities. A detailed review of the clinical and histopathological findings was conducted.
Results: The patient presented multiple erythematous papular cutaneous lesions distributed diffusely throughout the body. Histopathological analysis revealed a well-defined, non-encapsulated, monomorphic cellular proliferation located in the dermis, composed of cells with bland nuclei and abundant eosinophilic cytoplasm, arranged on a loose stroma with a positive Alcian Blue mucinous appearance. Perivascular lymphocytes and occasional mast cells were observed. Isolated multinucleated giant cells were present, without granulomas. Immunohistochemical study showed that the described cells were positive for PGM1, CD68, XIIIa factor and CD163, while they were negative for S100, CK AE1-AE3, lysozyme, CD1a, CD34, c-kit and NTRK.
Conclusion: The HPMH, described by Iglesias and Bork in 1988, is a benign form of non-Langerhans cell histiocytosis. Less than 20 cases have been reported, affecting different members of the same family with an autosomal dominant inheritance. Patients progressively develop multiple cutaneous nodules, mainly on the head and extremities, asymptomatic and without systemic involvement. This entity presents diagnostic challenges due to its clinical variability and histopathological similarity to other mucin-rich dermatoses.

E-PS-03-027

Microsatellite instability high risk in sebaceous adenoma: a case report

S. Ekmekci*, B.G. Özamrak, N. Güney, A. Olgun, Ü. Küçük
*Izmir Provincial Health Directorate, Izmir City Hospital, Department of Pathology, İzmir, Turkey

Background & objectives: Sebaceous adenomas are rare, slow-growing, benign sebaceous tumours. They are mainly observed in the head and neck and patients over 50. The treatment is total excision. Like other sebaceous neoplasms, Muir-Torre Syndrome can be seen as a cutaneous finding.
Methods: A 77-year-old male patient applies due to a mass on the scalp. An excisional biopsy is performed, with preliminary diagnoses of basal cell carcinoma (BCC) and squamous cell carcinoma. The patient had a BCC and CLL/SLL history from the nasal region, and JAK2 V617F mutation was present. A nodular lesion on the skin excision material was observed.
Results: Histopathological examination showed the proliferation of sebaceous and basaloid cells in the dermis, whose connection with the epidermis was not seen. The neoplastic proliferation consisted of cells with different shapes and sizes. Tumour cells showed focal positivity with CD10. Immunohistochemical evaluation of microsatellite instability (MSI) markers revealed the loss of nuclear expression by MSH2 and MSH6. Our case was signed out as sebaceous adenoma, and systemic evaluation accompanied by detailed family history (regarding visceral neoplasms, especially gastrointestinal system and urogenital system scans) was recommended.
Conclusion: Muir-Torre Syndrome is an entity characterized by multiple sebaceous tumours and visceral malignancies, especially in the gastrointestinal region. Such cases are reported to have lymphoid neoplasms as well. It should be kept in mind, especially when multiple sebaceous neoplasms are detected in cases under the age of 50; MSI testing for germline mutations is required. Genetic counseling and close follow-up with regular screening and genetic testing of the family members are also recommended if mutations are detected.

E-PS-03-028

Cutaneous follicular tumours and the experience of the pathological anatomy department of the Mohammed VI Marrakech University Hospital: about 67 cases

H. El Khadraoui*, H. Rais
*Anatomopathology department, Morocco

Background & objectives: . We report a series of 67 cases of adnexal tumours with follicular differentiation diagnosed at the Mohammed VI anatomy and pathology department in Marrakech, describing the epidemiological and anatomopathological profiles of these tumours.
Methods: This is a retrospective study concerning 67 cases of adnexal tumours with follicular differentiation diagnosed in the pathological anatomy department of the Mohammed VI University Hospital of Marrakech over a period spread over 15 years from January 2009 to December 2023.
Results: The average age of our patients was 36 years with extremes of age ranging from 17 years to 90 years. The M/F sex ratio was 1.2. The main reason for consultation was a skin mass in different locations. Benign tumours represent 95.8% while malignant tumours represent 4.2%. The predominant histological type is pilomatricoma found in 47 cases followed by trichoadenoma and trichoblastoma.
Conclusion: This work made it possible to study follicular skin tumours which are rare and very varied tumours, most often benign but characterized by their clinical polymorphism which explains that the confirmatory diagnosis cannot be done without correlation of clinical and histological data.

E-PS-03-033

Primary cutaneous apocrine carcinoma (PCAP) of the scalp: case presentation and review of the literature

M.C. Filip*, C. Socoliuc, C. Morjan, A.D. Stefana, E.N. Ignat, R. Andrei
*Pathology Department Synevo Romania; Colentina University Hospital, Romania

Background & objectives: Apocrine carcinoma is a rare cutaneous adnexal neoplasm that demonstrates clear signs of malignancy, apocrine secretion and lacks the distinctive microscopic features found in other well-defined lesions with apocrine differentiation.
Methods: We present a case of 65-year-old man with an ulcerated cutaneous tumour on the occipital scalp, measuring 40/25/15 mm and having a long standing evolution (of approximately 10 years).
Results: Microscopic analysis reveals a glandular, cystic, papillary and solid proliferation within the dermis and subcutis, consisting of large epithelioid cells with granular eosinophilic cytoplasm, displaying large areas of apocrine secretion, moderately nuclear pelomorfism and frequent mitoses, grade 2 (score 6 using Nottingham system). No in situ component or benign pre-existing tumour was identified.
The tumour proliferation shows positive immunohistochemical staining for GCDFP15, CK19, Mammaglobin and Androgen Receptor and negative for ER, PR, HER2, D2-40, GATA3 and p63 among others.

The patient also exhibits one lymph node metastasis in the occipital region, while CT and PET-CT fails to show additional tumours.
Conclusion: PCAP is an exceedingly rare tumour, with limited documented cases, typically found in the axilla, while scalp involvement is highly unusual.
The main differential diagnosis involves a cutaneous metastasis originating from a mammary ductal carcinoma, our case having a similar immunohistochemical profile and no associated precursor lesion. Hence, the final diagnosis of PCAP was supported by clinical and imaging examinations.

A comprehensive multidisciplinary approach is vital for enhancing patient outcomes in cases of PCAC.

E-PS-03-034
Fibrous hamartoma of infancy: when molecular studies give us a hand
H. Galindo Guzman*, B.B. Ardaya Lopez, F. Arias, V. Parra Blanco
*Hospital General Universitario Gregorio Marañón, Spain

Background & objectives: Fibrous hamartoma of infancy is a benign tumour that can present a challenge when it presents with atypical clinical features and the diagnosis is made in small biopsies. We present a case of a 7-month-old child with a vascular-like tumour.
Methods: The patient presents a rounded, raised lesion of 5.5 cm, elastic, depressible and skin-colored with bluish vessels in the upper mid-dorsal region. Positive Darier sign. Initially diagnosed with infantile hemangioma vs tufted hemangioma vs lymphatic malformation, an incisional biopsy of 0.5 cm in diameter was performed.
Results: The biopsy revealed a subcutaneous lesion in the deep dermis, composed of a mixture of mature tissues with two components: lobes of mature adipose tissue interrupted by occasional fascicles of collagen and myofibroblastic cells. Isolated and poorly defined bundles of small spindle cells without atypia and mitotic activity with doubtful staining for CD34 were observed. Immunohistochemistry for GLUT1 was negative. Molecular studies revealed an insertion in exon 20 of the EGFR gene, which ruled out the diagnosis of infantile hemangioma or other vascular lesion. With these findings, the lesion was surgically removed, which morphologically confirmed the diagnosis of fibrous tumour of infancy.
Conclusion: Fibrous hamartoma of infancy is a rare entity that presents in paediatric age and in some cases, its histological characteristics in a superficial and partial biopsy can lead to considering other differential diagnoses. Genetic studies are becoming increasingly important since they can help reach the diagnosis in small specimens without typical histology. It is important to consider this entity in the differential diagnosis of subcutaneous tumours in childhood since despite being benign, its correct diagnosis can avoid incorrect management.

E-PS-03-035
Edematous face in a young man. What's wrong?
M.J. Gálvez-Medina*, A. Sanz Zorrilla, M.J. Jurado Rivera, V. Davila Flores, I. Sánchez Ramírez, J. Osuna Soto, S. Haro Yuste
*Hospital Universitario Reina Sofía, Spain

Background & objectives: In dermatopathology, in most cases, it is easy to recognize neoplastic lesions. However, there are symptoms that may appear banal though masking a serious pathology; either because they have atypical presentations or because they show a partial responseto treatments.
Methods: We present the case of a young Caucasian male with edematous lesions in the facial region simulating chronic erythema persistants. These are diffuse lesions, more palpable than visible, on bony prominences, without pain or itching. After several visits to dermatology, a skin biopsy was performed which showed shocking results and led to take samples from different body regions.
Results: The skin biopsy showed monomorphic lymphocytic infiltrate around vascular structures at both superficial and deep levels. These lymphocytes have increased size with dense chromatin and they were clearly diagnostic of a malignant lymphoid process. Basic immunohistochemical techniques were performed, moreover, it had to be expanded due to the negativity of a large number of markers (CD20, CD3, MUM1, Myeloperoxidase). PAX5 and CD19 had to be relegated to guide the diagnosis, which, together with TDT and the negativity of other markers pointed to B lymphoblastic leukemia. Bone marrow biopsy showed clear infiltration by leukemia.
Conclusion: B lymphoblastic leukemia is a typical pathology in children but can also occur in adults. The literature reports a higher frequency of leukemia cutis presentations in T lymphoblastic leukemia.

This example is not intended to promote the indiscriminate use of biopsies by dermatologists, but to highlight the importance of having good communication between dermatologists and pathologists and taking a skin biopsy on time.

E-PS-03-036
Multisite extramammary Paget disease: an unusual malignancy in a Caucasian male
S. García-Fuertes*, N. Franco, E. Ponce-Casas, R. Vilorio, M. Garcia Garcia, C. Cabañuz, F. Felipo Berlanga

*Hospital Clínico Universitario Lozano Blesa, Spain
Background & objectives: Extramammary Paget disease (EMPD) is a rare cutaneous neoplasm that frequently develops in areas where apocrine glands are abundant, as erythematous, well-demarcated plaques. Primary EMPD involving more than one location is unusual, with most cases reported in Asian patients.
Methods: We present an 86-year-old man with a 2-year history of two independent erythematous plaques located in the right groin and the left pubic region. There was no history of malignancy and no palpable regional lymphadenopathy. Dermatologists thought of fungal infection as first diagnostic option, so skin punch of both sites were referred to our department.
Results: Histologically, skin biopsies revealed nests of Paget's cells with large nuclei and abundant clear cytoplasm involving the full thickness of the epidermis and the papillary dermis, basal cells with mild atypia and apocrine glands affected by the neoplasm. Immunohistochemistry showed that those cells were positive for CK7, CK8/18, GCDFP-15, EMA, CEA, MUC1 and Ber-EP4, while S100, MUC2 and CK20 were negative. An abdominopelvic computed tomography revealed no signs of malignancy or metastatic disease. A diagnosis of multisite EMPD was confirmed. Given the presence of invasive disease on initial biopsy, the patient was proposed to definitive surgical resection of both lesions, with wide peripheral and deep surgical margins.
Conclusion: EMPD is an unusual intraepidermal carcinoma usually occurring on apocrine gland-containing skin. Single-site disease has a Caucasian and female predominance, but multifocal EMPD has been occasionally reported in Asian males. In our knowledge, we present the first case of EMPD in a Caucasian patient. In absence of metastatic disease and underlying malignancy, a wide excision is the gold standard treatment for multifocal EMPD, with favourable prognosis. Early detection of multisite EMPD is prior to avoid misdiagnosis and prevent malignancies.

E-PS-03-037
Trichoblastic carcinoma in a patient with Brooke-Spiegler syndrome: a entity uncommon

J. García-Gómez*, A. Quer, M. Aquino, A. Jaka, C. Perello-Fabregat, I. Beleña, P. Luizaga
*Hospital Universitari Germans Trias i Pujol, Spain

Background & objectives: Brooke-Spiegler syndrome (BSS) is a rare genodermatosis leading to usually bening adnexal neoplasms. Malignant transformation, like trichoblastic carcinoma (TBC), is uncommon. TBC exhibits dual differentation toward follicular stroma and germinative cell, with malignancy in the epithelial component.
Methods: We present the case of a 85-year-old man with Brooke-Spiegler syndrome and a history of multiple basal cell carcinomas, trichoepitheliomas, and cylindromas. The patient had multiple widly distributed lesions, but it was decided to excision a preauricular ulcerated lesion with poorly defined edges measuring 1,9 x 0,6 x 0,3 cm.
Results: The histological study of the lesion identified an ulcerated, poorly delimited, invasive neoplasm with double differentiation towards follicular stroma and epithelium which the epithelial component presented marked atypia and necrosis. In addition, clearly identifiable transition zones will be observed between the benign component (trichoblastoma) and the malignant component. The resection margins were affected by the benign component but the patient was advised to reoperate to expand the affected area. Our patient is disease-free after 8 month of follow-up.
The diagnosis was TBC, a neoplasm that arises from the malignant degeneration of benign follicular tumours where the benign and malignant components converge.
Conclusion: Trichoblastic carcinoma (TBC) is a rare and aggressive malignancy, with its clinical feature, treatment, and outcomes poorly understood due to limited data from only 93 reported cases. Metastases and aggressive progression, notably after incomplete resection, have been observed. Syndromic association (BSS) may offer a better prognosis. The scarcity of cases impedes a comprehensive understanding of TBC´s natural history and prognosis.

E-PS-03-038
Miliary osteoma cutis: clinical characterization and histopathological analysis of an unusual case
M.A. Gil Galvín*, E.I. Ortega Pinto, A. Diez Fernández, M.C. Garrido
*Hospital 12 de Octubre, Spain

Background & objectives: Miliary osteoma cutis represents a rare variant of cutaneous osteoma, an entity of unknown etiology characterized by the formation of multiple small-sized nodules clustered in the dermis composed of bone tissue, especially affecting the face.
Methods: We present the case of a 54-year-old female patient with multiple asymptomatic cutaneous papules on her cheeks, indurated and without changes in coloration. The clinical orientation was papular rosacea, and she was treated with isotretinoin. After the treatment failure, a skin punch biopsy was made. After fixation in formalin and embedding in paraffin, histological sections were analysed.
Results: Histopathological evaluation revealed the presence of multiple nodules composed of mature trabecular bone tissue surrounded by adipose and fibroconnective tissue in the deep dermis and hipodermis. A perivascular lymphocytic infiltrate was observed in the papillary and reticular dermis. Based on these findings and their correlation with the patient's clinical presentation, the diagnosis of miliary osteoma cutis was established.
Conclusion: Miliary osteoma cutis is a rare entity that may be a diagnostic challenge due to his clinical similarity to other cutaneous lesions such as rosacea and other acneiform eruptions, highlighting the crucial role of the pathologist in the diagnosis. It is essential to consider this entity in patients with multiple cutaneous nodules, especially in cheeks, forehead, and scalp. Although it is a benign and asymptomatic condition, an accurate diagnosis is fundamental to avoid unnecessary treatments and provide appropriate clinical guidance.

E-PS-03-039
Perineal nodular induration of the cyclist - case series and literature review
Y. Guzmán Gómez*, A. Santos-Briz Terrón, S. Alvarez Alonso, J.L. Revilla Hernández, M. Angoso Clavijo, R.M. Escribano de la Torre, J.J. Jiménez Velasco, N. Fontanil Vior
*HUMV, Spain

Background & objectives: Perineal nodular induration (PNI) of the cyclist, also called "third testicle", is a rare benign proliferation of soft tissue in the perineal region. The aim of this paper is to present the histological findings of four new cases.
Methods: The archives of our department for the last eight years were reviewed and four cases of PNI were found, representing the longest series of cases ever described in the English literature. In addition, a review of published cases in the existing literature was undertaken using the Pubmed database with the search terms 'perineal nodular induration' and 'cyclist's nodule'.
Results: We present four cases of PNI, three male amateur cyclists and one female professional cyclist. The four patients manifested unilateral painfull perineal lesion, slowly-growing during several years. Recurrent inflammation was present in one case. Surgical excision was performed in all patients. The histological examination showed a proliferation consisting of a prominent fibrocollagenous tissue with a low density of mature spindle cells, damaged elastic fibres and an entrapment of mature adipocytes. One case showed concomitant deep cystic folliculitis. The patient's history, clinical and histopathological findings, suggested a diagnosis of PNI. A literature search identified 15 PubMed articles reporting 23 cases of perineal nodular induration (PNI) or cyclist's nodules.
Conclusion: PNI is associated with "saddle sports", particularly road cycling, and is not exclusive to men; female cases have also been reported. Due to the paucity of literature, PNI is a rare condition that is relatively well known to sports medicine specialists, but appears to be under-recognised by general practitioners and pathologists. With the increasing popularity of cycling, PNI must be included in the differential diagnosis of an elite or amateur cyclist presenting with a perineal mass.

E-PS-03-040
Desmoplastic neurotropic melanoma: case report
H. Kandemir*
*Health Sciences University Izmir, Turkey

Background & objectives: Desmoplastic melanoma(DM) is a rare variant, less than 4% of melanomas.Sun exposure and age are risk factors.Lesions present as nodules, papules, plaques.A subtype of DM, accounting for approximately 33% of cases, exhibits neurotropism, characterized by tumour cells infiltrating neural structures
Methods: In order to contribute to the literature, presenting a case report of desmoplastic malignant melanoma, a rare variant.
Results: A 29-year-old female patient presented with a 7 mm diameter, slightly raised, firm nodular lesion on her back. The lesion was excised. Upon examination of the sections, irregular acanthosis, thinning, and serum accumulation were observed in the epidermis, with no signs of ulceration.The tumour, originating from the papillary dermis, completely involved the skin and infiltrated the subcutaneous fat tissue with slight pleomorphism in spindle cells. There was no melanocytic atypia in the epidermis. Lymphoid aggregates were seen in the stroma, and there was no evidence of lymphovascular invasion.Two mitoses were observed in the tumour. Immunohistochemical examination revealed S100(+) and SOX-10(+) in the tumour cells, while HMB-45 and Melan-A were (-).
Conclusion: Desmoplastic melanomas lack pigment. During diagnosis, they are infiltrative and have irregular borders. The tumour consists of

hyperchromatic nucleus cells resembling fibroblasts and is surrounded by collagen fibers. Lymphoid aggregates are indicative for diagnosis. Neurotropism is associated with poor survival outcomes. Immunohistochemically, S-100 and SOX-10 are positive, while other melanocytic markers may be negative. In the differential diagnosis, tumours such as neurofibroma, dermatofibroma, atypical fibroxanthoma, cutaneous leiomyosarcoma, spindle cell carcinoma, and malignant peripheral nerve sheath tumour should be considered.

E-PS-03-041

Endocrine mucin producing sweat gland carcinoma (EMPSGC) in an extrafacial site

U. Kiriwandeniya*, A. Ali
*Department of Histopathology, Mid and South Essex NHS Trust, United Kingdom

Background & objectives: Endocrine mucin producing sweat gland carcinoma (EMPSGC) is a low grade mucin-producing neuroendocrine neoplasm of sweat gland origin with a predilection for the eyelid and periorbital skin. It is a precursor to mucinous adenocarcinoma with neuroendocrine differentiation.Women affected more.
Methods: A 58 year old woman presented to Dermatology clinic with a nodule on right posterior scalp measuring approximately 30mm in size. Wide local excision was done with the clinical differential diagnoses of keratoacnathoma or squamous cell carcinoma. On macroscopic examination this lesion was measuring 30x28mm with a central elevation of 20mm .It was lobulated and pinkish on surface.
Results: On microscopy this was predominantly a fairly circumscribed expansile tumour in dermis composed mainly of nodules of small polygonal tumour cells floated in extra cellular mucin pools. Cribriform architecture is noted within nodules focally. A few clusters of tumour cells were noted suspicious of focal infiltration. Nuclear atypia was mild and mitoses was sparse. A single focus of peri neural invasion is noted beyond the dermis. No areas of necrosis or lymph vascular invasion identified. The cells were positive with Ber-Ep4, CEA, CK7, ER/ PR, BCL2, GATA3 and Synaptophysin, weakly positive with Chromogranin and negative with CDX2, CK20, CK5, P63, SMA, Desmin and TTF1. Ki 67 activity was around 5%.
Conclusion: Main differential diagnoses included primary cutaneous mucinous carcinoma and metastatic mucinous carcinoma. In our patient there was no clinical history of diagnosed malignany. EMPSGC is considered cutaneous analogue of solid papillary carcinoma of the breast. In some cases, it is associated with adjacent mucinous sweat gland carcinoma with neuroendocrine features, and most likely represents a precursor lesion.

However as morphology or immunohistochemistry can not exclude metastatic breast (mucinous)carcinoma clinicopathological, ragiological correlation, MDT discussion are recommended.

E-PS-03-042

Eccrine poroma, spiradenoma and trichoepithelioma arising together, a rare combination skin adnexal tumour case report

F. Kubba*, F. Teixeira
*Ealing Hospital, London North West University Healthcare NHS Trust, United Kingdom

Background & objectives: A skin tumour was excised from a 95-year old male clinically presented as a slowly growing groin nodule. The clinical differential diagnosis included extramammary Paget's disease and a benign skin appendageal tumour. The patient had no previous skin cancers.
Methods: Macroscopically the lesion appeared nodular measuring 20 x 16mm.
Microscopically it was easy to identify a main lesion of an eccrine poroma with a smaller element of a trichoepthelioma and a minor element on the side resembling a spiradenoma/apocrine adenoma. All three elements had benign features and no obvious necrosis, cytological atypia or increased mitosis was seen.
Results: CK7, CK19 and CEA immunohistochemical stains were also applied to highlight the ductal differentiation. Rare areas of eccrine ducts were noted. No further molecular genetic tests were applied.
No other tumours elsewhere were seen to suggest a syndromic type of clinical presentation and there was no family history of multiple skin tumours.
On literature review, combined appendageal skin tumours usually occur from the same cell lineage. Although rare tumours are reported to combine two or even three of the follicular, eccrine and sebaceous gland differentiation. This support the pluripotent cell theory.
Our patient had their tumour excised at the first instance and no recurrence or regional metastasis was reported.
Conclusion: We have described a rare appendageal tumour of a combined eccrine poroma, trichoepithelioma and a minor spiradenoma element. Combined lesions from the same cell lineage can occur however combined eccrine and follicular tumour are quite rare suggesting good evidence that such differentiation is possible due to the presence of pluripotent cells. There were no clinical sequelae and the tumour did not recur. Being aware of such combinations may help us in further future understanding and studying factors involved in tumourigenesis.

E-PS-03-043

A case report of basal cell carcinoma of the anus: rarity in anal cancer

B.A. Lazar*, A. Ungureanu, A. Mocanu, O.S. Cotoi
* Mures Clinical County Hospital, Romania

Background & objectives: Basal cell carcinoma is the most prevalent form of skin cancer, typically arising on sun-exposed areas of the skin, its occurrence in uncommon sites such as the perineum accounts for less then 0,2 % of all basal cell carcinoma cases.
Methods: We present a case of a 82-year-old female with a perianal lesion of 6 months progression that reached 2 cm in diameter causing anorectal bleeding, pain and pruritus. Following unsuccessful topical treatment, the patient underwent an incisional biopsy. Paraffin-embedded sections were prepared, and the specimen was examined using hematoxylin and eosin staining, followed by immunohistochemistry reactions.
Results: Microscopic examination revealed abasophilic tumour with central ulceration consisting of nests of small basaloid cells emanating from the epidermis with peripheral palisading, displayed areas of cystic architecture, desmoplastic changes, and retraction artifact. The tumour cells were basaloid, small, hyperchromatic, with occasional mitotic figures. The stroma exhibited edema accompanied by the presence of mononuclear inflammatory cells. Immunohistochemical staining demonstrated tumour cell positivity for Bcl2, BerEp4 and p40. The role of immunohistochemical markers was to differentiate cutaneous basal cell carcinomas from squamous cell carcinomas. The surgical margins were infiltrated by tumour proliferation. These findings were consistent with the diagnosis of nodular, superficial and cystic basal cell carcinoma with infiltrative features.
Conclusion: Perianal basal cell carcinoma is a rare type of skin tumour encountered infrequently in dermatopathology practice. Considering the notable histological resemblance yet disparate biological characteristics and management approaches, it is imperative to discern between basal cell carcinoma and basaloid squamous cell carcinoma.This case highlights that basal cell carcinoma can develop in unexposed sun area, such as perianal region.

E-PS-03-044
Scarring alopecia as an undescribed side effect of Dupilumab
F. Leiva-Cepas*, A. Sanz Zorrilla, I. Sánchez Ramírez, J. Osuna Soto, V. Amorrich
*University of Cordoba, Spain

Background & objectives: Dupilumab is a drug used in the treatment of atopic dermatitis (monoclonal antibody that blocks IL4-IL13 receptors). Side effects such as conjunctival swelling, blurred vision, urticaria and fever are described. However, alopecia has not been reported as a side effect.
Methods: The histology of two biopsies from a 16-year-old treated with Dupilumab, who began developing inflammatory alopecia patches on the scalp a week after starting medical treatment, was studied.
Results: There was a normal count of the number of hair follicles without alteration of the percentage of anagen, telogen, or catagen phases. Incipient scarring alopecia with focal lichenoid inflammation in the isthmus of the hair follicles was observed, a similar finding to that found in Lichen planus.
Conclusion: Are we facing a side effect of Dupilumab? Or is it a coincidence that the patient presents a scarring alopecia just at the beginning of the treatment? Our dermatologist suggested that it was due to his severe atopy or that it was a combination of trichotillomania with alopecia areata, but the epidermis showed no signs of spongiosis, no pigment cast, and there was no inflammation in the hair bulb.

E-PS-03-045
Fibrous epithelioid histiocytoma: clinical presentation, histopathological features, and diagnostic challenges - a case report
R. López Henríquez*, M.A. Krupinska, J.S. Marrero Afonso, C.N. Hernández León
*Hospital Universitario de Canarias, Spain

Background & objectives: Fibrous epithelioid histiocytoma is a benign cutaneous neoplasm of unknown histogenesis. Although it was formerly recognized as a rare variant of dermatofibroma, it is now considered an independent entity, with ALK rearrangements present in 90% of cases.
Methods: A 63-year-old female patient with no significant personal history presented to a dermatologist with a 6 mm pink papule on the right thigh. Examination revealed nonspecific dermatoscopy. The dermatologist considered a differential diagnosis including dermatofibroma, basal cell carcinoma, and dysplastic nevus. Excision was performed. Conventional and immunohistochemical techniques for S100, HMB45, CD68, and ALK were employed.
Results: A 0.7 x 0.3 cm skin punch biopsy was obtained. Microscopic examination revealed a dermal lesion composed of a proliferation of large epithelioid cells with eosinophilic cytoplasm and abundant lymphoplasmacytic inflammatory infiltrate. No atypia or obvious mitotic figures were identified. Immunohistochemically, these cells exhibited positivity for CD68 and ALK and negativity for S100 and HMB45. The morphological and immunohistochemical findings were consistent with fibrous epithelioid histiocytoma.
Conclusion: The histological differential diagnosis of fibrous epithelioid histiocytoma is broad and encompasses melanocytic lesions such as Spitz nevus, lesions with myoepithelial differentiation such as cutaneous syncytial myoepithelioma, and mesenchymal lesions such as epithelioid sarcoma and cellular neurothekeoma. However, fibrous epithelioid histiocytoma is a benign entity that rarely recurs, so careful examination is necessary to identify it.

E-PS-03-046
Sebaceous carcinoma arising from sebaceoma in a patient with lynch syndrome: case report and literature review
R. Lyrio*, A. Pestana Lopes, R. Veiga
*Hospital da Luz Lisboa, Portugal

Background & objectives: The association between cutaneous sebaceous tumours and Lynch syndrome (LS) is well known. Malignant transformation of sebaceomas into sebaceous carcinomas (SC) is exceedingly rare. We aim to report a case of SC arising in a sebaceoma, in an LS patient.
Methods: A 55 year-old woman with a diagnosis of colonic adenocarcinoma in the context of multiple sebaceomas, and LS had a 13mm ulcerated nodule on the neck, which was excised and sent for pathologic examination. A PRISMA-driven literature review on SC arising in sebaceoma was carried out, using Pubmed, Scielo and Lens.
Results: Microscopically, a sebaceous neoplasm with cyto-architectural features mostly compatible with sebaceoma was found. Interestingly, in the deeper aspects of the tumour, an infiltrating component was identified, consisting of small nests and isolated epithelial cells, morphologically and immunophenotipically consistent with sebaceous histogenesis. The final diagnosis of SC arising from secabeoma was made.
Our review showed 2 other cases similar to ours, with lesions ranging from 10-17mm, located on the head and neck region. None were in the context of LS, nor were metastasis found. The disease-free interval ranged between 5-24 months.
Conclusion: The malignant transformation of sebaceomas into SC is extremely rare and still very poorly understood, with only 2 other cases reported in the literature.

Further studies may provide better understanding about the underlying pathogenic mechanisms of such a rare occurrence, and to the eventual subsequent identification of clinical and histologic features that might be useful in these patients' management and follow-up.

E-PS-03-047
Common characteristics in both primary cutaneous marginal zone lymphoproliferative disorder and primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder: a case series
S. Merino Baamonde*, E. Higueras Mora, M. Rubiera Valdés, F.J. Pérez Rastrollo, C. González Rodríguez, M. García Martínez, C. Fuente Díaz, J.R. Riera Velasco, P. Morales del Burgo, B. Vivanco Allende
*University Hospital of Asturias, Spain

Background & objectives: Primary cutaneous marginal zone lymphoproliferative disorder (PCMZ-LPD) and primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder (PCSM-LPD) both present an indolent course, and occasionally similar histopathological features, posing a diagnostic challenge. We aim to review cases to identify such common characteristics.
Methods: Cases were collected retrospectively, from 2015 to 2024. 10 cases of PCMZ-LPD and 2 cases of PCSM-LPD were identified. Clinical data was collected, and hematoxylin-eosin sections studied to record architecture, epidermotropism and location of infiltrate. Immunohistochemical studies were performed, analyzing CD3; CD4; CD8; CD20; PD1; MUM1; kappa-lambda, PD1, Bcl6, CD10, CXCL-13 and ICOS.
Results: Out of all the examined cases, 3 cases of PCMZ-LPD presented a diagnostic challenge. One presented with confusing features both in histomorphology and immunohistochemistry, with TCRG policlonal amplification. A diagnosis of PCMZ-LPD was made based on kappa chain restriction. The other 2 cases had common features with PCSM-LPD but were not as challenging. One had TCRG oligoclonal amplification, and presence of multinucleated cells with a monomorphic small cell infiltrate, but immunohistochemistry was diagnostic of PCMZ-LPD. The other case presented a pleomorphic infiltrate composed of atypical plasma cells with some blastoid cells, accompanied

by a small T-cell component with strong expression of TFH markers; it was diagnosed as PCMZ-LPD.
Conclusion: Both PCMZ-LPD and PCSM-LPD are rare, and have a number of clinicopathological characteristics in common. These disorders present with a dermal infiltrate of atypical lymphoid cells, which are frequently polymorphous. Immunohistochemistry and clonality analysis are vital to reaching a correct diagnosis. Approximately 25% of cases presented with characteristics common to both entities. The results of our case series are compatible with those found in the literature.

E-PS-03-048
Trichilemmal carcinoma: a case report of a rare entity
A. Milićević*, O. Živković, I. Petrovic, K. Obradović
*Institute for Oncology and Radiology of Serbia

Background & objectives: Trichilemmal carcinoma (TC) is a rare cutaneous malignant adnexal neoplasm with follicular outer root sheath (ORS) differentiation. It has a predilection for elderly patients involving sun-exposed areas of the body.
Methods: A 75-year-old female patient with a previous history of breast carcinoma was referred to the Institute for Oncology and Radiology of Serbia with a large lesion on the scalp in the frontoparietal region of the head. The tumour was removed surgically with a wide local excision arranged to confirm the diagnosis.
Results: Surgical excision was performed, and histopathological evaluation of the excised specimen revealed a TC with no lymphovascular invasion and clean surgical margins. Microscopic features show TC characteristics, including lobular proliferation centred on pilosebaceous structures connected to the epidermis, composed of small groups of round-shaped epithelial cells with clear, glycogen-rich eosinophilic cytoplasm, prominent atypical nuclei, high mitotic rate, and with foci of trichilemmal keratinization.
Conclusion: This rare tumour is the malignant counterpart of trichilemmoma and mimics many entities. It should be distinguished from other tumours of follicular origin. The diagnosis of TC is established through physical and histopathology examination. Although local recurrence is rare, it has been reported. The treatment of choice is surgical excision with tumour-free margins, which is essential due to the potential for local invasion and recurrence.

E-PS-03-049
Bullous dermatoses and the use of direct immunofluorescence
S. Moqran*, N. Hammas, F. Harmouch, S. Aitbrahim, L. Chbani, L. Tahiri
*Pathology department, University Hospital Hassan II, Morocco

Background & objectives: Bullous dermatoses (DB) are classified into two main categories: autoimmune and non-autoimmune. In order to establish a diagnosis, it is essential to correlate clinical and anatomopathological findings. our aim is to clarify the role of direct immunofluorescence in their diagnosis.
Methods: A retrospective study was conducted over a three-year period, encompassing all cases of DB diagnosed in the Department of Pathology. A total of 80 cases of DB were collected. In order to provide a diagnostic approach, two skin biopsies were taken from each patient. One biopsy was used for histological examination, while the other was used for direct immunofluorescence (DIF).
Results: There was a female predominance with a sex ratio M/F of 0.6. The mean age was 60 years. The IFD results indicated that 68 of the cases (85%) exhibit autoantigen expression, which is consistent with the autoimmune nature. A division was made between cases of IFD positive according to the level of skin cleavage. The resulting categories were as follows: autoimmune intraepidermal or pemphigus DB (n=19) and autoimmune subepidermal DB (n=49). Subepidermal DB AI were predominantly autoimmune bullous pemphigoid (31 cases), followed by epidermolysis acquired (9 cases), then gestational pemphigoid, dermatitis herpetiformis and linear IgA dermatosis. The pemphigus cases were classified into two categories: eight deep and ten superficial.
Conclusion: The diverse range of BD presents a challenge to accurate diagnosis. Clinical and histological examination alone cannot determine whether the condition is autoimmune or non-autoimmune BD. Therefore, additional diagnostic techniques, such as direct immunofluorescence testing, are necessary to rule out non-autoimmune BD and to determine the histological subtype of the autoimmune DB.

E-PS-03-050
Pathologist interobserver variability in the diagnosis of appendageal skin tumours
S. Moqran*, N. Hammas, S. Aitbrahim, F. Harmouch, S. Elloudi, F. El Mernissi, L. Chbani, L. Tahiri
*Pathology department, University Hospital Hassan II, Morocco

Background & objectives: Cutaneous adnexal tumours (CATs) are neoplasms that differentiate towards cutaneous appendages. Their diagnosis can be challenging due to their morphological heterogeneity and the aggressive behaviour of malignant tumours. This study aims to clarify the diagnostic challenge by examining interobserver variability.
Methods: A retrospective study was conducted over a period of 8 years (2015-2023), including all CATs diagnosed in the Department of Pathology. 114 cases of CATs collected during this period were blindly reviewed by a dermatopathologist and another pathologist. The kappa coefficient of interobserver variability (with 95% confidence interval) was calculated to measure the reliability of the correlation.
Results: There was a female predominance with a sex ratio M/F of 0.58. The mean age was 50 years. The head and neck were the most affected areas (78%). In this study, the agreement between three pathologists in the determination of the benign or malignant nature of the CAT was analysed. The results showed an agreement of 100%, with a kappa value of 1. When CATs were classified into groups based on their follicular, sebaceous and sudoriparous differentiation, there was substantial agreement between pathologists ranging from 87% to 91%, with a kappa value of 0.78 to 0.90. The disagreement between pathologists was mainly related to follicular and sweat gland differentiated tumours.
Conclusion: This study has identified inter-observer variability in the diagnosis of CATs, which was low but significant, particularly in the accuracy of the histological subtype. This variability may be attributed to the morphological heterogeneity of this type of tumour and its rarity. However, therapeutic management was not affected in any of the cases in this series, as there was complete agreement between pathologists regarding the malignant or benign nature of the tumour.

E-PS-03-052
One erythematous plaque: two different histological patterns
M. Narváez Simón*, A. González Fábrega, A. Remón Love
*UPIGAP-Hospital de Baza-HUVN, Spain

Background & objectives: Granuloma annulare and necrobiosis lipoidica are dermatosis which have rarely been reported to occur concomitantly in patients with diabetes mellitus.The relevance of our case is based on the scarce number of reported cases describing these two patterns as unique lesion.
Methods: We report a case of a 78-year-old woman with history of type II diabetes and psoriasis,who developed a new onset erythematous and violaceous eruption formed by infiltrative plaques in trunk,upper limbs and dorsal foot.Clinical diagnosis of granuloma annulare was made and, in order to confirm it, a 4mm skin punch biopsy was performed from a lesion on her right forearm.

Results: Microscopic examination revealed two distinct lesional patterns as part of the same clinical lesion.The most superficial lesion was localted in mid-dermis and it was characterized by alternating areas of inflammatory infiltrate and necrobiotic collagen horizontally oriented parallel to epidermis.The inflammatory infiltrate was composed of an admixture of lymphocytes,plasma cells,multinucleated histiocytes and histiocytes forming ill-defined palisading granulomas around the necrobiotic collagen.No dermal mucin was found.In deep dermis,a second lesion with focal interstitial granulomatous infiltrate with altered collagen and with increased dermal mucin in the central portion was seen.Plasma cells were absent.Diagnosis of Granulomatous intersticial dermatitis with necrobiosis lipoidica-like pattern in mid-dermis and interstitial granuloma annulare-like pattern in deep dermis was made.
Conclusion: Necrobiosis lipoidica and granuloma annulare are granulomatous dermatosis of unknonw etiology with necrobiotic collagen. Some authors suggest that those two entities might represent different manifestations of the same process. Moreover, they have been described to occur concomitantly in patients with diabetes mellitus but as separated synchronic lesions. At the time we are writing this abstract and after reviewing the literature, we did not find any reference of concomitant necrobiosis lipoidica and interstitial granuloma annulare within the same clinical lesion.

E-PS-03-053
Ectopic cutaneous meningioma: a case report and review of the literature
I. Bahri, Z. Nfikha*, N. Abdessayed, H. Yoni, B. Sriha, M. Mokni
*Department of Pathology, University Hospital of Farhat Hached, Tunisia

Background & objectives: Cutaneous meningiomas (CM) are rare tumours most commonly located in the skin of the scalp. This work aims to report a case of CM, to emphasize the rarity of this entity, and to analyse his epidemiological and pathological characteristics.
Methods: A 44-year-old female presented with a slowly growing mass in the frontal area, evolving for 18 months. Physical examination revealed a 1.6 cm firm, subcutaneous mass adherent to the deep tissues without cervical lymphadenopathy. The patient underwent lesion excision with pathological examination of the specimen.
Results: Histological examination showed a proliferation of syncytial sheets of meningothélial cells arranged in nests and lobules inter-separated by fibro-collagenous tissue. Pseudovascular spaces were noted. There was no significant cytological atypia or necrosis. Mitoses were rare. The immunohistochemical study revealed positivity for vimentin, epithelial membrane antigen, and negativity for PS100, melan A, HMB45, CD34, CD68, and pancytokératine.
Conclusion: Ectopic meningiomas are rare tumours derived from meningothelial cells located in the dermis or the subcutaneous tissue. These are most commonly found in the scalp and occur in both congenital and acquired forms. CM is divided into three types: Congenital type, ectopic soft tissue meningiomas, and tumours extending from meningioma involving neuroaxis. The clinical features and imaging studies are most of the time inconclusive. The pathological examination is essential for the diagnosis and discrimination of differential diagnoses.

E-PS-03-054
Comparative analysis of six different IHC assays for epithelial cell adhesion molecule (EpCAM) in carcinomas
S. Nielsen*, J. LaMar, D. Wang, A. Saxena, V.M. Calero, R. Decamillis, M. Korsdal Stensballe
*NordiQC, Aalborg University Hospital, Denmark

Background & objectives: Immunohistochemistry (IHC) for EpCAM is commonly used to identify adenocarcinomas and distinguish cutaneous basal cell carcinoma (BCC) from squamous cell carcinoma (SCC). This study compares the diagnostic sensitivity and specificity of six EpCAM IHC assays in various carcinomas.
Methods: Four EpCAM antibody clones were optimized on three IHC platforms using TMAs with a range of normal tissues and carcinomas. Six combinations provided acceptable technical and analytical performance and were subsequently validated on 106 neoplasias; 85 carcinomas, including 9 BCCs and 8 SCCs, and 21 non-carcinomas. Results were scored by two observers using three cut-offs (1%, 10%, and 50%).
Results: The six EpCAM assays provided a diagnostic sensitivity of 78-94% for carcinomas depending on the positive cut-off level. The assay using clone VU-1D9 provided the highest diagnostic sensitivity at all three cut-offs but also the lowest diagnostic specificity to distinguish BCC from SCC. Irrespective of IHC assays applied, a 50% cut-off provided the highest diagnostic accuracy to separate BCC and SCC. 100% of BCC's exhibited homogenous strong positivity in all assays, regardless of cut-off. 13-88% of SCCs were positive for EpCAM, depending on IHC assays and cut-off applied.
Conclusion: This is the first study to evaluate the diagnostic sensitivity and specificity for six EpCAM IHC assays. When using a diagnostic sensitivity with a purpose of identifying carcinomas, EpCAM-positivity was homogenously distributed in all BCCs but can still be identified heterogeneously in a high proportion of cutaneous SCCs. However, a high diagnostic specificity is dependent on a higher cut-off level. Future studies with a larger number of cutaneous BCC and SCC are necessary to confirm these findings.

E-PS-03-055
Case report of proliferating trichilemmal cyst: a diagnostic challenge in small biopsies
I. Novosel*, M. Lund-Iversen, D. Viveca Haugen
*Sykehuset Østfold Kalnes, Seksjon for patologi, Senter for laboratoriemedisin, Grålum, Norway

Background & objectives: Proliferating trichilemmal cysts (PTCs) can develop from or within benign trichilemmal cysts originating from the outer hair root sheath, typically found on the scalp. While their exact etiology remains unknown, recent data often suggest autosomal dominant inherited genetical structural aberrations.
Methods: A 48-year-old woman presented with a partly cystic, partly solid subcutaneous tumour on her head, which had gradually enlarged over several years.Magnetic resonance imaging revealed conflicting findings, indicating potential malignancy due to a large extracranial soft tissue tumour with a complex structure but without significant skeletal involvement. Given recent rapid growth, the patient was referred for further investigation of sarcoma.
Results: A preliminary diagnosis based on needle biopsy suggested squamous cell carcinoma, leading to complete excision at a local hospital. Macroscopic examination revealed a 5 cm diameter tumour with a grayish-white, partly solid, and gelationous cut-surface. The tumour was cut and prepared for H/E microscopical analysis, which revealed a well-circumscribed squamous tumour characterized by a multicystic structure lined with stratified squamous epithelium lacking a granular cell layer, and containing dense eosionophilic keratin. The diagnosis of proliferating trichilemmal cyst was confirmed based on findings of pronounced proliferating squamous epithelium, mitotic activity, and varying degrees of atypia without infiltration into the surrounding soft tissue.
Conclusion: The diagnosis of skin adnexal tumours, especially in needle biopsies poses a challenge. Thorough and detail-oriented analysis is necessary to diagnose PTC accurately. Needle biopsies are not recommended for diagnosing PTC due to its complex nature. Failing to exclude differential diagnoses such as squamous cell carcinoma can have significant implications for patient treatment.

E-PS-03-056

Ectopic extramammary Paget's disease on the face: a rare case report

E.I. Ortega Pinto*, J.L. Rodríguez Peralto, M.C. Garrido Ruiz
*Hospital Universitario 12 de Octubre, Madrid, Spain

Background & objectives: Extramammary Paget's disease (EMPD) constitutes a rare malignant neoplasm of the skin that originates in its primary form in the ducts of apocrine glands. There´s an even rarer form called ectopic EMPD (E-EMPD) at skin places lacking apocrine glands.
Methods: We report a case of a 76-year-old man with red plaque on the left cheek of two years of evolution, with progressive growth until affecting the external ear canal. Beard loss was shown in the affected area for the past 6 months.
Results: The skin biopsy shows that the epidermis presents a cellular proliferation forming nests located between normal epidermal keratinocytes, made up of atypical cells with extensive eosinophilic cytoplasm and large nuclei with evident nucleoli. Immunohistochemical techniques reveal that the atypical cells are positive for cytokeratin (CK) 7 and negative for CK20, CK10 and p63.
Conclusion: The E-EMPD is an uncommon presentation form of EMPD. Until 2021, there were less than 50 cases published in literature. Correct clinical-histopathological correlation is essential to reach the diagnosis, always ruling out the possibility of other associated tumours. For the histological diagnosis, it is crucial to combine morphological study using hematoxylin-eosin with immunohistochemical techniques such as CK7, CK20, CK10, p63 and GCDFP15. When possible, the course of treatment mostly used is the surgical excision with clear margins.

E-PS-03-057

Hereditary progressive mucinous histiocytosis: a case report

E.I. Ortega Pinto*, M.C. Garrido Ruiz, J.L. Rodríguez Peralto
*Hospital Universitario 12 de Octubre, Madrid, Spain

Background & objectives: Hereditary progressive mucinous histiocytosis (HPMH) was first described in 1988 by K. Bork and N. Hoede. HPMH is a rare progressive non-Langerhans cell histiocytic disorder that only shows cutaneous manifestations. Unlike other benign cutaneous histiocytoses, the lesions don't regress spontaneously.
Methods: We report a 45 years old male patient, that presents multiple brown-reddish papulo-nodular lesions between 3 and 9 mm in diameter, on the forearms, legs, face and scalp. These lesions began to appear about 4-5 years ago. The lesions were mostly asymptomatic. The patient denies any known family history of skin diseases or lesions similar to his own.
Results: The skin biopsy shows a well-defined but not encapsulated cell proliferation, located in the dermis and consisting of monomorphic cells with oval nuclei and finely punctate chromatin that present broad eosinophilic cytoplasm and other more spindle-celled and stellate cells on a loose stroma with a mucinous appearance, positive with Alcian Blue. Immunohistochemical techniques reveal that the cells described are histiocytic in nature and are positive with CD68. The clinical and histopathological findings were compatibles with HPMH.
Conclusion: HPMH is a very rare disease (only 26 cases have been described worldwide). It affects members of the same family and is believed to be inherited in an autosomal dominant fashion, nevertheless sporadic cases have been reported. The diagnosis is difficult when there is no family history and because it is a little-known entity. The course of trearment with thalidomide stopped the progression or in other cases decreased the severity of the disease according to the latest published data.

E-PS-03-058

A rare case of malignant mixed tumour of the toe: a case report

B. Özcan*, S.K. Dursun, Z. Tosuner
*Basaksehir Cam and Sakura City Hospital, Turkey

Background & objectives: Chondroid syringoma, also known as a mixed tumour of the skin, is a rare tumour derived from sweat glands. Histologically, it comprises epithelial and mesenchymal components. Although it is rare, those located on foot carry an increased risk of malignancy.
Methods: A 68-year-old male presented with a mass on his left second toe, persisting for 20 years with recent progressive growth. Physical examination revealed a firm, palpable mass. Magnetic resonance imaging showed a heterogeneous 4x3 cm lesion on the left foot with smooth, lobulated contours, raising suspicion of malignancy. Subsequently, an excisional biopsy was performed.
Results: Histomorphological examination revealed a cellular mesenchymal-epithelial mixed neoplasm, displaying an atypical poorly differentiated tumour with focal eccrine-apocrine differentiation and chondroid stroma. No tumoural necrosis was observed, and the lesion exhibited infiltrative borders. Immunohistochemical staining showed positivity for S-100, EMA, CEA, Pancytokeratin, p16 (focal), GCDFP15, and PLAG1, with a Ki-67 proliferation index of 12%. No staining was observed with p40. Morphological findings, supported by immunohistochemical results, suggested a diagnosis of "Malignant Mixed Tumour of the Skin."
Conclusion: Chondroid syringoma, a rare tumour originating from sweat glands, rarely undergoes malignant transformation. However, in the foot region, there is a higher risk of malignancy, with approximately 82% of malignant lesions reported in this area. Histologically, it is characterized by chondromyxoid and fibrous stroma surrounding epithelial component. Malignant cases often display tumour necrosis, atypia, and poor differentiation. Notably, in this case, atypical appearance and poorly differentiated morphology, along with the rapid tumour growth and location on the foot were observed.

E-PS-03-059

Cutaneous non-tuberculous mycobacteria infection - a case report and literature review

M. Pinho Fialho*, M. M. de Carvalho, A. Miroux Catarino, S. R. Casanova, R. Sampaio
*Department of Pathology - Unidade Local de Saude Santa Maria (ULSSM); Instituto Politécnico de Lisboa (ESTeSL), Portugal

Background & objectives: Non-tuberculous mycobacteria (NTM) are often overlooked as opportunistic agents causing cutaneous infections. While histological findings may resemble cutaneous tuberculosis, treatment and clinical management differ significantly. We present a case of NTM skin infection and a literature review.
Methods: A 62-year-old female with autoimmune hepatitis, on immunosuppression, received corticosteroid injection in the elbow joint. Six months later, she presented with a skin nodule at the injection site, histologically diagnosed as cutaneous tuberculosis. Despite being asymptomatic and lacking epidemiological context or chest X-ray abnormalities, a second adjacent skin nodule developed and was subsequently biopsied.
Results: The skin biopsies showed poorly formed epithelioid non-necrotizing granulomas with neutrophilic microabscesses (suppurative granulomas) and Langhans-type multinucleated giant cells in the reticular dermis and subcutaneous tissue. Gram and Grocott stains were negative, and acid-alcohol resistant bacilli were observed using the Ziehl-Neelsen stain. As suggested by Song et al., we identified small vessel proliferation with sparse fibroblasts within the lesions. The histological examinations were consistent with NTM skin infection and confirmed by polymerase chain reaction (PCR).

Conclusion: The case underscores the diagnostic challenge posed by NTM infections, often mimicking cutaneous tuberculosis. These histopathological findings should help pathologists decide when to suspect a NTM infection, avoiding a delay in diagnosis and a tuberculosis label that could lead to overtest and unnecessary treatments.

E-PS-03-060

A rare and aggressive cutaneous neoplasia: primary cutaneous γ/δ T-cell lymphoma

D. Sá*, S. Neves, I. Araújo, A. Coelho, D. Tente, F.E. Costa, J.R. Vizcaíno
*Anatomic Pathology Service, Pathology Department, Unidade Local de Saúde de Santo António, Portugal

Background & objectives: Primary cutaneous γ/δ T-cell lymphoma (PCGDTCL) is a rare and aggressive cutaneous malignancy that usually affects the extremities of adults of either sex, frequently spreading to mucosa and extra-nodal sites but generally sparing lymph nodes, spleen, and bone marrow.
Methods: We report a case of an 80-year-old man that was referred to a dermatology consultation due to a 4-month history of erythematous patches and nodules dispersed throughout the thorax and limbs, some of them with an annular pattern. B symptoms such as night sweats and unintentional weight loss were also reported. The patient was then submitted to a skin biopsy.
Results: We received a skin punch biopsy specimen with 0,8 cm of diameter and 0,6 cm of depth showing a white epidermal surface and white and homogenous cut surface. Histologic examination showed psoriasiform acanthosis and parakeratosis of the epidermis associated with the presence of epidermotropism. The lymphocytes were of intermediate size and showed irregular nuclear contours. All the compartments of the skin were infiltrated by the lymphoma. Immunohistochemistry revealed positive reaction for CD2, CD3, CD7 (heterogeneous) and TIA1 in the atypical lymphocytes and no expression of CD20, CD5, CD4, CD8, CD56, CD30 and CISH EBER. Flow cytometry showed a T-cell infiltrate composed of small, atypical cells with gamma/delta T-cell receptors phenotype.
Conclusion: Tumour cells are TCR-γ and TCR-δ positive and TCR-β negative, with expression of at least one cytotoxic protein, including granzyme B, perforin and/or TIA1. CD30 is found in 41% of cases and its expression can be useful as a therapeutic target of anti-CD30 monoclonal antibodies. Some studies showed five-year overall survivals for patients with no epidermotropism, any epidermotropism, and predominantly epidermotropic presentation of respectively 32.8%, 28.9%, and 40.0%. Our patient is still alive 30 months after the initial diagnosis.

E-PS-03-061

A very rare case of melanocytic matricoma with lymph node metastasis: case report and review of the literature

S.M. Sabo*, A. Birceanu, A. Evsei, C. Costras, A. Cernat-Stefan, A. Toma, T. Magdici, R. Roman, A. Dima
*Colentina Clinical Hospital, Romania

Background & objectives: Melanocytic matricoma (MM) is a very rare biphasic neoplasm composed of matrical and supramatrical epithelial cells and pigmented dendritic melanocytes. There are few reported cases showing malignant features. We report a case with sentinel lymph node metastasis.
Methods: We searched the literature for cases of disseminated melanocytic matricomas to compare clinical and histological features with our case. We found 12 cases of malignant melanocytic matricoma (MMM). Their criteria used for defining malignancy were ill-defined infiltrative arhitecture, high mitotic rate, necrosis and local reccurrence. There were no cases with lymph node or visceral metastasis at diagnosis or at follow-up.
Results: A 46-years-old male patient with a history of lateral thoracic skin tumour, diagnosed in another hospital with MMM and positive excision margins, presented in our clinic for axilar sentinel lymph node biopsy with intraoperative consultation and re-excision of the thoracic lesion. Frozen sections revealed a 1 mm metastasis in one lymph node. Microscopically, re-excision tissue demonstrated a dermal tumour with follicular origin, infiltrating into the subcutis, composed of islands of basaloid cells, with minimal pleomorphism, atypical mitotic figures, and pigmented cells with central keratinization and necrosis. Immunohistochemistry confirmed the presence of matrical cells admixed with dendritic melanocytes. Lymph node metastasis presented as a sheet of tumour cells with central keratinization.
Conclusion: Despite the absence of documented lymphatic spread in existing lite3rature, in our case the oncological-surgical team decided for sentinel lymph node biopsy, which revealed a metastasis on histological examination. This highlighted the potential for an aggressive behaviour, which is why the patient was further treated with radiotherapy. Followup after one year showed no evidence of local or distant recurrence. This particular case emphasizes the need for establishing guidelines for patient management in cases of melanocytic matricoma with histological malignant features.

E-PS-03-062

Artificial intelligence quantifies key prognostic factors of melanoma from H&E images

Y. Salhi*, J. Rynkiewicz, C. Bossard, A. Nakhjavani, S. Salhi, J. Chetritt
*DiaDeep, France

Background & objectives: Breslow Thickness and Ulceration are key to the assessment of Melanoma survival and relapse outcomes. We introduce and compare two approaches based on deep neural networks to quantify and assess these factors: a fully and weakly supervised approaches.
Methods: In this study, we use two datasets (n=350 and 540) and investigated two learning approaches. First, a segmentation model is trained with pixel-wise annotations. A second network is trained to learn from image-level labels. The performance in predicting Breslow thickness and identifying the presence of ulceration in Melanoma H\&E-stained whole slide images is assessed on a hold-out dataset.
Results: We show that a network can learn the representation of these pronostic factors without any annotation, precision of 0.85 and 0.92 for Breslow and Ulceration compared to 0.81 and 0.89 with fully-supervised network.
Conclusion: Training models without any pixel-wise annotation outperforms annotation-based learning. Its superior performance, combined with its practical advantages in terms of training requirements, suggests that it could serve as a valuable asset in the fight against melanoma, subject to further validation and integration into clinical workflows. Furthermore, we believe that this study lays a foundation for future AI systems to prognosticate not just melanoma severity but also potential patient survival duration and cancer recurrence probabilities.

E-PS-03-063

Histological discrepancies among various samples from a patient with systemic histiocytosis

I. Sánchez Ramírez*, A. Sanz Zorrilla, V. Davila Flores, M.J. Jurado Rivera, J. Osuna Soto, A. González-Menchén
*Hospital Universitario Reina Sofía, Pathology Unit, Spain

Background & objectives: Histiocytoses are characterized by accumulation of macrophages and/or dendritic cells. The specific diagnosis can be challenging. In our patient, discordant histological results, led us to consider the differential diagnosis between Langerhans cell histiocytosis (LCH), Erdheim-Chester disease (ECD), or mixed histiocytosis.

Methods: We present a 70 year old woman with multisystemic affection, specially in bone and skin. Two samples (cutaneous and bone) were analysed separately and compared. Molecular methods were performed to determine the BRAF status in case the patient could benefit from this therapy.
Results: The long bone biopsy showed diffuse infiltration of histiocytic-type foamy cells accompanied by intense fibrosis. This image, along with the immunohistochemical findings, suggested that it could be ECD, as clinicians suspected. In contrast, the skin biopsy showed discreet proliferation of Langerhans cells with epidermothropism, contrasting with that found in the bone sample. BRAF PCR was performed, revealing a mutation in BRAFV600E.
Conclusion: The presence of mutations in the BRAF proto-ocogene is found in more than 50% of LCH cases. However, this same mutation can be found in ECD, which is a multisystemic disease, sometimes with poor prognosis, whose typical characteristic is the involvement of the long bones, as our patient presents. Mixed Histiocytosis is also described when there are images of LCH and ECD in the same biopsy or in different ones from the same patient.

E-PS-03-064
Multicentricreticulo-histiocytosis: a case report and review of the literature
C. Ben Takaya, Y. Sarra*, D. Daghri, B.K. Marwen, N. Ouini, T. Tlili, I. Bahri, W. Mokni, N. Abdessayed, B. Sriha
*Department of Pathology, University Hospital of Farhat Hached, Sousse, Tunisia

Background & objectives: Multicentric reticulo-histiocytosis (MRH) is a rare non-Langerhans cell histiocytosis characterized by cutaneous eruption and erosive arthritis leading to systemic complications with fatal outcome.We present a case of MRH, detailing its clinical and histopathological features alongside with a literature review.
Methods: A 47-years-old woman, without medical history, presented with a non-pruritic papulo-nodular rash affecting the neck, ears helices, face, hands, and forearms. dermoscopic examination revealed numerous coral-colored papules on the face, neck, ears, hands and periungual areas, arranged in a coral necklace-like pattern. Joint examination showed destructive polyarthritis deforming the metacarpophalangeal joints.
Results: Histopathological examination revealed a diffuse dermal infiltrate consisting of histiocytic and giant cells with an eosinophilic "ground glass" cytoplasm. The nuclei was round sometimes crumpled with small nucleoli. Scattered inflammatory cells, including lymphocytes and rare eosinophils were also present. There were neither foamy macrophages nor Touton giant cells. The immunohistochemical study proved the non-Langerhansian nature of these histiocytes that were positivefor CD68 and negative for CD1a and PS100. The diagnostic of MRH was retained. The patient receivedan oral prednisolone treatment with improvement of cutaneous nodules
Conclusion: MRH is a challenging rare multisystemic and paraneoplastic disease of unknown etiopathogenesis. Most patients are adults aged >40 years with female predilection. All clinical symptoms are directly caused by the infiltration of reticulohistiocytes, which are histologically characterized by histiocytic multinucleated giant cells with eosinophilic ground glass cytoplasm. The clinical history is crucial for the accurate diagnosis. When presenting as a solitary cutaneous lesions, these histologic features may be confused with melanocytic lesions or oncocytic form of juvenile xanthogranuloma.

E-PS-03-065
Newly introduced skin adnexial tumour: NUT carcinoma
B.B. Senay*, N. Koc, G. Gumrukcu, F. Aker
*Haydarpasa Numune Training and Research Hospital, Pathology Department, Turkey

Background & objectives: A 51-year-old male presented with an erythematous nodule adjacent to old scar tissue in the right lumbar region. In 2016, he underwent excision from this area at another hospital, where it was diagnosed as 'squamoid ductal eccrine carcinoma'.
Methods: The morphology of the punch biopsy and the previous excision material was evaluated together, followed by immunohistochemistry and Next-Generation Sequencing (NGS) analysis.
Results: The punch biopsy revealed infiltrative atypical epithelial cell proliferation within a fibromyxoid stroma in the dermis, composed of poorly differentiated cells with small duct formation and basaloid differentiation. Focal ductal structures were labeled for CEA, and basaloid cells showed positivity for Ber-EP4. Numerous mitoses were evident. Both the punch biopsy and previous excision material exhibited similar morphology, leading to a diagnosis of malignant appendageal skin tumour. For a definitive diagnosis, NGS analysis was performed on the biopsy sample, identifying a gene rearrangement between *BRD3 Exon 9* and *NUTM1 Exon 5* in 98.6% of sequences. The final diagnosis was reported as Primary Cutaneous NUT Carcinoma.
Conclusion: The patient developed nodules confirmed as infiltrations by a poorly differentiated malignant tumour. After diagnosis, survival was 9 months. Here we report the seventh case (fourth involving the *BRD3:NUT1* fusion) of primary cutaneous NUT Carcinoma. Considering NUT Carcinoma in the differential diagnosis of poorly differentiated skin tumours is essential due to its poor prognosis and metastatic potential. This instance expands our understanding of this rare cancer, underscoring the necessity for further investigation into its molecular, histological, clinical, and prognostic variations.

E-PS-03-066
A rare case of temporal basomelanocytic skin tumour in a patient with multiple basal cell carcinomas
E. Papagianni, E. Spiteri*, E. Athanasiou, A. Therapontos, C. Vourlakou
*Department of Pathology, Evangelismos General Hospital, Athens, Greece

Background & objectives: A malignant basomelanocytic tumour is a rare finding. We present a case of a skin lesion of an 84-year-old male with multiple previus basal cell carcinomas (BCC) of the head, who went under excisional biopsy suspected for BCC.
Methods: We received a specimen of an unoriented skin excision measuring 2.5x2.1 cm to a depth of 0.6 cm. The epidermis shows a pigmented lesion 1.6x0.8 cm. The specimen sectioned to reveal a pigmented solid lesion with a depth of 0.2 cm which is located 0.4 cm from the deep margin. The specimen is entirely submitted serially and proceded histopathological examination.
Results: Evaluation of microscopic sections revealed an invasive pigmented nodular skin lesion with solid basaloid cells reminiscent BCC. Peripherally of the BCC, along the basal layer, there was a lentiginous to nested proliferation of atypical melanocytes compatible with in situ melanoma / lentigo malignant melanoma. Immunohistochemical studies demonstrated strong positive expression in all tumour cells of epithelial markers BerEP4, CK5/6, p64, p40 highlighted the basaloid nature of the lesion with coexpression of melanocytic markers SOX-10, Melan A, HMB-45 and Tyrosinase. Ki-67 showed heterogeneity positivity, up to 30%. These findings confirmed the diagnosis of malignant melanocytic tumour.
Conclusion: Different theories have been suggested about the pathogenesis of these rare lesions and the treatment of choice is not established yet. Each case is evaluated considering anatomical site of the lesion and patient comorbidities. Documenting these rare cases should be helpful to resolve the questions posed by both pathologists and clinicians in the future.

E-PS-03-067

CD117 expression in hidradenomas

A. Sykaras, C. Kouvidou, E. Spiteri*, E. Athanasiou, P. Vlahou, A. Therapontos, C. Vourlakou
*Department of Pathology, Evangelismos General Hospital, Athens, Greece

Background & objectives: CD117 is a receptor tyrosine kinase with a key role in signal transduction and in the pathogenesis of several neoplasms. We investigated the expression of CD117 in hidradenomas, which are benign adnexal tumours derived from the apocrine and eccrine glands.
Methods: We performed CD117 immunostaining in formalin fixed paraffin embedded tissue sections from 10 hidradenomas. Immunohistochemical positivity of CD117 was defined as cytoplasmic and membrane expression in at least 10% of the tumour cells. A cut-off of 50% positive cells was set to differentiate diffuse from focal expression. The intensity of the staining was graded as strong, moderate and weak.
Results: In normal skin the expression of CD117 is restricted to melanocytes, mast cells and secretory cells of sweat glands, while ductal and myoepithelial cells of the sweat glands are negative. 75% (6/8) of hidradenomas were CD117-positive. One tumour displayed diffuse, strong, cytoplasmic and membrane positivity. The other CD117 positive hidradenomas displayed a focal staining (25-30% of cells) of mainly moderate intensity (4/5 moderate, 1/5 strong staining). The focal, moderate CD117 expression was mainly cytoplasmic and less membrane (in 3 hidradenomas) whereas the one case with focal, strong CD117 staining displayed equally cytoplasmic and membrane staining. Two hidradenomas displayed cytoplasmic expression of CD117 in 5% of cells and were considered negative.
Conclusion: Our findings suggest that CD117 is focally expressed in a subset of hidradenomas and may represent a useful immunohistochemical staining for the differential diagnosis of this adnexal tumour. Our data are in line with the very limited literature on this topic and highlight the need of larger studies with combined immunohistochemical analysis of CD117 expression and molecular genetic analysis of c-KIT (CD117) gene mutations to identify hidradenoma patients who may benefit from imatinib.

E-PS-03-068

Evaluation of CD117 expression in Merkel cell carcinoma

A. Sykaras*, C. Kouvidou, A. Therapontos, E. Athanasiou, E. Spiteri, P. Vlahou, C. Vourlakou
*Department of Pathology, School of Medicine, University College Dublin, Ireland

Background & objectives: Merkel Cell Carcinoma (MCC) is an aggressive, neuroendocrine skin cancer. CD117 is a receptor tyrosine kinase protein, linked to the pathogenesis of several cancers, that is not expressed in normal Merkel cells. We investigated the expression of CD117 in MCC.
Methods: CD117 immunohistochemistry was performed in formalin fixed paraffin embedded tissue sections from 10 MCC patients. Cytoplasmic and membrane expression in at least 10% of MCC cells was required to classify a tumour as positive. Staining of more than 50% of MCC cells was graded as diffuse positivity. CD117 staining intensity was characterized as strong, moderate and weak.
Results: All the tissue sections displayed CD117 immunoreactivity and 75% (6/8) of them showed both membrane and cytoplasmic staining and were considered CD117-positive. Five of them displayed diffuse positivity (in 60-90% of the cancer cells) and one had focal, weak-moderate CD117 expression in 40% of the neoplastic cells. CD117 staining intensity was strong (2/5) or moderate-strong (2/5) in the diffusely positive MCC. The other two MCC specimens were considered negative because they displayed only cytoplasmic expression of CD117. One showed a focal, weak staining and the other had a diffuse moderate staining intensity.
Conclusion: Our findings suggest that the majority of MCC express cytoplasmic and membrane CD117. This result is in agreement with the very limited literature on the same subject, although we notice a higher percentage of MCC cells with strong, diffuse, membrane CD117 staining than previously reported. CD117 expression in MCC highlights a potential diagnostic pitfall. It is currently unclear if the activation of c-KIT proto-oncogene plays a role in MCC pathogenesis and if CD117-positive MCC patients may benefit from targeted therapies.

E-PS-03-069

Metastatic cutaneous melanoma with angiosarcomatous transdifferentiation - a peculiar diagnosis

D. Tapoi*, A. Dumitru, A. Ciongariu
*Department of Pathology, University Emergency Hospital Bucharest, Romania

Background & objectives: Cutaneous melanomas, particularly in metastatic settings, can display a wide range of histopathological and even immunohistochemical features, making the correct diagnosis a real challenge. In this respect, we present the case of a Metastatic cutaneous melanoma with angiosarcomatous transdifferentiation.
Methods: A 66-year-old man presented to the University Emergency Hospital in Bucharest, with amelanotic nodular lesion on his thorax. The man had been previously treated for a cutaneous melanoma a year before. The new lesion was surgically removed and underwent ample histopathological and immunohistochemical analyses.
Results: The histopathological analysis revealed the presence of a high-grade spindle cell proliferation with frequent atypical mitotic figures and numerous ill-defined vascular spaces, located in the dermis with now connection with the epidermis. These findings were highly suggestive of an angiosarcoma but bearing in mind the history of cutaneous melanoma, immunohistochemical tests for SOX10, PRAME, MelanA, ERG, and CD31 were performed. The tumour cells were focally positive for CD31 and ERG and completely negative for PRAME and Melan A. However, SOX10 was moderately positive in most of the tumour. Based on this pattern of expression and cosidering the patient's history, the diagnosis of metastatic cutaneous melanoma with angiosarcomatous differentiation was established.
Conclusion: Even though metastatic melanomas frequently undergo divergent differentiation, angiosarcomatous transformation, proved by immunohistochemical expression is an extraordinarily rare phenomenon. This is one of the very few reported cases and it proves that a diagnosis of melanoma should always be considered given the right clinical context. Therefore, we highlight the importance of performing extensive immunohistochemical tests, including multiple melanocytic markers in order to establish the correct diagnosis.

E-PS-03-070

The relationship between demographic status and clinical characteristics of Kaposi sarcoma: a single-centre study

A. Türkmen Dedeoğlu*, S. Gezmen, Y. Karabulut, Ü. Türsen
*Mersin University, Department of Pathology, Turkey

Background & objectives: Kaposi Sarcoma is an angioproliferative tumour characterized by distinct clinical variants. Regardless of subtype, all Kaposi Sarcoma variants are linked to HHV-8. Our study's objective is to demonstrate the correlation between demographic attributes and the clinical manifestations of Kaposi Sarcoma.

Methods: In this study, a retrospective cohort study was conducted to evaluate the clinical and demographic characteristics of patients with Kaposi Sarcoma of all types. The medical records of patients diagnosed with Kaposi Sarcoma in our department between 2009 and 2023 were retrospectively reviewed. Demographic and clinical characteristics were recorded, and HHV8 expression was identified immunohistochemically in all patients.
Results: Kaposi Sarcoma tends to affect older patients but presents at a younger age in HIV-positive patients. Male predominance and the classical type of Kaposi Sarcoma were consistent findings. We noted a higher prevalence of organ involvement in HIV-positive patients. Extremity primary sites were predominant, but non-extremity sites were associated with higher HIV positivity and advanced stages, suggesting a potential prognostic indicator. We found a significant correlation between blood type and primary tumour site, with certain blood types less common in extremity sites. Alcohol and smoking are linked to higher HIV positivity and the epidemic clinical type, reflecting broader socio-behavioural factors. We also found a correlation between birthplace and HIV serology.
Conclusion: Our study sheds light on the relationship between clinical features and demographic characteristics of Kaposi Sarcoma patients. It stands as one of the few conducted in our country and the second largest case series worldwide, offering valuable insights into this complex disease. Age, HIV status, and tumour site correlated with the literature. Our findings also highlight the impact of alcohol, smoking, and birthplace on disease presentation. Overall, our study contributes valuable insights for tailored management strategies and future research endeavors.

E-PS-03-071
Onychomatricoma in young patient: case report and literature review
L. Vasconcelos Cavalcante*, I. Santos Costa, M.d.F. Figueiredo, G. Gadelha Costa, G. Lopes Teixeira, L. Brasileiro Marques, A.L. Felipe Dias, J. Carneiro Melo
*University of Fortaleza, Brazil

Background & objectives: Onychomatricoma is a benign neoplasm specific to the nail complex. The most affected age group is middle-aged, prevalent in women.Clinical diagnosis is challenging due to the lack of knowledge about the tumour. It describes an atypical case of Onychomatricoma.
Methods: Woman, 17 years old, with xantonychia, nail hyperkeratosis, splinter haemorrhages affecting the nail plate and longitudinal and transverse hypercurvature of the nail plate of the right index finger. Antimycotic treatment was performed, without response. A fungal culture was requested, which was negative and a biopsy was requested with suspicion of neoplasia.
Results: Under microscopy, proliferation of subungual dermal spindle cells without atypia, arranged in short, storiform bundles. This case illustrates an atypical clinical presentation of the condition, as despite presenting the classic tetrad (xantonychia, nail hyperkeratosis, splinter haemorrhages affecting the nail plate and longitudinal and transverse hypercurvature of the nail plate), the age range and the absence of trauma to the nail plate nail region of the nail plate are extremely rare. This case highlights the importance of raising awareness about Onychomatricoma among healthcare professionals, especially dermatologists.
Conclusion: This study demonstrates the importance of differential diagnoses and the need for additional tests to assist in the correct diagnosis. Onychomatricoma is a rare condition in the patient's age group, however, differential diagnosis of nail injuries is important.

E-PS-03-072
The value of TERT, BRAF and NRAS gene expression in progression free survival in patients with melanoma
T. Zablocka*, S. Isajevs
*University of Latvia; Riga East University Hospital; Pauls Stradins Clinical University Hospital; Hospital of Traumatology and Orthopaedics, Latvia

Background & objectives: Despite recent insights into melanoma genetics, the value of co-mutation on melanoma prognosis is still controversial. The aim of our study was to compare the value of TERT, BRAF and NRAS gene mutations and its association with progression free survival(PFS).
Methods: 118 patients who underwent melanoma stage IA-IIC surgical treatment at Riga East University Hospital, Latvian Centre of Oncology, Riga, Latvia in 2012-2018 were retrospectively enrolled in the study. The Qiagen pac-cancer-multimodal panel gene kit was used for the assessment of TERT, BRAF and NRAS gene mutation.
Results: The PFS did not differ between wild type and BRAF mutant melanoma. Patients with NRAS mutant melanoma had significant worse PFS compared to NRAS wild melanoma (HR=12.30; 95%, C.I=5.78-26.21, P<0.0001). Furthermore, BRAF and NRAS co-mutant melanoma has significant worse PFS compared to BRAF mutant melanoma (HR=6.30; 95%, C.I=3.10-12.70, P<0.0001). Patients with TERT mutation had significant worse PFS compared to TERT wild melanoma. In addition, TERT and BRAF co-mutant melanoma has significant worse PFS compared to BRAF mutant melanoma (HR=8.25; 95%, C.I=2.90-13.40, P<0.0001). In addition, patients with TERT mutation and low TIL had significant better PFS compared to patients with TERT mutation and high TIL infiltration (HR=4.80; 95%, C.I=2.30-7.890, P=0.002).
Conclusion: To conclude, the patients with TERT/BRAF and NRAS/BRAF co-mutant Stage IA-IIC melanoma had worse progression free survival compared to NRAS wild, TERT wild and BRAF wild melanoma. The complex BRAF, TERT and NRAS assessment in melanoma in routine clinical practice is beneficial for the risk stratification of disease progression.

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E-PS-04E-Poster Session Digestive Diseases Pathology - Liver/Pancreas

E-PS-04-001
Case report: Kaposiform haemangioendothelioma in a liver transplant recipient with associated coagulopathy and graft failure
R. Agrawal*, D. Bartlett, D. Haldar, P. Trivedi, R. Brown, O. Cain
*United Kingdom

Background & objectives: Kaposiform haemangioendothelioma (KHE) is a rare and locally aggressive vascular neoplasm sometimes associated with the Kasabach-Merritt phenomenon. We present a case of KHE growing within the liver hilum and around the nearby blood vessels of a 23-year old female.
Methods: Our patient initially presented to her clinical team with the signs and symptoms of liver failure from the age of 12 and, despite multiple liver biopsies, was diagnosed with 'cryptogenic cirrhosis.' Progressive deterioration eventually necessitated a liver transplant. Macroscopic examination of the liver explant showed an atrophic right lobe and fibrotic hilum. Microscopic examination revealed an ill-defined vasoformative.
Results: ...tumour with slit-like vascular channels surrounded by fibrous tissue and extensively involving the liver hilum and wrapping around hepatic vessels. The tumour cells were epithelioid with wavy nuclei and immunohistochemistry was positive for ERG and CD31 and

negative for HHV8, confirming the diagnosis of KHE. The background liver showed regenerative nodular vascular changes without evidence of cirrhosis.
The transplanted allograft failed and was removed after 6 days. Macroscopic examination showed extensive occlusive thrombi involving the hilar vessels and hepatic vein. This was associated with parenchymal necrosis in the graft with striking localisation near the thrombi. The patient subsequently developed intractable melaena associated with multiple oozing bleeding points throughout the intestine.
Conclusion: This case shows a KHE first diagnosed in the perihepatic tissues of a liver explant for a case of 'cryptogenic cirrhosis.' In retrospect, the vascular changes within the liver parenchyma were deemed to be secondary to the tumour. Subsequent thrombotic complications within the graft and post-operative intractable melaena may be manifestations of the Kasabach-Merritt phenomenon, which is a consumptive coagulopathy that can be triggered by surgical manipulation of KHE.

E-PS-04-002
Expression of c-myc and p53 in pancreatic ductal adenocarcinoma and their association with clinicopathological, molecular, prognostic and survival variables in patients of Fundación Santa Fe de Bogotá University Hospital, between 2009-2022. A case-control study
J. Alvarez*, J.A. Baena del Valle, V. Barrera Penagos, A. Vera Torres, G. Rozo Paz, D. Castellanos Leguizamón, D.M. Grajales Urrego, R. López Panqueva
*Fundación Santa Fe de Bogotá, Colombia

Background & objectives: Pancreatic ductal adenocarcinoma (PDA), ranking 9th in global mortality, presents poor prognosis despite standard treatments. This study compares c-myc and p53 expression with clinicopathological, molecular and prognostic factors in surgical PDA patients at Fundación Santa Fe de Bogotá University Hospital.
Methods: In this analytical observational case-control study, 95 PDA patients were included. Cases (n=73) survived <3 years post-diagnosis, and controls (n=22) >3 years. Clinicopathological data was retrieved from histological analyses and electronic medical records. Immunohistochemical expression of c-Myc (positive cells/total # cells) and p53 (aberrant = 0% or > 60% expression) was determined. Statistical analyses were conducted using R-studio version 2023.12.1.
Results: In this group of study, 52 (54,7%) were female and 43 (45.3%) were male, with ages between 41 and 89 (M=66.8). p53 and c-myc were evaluated only in 39/55 surgical PDA patients due to lack of histopathological material. Among them, 38 expressed c-Myc and 39 expressed p53. There were no significant differences between cases and controls for expression patterns in both markers. However, aberrant p53 expression was associated with lower disease-free survival after surgical treatment ($t[23] = -2.42$; $p < 0.05$; Cohen's $D = 1.32$). Additionally, subjects with post-surgical disease recurrence showed a higher c-Myc expression ($t[21] = -2.28$; $p < 0.05$; Cohen's $D = 0.54$).
Conclusion: This study evidenced an association between p53 expression and low disease-free survival. Moreover, there is higher post-surgical disease recurrence when c-myc was expressed. Consequently, targeted therapies for these genes could favour the prognosis of patients with pancreatic ductal carcinoma. Nevertheless, there was no statistical difference between the p53 and c-myc expression patterns between cases and controls. Further studies are needed to assess other possible molecular markers and the difference in their expression among tumours and preserved pancreatic tissue.

E-PS-04-003
Portal cavernoma cholangiopathy – histological features to look after
A. Alves*, J. Amaral, J. Gama, R. Almeida, M.A. Cipriano
*Unidade Local de Saúde de Coimbra, Portugal

Background & objectives: Thrombosis of the extrahepatic portal vein and the consequent portal cavernoma can lead to portal vein hypertension and biliary changes, with well-known clinical and radiological findings but without well-described histological features in the literature.
Methods: We present a case of a woman in her 40's with history of liver transplantation twenty years ago due to biliary atresia, complicated by portal cavernoma, who never underwent shunt surgery despite episodes of hepatic encephalopathy. Due to elevated serum bilirubin and alkaline phosphatase levels and cholestasis related symptoms, hepatic retransplantation was decided and performed.
Results: Gross examination of the liver showed perihilar biliary ducts ectasia with cystic transformation, multiple venous collaterals and a greenish parenchyma, with no other remarkable findings. Histologically, at the hilum, the portal vein branches had a significant luminal reduction and the biliary ducts showed partially denuded epithelium, with reactive changes, parietal inflammatory infiltrate and marked peribiliary glandular dilation. The intrahepatic portal tracts showed portal vein alterations (absence, arterialized or with disproportionally small lumina). There was periportal ductular reaction, marked sinusoidal dilation and focal nodular regenerative hyperplasia. Discrete periportal copper deposits were present as a result of chronic cholestasis. A diagnosis of portal cavernoma cholangiopathy was rendered.
Conclusion: Certain histological features, when observed either in a liver biopsy or surgical specimen, although not pathognomonic, should prompt a diagnosis of portal cavernoma cholangiopathy. These include changes in portal vein and its branches along with alterations in the intrahepatic and perihilar biliary ducts. Being able to recognize these findings and integrate them in the proper clinical and imaging context is crucial as their recognition can lead to an accurate diagnosis

E-PS-04-005
Liver involvement by hematolymphoid neoplasia: histopathological features in Acute Myeloid Leukemia and T-Cell/Histiocyte-Rich Large B-Cell Lymphoma cases
J. Azevedo*, G. Miranda, M. Alzamora, C. Perez Duque, M. Jácome, R. Henrique
*Department of Pathology, Portuguese Oncology Institute of Porto (IPO-Porto), Portugal

Background & objectives: Hepatic involvement in haematological disorders may go unnoticed, with patients only exhibiting increased liver enzyme levels. In such cases, biopsy is crucial for diagnosis. We illustrate two cases of late liver involvement by distinct haematological diseases, focusing on histopathological findings.
Methods: Case 1, 61-year-old woman, with acute myeloid leukemia, achieved complete remission after chemotherapy and allogeneic transplant. Six months post-transplant, progressive hepatic dysfunction was disclosed. Case 2, 18-year-old man, with complete chemoradiotherapy response for nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL), stage IA. Thirty-six months later, liver dysfunction with multiple lesions on CT-scan was detected. Liver biopsy was performed in both cases.
Results: Case 1: Hepatic architecture was globally preserved, with sinusoidal dilation/expansion secondary to hypercellular areas composed of monomorphic neoplastic cell population. The cells disclosed a blastoid morphology with basophilic/amphophilic cytoplasm, folded nuclei with fine chromatin, and distinct nucleoli. Immunohistochemistry showed CD34+, CD117+, MPO-. A diagnosis of hepatic involvement by acute myeloid leukemia was rendered. Case 2: Hepatic involvement by a lymphoma composed of large cells with lobulated nuclei and abundant cytoplasm, with B immunophenotype (CD45+, CD20+, Pax5+, Bcl6+, MUM1+, BOB1-, CD3-, CD5-, CD30-, CD15-, EBER-) scattered among abundant reactive T cells. The diagnosis of T-cell/histiocyte-rich large B-cell lymphoma, as likely

progression from the previous nodular lymphocyte-predominant Hodgkin lymphoma was established.
Conclusion: In haematological malignancies, liver biopsy is essential for staging, especially when imaging techniques cannot discriminate from steatosis and neoplastic infiltration. Extramedullary relapse with involvement of the liver in acute myeloid leukemia is rare, entailing poor prognosis and short survival time.

NLPHL is a rare disease with most patients presenting limited-stage disease. Approximately 3–17% eventually progress to large B-cell lymphoma, including T-cell/histiocyte-rich large B-cell lymphoma, which is associated with a more aggressive clinical course, requiring different management.

E-PS-04-006
COVID-19 vaccination - induced autoinmmune hepatitis
Z. Calixto Alvarez*, M.d.M. Riveiro Barciela, A. Hidalgo Romero, A.P. Diazgranados Daza, J.F. Chabla Jaramillo, M.T. Salcedo Allende
*Vall d´Hebron University Hospital, Spain

Background & objectives: The COVID-19 vaccine has been linked with multiple autoimmune diseases as autoimmune hepatitis (AIH). The linked between a specific type of vaccine and liver injury is imprecise. We show four cases of AIH after COVID-19 vaccination.
Methods: We reviewed four biopsies with diagnosis of AIH after COVID-19 vaccination. Medical data were analysed, including gender, age, comorbidities, liver function tests and antibodies, type of vaccine and number of doses, time of onset of symptoms, treatment, clinical follow up and AIH score. Hepatotoxic drug, herbal remedies, alcoholism, infections, autoimmune disease and obstruction of the bile duct were ruled out.
Results: Two women and two men, ages from 30 - 61. Comorbities: hypothyroidism, vitiligo and postpartum. Between 10-22 days after Astra-Zeneca, Pfizer and Moderna vaccination presented jaundice with biochemical cholestasis, cytolysis and hypergammaglbulinemia. Three patients had ANAS positive. All biopsies showed acute necroinflammatory hepatitis with AIH pattern. In one case we also observed cholestasis and neutrophils involving bile duct lumens. All were treated with corticosteroids, azathioprine and/or mycophenolate mofetil (MMF). Currently three patients have normal hepatic function and are asymptomatic. Two of them continue with azathioprine or MMF. The other patient does not receive any medication. One case received liver transplantation with recurrence of AIH.
Conclusion: The COVID19-vaccine has an incidence of autoimmune adverse effects of one per 10 000 immunized. The histologic findings presents the differential diagnosis between drug-induced-AIH and trigger idiopathic AIH, but the clinical and histological characteristics overlap. We need to perform long follow-ups and accumulate evidence that demonstrates the existence of this syndrome as adverse effect of COVID19-vaccination.

E-PS-04-007
The clinicopathological significance and prognostic impact of SFN expression on patients with intrahepatic cholangiocarcinoma
I. Chang*
*Wan Fang Hospital, Taipei Medical University, Taiwan

Background & objectives: Intrahepatic cholangiocarcinoma (iCCA) stands as the second most prevalent primary liver malignancy. By data mining on public iCCA transcriptomic datasets from GEO, we focused on the Gene Ontology "cell proliferation" (GO:0008283). SFN was identified as the most significantly up-regulated gene.
Methods: Immunohistochemistry was employed to assess SFN expression, and our patient cohort was subsequently divided into low and high expression groups. The association between SFN expression and various clinicopathological features was analysed. Univariate and multivariate survival analyses were subsequently employed. The survival indices analysed included overall survival (OS), disease-specific survival (DSS), local recurrence-free survival (LRFS), and metastasis-free survival (MeFS).
Results: Elevated SFN expression in iCCAs (n=182) was associated with the absence of hepatitis, positive surgical margins, advanced primary tumour stages, and higher histological grades (all $p \leqq 0.011$). The survival analyses also unveiled the substantial prognostic significance of SFN expression in iCCAs. The log-rank test indicated a significant and negative association between SFN expression and all prognostic indicators, encompassing OS, DSS, LRFS, and MeFS (all $p \leqq 0.0004$). Furthermore, in the multivariate analysis, SFN overexpression demonstrated a significant correlation with poorer outcomes in terms of DSS, LRFS, and MeFS (all $p < 0.001$).
Conclusion: These results support that SFN may play a pivotal role in iCCA oncogenesis and tumour progression and serve as a novel prognostic biomarker.

E-PS-04-008
Underexpression of CPS1 as independent unfavourable prognostic factor in intrahepatic cholangiocarcinoma
I. Chang*
*Wan Fang Hospital, Taipei Medical University, Taiwan

Background & objectives: Intrahepatic cholangiocarcinoma (IHCC) is the second most common malignant neoplasm of liver. Dysregulation of urea cycle metabolic enzymes is found in different types of cancers. However, the genes associated with urea cycle (GO:0000050) have not been systemically evaluated in IHCC.
Methods: A comparative analysis of gene expression profiles was applied to the transcriptomic dataset with a focus on genes associated with urea cycle, where CPS1 was recognized as the second most significantly up-regulated gene. The expression level of CPS1 in IHCC (n=182) was assessed by immunohistochemistry. Statistical analyses of CPS1 expression and various clinicopathological factors as well as survival were performed.
Results: We noticed that lower immunoreactivity of CPS1 in IHCC was associated with tumour progression (pT status) to statistical significance ($P = 0.003$). CPS1 underexpression was not only negatively correlate to overall survival (OS), disease-free survival (DFS), local recurrence-free survival (LRFS) and metastasis-free survival (MeFS) in univariate analysis, but also an independent prognosticator forecast poorer clinical outcome for all prognostic indices (OS, DFS, LRFS and MeFs) in patients with IHCC (all $P \leq 0.001$).
Conclusion: These results support that CPS1 may play a crucial role in IHCC oncogenesis and tumour progression and serve as a novel prognostic factor and a potential diagnostic and theranostic biomarker.

E-PS-04-009
Ductulo-insular variant of pancreatic neuroendocrine tumour with cystically dilated ductules: report of a rare case and review of the literature
F.E. Costa*, J.R. Vizcaíno
*Anatomic Pathology Service, Pathology Department, Unidade Local de Saúde de Santo António (ULSSA), Porto, Portugal

Background & objectives: The rare ductulo-insular variant of pancreatic neuroendocrine tumours (PanNET) exhibits neuroendocrine nests with small ductules distributed throughout the tumour. Although ductular structures are not rarely observed in PanNETs, this variant is poorly recognized, with few cases/case-series reported in the literature.
Methods: We report a case of an asymptomatic 43 year-old man with no relevant past clinical history, who presented with a pancreatic mass, incidentally detected on a routine abdominal ultrasound for

life-insurance purposes. On Computed Tomography scan, the lesion was described as an 8cm heterogeneous hypervascular pancreatic tail mass, with hypocaptive areas suggestive of necrosis and the patient underwent distal pancreatectomy.
Results: On cut section, the distal pancreatectomy specimen showed a 5,7cm well-defined pancreatic tail tumour with a fleshy, whitish cut surface with cystic areas and haemorrhagic ones. Histologically, the tumour was an otherwise typical PanNET with a nested architecture and monomorphic cells with eosinophilic cytoplasm and round nuclei with stippled chromatin. Unlike the imaging studies suggested, there were no areas of necrosis. Instead, there were areas of haemorrhage and the presence of unevenly distributed, some centrally located, variably prominent ductular structures, closely intermingled with the neuroendocrine nests. Unlike the classical variant, however, a large proportion of the ductules was significantly and macroscopically dilated. There was no cytological atypia nor mitoses/high-proliferative index.
Conclusion: We report a rare case of a PanNET, ductulo-insular variant, uniquely presenting cystically dilated ductules. This variant is especially important to recognize as to not misdiagnose these tumours as mixed neuroendocrine/non-neuroendocrine tumours. Additionally, it is fundamental to highlight the benign nature of the ductules as the prognosis is dependent on the endocrine component alone. There has been ongoing debate about whether these ductules are neoplastic or represent non-neoplastic pancreatic ductules entrapped by the tumour, with recent studies suggesting the latter.

E-PS-04-010
Pathological diagnosis in extrahepatic cholangiocarcinoma - a challenge for the couple gastroenterologist-pathologist
I. Crecium*, R. Ionescu, S. Zurac, T. Voiosu, G. Micu, A. Florescu, C. Popp
*Department of Pathology, Colentina University Hospital, Bucharest, Romania

Background & objectives: Diagnostic of extrahepatic cholangiocarcinoma (ECC) is a real challenge for pathologists, since they are expected to formulate the diagnosis on very small tissue samples. This study aims to evaluate the adequacy of biliary biopsies and inter-observer agreement in detecting ECC.
Methods: We included, retrospectively, 43 biliary biopsies obtained through ECRP, from patients that were subsequently proven to have ECC (by surgery, imaging assessment and evolution). Two independent pathologists examined the slides using a simple reporting scale: inconclusive, benign, regenerative atypia, dysplastic atypia and malignant. Results were correlated with the volume of tissue samples, as simple assessment of tissue acquisitions quality.
Results: Observers provided identical diagnoses for 25 cases and differing diagnoses for 17 cases. Despite a higher frequency of consistent diagnoses among observers, both groups - those with unanimous diagnoses and those with differing diagnoses - exhibited an average sample volume of 0.012 cm^3. Notably, a negative correlation was observed between sample volume and interobserver agreement, as indicated by a Pearson correlation coefficient of -0.048. Interestingly, cases classified as inconclusive and regenerative atypia demonstrated unanimous agreement among observers, while the weakest consensus was observed for cases categorized as dysplastic atypia.
Conclusion: Despite a higher frequency of unanimous diagnoses among observers, the study found no consistent correlation between samples volume and diagnostic agreement. These findings emphasize the need for improve diagnostic methods to enhance consensus among observers in clinical practice.

E-PS-04-011
Microsatellite instabile medullary carcinoma of the gallbladder: histopathological characteristics of a rare case
S.K. Dursun*, B.N. Üge, N. Dursun
*Basaksehir Cam ve Sakura City Hospital, Department of Pathology, Turkey

Background & objectives: Medullary gallbladder carcinoma (MGBC) is a rare subtype characterized by unique histomorphological features. Due to limited literature, there is need for deeper understanding of this entity. We present a case of MGBC exhibiting microsatellite instability with distinct histomorphological features.
Methods: A 51-year-old female presented with a one-year history of epigastric pain. Magnetic resonance imaging showed asymmetric thickening in the gallbladder walls with hydropic appearance. Additionally, a 1.5 cm calculus was found in the gallbladder neck. Increased FDG uptake (SUVmax = 7.8) was noted in the wall thickening of the gallbladder fundus. Subsequently, the patient underwent gallbladder and liver bed resection.
Results: Macroscopic evaluation revealed a 15x6x5.5 cm cream-yellow tumour attached to the gallbladder fundus. Microscopic evaluation showed stroma-poor sheets of tumour cells exhibiting syncytial growth and pushing borders, accompanied by a lymphocytic infiltrate. In focal areas, the conventional morphology of gallbladder carcinoma (GBC) was seen. High-grade dysplasia, pseudopyloric metaplasia were detected adjacent gallbladder. Invasion into the muscular layer and lymphovascular invasion were noted. No perineural invasion and lymph node metastasis was observed. Immunohistochemical staining revealed nuclear loss of MSH2 and MSH6, indicating microsatellite instability, supported by PCR analysis. EBER was negative. The combined morphological and immunohistochemical findings indicated the diagnosis of MGBC.
Conclusion: Medullary or lymphoepithelioma-like carcinomas of digestive tract are rarely seen in the gallbladder. They present nodular growth pattern with pushing borders, composed of cells with large, round/ovoid nuclei with vesicular chromatin and prominent nucleolus, additionally variable lymphoplasmacytic infiltration. The evidence of EBV varies, loss of mismatch repair protein expression can occur. Although literature suggests that MSI GBCs have a better prognosis, data on MGBCs are insufficient. Documenting such cases is crucial for understanding their clinical behaviour in this less-explored area.

E-PS-04-012
Two cases of chromophobe hepatocellular carcinoma, an uncommon subtype of hepatocellular carcinoma
S.K. Dursun*, S. Bağbudar, E. Kınacı, S. Erdamar Çetin, N. Dursun
*Basaksehir Cam ve Sakura City Hospital, Department of Pathology, Turkey

Background & objectives: Chromophobe hepatocellular carcinoma (HCC) is a rare subtype of HCC, recently recognized entity by WHO. Tumour is characterized by distinct histological features: focal areas with chromophobic-eosinophilic cytoplasm, marked anaplastic nuclei, and pseudocyst formation, associated with alternative lengthening of telomeres (ALT).
Methods: Case 1: An 84-year-old male with chronic hepatitis C virus infection presented with edema. MRI revealed a 24 mm liver lesion. Case 2: A 55-year-old male with chronic hepatitis B virus infection presented with a suspicious liver mass measuring 56x60 mm found incidentally during follow-ups. Both lesions were resected with a preliminary diagnosis of hepatocellular neoplasms.
Results: Case 1: A tumoural lesion measuring 3x3x1.8 cm, with two satellite foci was found. Case 2: A tumoural mass measuring 7x5.2x5 cm was observed. The tumours were well-defined, with hemorrhage and necrosis. Histopathological examination of both lesions showed cells with prominent eosinophilic cytoplasm, exhibiting marked atypia-anaplasia in some areas, and containing occasional acinar, microcystic structures. The tumour expressed hepatocellular markers.

When histomorphological and immunohistochemical findings were evaluated, the cases were reported as "Chromophobe HCC." Next-generation sequencing analysis was performed. The first case revealed ATRX and PIK3CA mutations, while the second showed CTNNB1 and TP53 mutations. The ATRX mutation associated with the ALT phenotype supported the diagnosis in the first case.
Conclusion: Chromophobe HCC, a rare subtype included in the latest WHO classification, is associated with the ALT phenotype. It is more prevalent in females and has survival rates similar to traditional HCCs. Identifying these lesions can be challenging, especially when they contain dominant conventional HCC areas. Features such as eosinophilic cytoplasm, marked atypia, and anaplasia should prompt consideration. Tumours with ALT can be resistant to telomerase inhibitors. Recognizing these lesions, characterized by the ALT phenotype, can be crucial for targeted therapies.

E-PS-04-013
EUS-FNB in pancreatic neoplasm – where is the balance between difficulties of tissue acquisition and the difficulties of pathological diagnosis
A. Florescu*, R. Ionescu, S. Zurac, T. Voiosu, G. Micu, I. Creciun, C. Popp
*Department of Pathology, Colentina University Hospital, Bucharest, Romania

Background & objectives: Accurate diagnostic on pancreatic fine needle biopsies is a significant challenge for pathologists, being heavily influenced by the quantity of the tissue. This study aims to evaluate how the area of the examined tissue influences the diagnostic of pathologists.
Methods: We included 26 EUS-FNB biopsies in the study, obtained from patients with suspected pancreatic malignancy (clinical and imaging criteria). Two pathologists, one resident/novice and one with extensive experience in pancreatic pathology, examined the slides using a simple reporting scale: inconclusive, regenerative atypia, dysplastic atypia, and malignant. The results were correlated with the areas on which the sampled materials were spread.
Results: Diagnostic concordance was achieved in 88% of cases. The highest concordance between the two observers was observed in cases classified as "malignant" or "inconclusive" (100% concordance for both categories), while the lowest concordance was found in cases with "regenerative atypia" results. When the biopsy specimen area was larger (77 mm² on average), the two observers tended to agree on the diagnosis. Conversely, when the specimen area was smaller (37 mm² on average), concordance in diagnoses decreased. The results were compared with another parallel study conducted at our clinic, involving 43 ERCP-guided biliary tract biopsies. This comparative study aimed to correlate specimen volume with diagnostic concordance between two observers.
Conclusion: This study investigated the impact of tissue sample size on diagnostic concordance between novice and experienced pathologists in pancreatic biopsies. Our findings revealed a significant correlation, with larger tissue samples exhibiting higher concordance in diagnoses. This suggests that adequate tissue acquisition during biopsy procedures can potentially improve diagnostic accuracy for novice pathologists, ultimately leading to a reduction in diagnostic errors.

E-PS-04-014
Pancreatic solid pseudopapillary neoplasm (PSPN): a retrospective review at our institution
N. Fontanil Vior*, R. Mazorra, J.J. Jiménez Velasco, Á. Terán, M. Morís, G.G. Yange, M. Martino, S. Alvarez Alonso, Y. Guzmán Gómez, Á. Estébanez
*Hospital Universitario Marqués de Valdecilla (HUMV), Spain

Background & objectives: Initially considered a benign entity, PSPN was later reclassified as “Low grade malignant” (IVB category —“Neoplasm-Other”—, Papanicolau Classification 2014), and currently belongs to the VII category —“Malignant”— of the WHO Classification, 2022. We studied retrospectively the prevalence at our centre.
Methods: A retrospective descriptive study of pancreatic cytology performed by endoscopic ultrasound (EUS) was carried out from January 2021 to January 2024, reviewing the medical records of cases diagnosed with PSPN. We also examined the main publications regarding PSPN of the last five years and utilised the Papanicolau (2014) and WHO (2022) classifications.
Results: In three years, 325 endoscopic ultrasound–guided fine needle aspiration cytology (EUS-FNA) of pancreas were performed, four (1.23%) of which were diagnosed with PSPN. Three (75%) patients were women. The average age was 32 years (19 – 50 years). The lesions measured between 4.5 and 6 cm. Abdominal pain was the main symptom in three cases. All cases were limited to the pancreas, three (75%) of them to the head. Two cases were encapsulated. One of the cases occurred in combination with infiltrating adenocarcinoma. Three cases were cystic. Three cases showed calcifications. All cases showed nuclear and cytoplasmic positivity for beta-catenin. Three cases were cyclinD1 positive and two were synaptophysin positive.
Conclusion: All patients were diagnosed with EUS-FNA, whilst other series average a 63% of EUS-FNA performance. 75% were located in the head, while in other series it predominates in the tail (27%) over the head (25.4%). During follow-up, none of them presented metastasis, whereas in other series it occurs in 7.1%. All patients still alive, while in other series PSPN associates a mortality of 4.8%. Our data is limited since we only had 325 EUS-FNA.

E-PS-04-015
CD166/ALCAM immunohistochemical profile in pancreatic ductal adenocarcinoma and associated lymph node metastases
S.E. Giuşcă*, I. Caruntu, L. Lozneanu, D. Ciobanu, C. Amalinei, E. Avădănei, A. Rusu
*Department of Morphofunctional Sciences I, “Grigore T. Popa” University of Medicine and Pharmacy, Iasi, Romania

Background & objectives: CD166/ALCAM, a cell adhesive glycoprotein, has been associated with hyperproliferative or pro-metastatic phenotype in different malignancies. Our study focuses on CD166 immunoexpression in primary pancreatic ductal adenocarcinoma (PDAC) and corresponding lymph node metastases, and its correlation with classical clinicopathological parameters.
Methods: We investigated 75 PDAC cases and 43 associated lymph node metastases. Clinicopathological parameters were collected from medical records. Immunoreaction on paraffin-embedded tissues was appraised semi-quantitatively (positive tumour cells’ intensity and percentage), resulting two-tired classification: low- and high-CD166. Roc curve was applied for cut-offs of ratio of metastatic number to total number of harvested lymph nodes (LNR). Data were statistically analysed.
Results: Out of a total of 75 PDAC cases, semi-quantitative analysis of CD166 immunoscore revealed 24 cases (32%) with low-CD166 and 51 cases (68%) with high-CD166. In associated lymph node metastases, CD166 immunoscore was low in 33 cases (76.74%) and high in 10 cases (23.25%). Statistical analysis showed significant correlation of CD166 immunoscore with LNR ($p = 0.03$), high-CD166 score being associated with lower number of metastasized lymph nodes. Kaplan-Meier curves based on LNR cut-off (8.5% positivity percentage, equivalent to 1.5 lymph nodes) indicated significant differences in average overall survival, 29.20 months for patients with LNR < 8.5% and 15.22 months for those with LNR ≥ 8.5% ($p = 0.003$).

Conclusion: LNR allowed sub-classification of patients in pN1 stage into groups with different survival. CD166 immunoexpression level appears to be associated with number of metastasized lymph nodes, shaping a more aggressive PDAC subtype. According to our results, comparison of tumour behaviour in relation to CD166 immunoexpression suggests that a low-CD166 promotes tumour dissemination, worse prognostic and shorter overall survival. Thus, our study supports the potential role of CD166 in pancreatic carcinogenesis by enhancing the hyperproliferative and pro-metastatic profile of primary tumour.

E-PS-04-016

Hepatic adrenal rest tumour (hart) mimicking hepatocellular adenoma: a case report of an extremely rare entity

C. Gouta*, N. Antoniadis, Z. Efstathiadi, M. Sidiropoulou, S. Vasileiadou, E. Sakellariou, E. Katsiki
*Department of Histopathology, Hippokration General Hospital of Thesaloniki, Greece

Background & objectives: Heterotopic adrenal tissue is often detected in extra-adrenal locations such as the kidney, the retroperitoneum, the spermatic cord and the paratesticular region. Hepatic adrenal rest tumour is a quite rare entity, with only 12 cases been reported so far.
Methods: A 41-year-old woman with a history of contraceptive pills use was referred to our hospital due to a liver mass found incidentally during imaging examination. A CT scan was performed which revealed a round, well-defined, subcapsular lesion with a maximum diameter of 5 cm into segment I of the liver. Hepatocellular adenoma was regarded as the most probable diagnosis.
Results: A partial hepatectomy was performed and the specimen was received by our laboratory for further evaluation. Macroscopic examination showed a solid, well-circumscribed, non-encapsulated, subcapsular mass with a maximum diameter of 5,5 cm. Microscopically, the mass consisted of a monotonous population of middle-sized cells with mixed eosinophilic and clear cytoplasm and small ovoid nuclei with prominent nucleoli. Round azurophilic intracytoplasmic inclusions were occasionally observed. Immunohistochemical examination showed positivity of tumour cells for Melan-A, NSE and SF-1, while HepPar1, arginase 1 and glypican 3 were negative. Consequently, the diagnosis of benign hepatic adrenal rest tumour was established.
Conclusion: Hepatic adrenal rest tumour is a very rare entity with predilection for young adults. In most cases these tumours are non-functional and behave in a benign way presenting as incidental findings. All reported cases involve the right hepatic lobe and especially segment VII. Differential diagnosis includes ccHCC, hepatocellular adenoma, metastatic ccRCC and angiomyolipoma. Our case report contributes to the literature by presenting an extremely rare case of hepatic adrenal rest tumour with unusual intrahepatic locality and a challenging clinicopathological manifestation.

E-PS-04-017

Clinicopathologic, immunohistochemical, and molecular characterization of hepatic adenomas in males: a single institution study in the United States

S. Harada*, S. Anderson, D. Shimoga Chandrashekar, B. Goksel, D.B. Johnson, N. Khazanov, D. Hovelson, B. Bulen, J. Motyka, L. Lamb, D. Harbi, A. Osme, G. Lee, S. Al Diffalha, D. Dhall
*University of Alabama at Birmingham, USA

Background & objectives: Hepatic adenomas (HA) in males are very rare. We performed detailed clinicopathologic, immunohistochemical and molecular characterization of HA in males, to understand their pathogenesis and malignant potential by searching for "hepatic adenoma" and "male" in our institutional pathology archive (2010–2020).
Methods: A search identified ten patients. The histologic slides, clinical findings and follow-up information were reviewed and immunohistochemical stains were performed. DNA was extracted from FFPE tissue on the seven cases diagnostic for HA (all resections) and targeted sequencing was performed at STRATA using Ion Torrent chemistry. Filtered variants were annotated with Annovar tool and OncoKB database to identify pathogenic mutations.
Results: The age ranged 28-68 years and the lesions ranged 3.7-15 cm. 86% of patients were morbidly obese. All showed at least focal cytologic atypia. Four cases (57%) showed diffuse CRP and/or SAA staining, suggestive of inflammatory-type HA, one of which showed pseudo-map-like GS staining pattern. One other showed patchy GS staining. These two harbored CTNBB1 mutations. Three lesions (43%) were markedly steatotic and one was haemorrhagic, which makes interpretation of reticulin stain difficult, but one showed loss of reticulin in non-steatotic areas and nuclear beta-catenin, suggestive of HCC arising in HA. None of the cases showed complete LFABP loss, HNF1A, TP53 and TERT promoter mutations, or significant copy number alterations.
Conclusion: Majority of HA in males occurred in obese patients and were inflammatory-type in our population in Southeast United States. However, beta-catenin activated adenomas were seen in 43% of cases. Despite showing cytologic atypia, questionable reticulin loss and GS positivity, raising concern for the possibility of HCC, none of them showed mutations commonly observed in HCC. A subset (43%) of HA in males appear to show benign characteristics and if properly characterized on a biopsy, may not require upfront resection.

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E-PS-04-018

Low-grade endometrial stromal sarcoma in the jejunum and liver

S.E. Horoz*, B. Binici, Ç. Çelikel
*Marmara University Faculty of Medicine, Turkey

Background & objectives: Endometrial stromal sarcoma(ESS) is a rare uterine tumour (0,2% of all cancers and up to 15% of sarcomas). Extra-uterine ESS is even more rare, believed to originate from endometriosis externa.We present this rare case because of its atypical features and associations.
Methods: A 47-year-old woman presented with one-month history of epigastric pain.Imaging showed a 9 cm solid-cystic lesion in the omentum, thickening of the jejunal wall,liver lesions.Omentum, jejunum, and liver segment were resected.The morphology of the tumour in the liver,jejenum and omentum was characterized by Irregular cellular islands of monotonous oval to spindle cells with minimal cytologic atypia,vesicular chromatin and scant cytoplasm.
Results: Necrosis and pleomorphism were not observed,mitotic figures were rare.Neoplastic cells were positive for CD10,ER,PR;but negative for CD117,cyclin D1,and S100.Surrounding the tumour there were areas of endometriosis in the jejunum but not in the liver.Based on these findings,the case was reported as low-grade ESS(LG-ESS) in the jejunum and metastasis to the liver.Few months later,PET-CT revealed FDG uptake in multipl foci of the liver and colon.Liver segmentectomy,total abdominal hysterectomy with bilateral salpingo-oophorectomy,and colon resection were performed. Examination of the colon resection specimen revealed typical colonic adenocarcinoma.In TAH-BSO specimen,there was a single endometriosis foci in the myometrium,Both ovaries and tubas were normal. In the liver there were multiple foci of endometriosis, as well as LG-ESS.
Conclusion: Endometriosis can occur in unusual sites including liver,small intestine and omentum.Extra-uterine malignant transformation in endometriosis has been reported previously in liver and small intestine.In our case,there were foci of endometrioisis in both liver and jejunum so we cannot be sure whether the primary tumour is in the liver or in the jejunum.Besides,we can also argue that these were

both primary and concurrent tumours.In addition,to our knowledge,our case is the only report of ESS in a woman with concurrent colonic adenocarcinoma.

E-PS-04-019

Undifferentiated carcinoma with osteoclast-like giant cells of the pancreas: molecular genetic analysis of 13 cases

J. Hrudka*, M. Kalinová, V. Ciprova, J. Moravcová, R. Dvořák, R. Matěj
*University Hospital Kralovske Vinohrady, Charles University, 3rd Faculty of Medicine, Czech Republic

Background & objectives: Undifferentiated carcinoma with osteoclast-like giant cells (UCOGC) of the pancreas is a rare malignancy considered a subtype of pancreatic ductal carcinoma (PDAC), exhibiting diverse prognoses. UCOGC displays a notably similar array of oncogenic DNA mutations to PDAC.
Methods: The study enrolled a group of 13 patients with surgically treated or biopsied pancreatic UCOGC. We scrutinized the somatic mutation landscape in this cohort using a custom next-generation sequencing (NGS) panel to detect Single Nucleotide Variants (SNVs) and Indels in 73 genes associated with solid tumours. The NGS custom panel was designed to cover genes crucial in pancreatic carcinogenesis.
Results: Our analysis unveiled a spectrum of pathogenic or likely pathogenic mutations akin to those found in PDAC, mirroring previously reported findings: 10 KRAS, 9 TP53, 4 CDKN2A mutations, and singular occurrences of SMAD4, CIC, GNAS, APC, ATM, NF1, FBXW7, ATR, and FGFR3 mutations.
Conclusion: To our knowledge, this represents the largest UCOGC cohort analysed by NGS published thus far. The results affirm the idea that UCOGC shares a genetic profile with PDAC, despite its unique appearance under the microscope. However, identifying a distinctive genetic signature exclusive to UCOGC, as well as predictive markers, remains largely unexplored. Mutations in ATM and ATR, suggesting "BRCAness," as well as alterations in FGFR3, might have potential significance for targeted therapy.

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E-PS-04-020

Real-life pathological diagnosis in extrahepatic cholangiocarcinoma – inter-observer agreement in a tertiary centre

R. Ionescu*, I. Creciun, R. Neagu, A. Cibotariu, L. Stanciu, D.M. Marinoiu, A. Bordea, A. Voiosu, S. Zurac, C. Popp
*Department of Pathology, Colentina University Hospital, Bucharest, Romania

Background & objectives: Diagnostic of extrahepatic cholangiocarcinoma (ECC) is proven to be a challenge for pathologists. Our main objective is to evaluate inter-observer agreement in detecting ECC and to assess the correlation between diagnostic agreement and the volume of the sample.
Methods: We retrospectively examined available data in 43 biliary biopsies obtained by ERCP. All patients included were proven to have ECC by imaging assessment, surgery and evolution. Two pathologists examined the slides using a simple reporting scale: benign and malignant. Results were correlated with the volume of the samples.
Results: Observers had identical diagnoses in 83% of cases and differing diagnoses in 17% of cases. A total of 22% of cases were misdiagnosed by both the observers, probably due to the limitation of tissue acquisition (inadequate biopsies). The most unanimous diagnoses were associated with an average sample volume of 0.012 cm3, while differing diagnoses were associated with an average sample of 0.009 cm3. Notably, when the average sample volume was 0.016 cm3, both observers misdiagnosed the case, the big samples being non-tumoural.
Conclusion: The study found a consistent correlation between inter-observer agreement and sample volumes, but some of them were misdiagnosed, despite a good volume of the examined sample. This finding emphasizes the need for better tissue acquisition practice and sometimes, the need for multiple biopsies, performed and evaluated by experts.

E-PS-04-021

High tumour-infiltrating lymphocytes (TILs) infiltration surrounding cancer cells at venous invasion foci can predict immune-prone pancreatic ductal adenocarcinoma (PDAC) which shows better progression-free survival (PFS)

B. Jeong*, S. Hong
*Department of Pathology, Asan Medical Center, Republic of Korea

Background & objectives: TILs are crucial prognostic factors in PDAC. However, accurately assessing TILs is challenging due to peritumoural pancreatitis. We aimed to overcome these challenges by evaluating TILs at venous invasion (VI) foci for precise assessment of immune-prone PDAC.
Methods: Histologic patterns of VIs, including destructive, pancreatic intraepithelial neoplasia (PanIN)-like, and conventional patterns, were evaluated from 364 cases with surgically resected PDACs. Histologic features related to TILs, including intratumoural tertiary lymphoid structures (TLS), peri-venous invasion (peri-VI) TILs directly contacting VI tumour cells, and peri-VI stromal TILs, were assessed with the destructive pattern, then clinicopathologic and genomic features were analysed.
Results: VI was detected in 124 cases (34.1%) with 76 cases (61%) of destructive pattern, of which high peri-VI TIL was 21 cases (28%) and high peri-VI stromal TIL was 23 (30%) using ≥10% cut-off of high TIL criteria. Intratumoural TLS was in 17 cases (22%). Patients with high peri-VI TIL had more common intratumoural TLS (p=0.008) and better PFS (median, 27 vs 8 months, p=0.0021), even when categorized into three groups (34, 25, and 8 months, p=0.0053). Similarly, patients with high peri-VI stromal TILs had better PFS (23 vs 10 months, p=0.02). There were no significant differences in mutation burden or driver mutation distribution according to TIL groups.
Conclusion: Evaluating TILs at VI foci in surgically resected PDAC tissue can provide more precise information regarding immune-prone PDAC and potentially can be used as a biomarker for the application of immunotherapies after surgical resection of PDAC.

E-PS-04-022

Progression of NET G3 can lead to TP53 mutation-associated NEC-like transformation

A. Kasajima*, E. Moser, E. Mayr, N. Pfarr, A. Ura, L. Vogel, M. Pavel, K. Scheidhauer, A. Werder von, G. Klöppel
*Department of Pathology, TUM School of Medicine and Health, Munich, Germany

Background & objectives: Recent studies reported that NETs G3 share genetic features with NECs, such as TP53 mutations. However, morphomolecular evolution of NETs G3 is poorly understood. We aimed to clarify morphological and genetical changes during progression of NET G3.
Methods: 37 NETs G3 were histologically examined at least twice. Tumours that progressed from G1/G2 to G3 were called “transit G3” and differentiated from tumours primarily identified as “de novo G3“. Morphology, Ki67 index (delta Ki67), molecular features of the initial and last assessments were compared, and the preceding treatments were studied.

Results: 27 (73%) transit and 10 de novo (27%) G3 were identified. NEC-like histological features (high grade atypia, diffuse growth pattern and/or necrosis) were identified in 8 (21%) transit G3 (6 pancreas, 1 rectum, 1 unknown primary). Delta Ki67 was significantly higher in NEC-like G3 (54% vs. 19%) and the interval time was significantly longer than that in the other transit G3 (63 vs. 29 months). All NEC-like G3 had TP53 (100%), and rarely RB1 (12%) mutations, but retained NET typical mutations, such as MEN1 and DAXX (5 and 1 case, respectively). NEC-like G3 patients received more than three different treatments, e.g., somatostatin analog (n=6), PRRT (n=5), streptozotocin (n=5), temozolomid (n=3).
Conclusion: We identified 8/37 (21%) NETs G3 which developed NEC-like features associated with an abrupt Ki67 increase (delta 54%), TP53 mutation (100%) and maintained NET characteristic genetic features, such as MEN1, DAXX mutations, therefore, differ from typical features of true NECs. NEC-like transformation occurred after long clinical course of NET G1/G2, often after treatment of the patients with multiple agents including PRRT or alkylating drugs.

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E-PS-04-023
Clinicopathological significance of IQ motif containing GTPase activating protein 3 (IQGAP3) in pancreatic ductal adenocarcinoma (PDAC)
A. Kido*, A. Ishikawa, T. Fukui, N. Katsuya, K. Kuraoka, W. Yasui
*Department of Molecular Pathology, Graduate School of Biomedical and Health Sciences, Hiroshima University, Japan

Background & objectives: IQGAP3 is a member of the IQGAP family. In gastric cancer, we reported that IQGAP3 was overexpressed, and its expression was an independent prognostic classifier. This study aims to confirm the biological role of IQGAP3 in PDAC.
Methods: We analysed IQGAP3 expression in 81 surgically resected PDAC samples by immunohistochemistry, and assessed the correlation between IQGAP3 and clinicopathological factors including patient's survival. Immunohistochemical staining was considered positive in the cases in which IQGAP3 stained more than 50% of the cancer cells. RNA interference was used to inhibit IQGAP3 expression in PDAC cell lines.
Results: We firstly performed immunohistochemical staining for PDAC. IQGAP3 was expressed in the cytoplasm and cell membrane of PDAC cancer cells. In the immunohistochemical analysis, 44 (54.3%) of 81 PDAC specimens were positive for IQGAP3. Kaplan-Meier analysis showed poorer survival in IQGAP3-positive PDAC cases. Multivariate analysis indicated that IQGAP3 expression was an independent poor prognostic factor in PDAC cases. Our cohort and The Cancer Genome Atlas database indicated that IQGAP3 is co-expressed with kinesin family member C1, which we previously reported as a cancer stem cell-associated protein. IQGAP3 siRNA treatment decreased PDAC cell proliferation and spheroid colony formation via ERK and AKT pathways.
Conclusion: These results indicate that the expression of IQGAP3 might play an important role in tumour progression of PDAC in terms of stem cell-like features and survival.

E-PS-04-024
Patients with prolonged inflammation and cholestasis following hepatitis A infection: autoimmune hepatitis?
É. Kocsmár*, C.S. Lőrinczi, K. Fried, K. Nemesi, K. Werling, J. Halász
*Department of Pathology, Forensic and Insurance Medicine, Semmelweis University, Hungary

Background & objectives: Chronic hepatitis B and C are well-characterized forms of chronic hepatitis (1), but hepatitis A virus (HAV) can also cause chronic liver disease by inducing autoimmune hepatitis (AIH), a type of chronic hepatitis of unknown and known etiological factors.
Methods: Our aim was to assess the prevalence and to evaluate the clinicopathological features of AIH in patients with prolonged HAV infections. Liver biopsy specimens from the institutional archives of the Department of Pathology, Forensic and Insurance Medicine, Semmelweis University, from 2017-2024, that were from clinically therapy-refractory cases of AIH suspicion and HAV positivity were selected.
Results: Of the clinically therapy-resistant patients biopsied for elevated liver enzymes and prolonged jaundice, 111 cases were found to exhibit characteristic features of AIH, such as lymphoplasmacytic interface hepatitis, lobular activity and increased apoptosis, further 36 cases showed overlap syndrome with other autoimune disease. In six cases, HAV infection was found in the background. Clinically, prolonged jaundice and elevated transaminases were observed for a prolonged period after the primary infection cleared, as well as elevated gamma-globulin levels and negative immunoserological results. Biopsy specimens showed histopathological abnormalities suggestive of autoimmune hepatitis, with one case of additional lesions masking the histological diagnosis. All patients showed a good therapeutic response to the immunosuppressive therapy.
Conclusion: Persistently elevated transaminases and histologically active hepatitis after serologically cleared HAV infection suggest the possibility of AIH. HAV-induced AIH is characterized by anti-SMA seropositivity/seroconversion (instead of ANA) with prolonged seroconversion time. Immunosuppressive therapy is therefore recommended in cases with negative immunoserology but histologically diagnosed as AIH.

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Reference: (1) Lotz G, et al. Hepatitis viruses and hepatocarcinogenesis. J Physiol Paris. 2001;95(1-6):417-422. doi:10.1016/s0928-4257(01)00057-2

E-PS-04-025
Is hepatic arteriolosclerosis related to loss of canals of Hering: preliminary results
A. Kolaki*, I. Grypari, E. Stoupi, I. Vlachos, D. Myoteri, D. Tiniakos
*Greece

Background & objectives: Hepatic arteriolosclerosis (HA), a complication of diabetes and hypertension, may be related to biliary changes resulting from ischemia. We explored the relationship of HA with loss of canals of Hering (CoH) in patients with unexplained chronically abnormal liver biochemistry.
Methods: We evaluated 15 liver biopsies, 9 with HA (median age 66.5,range 32-82 years, 7/9 women) and 6 with normal liver histology (median age 52,range 33-66 years, 4/6 women). Keratin (K) 7 and K19 immunostains were used to assess presence of intermediate hepatocytes indicative of chronic cholestasis (K7 only), ductular reaction (DR),bile duct loss and to evaluate CoH numbers (K19 only).
Results: Chronic cholestasis and CoH loss were significantly more common in the HA group compared to control (p=0.005 and p=0.025, respectively, Pearson chi square). HA was correlated with the presence of chronic cholestasis (p=0.005). Bile duct loss with chronic cholestasis and bile duct loss with CoH loss were more common in the HA group (p=0.006) and p=0.039, respectively. There was no correlation of any of the above features with the presence of sinusoidal fibrosis.

Conclusion: Our preliminary results in this limited sample indicate that biliary changes in liver biopsies performed for unexplained abnormal liver function tests may be etiologically related to HA, possibly leading to increased ALP and mild chronic cholestasis. We speculate that ischemia caused by decreased perfusion in thickened arterioles may affect the proximal branches of the biliary tree leading to CoH loss, in line with evidence correlating HA with small bile duct loss in primary sclerosing cholangitis.

E-PS-04-027

Cytomatrix® 3D cell blocks. A feasible new method for pancreatic EUS-FNA cell block formation for molecular assessment. A pilot study

S. Lopez-Prades*, S. Alós, I. Archilla, N. Vega, M.T. Rodrigo calvo, M.R. Esteve, S. Hoya, R. Millan, M. Cuatrecasas Freixas
*Pathology department. Hospital Clinic. University of Barcelona. Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Spain

Background & objectives: Cytological cell blocks from pancreatic EUS-FNA frequently have scarce material for molecular analysis. Cytomatrix® 3D synthetic matrix captures fresh cells to obtain a FFPE cell block. We compared the feasibility of viable material obtained with conventional and Cytomatrix® cell blocks.
Methods: Twenty-three EUS 22-gauge pancreatic FNA samples were prospectively included. The first FNA material was entirely used for Cytomatrix® cell block. Then, standard ROSE was performed obtaining material for cytological smears and cell block. We aimed to state the feasibility of Cytomatrix®. The amount of tumour cells and stroma on both cell blocks were assessed by three pathologists and two cytotechnicians.
Results: Five cases were excluded for having no material evaluable in some cell blocks. Among the 18 remaining cases, 15/18 (83%) had more tumour cells in the Cytomatrix® cell block, which was preferred to perform molecular analysis. Interestingly, in two cases, the Cytomatrix® cell block was used to perform immunohistochemistry to complete the diagnosis, since the regular cell block contained insufficient material. Regarding stroma, there were no differences using either method, half of the cases had more stroma in the Cytomatrix®, and the other half in regular cell block.
Conclusion: Cytomatrix® is a feasible new method for in situ diagnosis with ex-vivo confocal microscopy. We demonstrated the use of Cytomatrix® for obtaining good EUS-FNA cell blocks for further molecular analysis, since it concentrates all the material. As limitations of our study, we used the first FNA material for Cytomatrix® cell block formation which did not represent the conventional EUS-FNA ROSE process.

E-PS-04-028

The metamorphosis of a liver multinodular metastasis into a primary tumour by histological examination: a case report

L. Lozneanu*, C.E. Andriescu, S.E. Giuşcă, I. Caruntu, R.A. Balan, C. Amalinei
*Department of Morphofunctional Sciences I, "Grigore T. Popa" University of Medicine and Pharmacy, Iasi, Romania

Background & objectives: The adrenal metastases are often spread by hematogenous pathway, contributing to their specific morphological patterns. We present a case of a patient who was diagnosed clinically and on CT imaging with liver metastasis and a primary adrenal gland tumour.
Methods: A non-smoker, 69-year-old female was admitted to the surgery department of "Sf. Spiridon" Hospital Iasi, Romania, with a large adrenal gland tumour, diagnosed as a primary left adrenal gland tumour (T2N1M1) with multiple secondaries (liver, left kidney and adjacent muscles). The patient benefited from surgical treatment, histological examination and immunohistochemical analysis of the surgical specimens being evaluated for diagnosis certification.
Results: The diagnosis was established on the surgical specimen from the left adrenal gland. The external examination findings revealed a 17.5/11/5.5 adrenal gland specimen, containing a 15 cm nodular tumour. The tumour cut section showed a heterogeneous, multilobulated appearance, with grey-yellow areas and firm-elastic consistency, alternating with fibrous septa, and a central mucinous area. Microscopically, the tumour exhibited trabecular, solid, and pseudo-glandular appearance. The cells were pleomorphic, with irregular nuclei, conspicuous nucleoli, and amphophilic cytoplasm, with hepatoid-like phenotype. Immunohistochemistry of the hepatoid-like cells showed Arginase, HSA, Cam5.2, Glypican, and CK8 positivity. Morphologic findings corroborated with immunohistochemical characteristics were consistent with metastatic moderately differentiated hepatocarcinoma in the left adrenal gland.
Conclusion: Massive unilateral adrenal metastases originating from liver are rare. Adrenal metastases are usually bilateral and arise from different lung, breast, kidney, thyroid, colon cancers, and melanoma. The similar morphology of primary and secondary tumours made the differential diagnosis very difficult in our case. The morphological findings revealed a different outcome than CT imaging: adrenal metastasis of a hepatic primary tumour. Our results emphasize the important role of morphological diagnosis in a multidisciplinary approach, followed by assessment of the oncological management.

E-PS-04-029

Hepatocellular malignant neoplasm, not otherwise specified (HCN-NOS) – a clinicopathologic challenging diagnosis

J. Madeira*, B. Sepodes, M. Jerónimo, I. Gonçalves, M.R. Silva, M.A. Cipriano
*Pathology department, Hospitais da Universidade de Coimbra, Unidade Local de Saúde de Coimbra, Portugal

Background & objectives: HCN-NOS is a "provisional category" of rare paediatric liver malignancies with overlapping histologic features of hepatoblastoma (HB) and hepatocellular carcinoma (HCC). It is identified in older children, carries characteristic molecular alterations, with poor prognosis, and has different treatment approaches.
Methods: We reviewed clinical files and histology microscope slides of malignant hepatocellular neoplasms with no background of chronic liver disease, between 2000-2023, at Coimbra Local Health Unit and classified them according to this new entity. A total of 14 paediatric patients were included: 12 HB and 2 HCN-NOS. The diagnosis relied primarily on resection/liver explant samples and rarely on pretreatment biopsies.
Results: Male predominance was seen in both groups. The median age at diagnosis in the HCN-NOS group (8.75-years; range 8.5-9-years) was higher than in the HB group (1.85-years; range 0.6-4.75-years). The HCN-NOS group had higher PRETEXT stage (III/IV) than the HB group (2/2vs2/12). The HCN-NOS group had morphology of hepatocellular carcinoma and focal nuclear beta-catenin staining. The HCN-NOS group had more metastasis (1/2) than the HB group (2/12), however the HB group had more local tumour recurrence (2/12vs0/2). The median follow-up period was 2.29-years (range 1.25-3.33-years) and 2.03-years (range 0.75-23.6-years) for the HCN-NOS and HB groups, respectively, with only one death for the HCN-NOS group. Our findings corroborate the published literature.
Conclusion: HCN-NOS is a rare entity, whose diagnosis is challenging, since there are no universal well-defined histological criteria. We want to emphasize that diagnosis becomes even more difficult when chemotherapy is given, which is why a biopsy prior to treatment is recommended for a better characterization of these more aggressive subtypes, ensuring an accurate diagnosis for appropriate and effective treatment strategies. We also want to highlight the importance of the

multidisciplinary teams and the international reference centres, which we must appeal.

E-PS-04-030

Comparison of the results of morphological and laboratory-instrumental studies in calculous cholecystitis

B. Magrupov*, T. Verevkina
*Center for Professional Development of Medical Workers, Republican Research Center of Emergency Medicine, Uzbekistan

Background & objectives: Gallstone disease is one of the main indications for surgical principles, second only to peptic ulcer disease. In Uzbekistan, developmental pathology is registered in every sixth resident over 20 years of age.
Methods: We examined 1130 gallbladders. Women accounted for 81.3%, men 18.7%. Acute cholecystitis amounted to 51.5%, chronic cholecystitis to 27.79%, chronic recurrent cholecystitis to 20.71%. In acute cholecystitis, simple inflammation is 20%, phlegmonous – 21%, gangrene – 11%. Oregano and histometry were performed in each group with a comparative analysis of the results obtained with ultrasound and laboratory data.
Results: We have identified an error coefficient between morphometry data and ultrasound examination. A significant difference in indicators was determined between destructive and non-destructive cholecystitis. In all forms of inflammation, there was an increase of basophilic leukocytes number and erythrocyte sedimentation rate. The result of the study was the development of a program for mathematical prediction cholecystitis form with the allocation of three classes: destructive cholecystitis, non-destructive cholecystitis and healthy patients.
Conclusion: 1. In calculous cholecystitis, a reliable difference is determined only between destructive and non-destructive forms. 2. The ultrasound data has a high error coefficient. 3. The developed program is based on the morphometry of retrospective analysis of laboratory data and allows you to predict the form of cholecystitis before surgery based on changes in the cellular composition of the blood of patients with calculous cholecystitis.

E-PS-04-031

Granulomatous liver diseases: tuberculosis or not?

I. Mallek*, R. Ayadi, E. Brahem, R. Yaiche, O. Ismail, S. Ben Slama, A. Ayadi
*Department of Pathology, Abderrahmen Mami Hospital, Ariana, Tunisia

Background & objectives: Hepatic granuloumas (HG) is an uncommon condition with a lengthy list of causes.It may be found accidentally, but are most commonly found to be associated with an underlying systemic process. This study discusses the causes and clinocopathological characteristics of HG.
Methods: This retrospective study included all patients with a pathologically confirmed diagnosis ofgranulomatous hepatitis treated at our department of pathology between 2004 and 2023.
Results: There were 4 male and 9 female patients, aged between 27 and 67 years with a mean of 50,75. Common laboratory abnormalities were cholestasis or cytolytic alterations. Ultrasound and computerized tomography were sensitive but non-specific. The diagnosis was made on liver biopsy in all cases.In microscopic examination, granulomatous reaction was composed of epithelioid cells and multinucleated giant cells with variable number of lymphocytes. These granulomatous lesions were centred by caseous necrosis in 6 cases overs 13 (46,15 %), the rest were non caseating (53,84%).Tuberculosis was the most common etiology(46,15%), followed by idiopathic with undetermined causes (30,76%), sarcoidosis (15,38%) and finally primary biliary cholangitis (7,71%).
Conclusion: Diagnosis of HG is challenging due to its nonspecific clinical presentation, the limitation of laboratory testing, and the similarities of radiographic evaluation to other diseases. Microscopic findings are variable and sometimes uncertain, especially with non caseating necrosis. The histopathological examination must be completed with an underlying systemic process, mainly when the clinic presentation suggests the diagnosis. Clinicians in tuberculosis-endemic regions should maintain a high index of suspicion for hepatic tuberculosis.

E-PS-04-032

Neoplasms developed post-liver transplantation in a paediatric population: a 30-year experience in a reference centre

J. Gama*, T. Botelho, M. Jerónimo, S. Ferreira, M.A. Cipriano
*Unidade Local de Saúde de Coimbra, Portugal

Background & objectives: Children submitted to liver transplantation are under an immunosuppressive status and the incidence of neoplasms is higher than in the general population.
Therefore, this study aims to understand the types of neoplasms developed after liver transplantation in the paediatric population.
Methods: A retrospective transversal study including all the paediatric liver transplants performed in the national reference centre was done. The following data were collected: age, gender, indication for liver transplantation, immunosuppression regimen, number and histological subtype of the neoplasm, post-LT time to development of the neoplasm, clinical follow-up and treatment. The EBV and HHV-8 status were assessed.
Results: Of the 260 children that were submitted to liver transplantation, 10 children developed neoplasms (3.8%). The neoplasms were equally distributed between genders. The age at surgery varied between 2 months and 13 years and the main indication was biliary atresia (6). Eleven neoplasms were diagnosed including lymphoproliferative and mesenchymal neoplasms, as follows: post-transplant lymphoproliferative disorder (2), Classic Hodgkin lymphoma (2) Castleman disease (1), Burkitt lymphoma (1), Kaposi sarcoma (3), sarcoma, NOS (1) and EBV-associated smooth muscle tumour (1).
In one child the diagnosis of Castleman disease and Kaposi sarcoma was done concurrently.
The time from transplant until the development of neoplasms varied between 3 months to 6 years.
Conclusion: Although a "life-saving" procedure, liver transplantation (LT) implies lifelong immunosuppression, and thus, LT recipients are more prone to develop neoplasms compared to the general population. Neoplasms associated with viruses, such as EBV and HHV-8, are of particular interest in transplanted patients.
In this series, the most common neoplasms developed were lymphoproliferative neoplasms.

Even though rare, “de novo” tumours after LT can be associated with significant morbidity. Awareness and surveillance of its clinical manifestations are essential for a timely diagnosis.

E-PS-04-033

Caspase 3/7 activity, autophagy, DNA damage via ROS mechanisms by flow cytometry methods in oral squamous carcinoma cell lines after applied usnea barbata oil extracts

E. Matei*, G. Cozaru, V. Schröder, L. Bucur, M. Aşchie, M. Cristian, N. Dobrin, M.C. Roşu, V. Popovici
*CEDMOG, Ovidius University, Constanta, Romania

Background & objectives: The pharmacological activity of Usnea barbata is antioxidant, anticancer, and anti-inflammatory.
Methods: Cytotoxicity of U. barbata extract in canola oil doses (UBO; 3:3; 3:2; 3:1) showed in oral squamous cell carcinoma CLS-354 cell

line highlighted by caspase 3/7 activity, autophagy, cell cycle, and reactive oxygen species (ROS) count by flow cytometry methods.
Results: In CLS-354 tumour cells, the highest UBO dose (3:3) stimulated the enzymatic activity of caspase 3/7 than both positive controls (36.89 ± 1.44 vs. C2P: 9.60 ± 0.75, p<0.01; C3UA: 27.02 ± 1.64, p<0.05). Autophagy was augmented in CLS-354 tumour cells compared to 1% DMSO negative control and 5% P407 positive control: 62.98 ± 2.06; 51.16 ± 0.69; 47.37 ± 1.18 vs. C1: 12.57 ± 0.92, p<0.01; C2P: 27.27 ± 1.37, p <0.01). In CLS-354 tumour cells, UBO (3:2; 3:1) doses determined cell cycle arrest in G0/G1 phase reported to negative control (87.17 ± 1.57; 74.37 ± 1.27 vs. C1: 92.13 ± 1.61, p<0.01).
Conclusion: This work reveals the ROS-mediated anticancer potential of UBO doses through DNA damage, apoptosis, and autophagy.

E-PS-04-034
Exploring the risks and added value of diagnostic biopsy in patients with hepatocellular carcinoma (HCC)
M. Mccain*, S. Zhang, L. Macdougall, R. Watson, S. Cook, B. Haugk, A. Darne, S. Raman, D. Parkinson, A. Burt, J. Wordsworth, D. Jamieson, J. Nsengimana, D. Tiniakos, H. Reeves
*Newcastle University, United Kingdom

Background & objectives: Previously, HCC diagnostic biopsy was reserved for radiologically atypical nodules or those in the absence of cirrhosis. In 2020 NHS England advised biopsy for all suspected HCC before medical therapies. We have evaluated the risks and benefits of this approach.
Methods: Patients were those undergoing diagnostic biopsy for suspected HCC (Newcastle 2010-2023) recruited to observational research studies. Pathology reports were used to identify HCC histological grade, WHO 2019 architectural pattern and subtype features. These were interpreted alongside clinical data, with adverse events noted. In 2021 a histopathology proforma was introduced to facilitate reporting of potentially relevant features.
Results: 456 biopsies included 69 missed lesions (15.1%), 352 HCC (77.2%), 72 'other' (15.8%). Adverse events: none (438;96.1%), minor (7;1.5%), moderate pain/bleed/bile leak (8;1.8%) and death (1;0.2% - abdominal sepsis). Two developed later tumour seeding (0.4%). HCC biopsy size was sufficient for extended evaluation in 312/352(88.6%). 294/312(94.2%) cases reported architecture, with trabecular and/or pseudoglandular the commonest. Predominantly solid pattern trended towards improved survival (median months 45.3 n=26 vs others 24.23 n=268, p=0.058). Proforma adoption increased reporting of subtype features (56;17.9% overall). Steatohepatitic features associated with improved median survival (32.1 months; p=0.043;HR 0.567;CI 0.328-0.981), neutrophil high cases with poorer survival (4.5 months, p<.001;HR 8.774;CI 2.739-28.101), compared to no-subtype (23.6 months)(independent of grade/BCLC/treatment).
Conclusion: Reliable reporting of HCC architectural patterns and histological subtypes typically requires large specimens (resection/explant) but reporting of these features may have value in diagnostic biopsies. The implementation of a proforma increased reporting of HCC pattern and subtype features, with prognostic associations for further evaluation in validation cohorts. This series will be used as a training cohort for the development of prognostic/predictive AI tools within the CRUK HUNTER and EU-funded THRIVE Consortia.

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E-PS-04-035
Feasibility of molecular tests in biliary tract cytology
A. Municchi*, F. Falcinelli, G. Volpi, E. Brunetto, G. Magliacane, M. Perin, L. Pecciarini, M. Rimini, P.G. Arcidiacono, M. Tacelli, M. Schiavo Lena, F. Pedica, M.G. Cangi
*Vita-Salute San Raffaele University, IRCCS San Raffaele Hospital, Pathology Unit, Milan, Italy, Italy

Background & objectives: Molecular testing for biliary tract malignancies has recently become mandatory in standard routine practice. Cytological samples may be the only available material for molecular analysis in patients who are unsuitable for surgery.
Methods: In the last two years, 113 patients received a diagnosis of bile duct adenocarcinoma through ultrasound-guided fine needle aspiration (FNA) cytology at our Institution. Herewith we present the results of molecular characterization, by both NGS and standard methods (FISH and RT-PCR), obtained from 8 patients, who were unsuitable for surgery.
Results: Seven out of eight cases underwent successful molecular characterization; one patients did not yield reliable results because of the low fraction of tumour cells. Most (6/7) patients showed molecular alterations. Importantly, four cases (57%) carried targetable markers: IDH1 pathogenic variant p.Arg132Cys, FGFR2 pathogenic variant p.Ser252Trp, HER2 amplification, and FGFR2 fusion. The patients were treated accordingly.
Conclusion: The diagnosis of bile duct adenocarcinoma routinely relies on FNA cytological samples at our Institution, where we are currently implementing molecular analysis on cytological samples for their selection to targeted therapy. Our results indicate that multiple molecular targets may be detected. The collection of adequate amount of cytological material is therefore critical for both accurate diagnosis and personalized treatment in patients not candidate to surgery.

E-PS-04-036
Validation of the prognostic significance of a newly proposed histological classification of pancreatic ductal adenocarcinoma with molecular relevance
D. Myoteri*, N. Paraskevopoulou, I. Grypari, K. Papadopoulos, E. Stoupi, I. Vlachos, V. Michalaki, C. Papadimitriou, A. Vezakis, M. Konstadoulakis, D. Tiniakos
*Aretaieion University Hospital, Greece

Background & objectives: Pancreatic ductal adenocarcinoma (PDAC) can be classified based on morphology into biologically relevant categories associated with known molecular subtypes. We aimed to validate the prognostic significance of this newly proposed morpho-molecular classification.
Methods: We reviewed tumour containing histological slides from 75 PDAC resection specimens performed in our centre between 2016-2021. Cases were assessed for the presence of four morphological patterns (conventional, tubulopapillary, squamous and composite) that grouped into two categories "gland forming" and "non-gland forming". Morphological patterns and tumour categories were correlated with clinical-pathological variables and patient overall survival.
Results: The 50-patients subgroup for whom follow up was assessed, included 9(19.6%) grade 1, 17(37%) grade 2, 20(43.5%) grade 3 and 12(24.5%) pT1, 25(51%) pT2, 10(20.4%) pT3 and 2(4.1%) pT4 cases. There were 31(62%) gland forming and 19(38%) non-gland forming PDAC, subclassified in 21(42%) with conventional, 10(20%) with tubulopapillary, 2(4%) with squamous and 17(34%) composite pattern. The non-gland forming category was positively correlated with higher tumour grade (r=0.435, p=0.003) and inversely correlated with the presence of pancreatic intraepithelial neoplasia-PanIN (r=-0.394, p=0.006). The two morphological categories and four morphological patterns did not correlate with overall survival (log rank test p=0.732 and p=0.843, respectively).
Conclusion: We have confirmed the applicability of the newly proposed binary morphological classification of PDAC. In our cohort the most common morphological category was "gland forming" with the majority of PDAC showing conventional pattern. The recently proposed

prognostic significance of the binary morphological classification has not been confirmed. Further studies in cohorts with larger number of cases with molecular subtyping are required to assess the prognostic implications of the morphomolecular classification of PDAC.

E-PS-04-037

Hepatic vascular tumours: understanding the spectrum of benign and malignant lesions

A. Nitu*, R.A. Barna, O. Vita, A. Jurescu, D. Herman, M. Iacob, R. Cornea, M. Cornianu
*Pathology Departament, "Pius Brinzeu" Emergency Country Clinical Hospital Timisoara, Romania

Background & objectives: Vascular liver tumours are mesenchymal lesions from endothelial cells. They vary from benign lesions such as hemangioma to rare malignant tumours such as hepatic epithelioid hemangioendothelioma and angiosarcoma. This study aims to examine the clinico-pathological profile of hepatic vascular tumours.
Methods: In this retrospective observational study, clinical and histopathological records of patients diagnosed with hepatic vascular tumours at Timisoara County Hospital were analysed from January 2013 to December 2023. Collected data included age at diagnosis, gender, clinical presentation, tumour localization, histological type, microscopic characteristics, and more.
Results: A total of 17 patients with hepatic vascular tumours were included in the study, comprising 12 women and 5 men. The mean age at diagnosis was 52 years (range 28-76), with a female predominance (84%). The study identified hemangiomas as the most common tumour type, along with three cases of hepatic epithelioid hemangioendothelioma, two cases of hepatic angiosarcoma, and one case of secondary (metastatic) hemangiopericytoma. Clinical presentations varied: three cases were suspected of metastases from intestinal tumours, possibly carcinoma; one was thought to be a gastrointestinal stromal tumour metastasis, and in two, a hydatid cyst was suspected. Primary liver tumours, some vascular, were suspected in the rest.
Conclusion: In conclusion, this study reaffirms the diverse spectrum of liver vascular tumours, ranging from benign hemangiomas to aggressive angiosarcomas. These tumours can manifest across ages, with a notable predisposition in women. Clinical presentations often mimic other lesions, emphasizing the need for improved diagnostic methods. Unlike hepatocellular or bile duct carcinomas, standardization is lacking in the diagnostic and therapeutic approach for vascular neoplasms, supporting the urgency for better clinical strategies in their identification and management.

E-PS-04-038

Liver metastasis of ovarian granulosa cell tumour: report of a rare case

B.G. Özamrak*, S. Ekmekci, M. Guner, H. Sahin
*Izmir Provincial Health Directorate, Izmir City Hospital, Department of Pathology, İzmir, Turkey

Background & objectives: Granulosa cell tumours (GCTs) are rare sex cord-stromal tumours (SCSTs). Although they have low-grade malignant potential, late recurrences can be encountered as pelvic/peritoneal dissemination, but distant metastases (to lung, brain, and liver) are also less commonly observed.
Methods: A 64-year-old female with a history of multiple surgeries and adjuvant chemotherapies due to an ovarian tumour was admitted after the detection of a liver mass during her follow-up visit, 11 years after her primary diagnosis. In 2023, PET-CT showed a hypodense subcapsular mass lesion of 90x84 mm with a heterogeneous appearance located at the right lobe of the liver.
Results: The patient had a history of total abdominal hysterectomy, bilateral salpingo-oophorectomy in 2012 due to ovarian SCST, and adjuvant chemotherapy. Later, in 2015, the patient underwent pelvic mass resection, followed by chemotherapy. The patient remained disease-free until 2019, then another recurrence was detected, and sigmoid colon and peritoneal implant resections were performed, followed by chemotherapy. After the detection of a large liver mass in the right lobe during her follow-up in 2023, she underwent a right hepatectomy procedure. Upon pathological examination of the specimen, a solid tumour of 12x7x6 cm, consisting of cells with "coffee bean-like" nuclear grooves, was observed. Immunophenotypic features helped confirm the diagnosis of GCT metastasis.
Conclusion: We report a rare case of GCT with late liver metastasis. Due to the patient's history, preoperative biopsy was not performed. Although GCTs are known to be low-grade malignant tumours with long disease-free periods, late recurrences may be observed. Clinicians should be aware that liver metastases may rarely be encountered, usually after long intervals, even raising the possibility of misdiagnosis with primary liver tumours. Therefore, long-term follow-up is required to monitor the treatment results and detect possible recurrences on time.

E-PS-04-039

Cholangiocarcinoma expressing Inhibin A, a mimicker of neuroendocrine tumours: a rare case of cholangioblastic variant of intrahepatic cholangiocarcinoma

B. Özcan*, S.K. Dursun, N. Dursun
*Basaksehir Cam and Sakura City Hospital, Turkey

Background & objectives: The cholangioblastic variant of cholangiocarcinoma is rare and typically occurs in young female adults. The pathologic features may mimic neuroendocrine or other tumours. The tumour cells are positive for biliary markers, inhibin, and have a novel recurrent gene fusion, NIPBL::NACC1.
Methods: A 22-year-old female, non-smoker and non-drinker, presented to the outpatient clinic with complaints of abdominal pain. She had no relevant medical or family history. Magnetic resonance imaging with contrast revealed a 25 cm diameter intrahepatic mass. A core liver biopsy was performed, which showed an adenocarcinoma composed of monotonous cells with eosinophilic cytoplasm. Immunohistochemical results supported the diagnosis of cholangiocarcinoma.
Results: Hepatectomy was performed. A solid mass lesion measuring 23x18x10 cm with focal cystic areas was detected. Histologically, the carcinoma displayed diverse architectural features, including trabecular, organoid, microcystic, and infiltrative glandular patterns, along with biphasic cytology featuring large, polygonal eosinophilic cells and smaller basophilic cells. Tubulocystic areas exhibited secretion. Immunohistochemically, the tumour showed diffuse labeling for Inhibin A, cytokeratin-7, and cytokeratin-19, with patchy labeling for chromogranin and synaptophysin. HepPar-1, arginase, glipican-3, and trypsin were negative. Next-generation sequencing identified various mutations, but unfortunately, the NIPBL::NACC1 gene was not included in the panel. Based on histomorphological and immunohistochemical findings, the case was diagnosed as "Cholangioblastic Variant of Intrahepatic Cholangiocarcinoma".
Conclusion: It is crucial to consider the cholangioblastic variant of intrahepatic cholangiocarcinoma when a large solitary liver mass in young patients encountered. These tumours often express neuroendocrine markers and exhibit a morphology similar to neuroendocrine tumours. In cases of bland cribriform liver masses in young adults, using Inhibin A could be helpful to prevent misdiagnoses. It is established that these tumours have a better prognosis than conventional cholangiocarcinomas and possess distinct molecular features. Therefore, making the correct diagnosis is essential.

E-PS-04-040

Clinicopathologic significance of quaking expression in hepatocellular carcinoma

C.K. Park*, S. Kim, J.W. Park, J.W. Lee, J. Choe, Y.A. Cho
*Seegene Medical Foundation, Republic of Korea

Background & objectives: The expression of RNA binding protein quaking (QKI) and its clinical implications have not been fully elucidated in hepatocellular carcinoma (HCC). In this study, we tried to investigate clinicopathologic and prognostic significance of QKI expression in HCC tissue specimens.
Methods: We performed QKI, zinc finger E-box-binding homeobox 1 (ZEB1), E-cadherin, and glutathione peroxidase 4 (GPX4) immunohistochemical staining in 166 HCC tissue samples. X-tile bio-informatics software was used to set cut-off value for high QKI expression. Clinicopathologic correlation between QKI expression and various clinicopathological parameters was assessed.
Results: The best cut-off value for high QKI expression was 12.5. High QKI expression was observed in 28 out of 166 patients (16.9%) and revealed as an independent prognostic factor for inferior recurrence-free survival (RFS). In addition, high ZEB1 expression and high GPX4 expression was correlated with high QKI expression, but not with the loss of E-cadherin expression.
Conclusion: We identified high QKI expression in HCCs and its association with poor RFS. QKI might be a prognostic biomarker of HCCs, related with epithelial-to-mesenchymal transition, and could be a potential candidate for therapeutic target.

E-PS-04-041

Fibrin-associated large B-cell lymphoma (FA-LBCL): report of two cases presented as abdominal pseudocysts with immunohistochemical and molecular study

A. Petit*, G. Ippoliti, J. Azcarate, J. Bosch, N. Fullana, A. Domingo, T. Serrano, N. Ruiz, X. SanJuan, E. Ramos, L. Secanella, E. Gonzalez-Barca, G. Rivera, F. Climent
*Departament d´Anatomia Patològica. Hospital Universitari de Bellvitge. Idibell, Spain

Background & objectives: FA-LBCL is a rare neoplasm of large B-cells found incidentally at sites of chronic fibrin deposition in confined natural or acquired anatomic spaces.
Methods: We report two cases of FA-LBCL presenting as abdominal pseudocysts involving the liver and the adrenal gland detailing its clinicopathologic characteristics and its immunohistochemical and molecular profile.
Results: Two immunocompetent women aged 61 and 55 presented with cystic lesions of 15cm and 11cm detected on imaging studies after abdominal pain. Histopathologically they consisted on pseudocysts with abundant fibrinous material. Large atypical lymphoid cells were admixed with fibrin. They were positive for CD20, PAX5, CD79a, CD30, MUM1, BCL2, and EBV-in situ hybridization and negative for T-cell markers, CD10, BCL6, and C-myc. EB-LMP1 and EBNA2 were positive. No rearrangements (BCL2,BCL6 and MYC) were found. Next Generation Sequencing Analysis (Ampliseq Lymphoid panel v2,ThermoFisher) detected no mutations in one case. Both patients remain free of disease after management with complete surgical resection and close follow-up after 2 years and 6 months respectively.
Conclusion: Although they are very rare, FA-LBCL are diagnostic challenging neoplasms that should be kept in mind whenever facing an abdominal cystic lesion with fibrin inside. The clinicopathological characteristics found in the two cases reported are similar to the ones described in the literature with a non-germinal centre phenotype and association with EBV infection with type III latency.

E-PS-04-043

Pancreatic adenocarcinoma associated with intraductal papillary mucinous neoplasm: a case series

A. Prat*, D. Piñol, I. Espadaler, I. Campazas, I. Espinosa, V. Fusté, J. Szafranska, C. Fumagalli
*Hospital of Santa Creu and Sant Pau, Spain

Background & objectives: Pancreatic adenocarcinoma (PAC) arising from intraductal papillary mucinous neoplasm (IPMN) (PAC-IPMN) is reported to have better prognosis compared to conventional adenocarcinoma. Aim of the study was evaluating clinical and pathologic characteristics of a case series of PAC-IPMN.
Methods: 14 consecutive cases of PAC-IPMN diagnosed between 2017-2023 were selected, including 6 women and 8 men with a median age of 72years-old and a median follow-up of 15months. Demographics, tumour features, molecular studies and patients' follow-up were collected. A descriptive comparison between dead (A) and alive (B) groups was additionally performed.
Results: 64% of IPMN involved both main and branch duct and 50% showed both pancreatobiliary and gastric cell differentiation pattern. PAC (median size: 2,7cm) was predominantly located in the head. Comparison between A and B groups (6 and 8 patients respectively) showed similar age (71vs72years-old) and tumour size (2,5vs2,8cm). 83% in group-A presented both ganglionar and metastatic disease, in contrast to 63% and 37% of group-B. Perineural invasion was present in 83% of group-A and 75% of group-B. Mucinous tumours and G1-PAC belonged to group-B. The other data didn't show differences between the groups. Due to the limited cohort, statistical analysis had not been performed.
Conclusion: Our study showed that perineural invasion, ganglionar or distant metastatic disease along with a high histologic grade (G2-G3) are factors frequently present in patients who died for PAC-IPMN. In these cases, it seems that the behaviour of PAC-IPMN is similar to conventional PAC, as reported in literature, probably due to advanced stage of the disease. More studies are needed to find which factors are related with poor prognosis in PAC-IPMN.

E-PS-04-044

Intrahepatic inflammatory myofibroblastic tumour with features of IgG4-related disease & elevated serum CA 19-9 – a diagnostic challenge

N. Radhakrishnan*, S. Naskar, S.M. Kamath, N.A.R. Rao, S.A.A. Moger, C.D. Wilfred, P.P. Kasukurti
*Department of Pathology, Ramaiah Medical College, Bengaluru, India

Background & objectives: IgG4-related disease (IgG4RD) usually involves multiple organs and often presents tumefactive lesions. Inflammatory myofibroblastic tumour (IMT) and IgG4-related inflammatory pseudotumours (IPT) share common clinicopathological features, but differentiating between them is important for a pathologist since their treatment modalities can differ.
Methods: A 46-year-old woman presented with upper abdominal pain for 3 weeks and markedly elevated serum CA 19-9 levels (>1000 u/mL). Imaging studies revealed pericholecystic edema/collection/lesion involving segment 4 of the liver and calculous cholecystitis, prompting suspicion of malignancy. She underwent cholecystectomy and segmental liver resection. Specimen received for histopathological examination.
Results: Histopathological and immunohistochemical analyses of the specimen identified a spindle cell lesion with focal nuclear atypia. Immunohistochemical study revealed the spindle cells are positive for SMA and calponin, and negative for ALK1. The spindle cells

were surrounded by dense aggregates lymphocytes and plasma cells, with plasma cells showing IgG4 (~60/HPF) and IgG (~125/HPF) positivity in hotspot regions. Additionally, areas of fibrosis, phlebitis and xanthogranulomatous reaction with bile ductular proliferation were observed. The final diagnosis was an "ALK1-negative IMT with overlapping features of IgG4-RD". Molecular studies for ALK1 gene mutation and serum IgG4 estimation were not conducted due to logistical and financial constraints. Patient is doing well 6 months post-surgery.
Conclusion: While both IgG4-RD and IMT share immunomorphological features, they can often be distinguished through strict criteria. Yet, there are cases, like ours, where distinguishing between the two becomes challenging due to overlapping characteristics. Most IMT cases show ALK-1 expression; however, our case is among the 40% lacking ALK-1 immunopositivity. A xanthogranulomatous reaction might initiate IMT/IPT development. IMT and IgG4-RD can resemble each other. Chronic cholecystitis and bile inflammation could trigger IMT. High CA 19-9 levels don't always indicate carcinoma.

E-PS-04-046
The liver in adult polycystic liver disease (ADPKD): analysis of morphologic characteristics of 38 cases describing intercystic parenchyma
Y. Rodriguez-Gil*, M. Veras, D. Curto Aguilera, C. Prados
*Hospital Univ 12 de octubre, Spain

Background & objectives: "Fibropolycystic diseases' of the liver are a group of heterogeneous disorders, the most frequent is ADPKD. It is known that cysts are lined by a simple biliary epithelium. But few descriptions have been made about intercystic parenchyma.
Methods: In order to describe morphologic findings in intercystic liver parenchyma from patients with ADPKD and correlate those findings with clinical presentation and evolution, we have reviewed the biopsies and clinical records of all the patients with ADPKD and available biopsy in our centre, managed during 24 years.We found 38 patients with diangosis of ADPKD and biopsies or surgical specimens available.
Results: We review slides and clinical records of 38 patient diagnosed of ADPKD. Sex distribution was equitative (18F:18M). Age ranged 44-93 yo(median 68). Only 18/38 (47%) underwent transplant, 13/18 caused by liver complications, and 5/18 in combined liver-kidney transplantation. Native liver weight ranged 860–15,770 g. Morphological intercystic parenchymal changes were related to different pathogenic mechanisms. Nodular regenerative hyperplasia (NRH) was in 5/18 (27%) native livers, 2/18 cases (11%) showed incomplete septal cirrhosis, micronodular cirrhotic changes were present in 8/18 (44%) associated to (4/8 HVC, 1/8 HVB, 1/8NASH, 2/8 Alcoholic-SH), only 3 cases had isolated compressive parenchymal changes without nodularity or fibrosis. All cases showed many microharmatomas (Von meyenburg complexes).
Conclusion: ARPKD usually manifests clinically as asymptomatic liver enlargement,well tolerated. Conservative management was posible in most cases (20/38). Although normal intercystic parenchyma is described for these patients, we found only 3/18 (16%) patients without significative intercystic fibrosis. Most severe cases showed micronodular cirrhosis caused by comorbidities (HVC, HVB, NASH and alcohol). Other frequent findings were NHR, probably caused by vascular compression and incomplete septal cirrhosis probably multifactorial (vascular-biliar compression-ischemia,alcohol and others).Intercystic parenchymal lesions help to predict the appropiate moment for intervention and complications.

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E-PS-04-047
Undifferentiated carcinoma with osteoclast-like giant cells of pancreas: 3 case reports
I. S. Nair*, S. Nair P, R. S, A. Suresh Kumar, E. Joy
*Regional Cancer Centre, Thiruvananthapuram, India

Background & objectives: Undifferentiated carcinoma with osteoclast-like giant cells (UC-OGC) is a rare and unique malignant neoplasm of pancreas with around one hundred cases reported in English literature so far.The pathogenesis and clinical course is still unclear needing more extensive clinicopathological studies.
Methods: A retrospective analysis in our department identified 3 cases of UC-OGC reported between January 2017 and February 2024. The morphological characteristics were analysed by reviewing the hematoxylin and eosin slides along with its immunohistochemistry. Clinical details were attained from patient charts.
Results: Case 1: 61 female with chronic pancreatitis (7 years),on imaging showed a 7 cm mass involving body and tail of pancreas.Microscopy showed UC-OGC with an associated mucinous cystic neoplasm. Case 2: 46 female, with abdominal pain,episodes of hypoglycemia and 7.6cm mass in head of pancreas.Case 3: 47 male with abdominal pain (2 months) and 3.9cm mass in uncinate process of pancreas.Histology-UC-OGC with associated ductal adenocarcinoma.Immunohistochemistry: CK highlighted epithelial component, CD68 positivity noted in mononuclear histiocytes and osteoclastic giant cells.
Two inoperable cases received chemotherapy alone and 1 case had chemotherapy following surgery.On follow up, all three cases are alive with one case showing metastasis to liver at the time of diagnosis.
Conclusion: Presence of giant cells in a pancreatic lesion should enable a pathologist to rule out this entity as it can behave unexpectedly well compared to conventional pancreatic adenocarcinoma.Early accurate diagnosis with long-term follow-up can contribute in standardisation of its treatment and prognostic variables.

E-PS-04-048
Tumour budding in pre-neoadjuvant biopsy and post-neoadjuvant resection specimen is associated with poor prognosis in intrahepatic cholangiocarcinoma - a cohort study of 147 cases by modified ITBCC criteria
R. Shi*, G. Wu, R. Luo, L. Yang, Q. Gao, K. Zhu
*Singapore General Hospital, Singapore

Background & objectives: Tumour budding (TB) has been associated with poor survival in a variety of cancers including. Our study aims to assess the prognostic significance of TB in pre- and post-NAT intrahepatic cholangiocarcinoma, by modified International Tumour Budding Consensus Conference (ITBCC) criteria.
Methods: A total of 147 intrahepatic cholangiocarcinoma (iCCA) patients who received NAT and underwent surgery in our centre between 2019 and 2023 were included. For biopsy specimen, we used the receiver operating characteristic (ROC) curve to determine the best cut-off value of TB counts to predict survival. For the resection specimen, we graded TB count based on modified ITBCC criteria.
Results: In pre-NAT biopsy cohort, TB-positive subgroup had lower overall survival (OS) in univariate analysis (hazard ratio [HR]: 3.101; 95% confidence interval [CI]: 1.303-7.382, P = 0.011). In post-NAT resection cohort, TB-positive subgroup had reduced OS (OS: HR: 3.491; 95% CI: 1.611-7.567, P = 0.002) and recurrence-free survival (RFS) (HR: 1.772; 95% CI: 1.126-2.789, P = 0.013) in univariate analysis. In multivariate analysis including ypTNM stages, microvascular invasion and perineural invasion, TB-positive in post-NAT resection was also found as an independent prognostic factor for both OS and RFS (OS: HR: 2.768; 95% CI: 1.228-6.239, P=0.014; RFS: HR: 1.748; 95% CI: 1.085-2.816, P = 0.022).

Conclusion: In conclusion, assessing TB positivity by modified ITBCC criteria provides robust prognostic information in the NAT setting of iCCA and can be considered to be included in the routine pathological reporting.

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E-PS-04-049

Squamous cell carcinoma of the gallbladder and extrahepatic bile ducts: a rare entity

J. Sobreiro Furtado Silva*, M. Ferreira
*Unidade Local de Saúde de Braga, Portugal

Background & objectives: Squamous Cell Carcinoma (SCC) of the gallbladder and extrahepatic bile ducts is considered a rare entity. We describe one case of SCC of the gallbladder and one of the extrahepatic bile ducts and discuss their clinical and pathological features.
Methods: Patient 1 – 58-year-old woman with a common bile duct cyst known for 17 years presents on control cholangioMRI with thickening of its wall. Patient 2 – 67-year-old woman presenting with asthenia, anorexia, anemia and weight loss was diagnosed with a gallbladder mass.
Results: Both patients underwent cholecystectomy, liver resection and regional lymphadenectomy with per operative histological examination.
Patient 1 – On gross examination, a 1,5x1,0cm white mass involved the common bile duct.
Patient 2 – On gross examination, a 10,4x10cm white mass involved the gallbladder and the liver.
Microscopically, they were composed of variably differentiated squamous cell nests with presence of lamellar keratin. Immunohistochemistry was performed and there was diffuse immunoreactivity for p40 antibody.
Both cases had R0 margins, and no lymph nodes or distant metastasis were found.
Patient 1 is alive and disease free for five years.
Patient 2 had surgical complications and hasn't started adjuvant therapy yet.
Conclusion: Pure SCC represents a rare subtype of carcinoma of the gallbladder and extrahepatic bile ducts. Its recognition is crucial given the better outcome and potential cure of these patients when identified early.

E-PS-04-050

An extremely rare case report: the coexistence of gallbladder carcinoma developed from ICPN and lobular breast carcinoma metastasis to the gallbladder

C. Sönmez*, E.B. Balaban, M. Çıkrıkçıoğlu, F. Aker
*Hatay Defne State Hospital, Department of Pathology, Turkey

Background & objectives: Metastasis to the gallbladder is extremely rare. Here we report a case that has the coexistence of gallbladder carcinoma within intracholecystic papillary neoplasm (ICPN) and metastasis of breast lobular carcinoma to the gallbladder.
Methods: An 83 year old female patient applied to the hospital with abdominal pain. In her medical history, she had breast carcinoma with extensive bone and pleural metastasis. MRI showed a 19x11mm lobule contoured polypoid lesion in the gallbladder with diffuse contrast enhancement. The patient underwent cholecystectomy.
Results: Gross examination revealed a 1 cm polypoid lesion in the gallbladder and diffuse erosion of the mucosa. Histopathologic examination revealed back-to-back epithelial units in papillary and tubular configuration in areas corresponding to the polypoid lesion. The lesion showed architectural complexity with severe dysplasia. An invasion in the lamina propria was observed in the one microscopic focus within the polyp. In addition, poorly cohesive cell infiltration was observed in the periconnective fibrous tissue unrelated to these lesions. Immunohistochemical examination showed positive staining with GATA-3 in weakly cohesive cells and no staining in polyps and invasive carcinoma areas within polyps.
Conclusion: The coexistence of both invasive carcinoma in the background of ICPN and invasive lobular breast carcinoma metastasizing to the gallbladder is extremely rare. It may lead to misdiagnosis when the clinical information of the patient is unnoticed. When gallbladder neoplasm is seen with dysplasia as in our case, the possibility of metastasis may not be considered. Therefore, it is very important to know the clinical and radiologic features of the patient.

E-PS-04-051

A case report of follicular pancreatitis with pancreatic islet cell hyperplasia

E. Spiteri*, E. Gioti, P. Vlachou, A. Mellou, O. Kouroukli, D. Efthymiou, C. Vourlakou
*Department of Pathology, Evangelismos General Hospital, Athens, Greece

Background & objectives: Follicular pancreatitis is a rare variant of chronic pancreatitis, which can appear as a mass lesion, thus mimicking a pancreatic neoplasm. We present a case of a 58-year-old male diagnosed with follicular pancreatitis combined with reactive pancreatic islet cell hyperplasia.
Methods: We received a pancreatoduodenectomy (Whipple) specimen with the clinical and radiological diagnosis of pancreatic carcinoma, lacking a previous biopsy. The frozen section was answered as "chronic pancreatitis". The pancreatic parenchyma was entirely submitted serially and the slides examined were stained with hematoxylin / eosin. Numerous immunohistochemical markers were also used.
Results: Macroscopically the cut surface of the pancreas showed a nodular white to tan grey sclerotic lesion. Histologic examination revealed medium lymphoplasmacytic infiltration and numerous variable-sized lymphoid follicles with reactive germinal centre diffusely distributed amidst atrophic pancreatic acini, ductal atrophy and medium to severe stromal fibrosis. The germinal centres showed positivity for Bcl-6 and negativity for Bcl-2 immunohistochemical markers. No increase of IgG4-positive plasma cells was observed.
Simultaneously, amongst the atrophic acini, the pancreatic isle cells seemed hyperplastic, mimicking neuroendocrine neoplasm. Supplementary immunohistochemical markers were performed. The islets were composed of different cells positive for either somatostatin, glucagon, insulin or PP, thus excluding the possibility of a neuroendocrine tumour.
Conclusion: Follicular pancreatitis as it appears in this case often mimics pancreatic neoplasm both clinically and radiologically. Conducting a biopsy prior to the surgery should prevent overtreatment of the patient. Moreover chronic pancreatitis in general is often accompanied by pseudoencrocrine hyperplasia of the islet cells, giving the impression of a neuroendocrine neoplasm. This case includes both mimickers of neoplastic lesions, making it a rare and interesting combination.

E-PS-04-052

The possible clinical importance of co-expression of VSIG1, TTF-1 and vimentin in hepatocellular carcinoma

R. Szodorai*, I. Jung, L. Banias, I. Kovalszky, K. Dezső, Z. Kovács, S. Gurzu
*George Emil Palade University of Medicine, Pharmacy, Science and Technology, Targu Mures, Romania

Background & objectives: The expression of V-set and immunoglobulin domain containing 1 (VSIG1), thyroid transcription factor 1 (TTF-1), and Vimentin (VIM) triad in hepatocellular carcinomas (HCCs) remains unidentified. The aim of the study is to examine the possible clinical importance of their interaction.
Methods: The immunohistochemical expression of VSIG1, TTF1, and VIM was checked on 217 paraffin-embedded tissue samples from patients diagnosed with HCC, correlating them with clinico-pathological parameters
Results: VSIG1 positivity was observed in 113 out of 217 HCC cases (52.07%). Co-expression of VSIG1 and cytoplasmic TTF-1 was observed in 71 cases (32.71%). VIM positivity was identified in 36 cases (16.58%). VSIG1 expression showed a positive correlation with TTF-1 expression and a negative correlation with VIM ($p < 0.0001$). The overexpression of VIM was associated with poor survival outcomes. "Gastric-type HCC," defined by double positivity for VSIG1 and TTF-1, proved to not express VIM. This subtype was identified in 52 cases (23.96%), mainly differentiated (G1/G2) carcinomas. Conversely, triple-negative HCC was observed in 56 cases (25.80%), being predominantly associated with high-grade (G3/G4) HCCs.
Conclusion: The co-expression of VSIG1 and TTF-1 may serve as a favourable prognostic factor, indicating improved overall survival rates, for patients diagnosed with HCC. Conversely, the overexpression of VIM indicates a poorer prognosis. These findings suggest that evaluating the expression of these three markers could serve as valuable prognostic indicators for patients with HCC.

E-PS-04-053
Revisiting solid pseudopapillary neoplasm of pancreas: a detailed clinicopathological and immunohistochemical evaluation
A. Tandon*, R. Yadav, P. Das, A. Narayan, S. Pal
*All India Institute of Medical Sciences, New Delhi, India

Background & objectives: Solid pseudopapillary neoplasm (SPN) of pancreas is an uncommon entity with low malignant potential. Varied clinical features and histopathological patterns make SPN a challenging diagnosis. We aimed to evaluate the clinicopathological and immunohistochemical profile of SPNs.
Methods: All the cases of SPN diagnosed over a period of last 9 years at our institute, were retrieved and reviewed for various clinical parameters. A comprehensive histopathological evaluation using structured proforma was done. Immunohistochemistry for chromogranin, synaptophysin, LEF1 and β-catenin was performed and expression patterns were analysed. Cases of neuroendocrine neoplasms (NENs) were included for comparison.
Results: 60 cases of SPN were studied including 55 females and 5 males, ranging from 12-69 years. Tumour size varied from 2 to 16 cm with majority located in tail of pancreas. Most patients had localized disease. Tumours showed irregular tumour borders with cells arranged in pseudopapillae followed by solid nested pattern. The tumour cells were uniform with pale, eosinophilic cytoplasm, round small nuclei, frequently demonstrating rosettes. Secondary stromal changes included hyalinization, cystic degeneration, foamy macrophages and cholesterol clefts. On immunohistochemistry, strong nuclear expression for β-catenin (100%) and LEF1 (100%) with negative staining for chromogranin (100%) helped rule out the differentials as synaptophysin (13.3%) showed focal expression in SPNs.
Conclusion: SPNs can frequently mimic NENs in young individuals and children. Morphological features overlap for these lesions. Synaptophysin expression may be seen in both tumours. A diligent histopathological evaluation and an immunohistochemical panel consisting of chromogranin, β-catenin and LEF1 can differentiate these entities well. An accurate diagnosis is important as the relative indolent behaviour of SPNs can be managed with only surgical resection, even when large in size, bringing excellent long-term outcomes as compared to NENs.

E-PS-04-054
Declining utility of intraoperative pathology consultations for assessment of margins during whipple surgeries in an academic institution over six years
T. Truong*, E. Olkhov-Mitsel, N. Sina, L. Chen, N. Coburn, P. Karanicolas, L. Sun, P. Roopchand, T. Jorden, C. Rowsell
*Precision Diagnostics and Therapeutics Program, Sunnybrook Health Sciences Centre, Toronto, Department of Laboratory Medicine and Pathobiology, University of Toronto, Canada

Background & objectives: Intraoperative consultations (IOCs) practice for pancreatic resections vary widely among institutions and surgeons. During its initial phase (2018-2020), our study found IOCs did not improve postoperative-R0 rates. We now assess IOCs for Whipple surgeries over six years at our institution.
Methods: Retrospective review of all patients who underwent pancreaticoduodenectomy (Whipple) at our institution was performed in 2 phases; 2018-2020 and 2021-2023. Initial phase (2018-2020) findings were presented and followed by an initiation of phase II (2021-2023). Pathological data was recorded, comparing the total number of Whipple surgeries with corresponding IOC margins requested by in house surgeons.
Results: 437 Whipple surgeries were performed by 4 surgeons at our institution: 212 from 2018-2020 and 225 from 2021-2023 (P=0.674). IOCs were completed for 186 (42.6%) Whipple surgeries; 108 in 2018-2020 and 78 in 2021-2023. Differences in IOC utilization were investigated among surgeons. Surgeon I performed 129 Whipple surgeries (29.5%), Surgeon II 100 (22.9%), Surgeon III 125 (28.6%), Surgeon IV 83 (19.0%). IOC utilization significantly varied among surgeons: Surgeon I 80.3% (2018-2020) and 65.1% (2021-2023); Surgeon II, 20.4% and 19.6%; Surgeon III, 46.6% and 14.9%; Surgeon IV, 50.0% and 36.7% (P<0.001). IOC requests for Whipple surgeries decreased by 16.3% from 2018-2020 (50.9%) to 2021-2023 (34.7%; P<0.001), following the initial phase study.
Conclusion: Our preliminary findings indicate that although a significant variability persists in the frequency of IOCs requested for margins among surgeons, there is an overall significant reduction in IOCs requested for Whipple surgeries at our institution over the two periods of study. Further reviews of individual cases are warranted to ascertain the necessity of IOC requests within this patient cohort.

E-PS-04-055
Identification of cribriform and micropapillary components predicts poor prognosis in patients with pancreatic ductal adenocarcinoma
C. Utku*, D.D. Ekizalioglu, G. Serin, T. Gumus, F. Yilmaz, D. Nart
*Department of Pathology, Ege University School of Medicine, Turkey

Background & objectives: Pancreatic ductal adenocarcinoma is an aggressive malignant neoplasm that can include various morphological components. Cribriform and micropapillary patterns have been associated with poor prognosis in lung adenocarcinomas. We aimed to investigate the association of these components with prognosis in PDAC.
Methods: A total of 71 primary PDAC cases, resected and untreated preoperatively between 2016 and 2023, were re-examined to determine the percentages of morphological components. The relationship between survival and clinicopathological parameters of cases with a cribriform and micropapillary pattern rate of 20% or higher was analysed.
Results: In 29.6% of cases (n=21), the cribriform or micropapillary pattern was observed at 20% or higher. Among these, the mean age was 65.6 (51-87), and 8 of the cases were female. The 1-year survival rate was 69.8% for those with pattern <20% (n=50), while for those with pattern ≥20%, this rate was 40.2% (n=21). Overall, the median survival time was 15 months (±1.9, 95% CI = 11-19), 8 months for

≥20% (±3.1, 95% CI = 1.7-14.2), and 18 months for <20% pattern (±3.5, 95% CI = 11-25). A lower survival rate was observed in the group with pattern ≥20%, and this difference was statistically significant (p=0.015).
Conclusion: Recent studies have shown that micropapillary and cribriform patterns are prognostically worse in lung adenocarcinomas. It is known that the invasive micropapillary subtype in PDAC (micropapillary pattern ≥50%) has a worse prognosis. According to the results of our study, having a cribriform or micropapillary pattern ≥20% is associated with poor prognostic outcomes.

E-PS-04-056
TRPS1 expression in pancreatic adenocarcinoma: a potential pitfall
C. Utku*, T. Zhang, M. Robert, J. Misdraji, I. Nalbantoglu
*Department of Pathology, Ege University School of Medicine, Turkey

Background & objectives: TRPS1 has emerged as a sensitive and specific marker for breast cancer which is negative in pancreatic adenocarcinomas (PDAC). However, the human protein atlas lists TRPS1 as a marker of unfavourable prognosis in PDAC. TRPS1 expression in PDAC was investigated.
Methods: Immunohistochemical staining for TRPS1 was performed on tissue microarrays (TMA) of 18 PDAC cases. Additionally, five PDAC resection slides were stained. Nuclear staining of TRPS1 was considered positive. Immunoreactivity scores were determined by multiplying the percentage of immunoreactive cells and intensity. Slides were reviewed independently by two pathologists and scored as negative, low, intermediate, or strong positive.
Results: The staining pattern in resections displayed greater heterogeneity, with the background pancreas also revealing weak staining in islets and acini. Cytoplasmic interference and background stromal staining were noted in a subset. Of the 30 samples (25 TMA, 5 resections), 80% tested positive. Among these, 15 were classified as strongly positive (50%), 4 as intermediate positive (13%), and 5 as weakly positive (17%). Additionally, 6 samples tested negative (20%).
Conclusion: Our study suggests that TRPS1 is strongly expressed in 50% of PDAC samples, challenging the initial notion of its rarity. Therefore caution is warranted when interpreting TRPS1 positivity, especially in cases of metastatic adenocarcinoma of unknown primary origin, as misinterpretations could lead to erroneous conclusions regarding breast origin. Pathologists should exercise diligence to avoid potential pitfalls in diagnosis. Further research is needed to refine the clinical utility of TRPS1 in distinguishing PDAC from other malignancies, especially in the liver.

E-PS-04-057
Impact of mitochondrial stress on the prognosis of acute T-cell-mediated liver transplant rejection: a decade of insights (2011-2020)
S. Yağcı*, P. Bayık, B. Özdemir, G. Özgün, M. Haberal
*Department of Pathology, Baskent University, Faculty of Medicine, Ankara, Turkey

Background & objectives: Mitochondrial dynamics and mitophagy play crucial roles in liver diseases but remain understudied in liver allografts experiencing T-cell-mediated rejection (TCMR). This study aims to explore the impact of mitochondrial stress and mitophagy on liver transplant patients diagnosed with acute TCMR.
Methods: Sixty-six TCMR-diagnosed recipients were studied, analyzing 132 biopsies—66 initial, 66 follow-ups. Immunohistochemical staining for OPA1 and PINK1 assessed mitophagy in hepatocytes, bile ducts, and inflammatory cells, with additional PINK1 evaluation in sinusoids. The histopathological and immunohistochemical differences between the initial and follow-up biopsies correlated with concurrently measured liver function tests, fibrosis and steatosis development, along with graft and patient survival.
Results: Persistently elevated serum AST, ALT, and GGT levels (p<0.001, p<0.001, p=0.006 respectively), alongside new fibrosis and steatosis development (p<0.001), were associated with shorter 10-year survival in follow-up biopsies, despite an unchanged total RAI score (p=0.003). Increased OPA1 staining in hepatocytes associated with more lobular necrosis, new steatosis, and fibrosis development (p<0.014, p<0.001, p<0.001 respectively). Elevated PINK1 staining in inflammatory cells and sinusoids was linked to enhanced lobular necrosis, ongoing lobular inflammation, cholestasis, and new steatosis and fibrosis development (p=0.021, p=0.034, p=0.034, p=0.003, p=0.041 respectively). Additionally, higher percentages of OPA1 and PINK1 staining in hepatocytes, inflammatory cells, and sinusoids (p<0.001, p<0.001, p=0.001 respectively) were associated with prolonged 10-year survival.
Conclusion: As our knowledge, no similar study has investigated the impact of mitochondrial stress on graft survival after liver transplantation, making our study pioneering in this field. In conclusion, our study suggests that mitochondrial stress and dynamics in post-liver transplant follow-up can significantly influence post-transplant prognosis and survival. These findings provide a crucial foundation for future research and clinical applications in the field of liver transplantation.

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E-PS-04-058
Exploring the prognostic significance of Epithelial-Mesenchymal Transition (EMT) in Pancreatic Ductal Adenocarcinoma (PDAC): insights into EMT morphology, the Lysyl oxidase-like 2 (LOXL2) protein expression and in silico analysis of GATA binding protein 6 (GATA6)
E. Yumuk*, Ö. Sağol, A. Aysal Ağalar
*Gaziantep City Hospital, Gaziantep, Turkey

Background & objectives: Pancreatic Ductal Adenocarcinoma(PDAC) has a dismal prognosis and limited treatment options. EMT is a complex process, promoting invasion and metastasis. Our study investigates the role of EMT-related morphological features, LOXL2 expression and GATA-6 transcription factor involved in EMT in prognosis.
Methods: In this study, 100 cases diagnosed with PDAC were included. Clinical and pathological parameters from tissue sections were examined. The relationship between EMT-related morphological features and Keratin, Vimentin, E-cadherin and LOXL2 immunohistochemical expressions with prognostic factors was investigated. Additionally, genes and mRNAs involved in EMT associated with GATA6 copy number changes in PDAC cases were analysed from cbioportal.org databases.
Results: The median survival time in our PDAC patients were 35.7 months. Overall survival was significantly shorter in patients with tumour budding (TB), larger cell nests beyond tumour budding (LCN), mesenchymal phenotype (MP) and necrosis (p<0.001). The presence of necrosis is an independent negative prognostic factor for overall survival and disease-free survival (p=0.023, p=0.015). Poor differentiation (p=0.002), positive surgical margins (p=0.001), lymphovascular invasion (p=0.037) and E-Cadherin loss (p=0.028) were associated with shorter survival. LOXL2 expression is not associated with survival. Four EMT-associated genes were identified in GATA6 copy number changes. These genes are statistically associated with subtype classification of PDAC and maintenance of the epithelial layer.
Conclusion: Tumour budding which a potential indicator of EMT, statistically correlated with LCN, MP, and necrosis, and all 4 morphological findings are associated with shorter survival. Evaluating

these 4 findings together may indicate EMT. Necrosis is an independent negative prognostic factor and very important to be noted in pathology reports. The relationship between LOXL2, EMT, and survival was not demonstrated in this study. GATA6 expression is associated with 18q gain and regulates EMT processes through various mRNA expression and gene changes.

E-PS-04-059

Mucinous adenocarcinoma of the gall bladder: a rare incidental finding

A.C. Pop*, M. Muresan, A. Orosz, S.-.A. Vese, A. Vigdorovits, A. Camarasan, A. Pascalau, O. Pop
*University of Oradea, Romania

Background & objectives: Mucinous adenocarcinoma of the gallbladder is a rare tumour that accounts for less than 5% of gallbladder malignancies. We report the case of a 74-year-old woman who was diagnosed with a mucinous adenocarcinoma incidentally after a routine cholecystectomy.
Methods: History and physical examination were performed and subsequently the patient underwent laparoscopic cholecystectomy. Routine H&E stained-slides were obtained, after which immunohistochemical analysis for CDX2, CK7, CK20, CEA (COL-1) was performed.
Results: The pacient had a history of cholecystitis. The current episode prompted his visit to the physician. Intraoperatively, multiple peritoneal adhesions were identified and the gallbladder was enlarged. On gross analysis, the gallbladder had thickened walls and upon the inspection of the mucosa, an exophytic mass was identified. Microscopy revealed that the tumour was mainly composed of glandular structures floating in pools of mucin that comprised more than 50% of the lesion. Immunohistochemical analysis revealed the following profile: CDX2 +, CK7 +, CK20 + , CEA(COL-1) +.
Conclusion: This case highlights the importance of careful histological examination of the gallbladder after routine cholecystectomy as well as the diagnostic approach when confronted with rare malignancies at this level.

E-PS-05E-Poster Session Endocrine Pathology

E-PS-05-001

Primary small cell carcinoma of the thyroid without medullary thyroid carcinoma features

J.C. Almeida*, C. Costa, P. Amoroso Canão, J. Cameselle Teijeiro, M. Sobrinho-Simões
*Department of Pathology, Centro Hospitalar Universitário de São João (CHUSJ), Porto, Portugal; Faculty of Medicine of the University of Porto (FMUP), Porto, Portugal

Background & objectives: Small cell carcinoma (SCC) of the thyroid is an aggressive entity with extremely rare cases described to date. We report a primary thyroid SCC and review the respective literature.
Methods: A HIV positive 54-year-old woman presented with a rapid growing cervical 7cm mass causing compressive symptoms, associated with cervical lymphadenopathies. Fine-needle aspiration was performed and serum biomarkers levels were evaluated. No any other masses were detected in the staging workup procedures. The patient underwent neoadjuvant chemotherapy prior to surgical resection. Total thyroidectomy and bilateral/central lymphadenectomy were performed.
Results: Fine-needle aspiration showed a hypercellular smear composed of neoplastic cells with high nuclear-cytoplasmatic ratio, granular chromatin, nuclear molding, frequent mitoses and apoptotic bodies. The surgical specimen revealed infiltration of the thyroid gland and adjacent soft tissue by a solid/nested pattern neoplasia without amyloid deposition. All lymph node compartments were involved. Immunohistochemistry studies showed AE1/AE3, CK8/18, CD56, synaptophysin, chromogranin, CEA and TTF1 positivity, without calcitonin, CGRP, thyroglobulin, PAX8 and CK20 immunoreactivity. Calcitonin serum levels were not elevated. A diagnosis of SCC was rendered. Molecular study revealed exon 3 c.345T>A mutation of EGFR gene (uncertain significance). Patient underwent subsequent radiotherapy and is alive 5-months after surgery, with local and disseminated disease.
Conclusion: This case highlights the diagnostic problems of thyroid SCC with neuroendocrine differentiation and no immunoreactivity for calcitonin and CGRP. There are only few cases reported in the literature, with different terminology, limiting the characterization of this rare entity. In order to distinguish primary from metastatic origin the diagnosis relies on histopathology and clinical staging workup procedures. Further research is necessary to improve the clarification of putative origin of SCC, provided one can rule out its relationship with medullary thyroid carcinoma.

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E-PS-05-003

Composite pheochromocytoma - presentation of two cases with molecular study

A. Azueta Etxebarria*, D. Rodriguez Villar, J. Rosselló Soria, L. Aguirrezabal Marcotegui, I. Fernandez de la Prieta, R.I. Alvarado Cuenca, P. Martín Soler, J. Garcia-Reyero, M.S. Rodriguez-Duque, E. Elvira Uriarte, I. Lopez de Gamboa
*Pathology Department-Basurto University Hospital, Osakidetza. IIS BioBizkaia, Spain

Background & objectives: Composite phaeochromocytoma (CP) is a mixed neuroendocrine-neural tumour, formed by the combination of a typical phaeochromocytoma with a component of neuroblastic origin (ganglioneuroma in 80%). Some may be associated with genetic alterations and a small percentage may be hereditary.
Methods: Due to CP is a rare entity with a frequency of less than 3% of all adrenal gland tumours and constitutes between 1-9% of pheochromocytomas, with an average size of 4-6 cm, we reviewed CP from several hospitals and only two cases were found.
Results: One tumour is a 5.7 cm composite pheochromocytoma (CP) and the other a 20 cm giant composite pheochromocytoma (GCP). Both patients are male, 46 and 66 years old, and both presented clinical manifestations before surgery. Histologically, both had pheochromocytoma with associated ganglioneuroma, although the GCP had a small component of ganglioneuroblastoma. Both tumours show same immunohistochemistry, with positive chromogranine A and synaptophysin in pheochromocytoma and S100 positive in ganglioneuroma histology with calretinin-positive ganglion cells. No distant disease at present. Both tumours were negative for RET and SDHD gene mutations.
Conclusion: The majority of CPs are sporadic, like ours, and the pathogenic mechanisms are unknown. A small percentage may be hereditary, being associated with other genetic disorders such as NF type 1, Von Hippel-Lindau or MEN II, so the genetic study, with genes such as SDHD, RET or VHL should be complemented to the histological study in this rare entity with familial implications.

E-PS-05-004

Intraoperative consultation in thyroid lesions: a study on effectiveness and competence

I. Bağcı*, E. Tekin, F. Canaz, M. Kılıç
*Eskişehir Osmangazi University, Turkey

Background & objectives: TIRADS and Bethesda Reporting Systems guides the clinical management of thyroid lesions. Literature conflicts on the contribution of intraoperative consultation(IC). Herein, we evaluated the compatibility of IC with paraffin diagnosis, TIRADS and Bethesda categories; and discussed the limitations of IC.
Methods: Clinical and demographic data, histopathological features, TIRADS and Bethesda categories of forty cases who underwent IC in our department between 2018 and 2023 were collected. The IC result was compared with the paraffin evaluation. Cases in which a definitive diagnosis could not be given during intraoperative evaluation (deferred results) were excluded from the correlation analysis.
Results: During IC 19 cases were reported as benign and nine as malignant. On the examination of paraffin blocks, the number of benign and malignant cases were equal. The diagnosis of 80% of malignant cases were papillary carcinoma, and 75% of the cases had a follicular dominant histological pattern. After the exclusion of 12 deferred results (30%), sensitivity was determined as 64%, specificity as 100%, and diagnostic accuracy as 82.14%. The concordance of frozen diagnosis was higher in cases with benign paraffin diagnosis compared to malignant cases ($p = 0.014$). In frozen examination, a higher rate of benign results was observed in well-circumscribed nodules (77,5%) compared to irregular masses ($p = 0.002$).
Conclusion: Most deferred and discordant results were observed with well-circumscribed and/or follicular patterned lesions. The fact that capsular and/or lymphovascular invasion is essential for the diagnosis of malignancy in follicular lesions without papillary nuclear features causes the necessity of multiple sections for accurate diagnosis and diagnostic limitations during IC. IC may contribute to the clinical management of Bethesda category 1, 3, and 4 lesions, but is controversial for well-circumscribed lesions with follicular pattern. Therefore, algorithmic approach and selective IC are recommended.

E-PS-05-005
Core needle biopsy of highly aggressive malignant thyroid tumours
E. Bakuła-Zalewska*, M. Kwapisz, P. Góralski, J. Długosińska, J. Gałczyński, M. Dedecjus
*Department of Pathology, Poland

Background & objectives: Rapidly growing malignant tumours with extensive necrosis pose challenges in the cytologic examination of thyroid masses. The objective of this study was to assess the utility of core needle biopsy as a complementary method to diagnose highly aggressive thyroid malignancies
Methods: Twenty-nine patients with thyroid tumours were examined by ultrasound guided core needle biopsy between 2019 and 2023. The patients were referred to the Maria Sklodowska-Curie National Research Institute of Oncology for evaluation of rapidly growing thyroid mass and suspicious of malignancy. All patients underwent fine needle aspiration of thyroid mass with inconclusive or equivocal results prior to core needle biopsy.
Results: Core needle biopsy yielded a sufficient tumour tissue in 28 cases. In one case a repeated biopsy was required. The final diagnosis was anaplastic thyroid carcinoma (15 cases), poorly differentiated carcinoma (2 cases), follicular tumour (1 case), pleomorphic sarcoma (2 cases), B-cell lymphoma (1 case), and NUT midline carcinoma (1 case). In 6 cases, the diagnosis of metastatic carcinoma was confirmed, including 5 cases of squamous cell carcinoma and 1 pulmonary adenocarcinoma. One specimen was diagnosed as a benign lesion. Complications following core needle biopsy procedures in the present study included minor local bleeding in two cases and seeding of malignant cells along the needle tract in one case
Conclusion: Core needle biopsy of thyroid offers greater diagnostic accuracy with minimal complication risk over repeated fine needle aspiration with a prior inconclusive or non-diagnostic cytology. The ability to sample larger amounts of tissue suitable for histopathological assessment and immunohistochemical / molecular analysis, allows for specific histologic diagnosis which is critical in cases of anaplastic or poorly differentiated thyroid carcinoma, metastases, sarcoma, and lymphoma.

E-PS-05-006
Oncocytic thyroid carcinoma's pathological prognostic factors
M.A. Bani*, F. Pani, R. Chehab, D. Hartl, J. Hadoux, L. Lamartina, E. Baudin, A. Al Ghuzlan
*Department of Medical Biology and Pathology, Morphological pathology laboratory, Gustave Roussy Cancer Campus, Villejuif, France Paris-Saclay university, Gustave Roussy Cancer Centre, Inserm US23, CNRS UMS3655, AMMICa, Villejuif, France

Background & objectives: Oncocytic carcinoma (OCA) of the thyroid are rare. Their prognosis depends essentially on the extent of vascular invasion. Other factors as high grade features appears to be involved in the prognosis but needs to be clarified.
Methods: Retrospective analysis of patients with OCA between 2003 and 2021. Pathological and clinical variables were recorded: tumour size, mitotic rate, Ki67, necrosis, capsular invasion, vascular invasion, extrathyroidal extension and status at last follow up. Tumours were were considered of high grade if at least one of the following items was present: mitoses ≥ 5 and/or Ki67 ≥ 5 and/or necrosis.
Results: 61 patients were included in this study. 55.7 % were women and the mean follow-up was 5.7 years. Mean age at diagnosis was 53.68. In the univariate study, factors that were associated with poor overall survival were: tumour size ($p=0.008$); high mitotic count ($p=0.01$); high ki67 index ($p=0.02$); presence of necrosis ($p<0.001$) and high grade ($p<0.001$). Factors associated with low recurrence free survival were: male gender ($p=0.023$); tumour size ($p<0.05$); high mitotic count ($p<0.001$); high ki67 index ($p<0.001$); presence of necrosis ($p<0.001$); lymphovascular invasion ($p<0.001$); and high grade ($p<0.001$). In the multivariate analysis for reccurence free survival, vascular invasion ($p=0.0389$) and the high grade ($p=0.00661$) were independent prognostic factors.
Conclusion: In this cohort of OCA, tumour size, proliferation, presence of necrosis, vascular invasion and high grade were associated with a poor prognosis. For recurrence free survival, vascular invasion and tumour grade are independent prognostic factors. These findings couldn't be confirmed for OS due to the low mortality in this cohort. We herein confirm the importance of grading based on mitoses ≥ 5 and/or Ki67 $\geq 5\%$ and/or the presence of necrosis but these data needs to be confirmed on a larger cohort.

E-PS-05-007
Follicular thyroid adenoma with papillary architecture: a new emerging entity
L. Bouzidi*, S. Graja, M. Miled, S. Hidouri, T. Sellami Boudawara, N. Gouiaa, M. Zghal
*Department of Pathology, Habib Bourguiba University Hospital, Sfax, Tunisia

Background & objectives: Follicular adenoma (FA) showing papillary architecture was classified as a variant of conventional FA called hyperfunctioning or toxic thyroid adenoma. Recently, in the 2022 WHO Classification of Tumours of Endocrine Organs this neoplasm is considered as a distinct entity.
Methods: The histological features of FA with papillary architecture occurring in a 46-year-old man who presented with a nodule in the left lobe of thyroid are described referring to the new classification of tumours of endocrine organs. The nodule was classified EUTIRADS 3 on ultrasound. Biochemical analysis revealed a hyperthyroidism. Fine needle aspiration was not performed. The patient underwent thyroid lobectomy.

Results: Gross examination revealed a well-defined nodule measuring 65 mm with distinct capsule. The cut surface showed colloid appearance with cystic formations. Histopathologic analysis showed a mixture of follicular and papillary structures. Follicles were often large associated with delicate papillary projections. Subfollicles within follicles were identified. The colloid showed peripheral scalloping. The epithelial cells were columnar. The nuclei were round and basally located without nuclear features of papillary thyroid carcinoma (PTC). There was neither capsular invasion nor angioinvasion. Immunostaining for keratin 19 was focally positive and negative for HBME-1. We were referred to the new classification of tumours of endocrine organs; the final diagnosis of FA with papillary architecture was retained.
Conclusion: FA with papillary architecture is a benign encapsulated neoplasm presenting intrafollicular papillary architecture without nuclear features of PTC. It is associated with autonomous hyperthyroidism. The tumour cells are often negative for HBME-1, Galectin-3 and BRAF-V600E. A focal immunoreactivity for Keratin 19 is reported. It is distinguished from conventional FA due to its specific gene mutations (EZH1, TSHR or GNAS). We report this case to emphasize the fact that the presence of papillae in a FA is not synonymous with carcinoma.

E-PS-05-008
Cribriform-morular thyroid carcinoma: a rare tumour in thyroid gland
S. Erkılıç, K. Bulut*
*Department of Pathology, Medical Faculty, Gaziantep University, Gaziantep, Turkey

Background & objectives: Cribriform-morular thyroid carcinoma (CMTC) is a rare tumour of thyroid. Previously considered a variant of papillary thyroid carcinoma, it is now recognized as a distinct entity by the 2022 WHO classification of thyroid neoplasm. Here we present a CMTC case.
Methods: A 29-year-old woman presented with a nodule in the left lobe of thyroid gland. Fine needle aspiration cytology of this nodule was reported as suspicious for malignancy. The patient underwent bilateral total thyroidectomy.
Results: The thyroid specimen weighted 26 gr and left lobe was 5x3.5x3.5 cm, right lobe was 4x2x2 cm. The sections of left lobe revealed an encapsulated, yellowish-tan colored nodule of 3 cm diameter. Microscopically the nodule was well circumscribed and composed of columnar cells with nuclear clearing and groove similar to conventional papillary thyroid carcinoma. The nodule has cribriform, papillary, solid/morular growing pattern and there wasn't any colloid. Immunohistochemistry showed that non-morular areas were positive for β-catenin, TTF-1, CK19, estrogen and progesterone receptors, and negative for thyroglobulin. The morulae stained for CDX2, CD10 and CK5/6. The case diagnosed as cribriform-morular thyroid carcinoma.
Conclusion: CMTC has morphologic and genetic features that distinguish it from papillary thyroid carcinoma. It is frequently associated with Familial Adenomatous Polyposis (FAP) but can also occur sporadically. Although FAP-related CMTC often presents as multifocal nodules, solitary nodules are more common in sporadic cases. Genetic alteration in the Wnt/ β-catenin pathway is specific. Screening for colonic polyps and genetic analysis is important for patients with this diagnosis.

E-PS-05-009
Unveiling a rare morphological variant: myxoid adrenocortical adenoma with pseudoglandular pattern - a case report
G. Carrola*, D. Sá, M. Mexia, J.R. Vizcaíno, J. Brandão
*Anatomic Pathology Service, Pathology Department, Unidade Local de Saúde de Santo António, Portugal

Background & objectives: An extremely rare variant of adrenal adenomas, myxoid adrenocortical adenoma with pseudoglandular pattern, exhibits a unique morphological pattern. Our objective was to examine a case in our department that aligns with this entity, which is scarcely documented in the literature.
Methods: We conducted a case review of a 38-year-old female who was referred for a left adrenalectomy after a 5 cm nodule was identified on radiological imaging during the investigation of uncontrolled hypertension. Although laboratory tests revealed the mass to be non-functioning, the radiological characteristics were not entirely typical of adenoma. Therefore, surgery was decided upon discussion and subsequent histopathological analysis.
Results: Pathological assessment revealed a protruding mass on the adrenal gland with a solid, firm, and whitish-yellow cut surface, measuring 4.5 cm. Microscopically, corresponded to an expansive neoplasia with well-defined contours, comprised of regular small cells with clear to eosinophilic microvacuolated cytoplasm. The cells were predominantly arranged in a pseudoglandular pattern, with occasional trabecular areas, and myxoid background. Immunohistochemistry showed reactivity for Melan-A, SF1, Beta-catenin, INI1 (preserved), and CAM5.2 (peripheral dot-like), plus the absence of immunoreactivity for Calretin, CD99, PAX8, WT1, GATA3, SALL4, Inibin, Synaptophysin, and Chromogranin. Proliferative index was 1-2%. According to the Weiss criteria, the scoring was zero. There is no evidence of recurrence after thirteen months.
Conclusion: Myxoid adrenocortical adenomas with a pseudoglandular pattern are uncommon tumours characterized by distinctive histological features. Given their benign behaviour, it is crucial to recognize this unique entity to avoid misdiagnosis and incorrect management, particularly in distinguishing them from metastatic adenocarcinomas or retroperitoneal tumours. Thus, immunohistochemistry plays a pivotal role in the differential diagnosis.

E-PS-05-010
Adrenal myelolipoma in the practice of pathologist
A. Dobriakov*, A. Polcovnikova, A. Tokmakov, O. Konstantin, A. Chellyukanov, M. Alexandrova, V. Salaeva, E. Kuznetsova
*F.I. Inozemtsev Moscow City Clinical Hospital, Russia

Background & objectives: Adrenal myelolipomas are benign, non-functional adrenal neoplasms predominantly composed of mature adipose tissue and mixed myeloid tissue (it is represented by all three hematopoietic cell lines).They comprise 3% to 16% of all adrenal incidentalomas.
Methods: In the pathological department of F.I.Inozemtsev Moscow City Clinical Hospital in 2023, 33 cases of surgical material from removed adrenal tumours were studied with the preparation of micro preparations, hematoxylin-eosin H&E staining and additionally, according to Van Gieson and Sudan 3.
Results: Adrenal myelolipoma was identified in 3 patients, aged 45,64, and 72 years in 2023. The lesion was unilateral in all three cases. The detection rate was 9,1% among adrenal tumours. Macroscopically the tumour was represented a soft-elastic lobular node of yellow color (resembling adipose tissue with focal haemorrhages (diametr of 5.0 to 8.0 cm). The tumour had clear boundaries in relation to the unchanged adrenal gland tissue. Microscopically the tumour was represented by clearly demarcated,non-encapsulated tumour tissue,consisting of combination of mature adipocytes with trilinear extramedullary hematopoietic nests with full cellular maturation and a slightly increased number of megakaryocites, represented in different proportions.
Conclusion: Adrenal myelolipoma is an uncommon, benign and hormonally inactive tumour. Most lesions are asymptomatic and usually are rar discovered. According to the data, the detection rate of adrenal

myelolipoma was 9,1%, which corresponds to literature data. For a final diagnosis, histological verification of the tumour is required.

E-PS-05-011

A thyroid nodule revealing a parathyroid carcinoma: a case report

R. Doghri*, A. Khemir, W. Ben Makhlouf, B. Laabidi, G. Sahraou, L. Charfi, K. Mrad
*Pathology department, Salah Azaiez Institute, Tunisia

Background & objectives: Parathyroid gland cancer (PC) counts for <0.005% of all cancers. It affects adults of the 6th decade and is the etiology of primary hyperparathyroidism in <1% of cases. In this study we'll recall clinicopathologic aspects and prognosis of PC.
Methods: A case of PC was diagnosed based on clinico-morphologic features and immunohistochemical staining.
Results: A 81-year-old woman presented with cervical swelling. Ultrasound revealed a nodule on the left lobe of the thyroid gland. The patient had left loboisthmectomy. Extemporaneous examination revealed a carcinomatous proliferation. The patient had right lobe totalization. Tumour cells were morphologically reminiscent of those of the parathyroid gland. They had solid growth pattern and were focally arranged in pseudo-rosettes. The stroma was of endocrinoid type. Neighboring thyroid parenchyma was regular. Tumour cells were Cytokeratin+, calcitonin- and thyroglobulin-. Our patient had, otherwise, hypercalcemia with very high PTH serum levels. Given these clinical, morphological and immunohistochemical datas, the diagnosis of parathyroid carcinoma was retained. No recurrence has been recorded until this date.
Conclusion: Parathyroid gland cancers are rare. The highest incidence rate was recorded in Japan. Treatment consists of complete surgical resection with ipsilateral thyroid lobectomy. Pre-tracheal and recurrent lymph node dissection is necessary. Post-operative radiotherapy can be useful in case of recurrence. Complete tumour resection is associated with the highest survival rates reaching 90% at 5 years of follow up.

E-PS-05-012

Clinical and morphologic features of an ETV6:NTRK3 translocated high-grade papillary thyroid carcinoma: a case report

S.K. Dursun*, F.M. Doğukan
*Basaksehir Cam ve Sakura City Hospital, Department of Pathology, Turkey

Background & objectives: Papillary thyroid carcinoma (PTC) is derived from follicular cells and is characterized by specific nuclear features. PTCs harboring ETV6::NTRK3 translocation are mostly seen in radiation-related and paediatric thyroid cancers. We report an ETV6::NTRK3 translocated high-grade PTC with distinct histomorphologic features.
Methods: A 37-year-old male presented with persistent left shoulder pain. Radiologically, a mass lesion was detected in his left humerus and the concomitant biopsy revealed a metastatic PTC infiltration. Ultrasonography and fine needle aspiration biopsy confirmed the diagnosis of papillary thyroid carcinoma. Subsequently, total thyroidectomy and cervical lymph node dissection were performed.
Results: Gross examination revealed a tumour of 6x5.8x4.5 cm with a yellow-brown cut surface. On microscopy, tumour cells displayed the typical nuclear features of PTC. In most areas, tumour cells lined up around the papilla with nuclei on the apical side of the cells, a phenomenon previously described as 'reverse polarisation'. The tumour exhibited various patterns of growth and cytomorphology including papillary/micropapillary, solid/trabecular, hobnail, and follicular patterns. Lymphatic and vascular invasion, lymph node metastasis (20 out of 64), necrosis, and capsule invasion were observed. 2 mitoses per 2 mm^2 were detected. These morphological findings suggested the diagnosis of PTC with high-grade features. Next-generation sequencing (NGS) revealed a translocation of ETV6::NTRK3.
Conclusion: ETV6::NTRK3 translocated PTC, while often associated with radiation exposure, may occur sporadically. This mutation, typically found in young female patients, presents unique morphologic features such as reverse nuclear polarization. Recognizing these characteristics is crucial, as ETV6-NTRK3 translocated tumours tend to be aggressive and prone to metastasis. The high-grade characteristics of our case and the presence of multiple metastatic foci are consistent in this regard. Understanding these clinical and histologic findings may facilitate prompt molecular testing and guide targeted therapeutic interventions.

E-PS-05-013

Primary thyroid lymphoma: a rare case report

S. Ekmekci*, G.G. Uz, Ş. Çoban, B.G. Özamrak, E.E. Pala, Ü. Küçük, Y. Pekcevik, H.Y. Yılmaz
*Izmir Provincial Health Directorate, Izmir City Hospital, Department of Pathology, İzmir, Turkey

Background & objectives: Primary thyroid lymphoma (PTL) is a rare entity, accounting for 5% of all thyroid malignancies and less than 2% of lymphomas. In the majority of cases, PTLs are classified as non-Hodgkin's B-cell lymphomas.
Methods: A 75-year-old female with hoarseness,shortness of breath and a rapidly growing thyroid mass was admitted.An 83x69x51 mm mass filling left thyroid lobe, extending to the isthmus, invading through thyroid cartilage, and reaching larynx was observed at screening.The left aryepiglottic fold,paraglottic fatty tissue at the left glottic level were also infiltrated.Anaplastic thyroid carcinoma and PTL were considered in the differential diagnosis.
Results: Tru-cut biopsy revealed a neoplastic lymphoid infiltrate with necrosis, consisting of medium to large cells with prominent nucleoli, and the infiltrate seemed to eliminate the normal structure. Neoplastic cells were CD20 and PAX5 (+). Most of these cells were positive for Bcl6 (30%) and CD30, and some were positive for c-myc (15%). CD5, CD23, cyclin D1, CD23, CD25, Bcl2, MUM1, CD10, Panck, Pax8, TTF-1 and p53 were negative. The Ki-67 proliferation index was approximately 90%. The findings were consistent with Diffuse Large B-cell lymphoma.
Conclusion: PTL is a rare malignancy that can cause diagnostic pitfalls and make management challenging. They usually manifest as rapidly growing masses in the neck, causing compression symptoms. Initial investigations of suspected PTL should include blood tests and ultrasound-guided biopsy, preferably core needle biopsy. A quick and accurate diagnosis by cytology is crucial for an overall prognosis and treatment plan, which will depend on the lymphoma subtype. Systemic imaging is required for staging. Surgery is reserved for diagnosis and airway management.

E-PS-05-015

RET mutation in C-cell hyperplasia: a premalignant lesion with deceptive morphology

S. García-Fuertes*, N. Franco, E. Ponce-Casas, R. Vilorio, G. Muñoz-González, N. Torrecilla Idoipe
*Hospital Clínico Universitario Lozano Blesa, Spain

Background & objectives: C-Cell hyperplasia (CCH) consists in an increase of C-cell population in thyroid due to reactive-physiologic or neoplastic primary process. Neoplastic CCH is considered to be precursor lesion to familial medullary thyroid carcinomas (MTC), caused by mutations in RET proto-oncogene.

Methods: We present a 61-year-old female patient with personal history of breast carcinoma and colonic adenocarcinoma, who is subjected to hereditary studies in peripherical blood, in which a pathogenic RET mutation is detected. Because of incremented risk of MTC, a prophylactic total thyroidectomy is performed. We received the specimen at our pathology department.
Results: Grossly, thyroid gland was anodyne. Microscopically, we could establish a predominantly conserved parenchyma with multifocal areas of small nests disperse among follicles. At higher magnification, these well-circumscribed groups showed nodular architecture and were formed by monomorphous cells, with large eosinophilic to grey cytoplasms and ovoid nucleus without significant cytological atypia. They were positive for calcitonin and neuroendocrine markers, such as chromogranin and synaptophysine. Ki67 proliferation index was inferior to 1%. In addition, NGS was performed in the specimen and showed the same RET mutation as the blood genetic test result. Given the morphology, genetics and clinical history, a neoplastic CCH was diagnosed in a context of RET mutation.
Conclusion: The mutation detected in RET (c.2410G>A (p.Val804Met)) is pathological and the allelic frequency close to 50% confirms the germline origin, considering CCH as a time-dependent premalignant lesion of MTC. C-cell quantification is not necessary for diagnosis and it can be challenging to differentiate it from nodular medullary microcarcinoma. Therefore, early diagnosis in carriers of these mutations is essential. Prophylactic thyroidectomy represents the gold standard treatment for these patients, as well as family genetic counseling.

E-PS-05-016
Pathological characteristics as predictors of multifocality in papillary thyroid carcinoma
N. Gardic*, I. Starčević, T. Vasiljević
*Institute for Pulmonary Diseases of Vojvodina, Serbia

Background & objectives: Detecting multifocal papillary thyroid carcinoma through preoperative radiological assessments can be challenging, sometimes leading to residual disease in near-total thyreoidectomy. The aim of the research was to investigate the relationship between potential pathological predictors of tumour multifocality.
Methods: Patients who underwent surgical treatment for papillary thyroid cancer over a seven-year period were included in the study. The significance of predictors (capsular invasion (CI), lymphovascular invasion (LI), extrathyroidal extension (EE), lymph node metastasis (LM)) for the presence of multifocal disease was examined using a logistic regression analysis model.
Results: Out of 330 patients, 273 (82.73%) were female, while 57 (17.27%) were males, with an average age of 49.32±13.95 years. A majority of patients had solitary nodules (201/60.91%), while 129 (39.09%) patients had multifocal disease. Verified lympho-vascular invasion, capsular invasion, the presence of lymph node metastases, and extrathyroidal extension were identified as statistically significant predictors of multifocal disease according to the logistic regression model ($\chi 2=23.417;p<0.001$), with pseudo R2 ranging 0.053-0.093. Among the examined predictors, LI emerges as the most significant. Its presence increases the likelihood of multifocal carcinoma by 2.3 times. The presence of CI, EE, and LM increases the likelihood of multifocal disease by 47.15%, 36.11%, and 323.07%, respectively.
Conclusion: The examined pathological characteristics are statistically significantly associated with the presence of multifocal papillary thyroid carcinoma.

E-PS-05-017
Investigation of the contribution of EZH1 expression to differantial diagnosis in thyroid tumours with follicular pattern
F.E. Gökalp Satıcı*, R. Bozdoğan Arpacı, Ö. Bucak, A. Dağ, G. Örekeci Temel, M.E. Erdal
*Tarsus State Hospital/Department of Pathology, Turkey

Background & objectives: Follicular tumours of the thyroid are, follicular adenoma (FA), follicular carcinoma (FC), oncocytic adenoma (OA), oncocytic carcinoma (OC) and some papillary thyroid carcinoma (PTC) subtypes. In our study, the expression EZH1 molecule was investigated in the differential diagnosis of these entities.
Methods: In our centre, 125 cases diagnosed with thyroid tumour exhibiting a follicular pattern were included in the study. EZH1 expression levels were determined in all cases using immunohistochemistry and real-time PCR methods. H-score method was used in immunohistochemical evaluation. As a result, morphometric measurements and EZH1 expression were compared with clinicopathological findings and histopathological types.
Results: No significant difference was detected between histological types in terms of EZH1 expression detected by PCR and immunohistochemical EZH1 score. In FAs, statistically significant strong (scor 3 / +++) staining was observed with EZH1 compared to PTC subtypes. More scor 2 (++) staining were observed in PTC subtypes compared to FA and FC. No significant difference were observed between FA and FC in terms of EZH1 score and staining intensity.
Conclusion: It is stated in the literature that EZH1 mutations are mostly detected in benign thyroid tumours. Another study evaluated that EZH1 may play a role in follicular cell proliferation. Our study represents the first investigation, to our knowledge, of EZH1 expression levels in thyroid tumours utilizing immunohistochemical methods. When the findings of our study are examined, as a result, EZH1 staining intensity may be useful in distinguishing between FA and PTC.

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E-PS-05-018
Intratumour heterogeneity in pancreatic NET (PanNET): when morphology meets proliferation and molecular alterations
M. Iuzzolino*, A.R. Destro, A. Zerbi, S. Uccella
*Italy

Background & objectives: PanNET are graded according to the proliferation index in a three-tiered system, that guides therapeutic strategies. However, spatial and temporal heterogeneity, documented by morphology and molecular features may be observed in these NEN, with important clinical implications.
Methods: A 59-years-old woman was diagnosed with an incidentally found PanNET G1 of the tail at EUS-guided FNA. She underwent distal pancreatectomy. Microscopically, the tumour showed two morphologically different NET components, one trabecular with mitotic index 1x2mm2 and the other in solid nests with mitotic index 13x2mm2. Both components were analysed using immunohistochemistry and NGS analysis (500 gene panel Oncomine Plus).
Results: The trabecular part occupied 75% of the tumour, was composed of elongated cells, showed a Ki67 proliferation index (PI) of 2.8% and retained ATRX expression. The second population was represented by clear cells arranged in small solid nests with a Ki67 PI of 23% and loss of ATRX. For NGS analysis, the two components were microdissected and studied with a 500 gene panel. In both components, a mutation of MSH3 gene was present.The trabecular slowly proliferating subpopulation showed no other significant alteration at molecular analysis, whereas the other component, with Ki67 PI in the G3 range, had CNAs and mutations in several genes, including MLH1, HLA-A, PTEN and FGFR2.

Conclusion: This is an illustrative case of spatial tumour heterogeneity in PanNET, observed using morphology and supported by immunohistochemical and molecular techniques. The potential progression of low grade NET into NET G3 should be taken into consideration since the early stages of the disease, in order to properly program the therapeutic strategy. Careful sampling of the surgical specimen and application of selected immunostains allow the identification of the higher grade component. Molecular analysis is potentially useful for identifying druggable targets.

E-PS-05-019

Mixed medullary and follicular-cell derived carcinoma: a case report

B. Jurić*, V. Bedeković, L. Pažanin, H. Čupić
*University Hospital Center Sestre milosrdnice, Croatia

Background & objectives: Mixed medullary and follicular-cell derived carcinoma (MMFCC) of the thyroid is a malignant neoplasm which consists of coexisting populations of both follicular and C cell–derived tumour cells intermixed within the same tumour.
Methods: Both tumour cell populations should be morphologically distinct, and their lineage confirmed by immunohistochemistry. Clinical features depend on the predominant tumour component, but the clinical behaviour is more similar to the medullary thyroid carcinoma (MTC). Lymph node and distant metastases arise in up to 25% of cases.
Results: Serum calcitonin levels are frequently elevated, and serum thyroglobulin can also be high. MMFCC accounts for <0.1 % of all thyroid malignancies, it can occur in the setting of MEN2A or MEN2B syndromes or sporadically. We present a case of a 55-year-old female with Graves' disease who was treated with thyroidectomy. Grossing of the resection specimen revealed a 9 mm lesion in the left lobe which was diagnosed as papillary carcinoma of the thyroid (PTC) with four lymph node metastases. However, the postoperative laboratory workup showed elevated calcitonin serum levels.
Conclusion: The original pathohistological report was revised, and after performing additional immunohistochemical analysis the tumour was diagnosed as MMFCC with components of papillary thyroid carcinoma and medullary carcinoma. The patient underwent selective neck dissection and the final pathohistological report revealed eleven lymph node metastases. This case report highlights the importance of measuring preoperative calcitonin levels and of conducting a meticulous histological and immunohistochemical examination in order to assist the precise and early diagnosis of MMFCC.

E-PS-05-020

Fine needle aspiration cytology of the thyroid: a comparison of 53 cytological with histological diagnoses

S. Kanoun*, S. Hidouri, M. Triki, F. Maalej, N. Gouiaa, T. Sellami Boudawara, S. Graja
*Department of Pathology, Habib Bourguiba University Hospital, Sfax, Tunisia

Background & objectives: The distinction between benign and malignant thyroid-nodules poses a challenge. Diagnostic strategies like fine-needle aspiration cytology (FNAC) were developed, but carry risks of false results. In our study, we assess FNAC's role in thyroid-nodule management, focusing on its diagnostic value.
Methods: A retrospective multicentric-study of 53 thyroid-nodule surgery patients at the Otorhinolaryngology-Departments over 8 years (January 2013-December 2020) was conducted. Patients with preoperative FNAC interpreted by the same cytopathologist were included. Sensitivity, specificity, Positive Predictive Value , and Negative Predictive Value were calculated. Bethesda IV, V, and VI were considered positive, Bethesda II negative, while Bethesda I or III were excluded.
Results: Our study comprised 53 patients: 22 underwent surgery at Habib Bourguiba University Hospital in Sfax, and 31 at Gabes University Hospital. Cytological examination revealed 41.5% were classified as Bethesda II nodules, 30.6% as Bethesda III, 15.1% as Bethesda IV, 7.5% as Bethesda V, and 9.3% as Bethesda VI. Analytically, all Bethesda VI nodules were histopathologically positive, with 75% Bethesda V, 25% Bethesda IV, 12.5% Bethesda III, and 13.6% Bethesda II. Excluding Bethesda III, we found 19 true negative, 8 true positive, 7 false positive, and 3 false negative cases. Finally, FNAC demonstrated 72.7% sensitivity, 73% specificity, 53.3% positive predictive value, and 86.3% negative predictive value.
Conclusion: Thyroid cytological examination is a dependable tool for therapeutic decision-making. However, its sensitivity and specificity are limited, particularly in cases of follicular neoplasms. Definitive diagnosis of benign or malignant nodules relies on histopathological examination of the surgical specimen.

E-PS-05-021

Metastatic breast carcinoma affecting a parathyroid adenoma: a case report

Z. Lajmi*, Y. Sarra, F. Yosra, A. Bdioui, M. Mokni
*University Hospital Sahloul, Tunisia

Background & objectives: Involvement of the parathyroid glands by metastatic tumour is very rare condition. The concurrence of a metastatic breast in a parthyroid adenoma (PA) is an even a more remarquable event, that could be misdiagnosed as a primary parathyroid carcinoma (PPC).
Methods: 67-year-old women, who underwent a radical mastectomy for an invasive breast cancer staged as pT3N1Mx breast cancer was referred to symptomatic hypercalcemia. Investigations revealed a primary hyperparathyroidism due to an ectopic mediastinal PA. Total thyroidectomy with excision of PA were performed.
Results: Microscopic examination of the parathyroid lesion showed a well circumscribed PA mainly composed of clear cells, and surrounded by a thin fibrous capsule. The tumour encompassed multifocal deposits of large and atypical cells showing a prominent nucleoli and multiple atypical mitosis contrasting with the rest of parathyroid cells. Immunohistochemistry investigations were held. Unlike parathyroid adenoma, chromogranin and synaptohysin stain were negative in atypical cells deposits that showed a positive stain for CK7 and GCDFP15. CK20, GATA3 were negative. Considering the patient's history, we made the diagnosis of a metastatic breast carcinoma within a PA.

Conclusion: Tumour-to-tumour metastases are a well-documented, albeit uncommon, finding. The significant blood flow of endocrine organs including parathyroid favours metastases implants. The most common primary sites of malignancies in parathyroid glands is breast carcinomas due to common lymphovascular supply. Metastasis in PA could lead to the misdiagnosis of PPC that should show clear signs of invasion like vascular and neural invasion. Parathyroid metastasis must be ruled out in front of sign of malignancy in every PA.

E-PS-05-022

Assessing the clinical utility of the 2021 International Medullary Thyroid Carcinoma Grading System: a validation study

V. Macarrón*, S. Quinones, M. De Uribe Viloria, M.I. Esteban-Rodríguez, R.M. Regojo
*La Paz University Hospital, Spain

Background & objectives: Recent publication of the 2021 International Medullary Thyroid Carcinoma (MTC) Grading System based in necrosis, mitosis and proliferation index has revolutionized MTC diagnosis. Furthermore, other factors, including desmoplasia, may provide valuable prognostic insights into this condition.
Methods: We categorised MTC cases diagnosed at our institution since 2009 following the 2021 International MTC Grading System and assessed desmoplasia presence. Moreover, we gathered prognostic clinicopathological features, including multifocality, extrathyroidal extension, lymphovascular invasion, tumour size, TNM staging, extranodal extension, CEA and calcitonin levels, calcitonin biochemical relapse or incomplete response, locoregional and distant relapse, and disease-specific mortality, for potential correlations.
Results: In our analysis of 40 MTC cases (29 female/ 11 male, mean age 53,05 years), 33 were categorised as low-risk and 7 as high-risk MTC. Desmoplasia was evident in 23 tumours and absent in 17. No significant age or sex differences were observed. High-risk MTC patients displayed significantly higher tumour size (p=0,026), pT stage (p=0,018), pN stage (p=0,03), extra-nodal extension in lymph node metastases (p=0,04), locoregional relapse incidence (p=0,004) and disease-specific mortality (p=0,026). Tumours presenting desmoplasia demonstrated significantly higher lymphovascular invasion (p=0,025), tumour size (p=0,021), pT stage (p=0,004), pN stage (p=0,0003), AJCC stage (p=0,005), presurgical calcitonin levels (p=0,021), calcitonin incomplete response or biochemical relapse (p=0,017) and locoregional relapse incidence (p=0,029).
Conclusion: The application of the 2021 International MTC Grading System for risk stratification in MTC reveals significant prognostic correlations with pathological and clinical features, supporting for its integration into routine clinical practice. Furthermore, given the robust association observed between desmoplasia and various clinicopathological prognostic factors, there is a strong justification for considering its inclusion as a potential future parameter of the grading system. Increasing sample size and conducting survival analyses would fortify the study's results and enhance its clinical relevance.

E-PS-05-023
Morphometry of thyreod cancer
B. Magrupov*, A. Rajapov
*Center for Professional Development of Medical Workers, Republican Research Center of Emergency Medicine, Uzbekistan

Background & objectives: Morphometric indicators of thyroid tumours depend on quantitative and qualitative changes in pathological changes prevailing in the process and are expressed by different indicators in different histotopographic types of tumours.
Methods: For morphometric examination, thyroid gland tumour tissue from intraoperative materials submitted to the Bureau of Pathological Anatomy of the Khorezm Region over a period of 5 years are was taken from 58 patients who were surgically removed and histologically diagnosed as malignant tumour. It was determined that the age of the patients was from 18 to 68 years.
Results: The length and width of the epithelial cells, of the nuclei, the longitudinal and width diameter of the follicles and the colloid were measured. Based on the obtained quantitative indicators, the area of colloid and follicles was calculated using the formula:
Conclusion: It was found that the size of the epithelium and nuclei of malignant tumours of the thyroid gland increased in high-risk forms, and accordingly, the cell size also increased accordingly. This, in turn, allows us to draw a conclusion that medullary cancer is more severe than follicular cancer.Among the most malignant tumours of the thyroid gland, the high frequency of follicular type of papillary carcinoma and the fact that it is very similar to follicular tumours.

E-PS-05-024
Pitx2 is a superior marker for detection of midgut WDNETs compared to CDX2 and serotonin
M. Manethova*, V. Stejskal, H. Faistová, H. Hornychová, F. Gabalec, A. Ryška, J. Soukup
*The Fingerland Department of Pathology, Charles University, Faculty of Medicine in Hradec Králové and University Hospital Hradec Králov, Czech Republic

Background & objectives: Different transcription factors are used for identification of WDNETs' primary site. Pitx2 was reported as highly specific and sensitive marker for midgut tumours, although comparison with other currently used markers is missing.
Methods: 122 cases of well differentiated neuroendocrine tumours (WDNETs) from various locations were analysed using whole sections or tissue microarrays. Immunohistochemistry of Pitx2, Serotonin, NKX6.1 and CDX2 was performed and scored using H-score.
The cohort included 16 foregut, 33 midgut, 14 hindgut, 19 pancreatic, 18 lung, and 22 metastatic (16 small intestine, 4 pancreatic, 1 lung, 1 caecal) WDNETs.
Results: In primary WDNETs, Pitx2 was expressed in 31/33 midgut WDNETs (sensitivity 94% and specificity 100% for midgut origin), CDX2 in 31/33 midgut WDNETs (sensitivity 94% and specificity 87%), and Serotonin in 29/33 midgut WDNETs (sensitivity 88% specificity 91%). NKX6.1 was negative in all midgut WDNETs and positive in 6/19 pancreatic WDNETs (32% sensitivity, 98 % specificity). In metastatic WDNETs, Pitx2 showed sensitivity 100%, specificity 100% for midgut origin, in contrast to CDX2 (sensitivity 94%, specificity 40%) and Serotonin (sensitivity 82%, specificity 100%).
In non-midgut WDNETs, CDX2 expression was observed in 2/10 stomach, 3/6 duodenum, 4/19 pancreas, 3/4 pancreatic metastases. Serotonin positivity was seen in 5/14 rectal, and 1/18 pulmonary WDNETs.
Conclusion: Pitx2 is a superior marker for detection of midgut origin compared to CDX2 and Serotonin.

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E-PS-05-025
Next-generation sequencing in thyroid cancer
M.A. Marmol Fabrega*, L. de León García Rico, I. Larizgoitia Salinas, C. Fula Cobos, C. Diego Hernández, E. Hernández Suárez, M.Á. Muñoz Fernández, P. Iglesias Gómez, M. Boiza Sánchez, C. Villanueva Sánchez, T. Meizoso Latova
*Hospital Universitario de Móstoles, Spain

Background & objectives: Next-generation sequencing (NGS) in thyroid cancer allows for the sequencing of variables alterations in multiple signal pathways. Identify relevant genomic alterations can be useful for prognosis and treatment decisions.
Methods: We analysed 22 patients with advanced thyroid cancer with distant metastases from Hospital Universitario de Móstoles. A pathologist selected tumour areas with 35% to 90% tumour content. We examined 16 primary tumours, including 14 distant metastases, using Oncoming Focus Assay (OFA) panel on IonS5XL platform that detects variants in 52 cancer-related genes, including substitutions, insertions/deletions, copy number alterations, and rearrangements/fusions.
Results: In the analysis of 22 thyroid carcinoma cases, 19 (86.3%) were papillary, 2 (9.1%) poorly differentiated and 1 (4.5%) follicular

carcinoma. Most patients showed distant metastases (77.3%) to lungs or bones, while others had local/regional disease involving soft tissue, trachea and/or lymph nodes (43.7%). The main mutation detected in 17 patients (56.6%) was in the MAPK pathway, including 13 (43.3%) BRAF V600E mutations, 1 (3.3%) BRAF fusion, 2 (6.6%) NRAS mutations, and 1 (3.3%) ERBB2. Additionally, mutations in TRK receptor kinase and the PI3K/AKT/mTOR pathway were found in 5 patients (16.6%). The majority were female (72.7%) with ages ranging from 37 to 89 years (median 69 years).
Conclusion: According to the literature, the most common alteration found in our study is in the MAPK pathway. However, the prevalence of BRAF V600E mutation and RAS is 46.6% and 6.6% respectively, slightly lower than reported in other series (60-65% and 10-12%). In contrast, the prevalence of mutations in the PI3K/AKT/mTOR pathway (16.6%) is much higher than the recorded 5.6%. Identification of molecular alterations in patients with advanced thyroid carcinoma informs prognosis, treatment and precise management strategies for patients.

E-PS-05-026
Mixed corticomedullary tumour of the adrenal gland with somatic GNAS mutation
P. Masa Ogando*, E. Pérez-Béliz, B. Thorpe Plaza, S. Rojo Álvarez, L.I. Rojo Álvarez, I. Abdulkader Nallib, J. Cameselle Teijeiro
*Departments of Pathology and General Surgery, Clinical University Hospital, University of Santiago de Compostela, Santiago de Compostela, Spain

Background & objectives: Mixed corticomedullary tumours (MCMT) of the adrenal gland are a very infrequent entity of tumours formed by the intermixed proliferation of adrenal cortical and medullary cells. These tumours can be hormonally active, and the histogenesis is controversial.
Methods: We describe the clinicopathological, immunohistochemical (IHC) and molecular study of a case of MCMT presented in a 56-year-old female with clinical symptoms of arterial hypertension and an adrenal mass. Laparoscopic resection of the left adrenal gland was performed.
Results: The adrenal tumour mass was a well-circumscribed, golden yellow and pink 3 cm nodule, with two cystic formations. Histologically, an admixture of two different cell populations was observed: a) cells with clear and eosinophilic cytoplasm and small round central nuclei (cortical adenoma component), b) others with large granular eosinophilic cytoplasm and pleomorphic nuclei that were sometimes multinucleated (phaeochromocytoma component). IHC showed positivity for alpha-inhibin and melan-A in the cortical adenoma component with chromogranin-A positive in the phaeochromocytoma component. Both cell populations were positive for synaptophysin. The Ki-67 index was 2%. No necrosis, vascular invasion or infiltration was observed. NGS analysis revealed a somatic pathogenic variant of the GNAS gene.
Conclusion: This case supports the existence of MCMT as an entity as yet to be included in the WHO endocrine tumour classification (5th edition). The GNAS gene mutation, typically associated with conventional cortical adenomas, suggests cortical cell proliferation as the initial pathogenic event in this rare tumour.

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E-PS-05-027
Primary thyroid lymphoma: a tertiary care cancer centre experience
N. Mittal*, K. Rabade, S. Rane, M. Bal, A. Patil
*Tata Memorial Center, India

Background & objectives: Primary Thyroid lymphomas (PTL) are rare and comprise less than 2% of all lymphomas. They may clinically and histologically resemble a high-grade thyroid carcinoma; especially in a core biopsy from the thyroid, a detrimental diagnostic error with dire consequences.
Methods: A retrospective observational study of clinical, imaging, and histological features of primary thyroid lymphomas from Jan 2014-Dec 2022. A total of 60 cases of PTL with a mean age of 57.4 years (range 33-82 years) and a M:F ratio of 1:1.86. Clinical presentation showed rapidly enlarging mass in 64.3%, thyroid dysfunction in 40.5% and hoarseness of voice in 24.3% cases.
Results: Stridor and B symptoms were seen in 36.1% and 13.5% respectively. Mean T-size was 9.7cm and 25.8% were stage IV at presentation. Histologically, Diffuse large B-cell lymphoma was most common (90%), followed by 2 cases of follicular lymphoma. Co-existing PTC was seen in 11.1% cases. Notably, 18 referral cases had incorrect submitting diagnoses ranging from thyroiditis to anaplastic thyroid carcinoma, on surgical specimens. Pleomorphism, spindle cells, rhabdoid cells, and cord-like clustering were seen in 40, 30, 3.3, and10% cases, respectively. On immunohistochemistry, CD20 was positive in 100%, Mum1 in 55.6% and CD10 in 61.9% cases. Chemotherapy was given in 89.2% and adjuvant RT in 35.1% patients. Two patients (n=37) died of disease.
Conclusion: Primary thyroid lymphomas may present as a clinical and histological conundrum due to overlapping features with high-grade thyroid carcinomas. A rapidly enlarging thyroid mass sans stridor, with associated lymphadenopathy, and a discrete population of cells with epithelial marker negativity warrants ruling out a lymphomatous process.

E-PS-05-029
Adrenal adenomatoid tumour, a rare case of benign tumour with osseous metaplasia
D. Oflas*, M.H. Sakarya
*Erzurum City Hospital, Department of Pathology, Turkey

Background & objectives: Adenomatoid tumours (ATs) are benign neoplasms originating from mesothelial cells, typically occurring in the male genital tract. Herein, we report a case of adrenal gland AT, a rarity with less than 50 cases reported in the existing literature.
Methods: Computed tomography (CT) scan of a 65-year-old male patient undergoing medical follow-up for diabetes mellitus and arrhythmia revealed a microcalcifying mass in the left adrenal gland measuring 77x35 mm. Following surgical resection, macroscopic, microscopic, and immunohistochemical analyses were conducted.
Results: Macroscopically, the well-defined oval-round-shaped mass exhibited a cystic and solid grayish-white cut surface. Histologically, the tumour comprised variable-sized and shaped tubules within a fibrous connective tissue stroma. Angiomatoid areas, characterized by anastomosing tubules lined with flat endothelial-like cells, predominated. Solid areas containing cells with eosinophilic swollen cytoplasm and cystic components with calcification and osseous metaplasia were less frequent. Scattered lymphoid aggregates were noted in the stroma. Nuclear pleomorphism, evident mitotic figures, and necrosis were absent. Neoplastic cells stained positive for pancK, CK7, WT1, calretinin, and D2-40 immunohistochemically.
Conclusion: Adenomatoid tumours, typically found in the genital system, may also arise in the adrenal gland from mesothelial residues. Adrenal ATs may present with calcification on radiological examination. The presence of dystrophic calcifications and osseous metaplasia on histopathological examination corresponds to radiological findings. It's important to recognize that adenomatoid tumours are rare benign neoplasms that can occur extragenitally, sometimes displaying osseous metaplasia.

E-PS-05-030

Scoring systems in the pathohistological diagnosis of primary tumours of the adrenal gland

Ž. Panić*, M. Đolai, J. Ilić Sabo, A. Ilić, M. Šunjević, S. Trivunić Dajko
*Faculty of Medicine, University of Novi Sad, Serbia

Background & objectives: Every pathologist specialized in adrenal gland pathology faces pitfalls in differential diagnosis, as biological behaviour cannot always be predicted based on tumour morphology. In these cases, scoring systems such as Weiss criteria and PASS scoring system are widely used.
Methods: This prospective-retrospective study analysed 140 cases of adrenal tumours processed after total adrenalectomy over a period of 8 years. Two scoring systems were used to definitely diagnose primary cortical and medullar tumours (pheochromocytoma): the Weiss scoring system to differentiate cortical adenoma from carcinoma and the PASS scoring system for pheochromocytoma.
Results: 140 patients were included in this study, with the adrenal tumour present in 87 females (62.14%) and 53 males (37.86%). After applying the Weiss score, its value ranged from 0 to 2 in all 64 adenoma cases; 10 of 17 patients with adrenocortical tumours were scored as 0-2, and 4 of 17 patients as 3-6. In 4 adrenocortical carcinomas, Weiss's score was >6. Among tumours of the adrenal medulla, pheochromocytoma was dominant in 23 cases. Using the PASS scoring system, 20 of 23 diagnosed cases of pheochromocytoma had values 0-3, and 3 of 23 cases had the PASS value ≥4.
Conclusion: The scoring systems of adrenal tumours should be part of the routine diagnostic process because they can be helpful in determining the histological type and predicting the biological behaviour of primary cortical and medullary tumours of the adrenal gland, and they could be of great importance. This is important, especially in cases when it is difficult to evaluate the neoplasm based on its morphological features.

E-PS-05-031

Pituitary Neuroendocrine Tumours (PitNET) in acromegaly: insights from a pathological perspective

S. Pedrosa*, J. Pinheiro
*Unidade Local de Saúde de São João, Portugal

Background & objectives: Acromegaly is a clinical syndrome caused by excess growth hormone production and it is usually caused by pituitary neuroendocrine tumours (PitNETs). Surgical resection remains the cornerstone of treatment. However, disease relapse is common and additional medical treatment is frequently required.
Methods: A retrospective study of acromegalic patients that underwent surgical treatment was conducted. Patient data including demographic information, radiological findings and hormonal profile were annotated. Histopathological re-evaluation was performed according the 5th edition of WHO classification. SSTR2a and SSTR5 expression was studied in a subset of cases. Long-term follow-up data was analysed, namely disease relapse and response to additional therapy.
Results: Our study included 74 patients:49 (66.2%)females, median age at diagnosis was 48 years(range 28-87).
36 cases (48.6%) were densely granulated (DG) somatotroph/mammosomatotroph PitNET; median age at diagnosis was 44(+/-12.8)years; 4:5 M:F ratio; microadenomas represented 33%(n=12). Disease persistence/relapse was observed in 52.9%.
30 cases (40.5%) were sparsely granulated (SG) PitNET;median age at dianosis was 48.5(+/-11.8)years; 3:7 M:F ratio; microadenomas represented 16.7% (n=5). They presented larger size on MRI ($p<0.001$) and lower median insulin-like growth factor 1 (IGF-1) levels ($p<0.001$). Disease persistence/relapse was observed in 53.3% of cases.
Other cases included 5 (6.7%) intermediate-type somatotroph tumours, 2 (2.7 %) mature plurihormonal PIT1-lineage PitNET and 1 (1.3%) mixed somatotroph-lactotroph PitNET.
Conclusion: The therapeutic approach to acromegaly is challenging. In our study we observed more than 50% of cases with disease persistence/recurrence after surgery. Of these, 42% disclosed persistent high IGF1 plasma levels despite first line pharmacologic therapy. The histopathological heterogeneity of PitNET may provide clues for better risk stratification and predicting therapeutic response to different somatostatin analogues, with variable action in different somatostatin receptor subtypes.

E-PS-05-032

Composite pheochromocytoma: a tumour to consider in adrenal pathology

E. Ponce Casas*, G. Muñoz Gonzalez, S. García-Fuertes, R. Vilorio, N. Torrecilla Idoipe, E. Mejia, T. Ramirez
*Hospital Clínico Universitario Lozano Blesa, Spain

Background & objectives: Composite pheochromocytoma is an uncommon adrenal tumour that combines a pheochromocytoma and a neuroblastic tumour. Approximately 110 cases have been reported in the literature.
Methods: We present the case of an 86-year-old woman with hypertension and recurrent syncopes, who underwent surgery for vulvar squamous cell carcinoma, and during follow-up, an adrenal tumour of 5.5 cm and elevated metanephrines were detected. Adrenalectomy was performed, and the specimen was sent to us for study.
Results: Macroscopically, the tumour was rounded, non-encapsulated, and well-defined, with a heterogeneous cut surface. Microscopically, it was well-defined from periadrenal adipose tissue and consisted of nests of basophilic cells with a neuroendocrine habit compatible with Zellballen nests of a pheochromocytoma. Mixed with these, was a spindle cell proliferation with Schwannian appearance and both mature and immature ganglion cells, compatible with a ganglioneuroma. Immunohistochemically, the pheochromocytoma was positive for chromogranin, synaptophysin, and CD56, and negative for S100, which was positive in sustentacular cells. The ganglioneuroma was positive for S100, among other techniques. Neurofilament was intensely positive in ganglion cells and in the Schwannian component of the ganglioneuroma, and negative in the pheochromocytoma.
Conclusion: Composite pheochromocytoma consists of a pheochromocytoma and a neuroblastic tumour, usually a ganglioneuroma as in our case. Diagnosis requires microscopic confirmation of both components and adequate sampling to rule out the presence of neuroblasts. Although several immunohistochemical markers have been described to differentiate the two components, most have cross-positivity and are not definitive. The marker that has been most useful for us to distinguishing both components is the Neurofilament, something that we have not found specifically reflected in the literature.

E-PS-05-033

Morular metaplasia in different types of tumours

G. Raskin*, D. Davydova, M. Mukhina, E. Kravtcova, U. Dobrynina, M. Popov, D. Rianzhin
*Dr. Berezin Medical Institute, Russia

Background & objectives: Morular metaplasia is a special type of neoplastic transformation, which has unique pathogenesis, immunophenotype, morphology that isn't associated with squamous differentiation, unrelated to the localization of the tumour. A comparison of morulaes in thyroid and endometrial carcinomas was carried out.

Methods: The specimens of the cribriform morular thyroid carcinoma and the endometrioid carcinoma of the endometrium from 2 different patients have been investigated: an immunohistochemical examination of formalin fixed and paraffin embedded specimens has been conducted with antibodies to beta-catenin, CD10, CDX2 and ER. The thyroid tumour sample have been investigated by NGS using the set of 82 genes.
Results: In both cases, the morular structures appeared as nesting clusters of medium-sized elongated cells, with a moderate amount of eosinophilic cytoplasm and low grade cellular atypia. In the literature review it was found that the pathogenesis of morulae is based on the breakage of the signal pathway WNT/beta-catenin, which may be caused by germline (APC) or somatic (CTNNB1, QRAS, AXIN1, TERT and PI3KCA) mutations. In immunohistochemical study the cells of the morules expressed CD10, CDX2 and beta-catenin - nuclear expression, expression of ER was negative. In thyroid tumour the mutations of genes APC, CTNNB1, AXIN1 and PI3KCA have not been detected by NGS.
Conclusion: Morular metaplasia occurs in many organs and has similar morphology, immunophenotype and pathogenesis despite of localization of the pathological process. The biological potential of this phenomenon is unknown, but the presence of morulae may be a sign of mutation and may affect the prognosis of the disease.

E-PS-05-034
Oncocytic adrenal tumours: report of 3 cases
P. Rodrigues Veiga*, A. Lapa, M. Jácome, A.L. Cunha
*Department of Pathology, Portuguese Oncology Institute of Porto (IPO-Porto), Portugal

Background & objectives: Oncocytic adrenal tumours are rare and usually non-functional tumours, being more prevalent in younger women. We present three cases of oncocytic adrenal tumours diagnosed at our institution since 2014, in which the Lin-Weiss-Bisceglia criteria was used.
Methods: Of the three cases, two of them were women and the other was a man, aged between 47 and 62-years-old, all asymptomatic at diagnosis. The tumours were in the right adrenal gland in two cases and in the left adrenal gland in the third. The tumour size on imaging varied between 4.5 and 13cm. All cases underwent surgery.
Results: Microscopically, the three cases presented a tumour with a diffuse pattern, consisting of more than 90% of oncocytic cells.
The first case was a 3cm tumour, without necrosis. There was no vascular, sinusoidal, or capsular invasion. The mitotic index was inferior to 1 mitosis/50HPF, without atypical mitoses.
The second was a tumour weighing 342g and measuring 10.5cm, with areas of necrosis and a mitotic index of 2mitosis/50HPF, without atypical mitoses. Capsular, vascular, or sinusoidal invasion was not observed.
The third was an 11.3cm nodule, with areas of necrosis and vascular invasion. The mitotic index was 57mitoses/50HPF, with atypical mitoses. No sinusoidal or capsule invasion was observed. Liver metastases were present.
Conclusion: Due to the oncocytic cells exhibiting eosinophilic cytoplasm, high nuclear grade, and a diffuse growth pattern, oncocytic adrenal tumours must be classified according to the Lin-Weiss-Bisceglia system. According to this system, the presence of any major criteria defines malignancy, the presence of any minor criteria indicates uncertain malignant potential and the absence of any criteria, major or minor, defines a benign tumour. The three cases were diagnosed as oncocytic adenoma, oncocytic tumour of uncertain malignant potential and oncocytic carcinoma, respectively.

E-PS-05-035
Morpho-functional adaptive changes in the pituitary-adrenal system of rats after long-term exposure to heavy metal salts and the use of L-tocopherol
A. Romaniuk*, N. Hryntsova, A. Maliuk, M. Lyndin, N. Hyriavenko, K. Sikora, Y. Lyndina
*Sumy State University, Ukraine

Background & objectives: The morphological and immunohistochemical (Hsp90α) features of the pituitary gland and adrenal cortex were studied under the conditions of adaptation to long-term exposure to heavy metal salts in the experiment and the use of protective therapy L-tocopherol.
Methods: The animals of the experimental group were treated with L-tocopherol for 30 days after a 90-day exposure to a combination of heavy metal salts. Determination of the expression of the heat shock protein 90 (Hsp90α) marker was performed using antibodies to the Hsp90α protein (1:200). The result was expressed as a percentage and evaluated according to an accepted scale.
Results: L-tocopherol increased the expression level of Hsp90α in glandulocytes of the adenohypophysis and adrenal cortex. A diffuse positive reaction of the cytoplasmic type was observed in 85-92% of adenohypophysis cells. In the corticocytes of the glomerular zone of the adrenal glands, a weak (+) and moderately positive (++) expression level of Hsp90α was detected in the cytoplasm of 70-84% of cells with a mosaic of the detected areas of Hsp90α expression. In the bundle and reticular zone, a weakly positive Hsp90 (+) expression level was observed in the cytoplasm of 56-61% of cells. In the reticular zone, cells positive for the marker were located in the form of islands.
Conclusion: L-tocopherol showed bright adaptive, protective, and restorative properties regarding the gradual restoration of homeostasis in the pituitary-adrenal system of experimental animals during the 30 days of adaptation, increasing the level of expression of Hsp90α in the cytoplasm of granulocytes of both central and peripheral units, with a predominance of restoration processes in the adenohypophysis.

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E-PS-05-036
Adrenocortical sarcomatoid carcinoma: a rare case report and review of the literature
L. Ruddy*
*Columbia University Medical Center, USA

Background & objectives: Sarcomatoid carcinoma is an extremely rare variant of adrenocortical cancer with fewer than 30 reported cases. This lack of data makes it difficult to characterize its clinical, morphologic, molecular, and genetic features. A novel case of ASC is reviewed here.
Methods: Following surgical resection of the adrenal gland in a 71-year-old male with a previously undiagnosed adrenal mass and vague symptoms, we analysed the patient's clinical, radiologic, macroscopic, microscopic, and immunohistochemical findings. We then performed an extensive literature search, correlating our findings with our patient's clinical presentation, pathogenesis, and prognosis in an effort to further characterize ASC morphology and behaviour.
Results: Gross examination revealed a 13.4 cm necrotic mass completely replacing the normal adrenal. Histologic analysis showed expansive sheets of malignant spindle cells and an immunohistochemical profile supporting a diagnosis of ASC. Within six weeks, the patient developed metastases to the contralateral adrenal, ribs, and brain, and succumbed to his disease within three months. Morphology and clinical behaviour are consistent with prior literature, with no known cases of patients living past one year. No clinically significant mutations were identified in our patient. Newer research suggests activation of the epithelial-mesenchymal transition process and its mediation by the

Wnt/B-catenin pathway are implicated in ASC tumourigenesis, but a definitive evidence-based consensus is still lacking.
Conclusion: We present a novel case of ASC to further characterize these rare tumours and more clearly define their clinical and prognostic implications, as our current lack of understanding combined with the high propensity for distant metastases is associated with a remarkably poor prognosis. Correlation of our findings with those of limited available literature suggests a general consensus regarding macroscopic and microscopic tumour morphology and clinical behaviour; however, additional research on tumour pathogenesis is needed to identify potential chemotherapeutic targets.

E-PS-05-037
Validation of thyroid fine needle aspiration rinse with indeterminate cytology results as a suitable sample type for molecular testing
P. Santiago Díaz*, S. Clavé Safont, A. Sánchez Cabrero, S. Prat Mendez, M. Bautista Castro, E. Torres Fernández, E. Moragón Massey, S. Torres Rodríguez, M.d.C. Vela Ortiz, B. Bellosillo Paricio, B. Lloveras Rubio
*Department of Pathology, Hospital del Mar, Barcelona, Spain

Background & objectives: Fine needle aspiration (FNA) constitutes a first-line approach for thyroid nodule diagnosis, yet indeterminate morphological results complicate patient management. Molecular testing may aid risk evaluation. This study assesses the feasibility of mutation testing on remaining cytological material from FNA rinse.
Methods: 72 Bethesda III/IV samples (2018-2022) were analysed. 40 had molecular data from matched surgical specimens. 6 FNA later corresponded with papillary thyroid carcinomas. DNA was isolated using QIAamp DNA Mini-Kit (Qiagen), with quality metrics noted. BRAF V600E was assessed by CAST-qPCR. FNA samples with non-BRAF mutations in surgical specimens underwent next generation sequencing (NGS) with Oncomine Focus Assay (Thermo Fisher).
Results: DNA extraction was successful in 72 samples, yielding a mean DNA concentration of 59.4 ng/µl. BRAF V600E assessment with CAST-qPCR was informative in 69/72 (96%) samples, with only one case mutated (1.4%). NGS analysis in 6 FNA samples with non-BRAF mutations in matched specimens revealed valid results, with 4 cases showing HRAS or NRAS Q61R/K mutations, consistent with matched surgical sample findings. Overall, 5 mutations were detected in FNA samples out of 8 (62.5%) found in 40 surgical specimens. Missed mutations on FNA (2 BRAF V600E, 1 rare KRAS P34R) were due to low sample concentration conditioning limit of detection or hypothesized clonal heterogeneity due to different lesional areas sampled.
Conclusion: FNA rinses are a suitable source to perform molecular analysis after morphological evaluation maximizing diagnostic efficiency. Additionally, BRAF V600E is not the sole pathogenic alteration in thyroid cancer, so expanding tests to include other molecular alterations may enhance diagnostic utility using this available material.

E-PS-05-038
Synchronous medullary and papillary thyroid carcinomas: a case report of thyroid collision tumours
C. Ben Takaya, Y. Sarra*, W. Mokni, I. Bahri, S. Frini, D. Chiba, R. Sedego, N. Abdessayed, M. Mokni
*Department of Pathology , University hospital of Farhat Hached, Sousse, Tunisia

Background & objectives: Thyroid collision tumours (TCT) are rare entities defined by the synchronous occurrence of multiple neoplastic processes within the thyroid. We report a TCT of Papillary thyroid carcinoma (PTC) and Medullary carcinoma (MC) in order to discuss the challenges encountered in this diagnosis.
Methods: A 68-year-old male patient, without familial history of neoplasia, presented with anterior low-cervical swelling with extremely increased calcitonin levels (5000 pg/mL). Ultrasound revealed a totolobar nodule with highly suspicious features (TIRADS V) and a suspicious right cervical lymph node. A total thyroidectomy with adenoidectomy, and bilateral functional and recurrent laryngeal nerve lymph node dissection was performed.
Results: Grossly, the right lobe was occupied by a nodule of 6x4x2.5cm with heterogeneous cut surface featuring white and yellow areas without evidence of extra-thyroid extension. Microscopically, the nodule revealed a mixed malignant tumour proliferation wherein two carcinoma types were extremely intermingled. The predominant component showed, amidst amyloid stroma, poorly cohesive and often plasmocytoid-like cells with uniform round nuclei and fine stippled chromatin characteristic of MTC. The 2ndcomponent consisted of PTC exhibiting follicular structure with crowded and deformed nuclei. Multiple bilateral lymph node metastases of both carcinoma types were observed, either intermingled or separated. Immunohistochemical analysis confirmed the diagnosis of this TCT of MTC and PTC.
Conclusion: TCT account for 1 % of all thyroid tumours, with MTC and PTC being the most common co-occurrence. A germline point mutation of RET may be involved in the pathogenesis of this combination. MTC may show variety of patterns, rendering its diagnosis difficult, particularly in TCT. One of the main differential diagnoses is MTC with papillary-like nuclear features. The management of TCT is challenging due to the presence of two distinct tumours with different aggressiveness, treatment and prognosis.

E-PS-05-040
Metastasis to the thyroid gland: a 17-year retrospective study in a tertiary hospital
J. Sobreiro Furtado Silva*, P. Cunha Brito, J. Pardal
*Unidade Local de Saúde de Braga, Portugal

Background & objectives: Metastasis to the thyroid gland (MTG) is still considered a rare entity and its diagnosis can be challenging. The aim of this study is to contribute to the knowledge of the correlation between cytology, histology and clinicopathology features.
Methods: A retrospective analysis of MTG cases diagnosed in the Pathology Department of a tertiary hospital was conducted from May 2006 to September 2023. Clinical and pathological data were collected and analysed.
Results: Eight cases of MTG were identified. The prevalence of MTG was 0,01%. The mean age at the time of diagnosis was 62 ± 13 years. In this series, 75% (n=6) of cases, the primary tumour originated from the lung. In 7 cases, there were concomitant metastasis to other organs. Metastases were synchronous with the primary tumour in 6 patients, and in four, the diagnosis of the primary tumour was made on thyroid cytology/histology examination. Two patients underwent total thyroidectomy. No thyroid specific treatment was made in the others. Currently, only two patients are alive and the median survival after the diagnosis of MGT was 6,5 months.
Conclusion: In general, prognosis for patients with MGT remains unfavourable and is related to the aggressiveness of the primary tumour. Despite being a rare entity, the incidence of MGT may increase due to the widespread use of diagnostic imaging, allowing for earlier detection of alterations at this level.

E-PS-05-041
Challenges in the diagnosis of adrenal hemangiomas through two cases mimicking malignancy
A. Syrnioti*, G. Petrakis, S. Laskou, K. Sapalidis, G. Raptou
*Department of Pathology, School of Medicine, Aristotle University of Thessaloniki, Greece

Background & objectives: Hemangiomas are benign vascular tumours that pose significant diagnostic challenges when they rarely arise in the

adrenal glands, due to their clinical, radiological, and histopathological similarity to a broad variety of both benign and malignant entities.
Methods: We present two cases of adrenal hemangiomas in adult female patients. Imaging revealed right and left adrenal gland masses measuring 6.2 cm and 8.2 cm in greatest diameter, respectively, mimicking malignancy. Laparoscopic adrenalectomy was performed. Gross examination revealed well-defined masses with a combination of white-tan solid areas and dark-red haemorrhagic cystic regions. Hematoxylin-eosin and immunohistochemical stained sections were examined.
Results: Microscopic examination of both adrenal masses revealed diffuse fibrosis, haemorrhagic necrosis, and hyalinization around vascular channels of various size, shape, and wall thickness. These were lined by a single layer of endothelial cells without significant nuclear atypia or pleomorphism and were occasionally filled with erythrocytes or fibrin thrombi. Calcifications were frequently noted near or within the wall of the vascular channels. On immunohistochemical evaluation, the endothelial cells were positive for CD34, CD31, and ERG, with rare cells showing positivity for the Ki67 proliferation index. The surrounding, compressed adrenal parenchyma showed no remarkable changes. Based on these findings, the diagnosis of adrenal hemangioma was established.
Conclusion: Our cases highlight the necessity for a comprehensive diagnostic approach, integrating clinical, radiological, and histopathological findings to accurately identify adrenal hemangiomas. They are typically detected incidentally during imaging. Suspicion should be high in a cystic or haemorrhagic adrenal mass. Notably, a subset of these tumours may coexist with epithelial tumours, emphasizing the need for extensive specimen sampling and thorough microscopic examination. Enhanced awareness among clinicians and pathologists is crucial to prevent misdiagnosis and ensure appropriate treatment strategies.

E-PS-05-042
An unusual case with anaplastic transformation of papillary thyroid carcinoma with liver metastasis
A. Therapontos*, C. Vourlakou, E. Spiteri, E. Athanasiou, P. Vlachou, A. Georgiou, C. Kouvidou
*Department of Pathology, Evangelismos General Hospital, Athens, Greece

Background & objectives: Papillary thyroid carcinoma (PTC) metastasizes to regional lymph nodes while distant metastasis is rare. Anaplastic thyroid carcinoma has a very poor prognosis. We present a very rare case involving anaplastic transformation of PTC with an unusual distant metastasis to liver.
Methods: A 67 year old woman with a history of total thyroidectomy due to PTC 13 years ago , recurrence to regional lymph nodes 6 years later that treated with high dose radiotherapy for three times. The patient presented to our hospital with dyspnea and increased liver enzymes and multiple metastasis at liver , lung , bones and brain at PET-CT.
Results: The core biopsy of the liver nodule revealed morphological features of PTC (intranuclear inclusions) while the classical features (nuclear grooves , clearing , overlapping) not found. The neoplastic cells were epithelioid , pleomorphic with hyperchromatic nuclei and prominent mitotic activity. Necrosis , spindle or sarcomatoid morphology was not observed. Immunohistochemical staining showed positivity for HBME-1 , Galectin-3 , CK7 , TTF-1 , Napsin while PAX-8 and thyroglobulin were negative. P53 nuclear staining was positive in 80% of cells and Ki67 in 35% of them. BRAF(V600E) showed cytoplasmic positive staining. The immuno-morphological findings in correlation with the aggressive clinical behaviour the diagnosis of anaplastic transformation was done.
Conclusion: The liver metastasis from PTC is rare with a reported incidence of 0,5%. Metastases to the liver appear to be an advanced manifestation of the disease in association with other metastatic sites. The liver metastasis is considered to represent the terminal face of the disease and the prognosis is poor. Several hypotheses regarding the mechanism of anaplastic transformation of (PTC) which are genetic mutations in genes as BRAF and TP53 , the history of radiation exposure and radioactive iodine therapy.

E-PS-05-043
Ectopic Cushing´s syndrome in small cell lung cancer: is there sufficient evidence?
A. Ura*, E. Moser, M. Evert, K. Evert, E. Sipos, M. Kremer, K. Steiger, C. Mogler, H. Hoffmann, A. Werder von, D. Kaemmerer, G. Klöppel, A. Kasajima
*Department of Pathology, TUM School of Medicine and Health, Munich, Germany

Background & objectives: Current literature describes small cell lung cancer (SCLC) as common cause of ectopic Cushing syndrome (ECS). However, since there is no critical review of published cases based on current diagnostic criteria, the true association of SCLC with ECS is unclear.
Methods: Pathological and clinical features of previously reported cases with ECS were systematically reviewed mainly using PubMed as a search engine. In addition, 63 SCLCs (30 resected, 33 biopsied) were assembled, immunohistochemically screened for ACTH expression. The presence of a clinically apparent ECS was excluded.
Results: Our literature review revealed 230 patients with ECS and SCLC published between 1928 and 2023. Other terminologies than SCLC included oat cell carcinoma (n=73, from 1928 to 1990) and reserve cell carcinoma (n=1 in 1960). Histological pictures were provided in 45 articles. The quality of these pictures allowed tumour reassessment in 27 cases. 24/27 (89%) cases were re-classified as neuroendocrine tumour (NET) based on morphology. In 3 cases, the diagnosis of SCLC could not be rejected. In our cohort, 4/30 (13%) resected SCLCs showed single cell ACTH expression. None of the patients had Cushing syndrome.
Conclusion: Most (203/230) of the reviewed SCLC cases with ECS provided insufficient information for reassessment of the tumour diagnosis. The tumours in cases (24/27) with appropriate information (i.e., histology pictures) corresponded to NET. Only in 3 cases, the diagnosis of SCLC remained likely. Since single ACTH cells were found in 13% of resected SCLCs, the development of ACTH positive SCLC seems to be possible, however, probably in much lower frequency than the reported cases suggest.

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E-PS-05-044
PitNET/adenoma with loss of expression of AIP protein
P. Vlachou*, A. Therapontos, E. Athanasiou, P. Xekouki, E. Pissadaki, K. Barkas, R. Kakatsidi, G. Kyriakopoulos
*Department of Pathology, Evaggelismos General Hospital , Athens, Greece

Background & objectives: Somatotroph PitNET/adenomas with loss of expression of AIP protein correspond to a rare entity which is linked to Familial Isolated Pituitary Adenomas (FIPA), typically manifesting as macro-adenomas in youth.
Methods: A 20-year-old male with Sella Turcica macroadenoma underwent transsphenoidal tumour resection. Hematoxylin/eosin staining was used in the submitted sections. Immunohistochemistry for PIT-1, SF-1, TPIT, CK8/18, e-cadherin, Cyclin-D1, GATA-3, ER, GH, PRL, β-LH, β-FSH, ACTH, α-subunit, TSH, SSTR2a, SSTR5,

p53, ki-67, SDHB, Menin, ATRX and AIP was also performed, as well as Reticulin histochemical stain.
Results: The histological characteristics consisted of a neuroendocrine cell tumour with abundant eosinophilic to pale cytoplasm, containing pale cytoplasmic fibrous bodies, and oval-shaped nuclei. The cells were organized in a solid pattern inside a hyalinized, vascularized stroma. The ki-67 proliferation index was 2%. Immunohistochemically, full expression of the transcription factor PIT-1 was observed, with an accompanying limited expression of GH and PRL hormones. Cell cycle protein Cyclin-D1 was overexpressed. Loss of expression of AIP protein was observed, while Menin and ATRX protein expression was retained. Following the immunohistochemical results, a background check to the family members of the patient was performed, which revealed the presence of pituitary adenomas in relatives.
Conclusion: Familial pituitary adenomas occur in the context of either MEN1, Carney Complex or Familial Isolated Pituitary Adenomas (FIPA). FIPA is a rare entity representing around 2-5% of pituitary adenoma cases. The most common germline mutation found in family members with FIPA is that of AIP protein encoding gene, which is a tumour suppressor gene. These tumours are typically large and resistant to treatment and emerge early in life.

E-PS-05-045
Spindle cell oncocytoma/oncocytic pituicytoma: a case report of a rare entity
P. Vlachou*, E. Spiteri, A. Georgiou, O. Kouroukli, D. Efthymiou, S. Avgousti, A. Bairamis, G. Kyriakopoulos
*Department of Pathology, Evaggelismos General Hospital , Athens Greece

Background & objectives: Spindle cell oncocytoma/ Oncocytic pituicytoma is a rare, low – grade pituitary tumour, which macroscopically can be misdiagnosed for other pituitary neoplasms. Surgical evaluation and management pose challenges due to macroscopic similarities.
Methods: A 63-year-old female patient with a pituitary lesion underwent transsphenoidal resection of the tumour. Hematoxylin/eosin staining was used in the submitted sections. Immunohistochemistry for PIT-1, SF-1, TPIT, CK8/18, AE1/AE3, SOX-10, S100, Chromogranin A, Synaptophysin, INSM-1, TTF-1, PAX-6, Olig-2, GFAP, CD34, STAT-6, Galectin-3, Annexin-1, Antimitochondrial antibody (AMA), NeuN, Neurofilaments, INI-1/SMARCB1, GATA-3, SDHB, PHH-3 and ki-67 was also performed.
Results: Histologically, neoplastic cells displayed spindle or epithelioid morphology with abundant eosinophilic cytoplasm and moderate to high grade nuclear atypia. The cells were organized in trabeculae forming whorls and perivascular rosettes, inside a hypocellular, hyalinized stroma. The ki-67 proliferation index was 8% and the mitotic index was 0,8 mitosis per 2mm2. Immunohistochemically, S100, Galectin-3, Annexin-1 and Antimitochondrial antibody (AMA) markers were diffusely positive in all neoplastic cells. In addition, transcription factor TTF-1was expressed in the majority of the cells. The rest of the markers were negative.
Conclusion: Spindle cell oncocytoma/ Oncocytic pituicytoma is a rare, low – grade neoplasm of the posterior pituitary with high recurrence rate. It can be difficult to diagnose because it resembles adenomas in both imaging and gross analysis. Histologically, it can be confused with other pituitary neoplasms and therefore, it requires a broad diagnostic approach. Conclusively, clinical, imaging and histological correlation is essential for the diagnosis.

E-PS-05-046
Prognostic factors in gastroenteropancreatic neuroendocrine neoplasms
A. Zammouchi*, R. Bennoui, F. Hadj Hammou, N. Moulai, S. Ahmed Allal, G. Ifaidi, W. Ouahioune
*CHU Blida, Algeria

Background & objectives: Digestive neuroendocrine neoplasms (NEN) are a heterogeneous group of tumours in terms of primary tumour site, functionality, differentiation, treatment and prognosis. The aim of this study was to determine the prognostic factors of patients with digestive NEN in our population.
Methods: We performed a retrospective and prospective monocentric study on a series of 128 cases of digestive NNE collected in the department of Anatomy and Cytology Pathology of the CHU Blida on a period of 5 years (January 2017-December 2021).
The tumour characteristics recorded were differentiaion, Ki-67 index, grade, stage, mutation of p53 and Rb detected by immunohistochemistry.
Results: The mean overall survival (OS) was 44,40 months. The estimated 1, 3 and 5 year OS rates for all patients were 78,9%,76,9% and 67,3% respectively. Using univariate analyses, we found that age ($p<0,0001$), differentiation ($p<0,0001$), grade ($p < 0,0001$), Ki-67 index ($p<0,0001$), disease stage ($p=0,013$), p53 mutation ($p < 0,0001$) and Rb loss ($p <0,0001$) were associated with poor survival. On multivariate analysis, age, p53 mutation and Rb loss were the only independent poor prognostic factors.
Conclusion: In addition, we conclude that a precise evaluation of these prognostic factors (age, differentiation, grade, Ki 67 index, disease stage, P53 mutation, Rb loss) in our population will allow a better prediction of the evolutionary risk of patients and will thus orient the therapeutic strategy.

E-PS-06E-Poster Session History of Pathology

E-PS-06-001
The collection of cardiac pathology derived from the Royal Pathology Museum of the University of Turin
L. Ferrari*, F. Zampieri, S. Micalizio, G. Vinardi, E. Duregon, M. Papotti
*University of Turin, Italy

Background & objectives: The Pathology Museum of the University of Turin houses a historical collection of cardiac pathology dating from the late nineteenth century to the early twentieth century. The samples were collected at autopsy and, after fixation, stored in the fluid.
Methods: In recent years, the re-evaluation of the Museum of Pathology has begun. The study of the samples is based on the original diagnosis reported on the label and, if possible, on the comparison with the autopsy report and on the macroscopic examination of the sample. Due to the peculiarity of these samples, histological sampling was performed only in selected cases.
Results: This study allowed the cataloguing of 63 cases of cardiac pathology, 29 of which are still in the original jar preserved in original liquid. Among them, there are cases of infectious diseases such as 8 cases of endocarditis and 5 of tuberculosis and a rare case of endocardial myxoma. The preservation of the specimens is good and no specific restoration was required. The sampled cases show a good preservation of histological details despite the long immersion in the fluid. The composition of the fluids is unknown, but it was certainly not formol, since it was not used at the time, at least according to the old textbooks of museum techniques.
Conclusion: This collection is relevant for the history of pathology, because it shows old diseases now disappeared thanks to modern therapies. Some of these diseases were very common in the past, such as tuberculosis. The peculiarity of this collection is their historical documentation due to the original labels with the original diagnosis and the number of autopsy reports. These specimens can be useful for educational purposes thanks to its macroscopic preservation but also for an atlas of gross and microscopic paleopathology.

E-PS-06-002

The death of King Jan III Sobieski – was the disease terminal or the treatment deadly?

J. Gulczynski*, P. Paluchowski, J. Kropidlowska, E. Izycka-Swieszewska
*Medical University of Gdansk Dept. of Pathology and Neuropathology, Poland

Background & objectives: King Jan III Sobieski died at age of 67. In letters we can trace development of symptoms and find confirmation of clinical diagnoses. Nevertheless we can still argue on the real cause of death - was it disease or treatment.
Methods: We analysed historical sources including personal letters and published articles presenting possible course of disease and following treatment of Polish King leading to his demise. We can also take into consideration his way of living, alimentation, sexual contacts, consequent acquired disease, later complete intolerance of any phyiscal activity and long term treatment. We had accessed also his autopsy report.
Results: After and before election as a King of Poland, Jan Sobieski led very active life as a warlord and politician, with indulgence in food and drinks developing soon obesity, hypertension, and later physical exercise intolerance, frequent dyspnea, arthralgia, gout, nephro- and cholelithiasis. In his letters he describes vividly symptoms of all his ailments. Apart from those he contracted from his future to be wife, Maria d'Arquien de la Grange, so called French disease. The last one was treated by royal physician with calomel (mercury chloride), well known almost panaceum for any disease. It was considered as panaceum for all ailments.

Conclusion: The autopsy report confirms common maladies, including cardiomegaly, stones in urinary bladder, bile ducts and gallbladder. Signs of chronic exacerbated circulatory failure were confirmed. Extreme obesity with ascites and subcutaneous oedema. Apart from that probable sepsis (purulent pleuritis and pneumonia, pyelonephritis) with description of probable early purulent peritonitis without signs of perforation. The liver also looked altered. The obducents stated that kidneys were the source of health breakdown. But was calomel the reason or just accelerated already existing renal failure.

E-PS-06-003

History and future of the Museum of Macroscopic Pathological Preparations of the Department of Pathology School of Medicine University of Zagreb (1914-2024)

M. Kolić*, S. Sikirić, S. Seiwerth
*University of Zagreb School of Medicine, Croatia

Background & objectives: The Museum was established in 1924 with the arrival of the prosector Aleksandar Govorov at the Department of Pathology in Zagreb. After Govorov, the collection was managed by Josip Mihaljević, who worked as a preparator from 1957 to 1985.
Methods: In researching the history of the collection, we utilized archival material from various archival institutions and preserved preparations.
Results: The Museum was established in 1924 with the arrival of the prosector Aleksandar Govorov at the Department. Govorov cataloged around 3,500 preparations before retiring in 1951. After Govorov, the collection was managed by Josip Mihaljević, who worked as a preparator from 1957 to 1985. The issue of organizing the collection became relevant again after the Zagreb earthquake on 22 March 2020. The main goal is to organize the collection in accordance with contemporary museum standards, following similar examples of pathological collections. The collection currently contains approximately 1.400 preserved preparations. We recognize the need to provide suitable spatial conditions for the collection and appoint an educated person to oversee it.

Conclusion: The biggest issue is the lack of professional care. Since 1985, the heads of the Department attempted to organize professional care for this collection without finding understanding neither at the level of the School nor at higher levels. Another problem is that the collection has never been legally regulated as a museum. However, the post-earthquake reconstruction of the Department building and the historical valorisation of the collection have provided an opportunity to revitalize it in line with contemporary standards.

E-PS-06-004

Virtual autopsy investigation of gallstones in a 18th century Sicilian mummy

L. Ventura*, V. Pensiero, G. Romeo, A. Causarano, C. Caruso, M. Traversari
*San Salvatore Hospital, L'Aquila, Italy

Background & objectives: Gallstones represent a relatively rare finding in ancient human remains, and they are almost always related to high social classes. We report gallbladder stone disease detected by computed tomography-guided virtual autopsy in a natural mummy dating back to 18th century.
Methods: The mummified body of an anonymous individual found in the church of S. Anna in Modica, south-eastern Sicily was conservatively investigated by external examination and computed tomography (CT) scanning. 3D rendering and virtopsy approach enabled us to recognize multiple stones in the gallbladder, whereas densitometry allowed to reconstruct the exact stone morphology and to establish chemical composition.
Results: The mummy belonged to a plump elder man with poor dental status, calcified lung nodules, pelvic phleboliths, and severe osteoarthritis of the spine and the right hip. Seven gallstones measuring 1.3 to 2.0 cm in largest diameter were observed. They had ellipsoid shape and inhomogeneous morphology with central hypodense cores and density values ranging from 70 to -289 Hounsfield Units (average: -40). These features suggested combined cholesterol gallstones. Literature review allowed to find 21 cases of ancient cholelithiasis dating back from 2nd millenium BC to 16th century AD. The age at death was between 25 and 60 years old, with a female predominance, and a 3:1 ratio of cholesterol:pigmented stones.

Conclusion: Gallstones may be easily recognized in natural mummies through CT-guided virtopsy approach, whereas densitometry may help to establish their chemical composition. In the present case, cholesterol-based stones were probably due to dietary factors and genetic predisposition like their modern counterparts. Along with the other pathological findings (obesity, phleboliths, dental status) gallbladder stones represent a good bioanthropological marker of high social class.

E-PS-06-005

The brucellosis of the Blessed Sante from Montefabbri (1343- 1394) in direct and textual sources

L. Ventura*, L. Arrizza, M.G. Palmerini, C. Mercurio, M. Polidori, G. Mandolini, G. Fornaciari, A. Fornaciari
*San Salvatore Hospital, L'Aquila, Italy

Background & objectives: Giansante Brancorsini was born to a noble family in Montefabbri, Italy. He joined the Franciscans after killing an aggressor, to live a life of penance for his sin. Recently, shotgun metagenomics allowed to identify Brucella melitensis DNA in his remains.
Methods: His skeletonized remains underwent external inspection, on site radiographic survey, and tissue sampling for additional

investigations. Some of the nodules found in his abdomen/pelvis were investigated by stereomicroscopy (SM), scanning electron microscopy with energy dispersive X-ray analysis (SEM-EDX), histology, X-ray diffraction (XRD) analysis, and Fourier's transformed infrared (FTIR) spectrometry. Hagiographic sources were studied in order to look for medical citations.
Results: Several calcified polylobate nodules were found in the abdomino-pelvic cavity near the lumbar vertebral tract. BSM, SEM, and histology/histochemistry showed the presence of an external fibrous capsule containing inner amorphous material, corresponding to necrotic debris. SEM-EDX and XRD highlighted the presence of apatite in the nodule, whereas FTIR demonstrated DNA and human serum proteins as organic compounds. Moreover, high resolution SEM with back scattered electrons allowed to visualize several micrococci measuring 1-3 micrometers in largest diameter in the inner portions of the nodule. Hagiographic sources reported that he suffered for many years a large and deep sore in the right groin and recurrent fever, until he died in august 1394.

Conclusion: Advanced morphologic and analytical investigation allowed to establish that the nodules found in the body were lymph nodes affected by granulomatous necrotizing lymphadenitis caused by Brucella melitensis. The micrococci observed by SEM morphologically corresponded to Brucellae. These findings are in agreement with multifocal periostitis and spondylodiscitis recognized in the skeleton as well as with the clinical history referred by hagiography. In conclusion, this represents the most ancient case of a morphologically documented brucella lymphadenopathy also with ultrastructural evidence of bacteria.

E-PS-06-006

Questionnaire portrait of the outstanding Russian scientist-pathologist academician of the Academy of Medical Sciences of the USSR Professor Donat Semyonovich Sarkisov (05.09.1924–16.11.2000)
A. Zubritsky*
*Russia

Background & objectives: Born in Moscow into family of doctors. He graduated from Military Medical Academy (MMA) (1947), which was evacuated to Kirov. He began his scientific creative activity with series of works on studying reversibility of chronic pathological changes in internal organs.
Methods: Defense of his candidate's dissertation on the topic "On the issue of the toxicity of tannic acid for the liver and kidneys logy and function of the brain on the occurrence, course and outcome of experimental pneumonia (1955). Researcher, Marine Medical Research Institute (1947–49); assistant, Senior Lecturer, Department of Pathological Anatomy, MMA (1949–58); demobilized (1958).
Results: Head, Department of Pathological Anatomy, Institute of Surgery named after A.V. Vishnevsky Academy of Medical Sciences of the USSR (1958–2000); he created the theory of intracellular regeneration, which in its philosophical essence is the development of the position of motion as a form of existence of matter, developed at the current level of medical knowledge the recombination mechanism of the occurrence of pathologies and protective reactions of the body – the doctrine of combinational transformations ("the law of combinational transformations" – the 4th law of philosophy, D.S.Sarkisov's law). He is the author of 170 scientific publications, including 18 monographs on various problems of pathology.

Conclusion: Distinctive feature: Love of science, possessed great sense of humor, unusually friendly and at the same time absolutely principled person. Hobbies: History of Russian literature and medicine, issues of culture, art, politics, public life. Laureate of the N.I.Pirogov Prize, the USSR State Prize (1981) and the Russian Federation (1996). He died at the age of 77th from colon cancer. He was buried at the Vagankovskoye cemetery in Moscow.

E-PS-07E-Poster Session Nephropathology
E-PS-07-001
A retrospective analysis of the spectrum of renal diseases at a regional tertiary centre for renal pathology
A. Al-Omari*, H. Issa, L. Brammar, A. Kret, B. Wagner
*Sheffield Teaching Hospitals NHSFT, United Kingdom

Background & objectives: The incidence of renal disease varies both regionally within the United Kingdom and globally. The pathological analysis of renal specimens is complex and requires integrating light-microscopy, special-stains, immunohistochemistry, direct immunofluorescence-studies, and electron-microscopy (EM), along with clinical input, to enhance diagnostic precision.
Methods: A retrospective analysis of histopathology reports of predominantly renal biopsies, in addition to a smaller number of nephrectomies, spanning 2018 to 2021 was conducted. This encompassed 692 cases which included native, transplant and donor kidney specimens. Data was categorised into age distribution, gender, diagnosis, and overall type of renal pathology.
Results: The gender distribution revealed 306 females and 386 males, with ages ranging from 16 to 96 years. Of the 692 cases, 491 were native kidney specimens, which exhibited a range of pathologies including glomerular, tubulointerstitial, vascular and infective disorders. Notably, IgA nephropathy was the most frequently encountered disease, with a total of 84 cases. The diagnosis of 21 cases (including Fibrillary Glomerulopathy, Monoclonal Immunoglobulin Deposition Disease, Immunotactoid Glomerulopathy and various genetic diseases of collagen) was reliant on EM. The majority of transplant and donor kidney specimens showed tubulointerstitial disorders.

Conclusion: This study explores the spectrum of renal diseases observed locally in South Yorkshire, in native, transplant and donor kidney specimens. These findings offer valuable insights for clinicians and pathologists, underscoring the imperative for precision in diagnosing renal diseases. It also highlights the crucial role of EM in diagnosing certain challenging renal disorders.

E-PS-07-002
Dendritic cells and interstitial fibrosis in IgA nephropathy patients - new relations to an old story
Y. Ananiev*, E. Aleksandrova, M. Nikolova, I. Erkanyan, E. Tilkiyan
*Department of General and Clinical Pathology, Forensic Medicine, Deontology and Dermatovenerology, Medical Faculty, Trakia University, Bulgaria / Department of Pathology, Military Medical Academy, Sofia, Bulgaria

Background & objectives: IgA nephropathy is the most common glomerulonephritis. The progression is different depends of infiltrating with immune cells and dendritic cells. The purpose of this study is to compare infiltration with CD8+lymphocytes and dendritic cells with fibrosis and expression of TGF-beta1.
Methods: We investigated 22 patients with IgA nephropathy in different classes according to Haas and Oxford IgA Nephropathy Classification immunohistochemically, with antibodies against CD1a, CD83, CD8 and TGF-beta1. The clinic-laboratory parameters and histology findings were analysed.

Results: We found that 17 of all cases were positive for TGF-beta1. Cases with interstitial fibrosis >25% (T1 and T2) had more CD1a-positive and CD83-positive dendritic cells compared to these <25% (T0) (3.24+/-1.23 and 1.5+/-3.22 vs. 1.09+/-1.22 and 0.8+/-2.1 cells/mm2, p=0.001, Mann–Whitney U test). The number of CD8-positive T-lymphocytes was higher in cases with high infiltration with CD83-positive dendritic cells, but not significant higher compared with CD1a-positive dendritic cells (x2=13.2; p=0.028 vs. x2=1.98, p=0.134). In addition CD83 were higher in number for TGF-beta1 positive cases compared to TGF-beta1 negative cases (p=0.009, Mann–Whitney U test).
Conclusion: Our results suggest that cases with higher infiltration with CD83-positive dendritic cells had expression for TGF-beta1, grater interstitial fibrosis and more CD8-positive lymphocytes compared with cases with lower infiltration with mature or immature dendritic cells.

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E-PS-07-004
Correlation of hsa-mirna-342-3p and SOX 6 expressions with diabetic nephropathy classification, prognostic histomorphological parameters and laboratory findings in renal biopsy diagnosis with diabetic nephropathy
G. Arslan*, Y. Karabulut, İ. Yeleser, M.E. Erdal, S. Demir, A.A. Özdemir
*Mersin University, Department of Pathology, Mersin, Turkey

Background & objectives: Diabetic nephropathy(DN) is one of the leading causes of end-stage renal disease. We focused on the genetic and immunohistochemical expression of SOX 6 and hsa-miR-342-3p in DN biopsies and correlation with clinical findings for new methods of diagnosis and treatment.
Methods: In our study, 110 cases with DN confirmed by biopsy were included. Genetic expressions of hsa-miR-342-3p and SOX 6 by Real Time PCR and immunohistochemical staining of SOX 6 in tissues were studied, and their relations with clinical and histomorphological parameters were evaluated.
Results: An inverse relationship between genetic expressions hsa-miR-342-3p and SOX 6 has been demonstrated. SOX 6 genetic expression was correlated with serum creatinine and tubular basement membrane thickening. Immunohistochemically SOX 6 staining was observed with mesangial cell and podocyte in 21, tubular staining in 45, and interstitial staining in 27 patients. It was shown that tubular staining was associated with proteinuria, interstitial fibrosis and inflammation; interstitial staining was associated with creatinine; and staining in the glomerular compartment was associated with advanced DN class.
Conclusion: Our study is the first in the literature in which SOX 6 was applied immunohistochemically in human kidney tissue, and its relation with DN classes was examined. It is also valuable regarding its correlation with laboratory and histomorphological parameters. Our findings provide a valuable contribution to the literature for future studies on larger patient groups and will contribute developing new biomarkers regarding DN therapy and predicting the course of the disease.

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E-PS-07-005
Evaluation of the number of eosinophils in interstitium of kidney biopsies of patients with diabetic nephropathy: can it predict the prognosis?
J. Carrillo Checa*, J.A. Torres Ortiz, A.J. Hernández García, M.N. Villca Huayta, A. van der Biezen, M.Á. Tribaldos Villar, D. Arroyo Rueda, F.J. Díaz Crespo
*Service of Pathological Anatomy, Regional University Hospital of Málaga, IBIMA Plataforma BIONAND, Spain

Background & objectives: Previous studies have found an association between eosinophilic interstitial infiltrate and worse renal function in patients with diabetic nephropathy (DN). We performed a study to evaluate the relationship between eosinophils in interstitium and glomerulus with clinico-histological findings and prognosis.
Methods: Retrospectively, we collected different clinical and histological variables from 23 diabetic patients diagnosed in our hospital between April 2017-July 2022 in whom a renal biopsy was performed due to worsening of proteinuria or renal function. Histological data were reviewed in hematoxylin-eosin, PAS, silver-methenamine and Masson's trichrome stains. Number of eosinophils/mm2 were assessed in the interstitium, tubules and glomeruli.
Results: Of the 23 patients, 18 were men and 5 women, with a mean age of 59.9 years (26-72). According to Tervaert classification: class I (1 patient), class IIa (3), class IIb (2), class III (10) and class IV (7). 3 patients were diagnosed of acute tubulointerstitial nephritis and 6 with other renal pathologies in addition to DN: 1 patient with IgA nephropathy, 1 with endocapillary glomerulonephritis, 1 extracapillary glomerulonephritis, 2 with focal and segmental glomerulosclerosis and 1 with thrombotic microangiopathy. In the statistical analysis, a higher number of interstitial eosinophils was associated with a greater need for dialysis (t student = -0.933, p = 0.034), regardless of associated glomerulopathy.
Conclusion: We have not detected any differences in interstitium changes of biopsies of patients with DN alone or with other glomerulopathies. But, we have found a correlation between the number of interstitial eosinophils and need for dialysis, regardless of associated glomerulopathy. A higher number of eosinophils could predict a greater need for renal replacement therapy. Studies with a large number of patients are necessary to confirm these results.

E-PS-07-006
Surveillance biopsy in recipients of kidney transplantation
I. Caruntu*, R. Avram, A. Covic, T. Andrian, A. Covic, S.E. Giuşcă
*Department of Morphofunctional Sciences I, "Grigore T. Popa" University of Medicine and Pharmacy, Iasi, Romania

Background & objectives: Banff Classification is the working tool for the antibody-mediated rejection (AMR) and T-cell mediated rejection (TCMR) diagnosis, in recipients of kidney transplantation. Our study focuses on lesion spectrum identified in periodic assessment of allograft status by surveillance or protocol biopsies.
Methods: Study group comprised 44 patients who underwent, between February 2020 and March 2024, surveillance biopsies at one year after kidney transplantation. Renal specimens were processed for light microscopy (H&E, PAS, trichrome and methenamine silver stains) and immunofluorescence (anti-Cd4) exams. Histopathological changes were assessed by using Banff lesion scores. Diagnostic classes have been set up in accordance with 2022 Banff Classification.
Results: Histology revealed normal biopsy or nonspecific changes (Banff Category 1) in 4 patients. Morphological changes and semiquantitative scores sustained chronic active AMR (Banff Category 2) in 4 cases, acute TCMR (Banff Category 4) in 2 cases, chronic active TCMR (Banff Category 4) in 5 cases, interstitial fibrosis and tubular atrophy (Banff Category 5) in 23 cases. 5 cases presented other changes not considered to be cause by acute or chronic rejection (Banff Category 6). In a single case, the material was insufficient. Active or chronic AMR (Banff Category 2) or borderline for acute TCMR (Banff Category 3) were not diagnosed.

Clinico-biological parameters of patients were consistent with Banff diagnostic categories.
Conclusion: The original Banff Classification registered updates reflecting the in-depth understanding of relationship between immune mechanism involved in transplantation and allograft microscopic lesions. Although Banff criteria are applied in monitoring transplant recipients, few studies report on surveillance or protocol biopsies for which no standardised follow-up algorithm has been established. Our study points out that monitoring of patients through protocol biopsies allows early recognition of histological changes, detection of subclinical renal pathology, adjustment of treatment and improvement of long-term allograft outcomes.

E-PS-07-007
The function of renal cortex and proteinuria: a human biopsy study
M.B.C.Y. Chow*, S. Brodsky, A. Chow
*North District Hospital, Hong Kong

Background & objectives: Proteins filtered from blood through the glomerular filtration barrier are reabsorbed by proximal tubular epithelial cells (PTECs) in form of tubular protein reabsorption droplets (TPRDs). Here we investigate the correlations between proteinuria, TPRDs and histologic markers in human kidney biopsies.
Methods: Consecutive native kidney biopsies performed at the OSU-WMC for a 1-year period were analysed. Cases with acute glomerular diseases and inadequate biopsies were excluded. The staining intensity and percentage of TPRDs by immunofluorescence and other histologic parameters were assessed.
Results: 109 cases were included into the study. A reverse correlation was found between the percentage of albumin TPRDs and proteinuria (p=0.047). There was positive correlation between proteinuria and the degree of acute tubular necrosis (ATN) (p=0.015). In patients with no ATN, positive correlations between proteinuria and albumin TPRDs and IgG TPRDs were seen, whereas in patients with ATN these correlations were lost. A positive correlation was seen between proteinuria and the number of globally sclerosed glomeruli and interstitial fibrosis.
Conclusion: Our data indicates that the degree of proteinuria is correlated with the function of PTECs and their ability to absorb proteins from the urinary filtrate. When PTECs are injured, proteinuria increases simultaneously with the degree of ATN. Similarly, proteinuria positively correlates with the degree of chronic kidney injury. Therefore, functioning renal cortex is necessary in the regulation of proteinuria.

E-PS-07-008
Nephrotoxicity of chemotherapy: ten years' experience
M. De Uribe Viloria*, V. Macarrón, G. Escuer-Albero, S. Quinones, C. fuentes Fernández, M.C. Vega Cabrera, B. Rivas, E. García Fernandez, L. Yebenes
*La Paz University Hospital, Spain

Background & objectives: The kidney is one of the main drug elimination pathways for antineoplastic compounds and their metabolites. Chemotherapy-related nephrotoxicity is a deleterious adverse drug event that is on the rise, greatly limiting the efficacy of cancer treatment and increasing morbimortality.
Methods: We reviewed our files from 2004 to March 2024 and found 9 patients with kidney biopsies taken while undergoing chemotherapy treatment. We performed routine staining and direct immunofluorescence studies in all cases. Then we evaluated each of the compartments (glomerular, tubulointerstitial and vascular). Epidemiological data, symptomatology and treatment information were obtained from the clinical history.
Results: Our study included 9 patients (2 female, 7 male; median age 67.5). 1/9 patient was treated with alkylating agents, 3/9 with tyrosine-kinase inhibitors, 1/9 with checkpoint inhibitors (CPIs), 1/9 combined Antifolates and CPIs, 1/9 combined platinum-based drugs (PBDs) with taxanes and CPIs, while 2/9 combined PBD and antimetabolites. Out of all patients 7 showed varying degrees of Acute tubulointerstitial nephritis (ATIN) (3/7 severe, 3/7 moderate and 1/7 mild). One of which had severe arteriolar hyalinosis and focal and segmental glomerulosclerosis. One of the patients treated with PBD-antimetabolites (Gemcitabina) presented with thrombotic microangiopathy (TMA) while showing no sings of ATIN. In four cases tubular acute necrosis was found.
Conclusion: Chemotherapeutic agents, both conventional cytotoxic agents and targeted agents, may damage any segment of the nephron. Our study showed varying degrees of damage in all three compartments studied, though tubulointerstitial damage should be highlighted. After our diagnosis treatment was suspended in 6 patients, 2 of whom died shortly after. Recognising and reporting these changes will improve early detection of chemotherapy-associated complications and may affect patients outcomes through modification, interruption, or suspension of therapy.

E-PS-07-009
Kidney biopsy evaluation in ANCA-associated vasculitis: a diagnostic and prognostic tool to be empowered
C.A. Gomez Gonzalez*, B. Sarsık Kumbaracı, F. Tastekin, Z. Akcali, S. Sen
*Department of Pathology, Ege University Faculty of Medicine, Turkey

Background & objectives: End-stage renal disease (ESRD) is a worldwide concern due to its impact on public health and patients' lives. Rapidly progressive glomerulonephritis, such as ANCA-associated vasculitis is a group with morbidity to be focused on.
Methods: 111 kidney biopsies performed in Ege University Hospital,Izmir,Turkey; between January 2012-2019, with ANCA-positive status were reevaluated. Berden histopathological classification,Mayo Clinic Chronicity Score, and Renal Risk Score were calculated, with detailed histopathology descriptions. Serum creatinine,eGFR,hematuria, proteinuria at baseline; treatment,eGFR in 1 and 5 years- follow-up, dialysis requirement, and death for survival rate. Statistical significance (SPSS software) was evaluated with a p-value<0.05.
Results: The median age of cases was 58 years old, with 62(55,9%) female and 49(44,1%) male cases. Cases grouped by clinical syndrome EGPA n=2, GPA n=38, MPA n=34, and unclassified n=37. Cases grouped by ANCA-type were MPO-ANCA n=73, PR3-ANCA n=35, MPO/PR3-ANCA n=1, MPO/ANA n=1, and MPO/AntiGBM n=1. Mixed and sclerotic classes of Berden classification had a higher prevalence of 35,5% 28,2%respectively; Mayo Clinic Chronicity Score, moderate and minimal categories had high frequency 30,9% and 28,2%. 45,5% of the cases had medium Renal Risk Score. Statistical differences were noticed in the age of presentation,eGFR at diagnosis, and IF/TA. Survival analysis detected a relation between lung compromise and IF/TA.
Conclusion: Chronicity findings in biopsies were noticed in 66,7%. Evaluation of interstitial inflammation, fibrosis, and tubular atrophy are remarkable for the outcomes of patients. Kidney biopsy for the diagnosis of ANCA-vasculitis has a high impact on the care flowchart of patients, detailed interpretation with clinical data might light up the treatment and further follow-up, attending the risk of developing ERSD with survival rate impact.

E-PS-07-010
Renal changes as adverse effects of VEGF inhibitor therapy in patients with malignant diseases

M. Horacek*, P. Šenjug, J. Josipović, G. Radulović, K. Altabas, D. Galešić Ljubanović
*Department of Pathology, University of Zagreb School of Medicine, Zagreb, Croatia

Background & objectives: Bevacizumab is a monoclonal antibody to vascular endothelial growth factor (VEGF) used for treatment of various malignant tumours. A significant adverse effect of bevacizumab is nephropathy that resemble those in thrombotic microangiopathy (TMA), FSGS, or cryoglobulinemic glomerulonephritis.
Methods: Herein, we present five patients, average age 63 years who underwent kidney biopsy between 2019 and 2024 due to proteinuria and/or chronic kidney failure and suspicion of the toxic effect of bevacizumab. Two males with colon cancer and three females with ovarian cancer were included.
Results: The average 24-hour proteinuria was 3 g, average serum creatinine 86,3 μmol/l, and average eGFR 78,3 mL/min/1,73m2. Light microscopy revealed an average of 20,6 glomeruli, with 4,6 showing global and 3,4 segmental glomerulosclerosis. Pseudothrombi were present in all biopsies, with mean diameters of the largest pseudothrombus per glomerulus for each patient measuring 23,2 μm; 19,7 μm; 22,7 μm; 23,5 μm and 26,9 μm. Additionally, duplication of the GBM was observed in the glomeruli. Interstitial fibrosis and tubular atrophy affected in average 10 % of the parenchyma. Mild fibrointimal thickening of the artery wall and moderate to severe arteriolar hyalinosis were present. Electron microscopy showed psudothrombi with loss of endothelial cells.
Conclusion: Bevacizumab-induced nephropathy is a relatively new entity with TMA-like elements, distinguished by the presence of hyaline pseudothrombi. It is important to consider it as a differential diagnosis in patients with malignant disease undergoing bevacizumab therapy and presenting with proteinuria. Diagnosis is established by kidney biopsy, however, clinical data, including therapy information, are essential for an accurate diagnosis.

E-PS-07-011
Unusual onset of a CCRCC with metastases in the vagina
A. Mazuch*, D. Anderco, A. Cumpanas, A. Dema
*County Emergency Clinical Hospital "Pius Brinzeu" Timisoara, Romania

Background & objectives: Clear cell renal cell carcinoma is the most common renal epithelial tumour, typically presenting as a solitary cortical mass within the kidney. Primary metastases frequently occur in the lungs and pleura, with exceedingly rare instances observed in female genital organs.
Methods: We present the case of a 56-year-old woman who presented with vaginal bleeding to the Gynecology Department. A polypoid vaginal mass, initially suspected as a primary vaginal tumour, was resected. Our laboratory was consulted for a second opinion. Immunohistochemical (IHC) study employed anti-PAX8, CA9, CK7, ER, p16, and S100 antibodies. Following 6 months of immunotherapy, the patient underwent left nephrectomy.
Results: Upon local examination, a polypoid mass of the vaginal wall was discovered, which on microscopic examination was determined to be a high-grade clear cell carcinoma. The immunohistochemical profile PAX8+/CA9+/CK7-/ER-/p16-/S100 suggested a renal origin rather than a primary genital tumour. A CT scan was performed which showed a tumour in the left kidney. After 6 months of immunotherapy, a decision was made to proceed with nephrectomy. Gross examination of the kidney revealed a tumour with multinodular growth. Microscopic examination confirmed the diagnosis of clear cell renal cell carcinoma (CCRCC) with rhabdoid features, G4, ypT3aNxV1M1. The patient is alive 2 years after the diagnosis.
Conclusion: The case highlights the unusual presentation of a CCRCC metastasis and emphasizes the importance of considering such metastases when encountering clear cell histology. Additionally, it advocates for the use of immunohistochemistry to assist in confirming the diagnosis.

E-PS-07-012
Collagen-specific molecular chaperone (Hsp47) could reveal cells involved in renal fibrogenesis - a potential target for future therapies?
A. Mioljevic*, G. Nikolic, M. Pecic, D. Milivojevic, P. Djuric, A. Jankovic, R. Naumovic, S. Radojevic Skodric, N. Bogosavljevic, M. Zivotic
*Institute of Pathology, Faculty of Medicine University of Belgrade, Serbia

Background & objectives: Excessive collagen production underlies chronic kidney disease progression. The aim was to correlate clinical parameters and degrees of tubular atrophy and interstitial fibrosis with the extent of Hsp47 (Collagen-Specific Molecular Chaperone) expression in kidney biopsies to identify collagen-producing cells.
Methods: Study included 30 human kidney samples stained with Hsp47 antibodies. Patients were divided into two groups: those with single cells and/or rare focal Hsp47 expression, and those with numerous interstitial foci and/or diffuse expression.
Results: The dominant expression pattern of Hsp47 was characterized by immunopositivity in renal interstitial cells. The amount of Hsp47 interstitial staining was significantly higher ($p<0.001$) in cases with more than 25% of tubulointerstitium affected with interstitial fibrosis and tubular atrophy. Clinical parameters of renal function (serum creatinine, urea, proteinuria, and estimated glomerular filtration rate), were worse in patients with higher Hsp47 expression, although these differences weren't statistically significant. Beside interstitial cells, some atrophic tubule cells expressed Hsp47 and cases with glomerulosclerosis also. Expression in pericytes and in the endothelium of capillaries and larger blood vessels was not confirmed by this staining method.
Conclusion: The study reveals a strong correlation between Hsp47 expression in renal interstitial cells and increased degree of interstitial fibrosis and tubular atrophy, suggesting Hsp47 as a marker for chronic kidney disease severity. The significance of this study lies in its potential for the application in new therapeutic modalities that could suppress collagen biosynthesis, even in cases of terminal renal insufficiency, potentially making the process of fibrogenesis a reversible condition in the future.

E-PS-07-013
Severe cryoglobulinemic vasculitis associated with monoclonal gammopathy: a challenging case of masked deposits
G. Nogueira Fontinha*, B. Fernandes, L. Rodrigues, A. Esteves, A.C. Pimenta, J. Amaral, R. Alves, V. Sousa
*Institute of Anatomical and Molecular Pathology, Faculty of Medicine of the University of Coimbra, Coimbra, Portugal

Background & objectives: Cryoglobulinemic vasculitis is a rare small vessel vasculitis commonly affecting the skin and the kidneys with a female sex preponderance. Its causes include infection being Hepatitis C virus the most common agent, autoimmune conditions and lymphoproliferative disorders.
Methods: A 56-year-old man presented with bilateral distal digital necrosis and surrounding soft tissue infection. Symptoms started the previous week. Blood analysis revealed increased inflammatory kinetics and acute kidney injury (serum creatinine (sCr) 2,17 mg/dL and serum urea 35,0 mg/dL). The patient started antibiotic therapy with a further need for finger amputation.

Results: Additional investigation revealed type II cryoglobulins (cryoprecipitate consistent with polyclonal immunoglobulin (IgG) and monoclonal lambda light-chains), mildly increased rheumatoid factor and normal complement levels. Urine showed an active sediment. Serum electrophoresis and urine immunofixation showed monoclonal heavy IgG and lambda light chains. Bone marrow analysis was consistent with MGUS.
Kidney biopsy revealed proliferative glomerulonephritis, with endocapillary, mesangial, and extracapillary proliferation (15% crescents), leukocytoclastic vasculitis, tubulointerstitial edema and diffuse acute tubular necrosis. Immunofluorescence demonstrated C3 (2+/3+) granular mesangial deposits. IF on formalin-fixed, paraffin-embedded tissue after protease digestion revealing granular capillary and mesangial lambda light chain deposits. Electron microscopy showed focal podocyte effacement and immune mesangial and subendothelial space deposits.
Conclusion: The diagnosis of cryoglobulinemic vasculitis secondary to MGUS of clinical and renal significance was assumed and the patient was initially treated with methylprednisolone and rituximab, followed by cyclophosphamide and bortezomib.

This case illustrates a severe small vessel vasculitis with acute and rapidly progressive cutaneous and kidney injuries in the context of type II cryoglobulinemia. In non-infectious cryoglobulinemia, a hematologic condition is usually present, with up to 65% of patients presenting an MGRS. Kidney biopsy was key to confirm the diagnosis.

E-PS-07-014
Double kidney trasplant due to IgA nephropathy and chronic active antibody-mediated rejection
J. Osuna Soto*, F. Leiva-Cepas, M. Huelva López, I. Sánchez Ramírez, M.J. Gálvez-Medina, R. Sánchez-Sánchez, R. Ortega Salas
*Hospital Universitario Reina Sofía, Pathology Unit, Spain

Background & objectives: IgA nephropathy (IgAN) is the most common primary glomerulopathy worldwide and the one that relapses the most post-transplant. Chronic Antibody-mediated Rejection (CAMR) is a common cause of allograft loss; both entities may coocur more frequently than thought.
Methods: 40-year-old man with chronic kidney disease secondary to IgAN who received two kidney grafts. In the sequential biopsies, histological signs of relapse of proliferative IgAN with hypertensive vasculopathy and Active CAMR were eventually observed. At the moment, kidney function is deteriorated but stable.
Results: First allograft biopsies: mild CAMR, chronic transplant glomerulopathy, hypertensive vasculopathy and mild mesangial IgA deposits. The allograft was explanted due to malignant hypertensive episode.
Second allograft biopsies: the latter showed glomerulomegaly, mesangial hypercellularity with IgA deposits, endocapillary proliferation, presence of histiocytes, mild glomerulitis, capillaritis, mesangial and focal glomerular deposition of C4d in immunohistochemistry. Electron microscopy showed double contours, electron-dense deposits in mesangium and multilamination of the basement membrane in the peritubular capillaries.
Conclusion: The incidence and prognosis of post-transplant recurrence of IgAN are variable; Malignant Hypertension is a rare manifestation, but a severe bad prognostic factor. CAMR is the most common cause of allograft loss in our country. Its diagnosis depends on histollogical or ultrastructural signs, independently of the presence of circulating antibodies. The association of these two entities may occur frequently and the microscopic study is mandatory for the diagnosis and therapeutic management.

E-PS-07-015
Case series of fibrillary glomerulonephritis with the DNAJB9 expression
H.K. Uzkuç*, B. Sarsık Kumbaracı, Z. Akcalı, A. Çeltik, M. Seziş, S. Şen
*Turkey

Background & objectives: Fibrillary glomerulonephritis (FGN) is a rare disease characterized by fibrillar deposits 12-24 nm in diameter. Electron microscopy (EM) was thought to be the gold standard for the diagnosis. However, DNAJB9 discovery has revolutionized the diagnosis and become an alternative diagnostic tool.
Methods: In this study, DNAJB9 and C4d were immunohistochemically applied to the kidney needle biopsy material of twenty-four cases with membranoproliferative and membranous patterns and different glomerular morphologies. The pathological and clinical findings of the cases were recorded.
Results: DNAJB9 was negative in twenty case and the diagnosis were as follows: IgA-nephropathy (4/24), membranous nephropathy (4/24), amyloidosis (2/24), postinfectious glomerulonephritis (2/24), focal segmental glomerulosclerosis (FSGS) (2/24), transplant glomerulopathy (2/24), diabetic nephropathy (1/24), lupus nephropathy (1/24), C3 nephropathy (1/24) and chronic glomerulonephritis (1/24). Four cases with DNAJB9 diffuse positive were evaluated as FGN and the mean age was 47,5 (15-64) years. While polytypic IgG, C1q and C3 accumulation was detected in the immunofluorescence (IF) examination of the three needle biopsy, morphologically it showed membranous-nephropathy, FSGS and membranoproliferative pattern. The biopsy of the remaining case was a consultation material and there was membranoproliferative pattern in the glomeruli.
Conclusion: FGN which is likely to be seen together with malignancies, autoimmune diseases and infections is associated with a wide range of glomerular pathologies. The true incidence is unknown because their non-typical clinicopathological findings. DNAJB9 is highly sensitive and specific at the diagnosis of FGN. In this preliminary study, no specific morphological or clinical clues was observed other than immune-complex deposition. FGN should be kept in mind by pathologists, especially in patients with glomerular pathology and immune-complex accumulation.

E-PS-07-016
The role of pronase digestion and electron microscopy in the diagnosis of monoclonal gammopathies of renal significance
M. Veras Lista*, B. Garzón, M. Alonso Riaño
*Hospital 12 de Octubre, Spain

Background & objectives: Light microscopy (LM) and direct immunofluorescence on frozen tissue (IF-F) are not highly sensitive techniques for diagnosing monoclonal gammopathies of renal significance (MGRS). This case series studies how using pronase digestion (IF-P) and electron microscopy (EM) might improve the sensitivity.
Methods: A retrospective analysis from the last 6 years of all the renal biopsies diagnosed with MGRS in Hospital 12 de Octubre, Spain, excluding AL amyloidosis, was carried out. Clinical and histological variables were reviewed, as well as the role of LM, IF-F, IF-P and EM in the histological diagnosis, and its sensitivity.
Results: 30 cases were included (ratio M-F:16-14, average age: 66.5 years). 15 had known B cell/plasma cell malignancies. 17 cases were clinically suspected of MG. Most common symptom was proteinuria. Techniques other than LM were needed in 28 cases. IF-F was positive in 4/7 patients (57.1%). IF-P showed positivity in 100% of cases; it uncovered light chain restriction in 4 cases with negative or no IF-F study, and confirmed it in 2 with positive IF-F. EM yielded a diagnosis in 28/29 cases (96.6%).

Most frequent pathologies were light chain proximal tubulopathy (n=14, 46.6%) and light chain deposit disease (n=11, 36.7%).
Conclusion: IF-P and EM uncover cases that would otherwise go undiagnosed. In this series, sensitivity with only IF-F is 57.1%, whereas it reaches 96.4% with EM and 100% with IF-P. The sample size of IF-P cases is limited, since many cases were referred from other hospitals for ultrastructural examination only; still, it highlights the value of this technique. While EM is not available everywhere, IF-P is an inexpensive, easily obtainable diagnostic technique that may be used in any department.

E-PS-07-017
Light chain-associated acute tubulointerstitial nephritis: two case reports and literature review
C. Vieru*, M.L. Abascal Camacho, R. Melero, C. Encinas, B. Sualdea Peña, A.J. Van Der Biezen, M.N. Villca Huayta, F.J. Menarguez Palanca, F.J. Díaz Crespo
*Hospital General Universitario Gregorio Marañón, Spain

Background & objectives: Light chain-associated acute tubulointerstitial nephritis (LC-ATIN) is an uncommon pattern of renal involvement in patients with multiple myeloma (MM). Little is known about this entity as only few case series have previously been reported.
Methods: Two cases were identified in hospital´s pathology archives over a 5-year period (2018-2023). In both cases light microscopic examination, immunohistochemical staining for tubular injury markers (p53, bcl2 and Ki67) as well as for light chains (kappa and lambda), direct immunofluorescence and electron microscopic examination were performed. We describe the clinicopathologic characteristics of these cases.
Results: They are two men aged 68 and 84, with clinical history of MM and rapidly progressing renal injury (Cr 2.7 mg/dL and Cr 3.5 mg/dL). Renal biopsies revealed tubular-interstitial changes with moderate lymphocytic inflammation, scattered polytypic plasma cells, neutrophils and eosinophils, associated with tubulitis and tubular damage, confirmed by three immunohistochemistry markers. One case exhibited intratubular light chain casts. This inflammatory response is consequence from abnormal light chain deposition within proximal tubular cells and along tubular basement membranes (TBM), highlighted via linear and granular lambda light chain positivity by immunohistochemistry and immunofluorescence. Electron microscopy displayed granular punctate electron-dense material deposition along TBM's outer aspects. Glomerular and vascular compartments were unremarkable.
Conclusion: LC-ATIN is an uncommon pattern of renal disease in patients with plasma cell dyscrasia, not well recognized clinically nor pathologically. Solely through light microscopy, distinguishing this entity from other forms of ATIN can be challenging, leading to potential misdiagnosis. Its identification requires ancillary diagnostic techniques such as immunofluorescence and electron microscopy. Its accurate diagnosis holds significant importance due to prognostic implications, as appropriate therapeutic intervention may facilitate renal injury correction.

E-PS-07-018
The importance of quality in renal biopsies
M. Vincis*, T. Gul, A. Canino, B. Doyle
*Università degli studi di Cagliari, Italy

Background & objectives: Kidney biopsy is the gold standard for the diagnosis of many renal conditions and can be used in conjunction with clinical signs to diagnose a variety of kidney diseases. The objective is to evaluate the diagnostic adequacy of renal biopsy.
Methods: We retrospectively reviewed 100 renal biopsies reported in the histopathology department of Beaumont Hospital, Dublin. Each renal biopsy was analysed by light microscopy, where possible, immunofluorescence, and electron microscopy. The following features were evaluated: number of cores, length in millimeters, number of glomeruli, and whether the biopsy was considered adequate by the pathologist even when there were not enough glomeruli.
Results: Out of the 100 cases analysed, 79 cases were adequate for diagnosis, and 21 cases had a glomerular count of less than 12. Out of these 21 cases, 5 cases were insufficient for diagnosis.
Conclusion: The study highlights the importance of light microscopy used in conjunction with immunofluorescence and electron microscopy to diagnose cases even if the glomerular count is inadequate.

E-PS-07-019
Evaluation of COVID-19 expression in kidney biopsies after COVID-19 vaccination and/or infection
Y. Karabulut*, G. Aydın Demir, A.C. Çiftçi, A.B. Eser, K. Turgutalp
*Mersin University, Turkey

Background & objectives: Coronavirus disease 2019 (COVID-19) has been causing severe respiratory disease (SARS-CoV-2) since December 2019 and can progress with many organ involvement. Kidneys, which are frequently affected organs, can be damaged by direct or indirect mechanisms.
Methods: Immunohistochemical expression of viral particles was investigated in biopsy materials of kidney diseases that may be related to COVID-19 infection and COVID-19 vaccine. After the histopathological examination of the kidney biopsy material of 90 patients who underwent kidney biopsy within 3 months after COVID-19 infection or COVID-19 vaccination between March 2020 and February 2023, COVID-19 antigen expression was evaluated immunohistochemically.
Results: The average age of the patients was 50. Of the 63 patients who underwent post-vaccination biopsy, 52 were patients with Biontech and 11 were patients with renal dysfunction after the Sinovac vaccine. 16 of 90 patients had Membranous Nephropathy (9 from Biontech, 2 from Sinovac, 5 after infection), 12 from Diabetic Nephropathy (8 from Biontech, 3 from Sinovac, 1 after infection), 9' u He was diagnosed with IgA nephropathy (6 from Biontech, 2 from Sinovac, 1 after infection). Staining was detected by COVID-19 immunohistochemistry study in 2 of the patients who underwent biopsy after COVID-19 infection and in 3 of the patients who underwent biopsy after Biontech vaccine.
Conclusion: Of the patients with COVID-19 immunohistochemical expression detected after vaccination, 2 were diagnosed with IgA Nephropathy, 1 with Diabetic Nephropathy and Non-AA Amyloidosis. Patients with COVID-19 immunohistochemical expression after COVID-19 infection were diagnosed with Focal Segmental Glomerulosclerosis and Tubulointerstitial Nephritis. Renal involvement mainly manifests itself as proteinuria and acute kidney injury. Additionally, as we experienced here the development of SARS-CoV-2 infection may cause exacerbation of pre-existing autoimmune and alloimmune conditions.

E-PS-08E-Poster Session Cardiovascular Pathology

E-PS-08-002
Primary cardiac undifferentiated pleomorphic sarcoma: report of a rare entity
S. Charfi*, S. Makni, S. Graja, T. Ellouze, L. Bouzidi, S. Hidouri, A. Hentati, T. Sellami Boudawara, M. Zghal
*Department of Pathology, Habib Bourguiba University Hospital, Sfax, Tunisia

Background & objectives: Primary cardiac tumours are exceptional. Undifferentiated pleomorphic sarcoma (UPS) is exceedingly rare and occurs frequently in the left atrium. The diagnosis can be challenging

considering similarities with myxoma. UPS is known to be aggressive; early detection and treatment are essential.
Methods: Herein, we describe the case of a 41-year-old woman with no previous history presented to the Cardiology Department with dyspnea and palpitations. The electrocardiogram revealed atrial fibrillation. Echocardiography showed a large left intra-atrial mass suggesting myxoma. Surgical excision of the tumour was performed. The diagnosis of cardiac sarcoma was initially retained.
Results: Four months later, the patient was readmitted due to worsening dyspnea. A computed tomography imaging was performed and revealed a large mass, measuring 9 cm with extension into the pulmonary veins. The patient underwent pneumonectomy with resection of the left atrium. Microscopic examination showed diffuse sheets of tumour cells with extensive necrosis and a scarce lymphocytic infiltrate. Neoplastic cells were epithelioid or spindle with pleomorphic nuclei. The tumour showed myocardial infiltration and pulmonary vein extension. Immunohistochemistry for PS100, SMA, TTF-1 and CD31 was performed showing focal expression. Immunostaining for MDM2, HHV8, cytokeratin, CD34 and desmin were negative. We concluded with a cardiac UPS. Unfortunately, the outcome was fatal.
Conclusion: UPS occurs frequently in extremities, trunk and retroperitoneum. Our case is distinguished because of its unusual location. Cardiac UPS is characterized by a worse outcome with median overall survival at 6 months. The recurrence risk is significantly increased with tumour size, invasion of adjacent tissues, and advanced AJCC staging. Immunohistochemical analysis is useful in establishing diagnosis, but there are no specific immunomarkers. Molecular testing could help make the right diagnosis. Prompt recognition of this tumour allows for early curative treatment.

E-PS-08-004
A rare case of segmental arterial mediolysis presenting with life-threatening haemorrhage following multivisceraltransplantation
J. Coelho Lima*, S.D. Preston, N. Russell, I. Amin, A. Butler, A. Paterson
*Department of Histopathology, Addenbrooke's Hospital, Cambridge University Hospitals NHS Foundation Trust, United Kingdom

Background & objectives: Segmental arterial mediolysis (SAM) is a rare non-inflammatory vasculopathy of uncertain aetiology that frequently manifests with abdominal pain and haemorrhagic shock in males. We present a case of SAM manifesting with life-threatening bleeding complicating the post-operative period of multivisceral transplantation.
Methods: Clinical, radiological, and histopathological data for this case were reviewed. This case report adheres to the Declaration of Helsinki and no identifiable patient information is presented.
Results: A 40-year-old male with liver cirrhosis underwent multivisceral (liver, pancreas, small and large bowels) transplantation due to extensive porto-mesenteric venous thrombosis. Two days post-operatively, the patient developed acute bleeding (Hb 45g/L). Exploratory laparotomy revealed a large-volume retroperitoneal haematoma. Intraoperative computed tomography angiography showed multiple splenic artery aneurysms, with active haemorrhage related to a distal ruptured aneurysm. Due to splenic ischemia, splenectomy was performed. Macroscopically, the spleen had prominently dilated blood vessels. Histologically, one artery showed segmental intimal fibrosis, attenuation of the elastic lamina, and medial degeneration, forming a local aneurysm, without infection or vasculitis. Subsequent imaging studies revealed two right renal artery aneurysms and right internal carotid artery fusiform dilatation.
Conclusion: This is the first reported case of SAM presenting with massive haemorrhage after multivisceral transplantation. Pathologists should be aware of this entity, as histopathological diagnosis of splenic SAM prompted imaging studies that identified additional renal and carotid vascular lesions. These vessels are frequently affected along with the mesenteric, hepatic and coeliac arteries. Although there is no specific therapy for SAM, acute haemorrhagic emergencies require surgical or endovascular intervention. Most vascular lesions resolve or stabilise, but radiological follow-up may be indicated.

E-PS-08-005
Arrhythmogenic cardiomyopathy phenotype associated with an ACTN2 and LMNA gene variant of uncertain significance (VUS)
J. Coelho Lima*, H. Cox, E. Curtis, H.S. Lim, C. Chue, D. Neil
*Department of Histopathology, Addenbrooke's Hospital, Cambridge University Hospitals NHS Foundation Trust, United Kingdom

Background & objectives: Alpha-actinin-2 (ACTN2*)* is an actin-binding protein that stabilises the contractile apparatus at the Z band. *LMNA* encodes lamin A/C, which forms the nuclear envelope scaffold. We present a case of arrhythmogenic cardiomyopathy (ACM) associated with an *ACTN2* and *LMNA* VUS.
Methods: Clinical, histopathological, immunohistochemical (IHC), electron microscopy (EM), and molecular genetics data for this case were reviewed. This case report adheres to the Declaration of Helsinki and no identifiable patient information is presented.
Results: A 45-year-old male underwent heart transplantation for dilated cardiomyopathy. Macroscopically, the heart showed biventricular dilatation with marked attenuation of the right ventricular walls. Microscopically, there was diffuse fibrofatty replacement of the right ventricle with no significant myocyte disarray or dysplastic vessels. Electron microscopy showed 2 – 5um electron dense lattice areas within the sarcomeric components associated with the Z-bands. There was perinuclear staining with lamin A/C on immunohistochemistry. Genetic screening revealed variants of uncertain significance in the *ACTN2* and *LMNA* genes. No other common genetic abnormalities were present.
Conclusion: This is the second reported case of an *ACTN2* variant associated with ACM phenotype and the first including EM findings. The Z-band-associated structures are similar to nemaline rod myopathy in skeletal muscle, for which *ACTN2* mutations are a known cause. This association is supported by a human *ACTN2*-mutant pluripotent stem cell-derived cardiomyocyte study. There was no histological support of lamin A/C involvement. IHC and EM are likely to be useful in determining the significance of genetic VUS in cardiomyopathies.

E-PS-08-006
Intracardiac cavernous hemangioma: case report
H. Erdoğan*, N.S. Şeker
*Turkey

Background & objectives: Primary cardiac tumours are rare and the majority of these tumours are benign. Intracardiac cavernous hemangioma is very rare and constitutes less than 5% of benign cardiac tumours.
Methods: The biopsy specimen was processed for routine paraffin embedding, and 4 μm paraffine sections were stained with H&E stain and used for immunohistochemical analysis with appropriate retrieval techniques, antibody dilutions, and controls.
Results: A 70-year-old female patient applied to the cardiology service with complaints of shortness of breath and fatigue. Echocardiography revealed a mobile mass containing cystic spaces, measuring 50x50 mm filling the right atrium, entering and exiting the right ventricle during systole-diastole. A biopsy was performed for histopathological examination. Microscopically, there were thin and thick-walled vascular structures lined with endothelial cells of varying diameters, stroma showing myxoid changes in places, inflammatory cells and fibrosis in places. The applied immunohistochemical vascular markers were

found to be positive. When the morphological and immunohistochemical findings were evaluated together, the case was evaluated as "intracardiac cavernous hemangioma".
Conclusion: Cardiac hemangioma cases are reported very rarely in the literature. Even if it is a benign tumour, cases can be referred for transplantation in cases where it cannot be completely excised. Although rare among cardiac tumours, it is a group of tumours that should be kept in mind.

E-PS-08-007
Histopathology of the heart atrial appendages in atrial fibrillation after cardiac surgery
Z. Gioeva*, N. Gutyrchik, L. Kakturskij, D. Areshidze, M. Kozlova, A. Stonogin, V. Savina, L. Mikhaleva
*Petrovsky National Research Centre of Surgery, Russia

Background & objectives: Postoperative atrial fibrillation (AF) is associated with a higher risk of thromboembolism and stroke. The study aimed to describe the histopathology of the heart atrial appendages removed during cardiac surgery complicated by AF
Methods: Histological analysis included 26 atrial appendages resected during heart valve replacement, aorto-coronary bypass surgery, mitral commissurotomy, and aortic prosthetics complicated by AF. The comparison group comprised 18 atrial appendages without AF complications after similar operations. The age of the patients ranged from 65 to 85 years. Paraffin tissue sections were stained by H&E, van Gieson, Mallory, and Lie.
Results: Coronary heart disease manifestations (CHD) – cardiosclerosis, perivascular fibrosis, stromal lipomatosis, endocardial fibrosis, venous fullness with sludge phenomenon were equally frequent in both groups. In AF cases, intracellular cytolysis in cardiomyocytes with discomplexation and dissolution of myofibrils, sarcoplasm devastation with sarcolemma exposure, were significantly more common. Contractile impairment and wave-like deformation of muscle fibers were present. Focal interstitial mucoid edema and areas of endocardial edema were detected. An increase in vascular permeability with swelling and proliferation of the endothelium, plasmorrhagia and perivascular edema was observed in myocardial microvessels. Lymphohistiocytic infiltrates were significantly more frequent in the stroma. In 3 AF cases, fresh parietal microthrombs were detected within endocardial edema sites.
Conclusion: Thus, the characteristics of chronic CHD manifestations and acute circulatory disorders, potentially associated with surgery, were common for the groups with and without AF. The distinguishing features of the AF group included intracellular myocytolysis of varying degrees, contractile impairment, mucoid edema of the myocardial stroma, perivascular edema with signs of increased vascular permeability, focal endocardial edema with individual parietal microthrombi.

E-PS-08-008
Pathomorphological characteristics of the heart involvement in systemic amyloidosis
Z. Gioeva*, L. Mikhaleva, A. Volkov, V. Pechnikova, L. Erofeeva, M. Mnikhovich, T. Bezuglova, N. Shakhpazyan
*Petrovsky National Research Centre of Surgery, Russian Federation

Background & objectives: Cardiac involvement in systemic amyloidosis is associated with a poor prognosis. The study describes the pathomorphological features of amyloid deposits in patients with the most common types of amyloidosis.
Methods: We analysed 85 cases of cardiac amyloidosis: 45 endomyocardial biopsies and 40 autopsies. All sections were H&E and Cong-red stained. Immunohistochemical amyloid typing was performed with an antibody panel to different amyloid proteins. The severity of amyloid deposits was evaluated using a scale of Grade 1-3: Grade 1, amyloid deposits occupy ≤25%; Grade 2, 25-50%; and Grade 3, ≥50%.
Results: In all cases Congo red-stained amyloid showed apple-green birefringence in polarized light. Pericellular amyloid deposition was common for AL amyloidosis, multifocal amyloid deposits occurred more frequently in patients with ATTR . More extensive amyloid deposits were observed in cases of AL-kappa amyloidosis, Grade 3 of severity prevailed. 45% of patients with AL-lambda amyloidosis had Grade 2 of severity and 40% - Grade 3. In 50% of ATTR amyloidosis cases the severity of Grade 2 was determined. Grade 2 was more common in patients with AA amyloidosis. The following types of amyloidosis were diagnosed: ATTR in 36 patients (42%), AL-kappa – 17, AL-lambda – 25, and AA in 6 cases.
Conclusion: Most of the patients in our study had AL amyloidosis. ATTR amyloidosis was usually identified after death in people over 90 years of age, more frequently in men. Pericellular diffuse amyloid deposition was more common for AL amyloidosis and multifocal amyloid deposits - for ATTR amyloidosis.

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E-PS-08-009
The role of cardiac amyloidosis in thanatogenesis of familial Mediterranean fever
S. Hambardzumyan*, D. Ghazaryan
*State Medical University Heratsi, Armenia

Background & objectives: Cardiac amyloidosis is a rare and clinically silent affection of familial Mediterranean fever. Early diagnosis and treatment of amyloidosis can prevent an amyloidogenesis and accumulation of amyloid deposits of the heart and other organs.
Methods: Morphological analysis of 105 autopsy observations with thoracic, abdominal and mixed forms of familial Mediterranean fever (P±m=5.71±2.27, 22.86±4.09, 71.43±4.4) distributed in 3 groups, by age of first manifestation of disease during the life: under 5, 5-20 and above 20 years (P±m= 28.57±4.4, 56.19±4.84, 15.24±3.5) respectively were done. For morphological studies Congo red, specific serum of Monoclonal Mouse Anti-human Amyloid-A used.
Results: Cardiac lesions at familial Mediterranean fever in 47.6% ($p<0.05$) of cases were clinically latent, and morphological changes in autopsy material in 52.4% ($p<0.05$) of cases were detected. Amyloidal cardiopathy in the presence of morphologically pronounced cardiomegaly with massive amyloid in the myocardial stroma in 23.8% ($p<0.05$), in the background of amyloidal cardiopathy atherosclerosis of the coronary vessels in 15.2% ($p<0.05$) of cases were detected. Amyloidal angiopathy played an important role, aggravating atherosclerotic vascular lesions in 3.8% ($p>0.05$) cases.
By immunocytological investigation of blood monocytes of patients, in amounts of 7,0±0,72 in the chronic renal failure and 4,93±0,45 in latent stage of disease, the fragments of amyloid fibrillar protein were detected.
Conclusion: Cardiopathic lesions are more found in the autopsy material than being diagnosed clinically. Amyloidal cardiopathy with pulmonary amyloidosis leading to cardiopulmonary failure can prevail in thanatogenesis. Amyloidal angiopathies are playing a role in morphogenesis of myocardial ischemia.

The presence of blood monocytes, containing fragments of A-amyloidal fibrillar protein, indicate their involvement in the process of incomplete degradation of the serum amyloid-A protein and amyloidogenesis. The initial ring of amyloidogenesis is blood, and blood cells act as amyloidoblasts.

E-PS-08-010
Extremely rare location of a heart tumour
R.H. Henriques De Gouveia*, C. Carreira, F. Corte Real
*Universidade da Madeira, Portugal

Background & objectives: Heart Primary Tumours are not frequent and may arise from any cardiac structure. The authors aim to present a begnin primary tumour displaying an extremely rare intracardiac location, that was discovered during medico-legal postmortem investigation.
Methods: A 49-years old male died after a massage session due to backpain (posterior to road trip). He began complaining of backpain and episodes of shortness of breath for 6-15 days. The last health check-up was well. A postmortem study was performed at a Branch of our National Medico-Legal and Forensic Sciences Institute, which included autopsy with toxicological and anatomo-pathological examinations.
Results: Relevant findings of autopsy were cardiopathy, prominent generalized organ vascular congestion and moderate alveolar oedema. The Cardiopathy included lesions of chronic ischaemic pathology (due to coronary atherosclerosis) and a tumoural "mass", located inside the right atrium, polypoid, inserted exclusively in the atrial side of the Eustachian Valve, soft-gelatinous, gray-withish with red foci and measuring 2cm (diameter). Microscopic evaluation of the tumour confirmed the diagnosis of Myxoma. Toxicology results were within/under therapeutic doses for Diazepan/Nordiazepan and negative for alcohol, illicit drugs, pesticides. Death was declared natural, due to Cardiopathy.
Conclusion: The Eustachian valve is an embryological remnant of the inferior vena cava (IVC) valve. Usually, it is absent or inconspicuous. When present, it may extremely rarely be the source of this cardiac tumour, which, despite being begnin, may lead to severe complications, as mechanical occlusion of the IVC orifice, embolization or sudden death. Complete Medico-Legal postmortem examination (including anatomo-pathological and toxicological studies) play an important role, by contribute to reveal, localize and characterize the tumoural lesion, namely in out-of-hospital deaths.

E-PS-08-011
An autopsy case of secondary dilated cardiomyopathy with unexpected endocrine tumour
M. Jovanović*, J. Petrović, S. Tatić, M. Đuknić, I. Petrovic, R. Janković, S. Glumac
*Institute for pathology, MFUB, Serbia

Background & objectives: Dilated cardiomyopathy (DCM) is a disease of the heart muscle characterized by enlargement and dilation of one or both ventricles accompanied by impaired contractility. Secondary DCM is driven by acquired factors (metabolic disorders, infectious myocarditis, ischemic disease, hypertension, drugs, alcohol).
Methods: Detailed gross examination of body (obesity and full-moon face, with stretch marks on abdominal and hip skin), and all internal organs with representative tissue samples have been collected for histopathologic (HP) analysis, which have been routinely processed (formalin fixation, paraffin embedding, 4-5 μm cut slides, hematoxylin-eosin staining). Comparison of clinically diagnosed comorbidity and histopathological correlation.
Results: We present a case of a 52-year-old female who was admitted to the Institute for Cardiovascular diseases "Dedinje" due to radiofrequent ablation treatment of paroxysmal ventricular tachyaritmia, who died four hours after the procedure. Available medical records states she had non specified cardiomyopathy, hypothyroidism, mixed dyslipidemia and myocardial infarction with non-obstructive coronary arteries (MINOCA) in 2020. Grossly, heart was rounded, dilated, with fibrotic and thinned internal third of the anterior and inferior walls of the left ventricle, and the entire septum, without atherosclerosis of coronary arteries. Both adrenal glands were slightly enlarged, nodular, with cortical calcifications, which microscopically proofed to be myelolipomas. Microscopic analysis of thyroid gland conformed Hashimoto's thyroiditis.
Conclusion: This case highlights relationship between cardiovascular and endocrine diseases, particularly in the context of hidden ethology of MINOCA and secondary DCM. The pathological findings of concomitant endocrine diseases like Hashimoto's thyroiditis and clinically non diagnosed bilateral adrenal benign tumours (myelolipomas) in patent with MINOCA and secondary DCM provide valuable insights into the underlying pathophysiological mechanisms. Further research and clinical attention is needed to understand the complex interplay between these entities, improve diagnosis, monitoring and management of patients with secondary DCM.

E-PS-08-012
A case of fibromuscular dysplasia of coronary arteries and congenital heart disease in a newborn
Y. Kuzyk*
*Danylo Halitsky Lviv State Medical University, Ukraine

Background & objectives: Fibromuscular dysplasia (FMD) is a non-atherosclerotic non-inflammatory vascular disease with primary damage to the renal and internal carotid arteries. FMD is known to be a disease of women aged 40-60 years. This pathology occurs exceptionally rarely in children.
Methods: Our study aimed to analyse a rare case of FMD of the coronary arteries in combination with congenital heart disease in an infant.
An autopsy was performed on a 2-day-old child. Histopathological changes of the coronary arteries were studied by standard and elective histological techniques (Hematoxylin & Eosin, Hart's elastin, Heidenhain's azan).
Results: An autopsy of two-day old child revealed along the course of the coronary arteries, numerous rounded protrusions with a diameter of 0.3 to 1.0 cm of the "string of beads" type were found. The oval window was closed by a thin tension membrane, which formed a valve that opened into the left atrium. The mouth of the pulmonary artery in the right ventricle was missing.
Histologically, stellate stenosis was found in the coronary arteries due to severe fibrosis of the vascular wall with pillow-like protrusions. The coronary artery wall appeared to be a continuous array of scattered elastic fibers with multiple fragmentation, lysis, and hypochromia, without division into layers.
Conclusion: This case demonstrates FMD in an infant and is likely congenital. This lesion of coronary arteries of various calibers, from the main trunk to intramural branches, has a rare localization. Histological changes in coronary arteries are characterized by diffuse fibrosis with loss of elastic framework, that is, total fibroplasia. Thus, the peculiarity of this case is a casuistically rare form of combination of FMD of the coronary arteries with a congenital heart defect, such as atresia of the pulmonary artery.

E-PS-08-013
A unique case of the combination of giant cell aortitis, arteritis, and coarctation of the aorta in the 3.5-month child
Y. Kuzyk*
*Danylo Halitsky Lviv State Medical University, Ukraine

Background & objectives: Giant cell arteritis (GCA) mainly damages cranial arteries. It's more common in women and the elderly.
Our study aimed to analyse unique case of GCA in the 3.5-month child to determine the features of clinical symptoms and pathomorphological manifestations.
Methods: We performed to analyse data of clinical signs, laboratory parameters, clinical manifestations, posmorten datas.
A histological examination of the aorta wall and its branches was performed using hematoxylin-eosin staining and additional histochemical

staining: Hart resorcin-fuchsin, Veigert picrofuchsin, Masson trichrome.
We reviewed articles over a 20-year period to compare our case with a similar one.
Results: We present the case of a 3.5-month-old girl died 20 hours after hospitalization due to an acute viral infection involving many internal organs. Viral infection manifested as acute nasopharyngitis, enterocolitis, and acute meningoencephalitis. Postmortem examination revealed giant cell aortitis and arteritis with coarctation of the aorta. GCA, in our case, had pathomorphological features. First of all, many plaques released into the lumen of the aorta had a conical end, which resembled a rash appearance. Secondly, granulomatous inflammation was localized in the intima of the aorta and all layers of small aortic arteries. This makes this case unique from a pathomorphological point of view.
Conclusion: In a 3.5-month-old girl, we found a unique case of GCA that has not been seen before in the literature. Our patient is the youngest with this pathology. The case involved coarctation, aneurysm of the ascending aorta, and aortitis, which had not been described before. GCA, in this case, had pathomorphological features, including conical plaques and granulomatosis inflammation in the aortic intima and small aortic arteries.

E-PS-08-014
Cardiac blood cysts – case report and literature review of a rare entity
H.Y. Chang*, S.H. Lai, L.S. Punjabi, W.S.J. Ong, Y.S. Keh, M.R. Amanullah
*Singapore General Hospital, Singapore

Background & objectives: Cardiac blood cysts are extremely rare benign tumours of uncertain pathogenesis, primarily associated with the valvular apparatus of newborns and infants. We report a right atrial blood cyst in an adult and briefly share the findings from our literature review.
Methods: A previously well 59-year-old female presented with acute-onset chest pain. Echocardiography revealed a 5.8cm right atrial mass attached to the interatrial septum. It is predominantly echolucent with possible internal calcification. Cardiac catheterization showed only mild coronary artery disease. Excision of the mass was performed. Grossly, the mass had a smooth blue-grey glistening exterior.
Results: Histology revealed cystic lesion containing fresh blood. The fibrous wall shows scattered partially organized fibrinous and fibrous foci with dystrophic calcification and is lined by benign-appearing CD31-positive endothelium, consistent with a cardiac blood cyst.
Cardiac blood cysts are predominantly found arising from cardiac valves, most commonly the mitral valve. The right atrium is an uncommon location, with only fifteen cases published thus far. Most patients are asymptomatic or present with non-specific symptoms. Potentially fatal sequelae include embolic stroke and cardiac tamponade. The cysts are predominantly small and round, frequently below 4cm in size, and occasionally pedunculated. Histology consistently shows a cystic lesion lined by bland endothelium, frequently containing non-organized blood.
Conclusion: The pathogenesis of cardiac blood cysts remain unclear. Postulations include trapped blood during valve development, heteroplastic changes in primitive mesothelium, and development from endocardial hematomas. Cardiac blood cysts are extremely rare and are yet to be included in the World Health Organization diagnostic guidelines. With increasing use of radiographic techniques, the detection of blood cysts is expected to increase. Histopathologists, radiologists and clinicians should be aware of this entity.

E-PS-08-015
A unique case of post-transplant progression in a cardiac allograft with pre-existing transthyretin amyloidosis
L. Lockau*, S. Smith, E. Tweedie
*Department of Diagnostic and Molecular Pathology, London Health Sciences Center, Canada

Background & objectives: Cardiac amyloidosis is a form of restrictive cardiomyopathy caused by amyloid infiltration in cardiac muscle, most commonly transthyretin (wild-type or hereditary) or light-chain proteins. We outline a unique case of cardiac transplantation with amyloidosis unexpectedly identified on post-transplant allograft biopsies.
Methods: This case report reviews histology from multiple antemortem cardiac allograft biopsies along with findings from the postmortem examination conducted seven years post-transplant.
Results: Amyloid deposition was identified unexpectedly in biopsies only one-week post-transplant. The patient developed significant heart failure after four years. Postmortem examination seven years post-transplant revealed a heavy (805 g, normal range 244-425 g) heart with marked concentric hypertrophy (left ventricle thickness 2.4 cm, normal range 1.2-1.5 cm) and a firm, waxy, pale myocardium. Allograft atria were dilated with patchy, granular endocardial plaques. Histologically, widespread interstitial amyloid deposition throughout the myocardium (around 50% of myocardial tissue) as well as endocardial deposits were highlighted immunohistochemically with Congo red and transthyretin stains. No amyloid was identified in other tissues. Genetic analysis of the allograft revealed no known pathogenic mutations associated with familial amyloidosis.
Conclusion: This unique case of cardiac amyloidosis has important implications for transplant-recipient health. The allograft previously functioned adequately, and there was evidently ongoing deposition of the recipient's transthyretin protein post-transplant. Animal models and liver transplant studies have demonstrated such progression can occur through amyloid seeding, which operates similarly to prion transmission; this has not previously been described in a cardiac case. We explore how seeding likely contributed to amyloid progression in this patient, resulting in significant heart failure and, ultimately, death.

E-PS-08-016
Coronary stents examined with a scanning electron microscope
B. Magrupov*, V. Ubaydullaeva
*Center for Professional Development of Medical Workers, Republican Research Center of Emergency Medicine, Uzbekistan

Background & objectives: Coronary heart disease is a major problem in the clinic of internal medicine. According to WHO, the mortality rate from cardiovascular diseases is 31% and is the most common cause of death worldwide.
Methods: Coronary stents (n=40) made of cobalt-chromium alloy coated with rapamycin drug were examined using scanning electron microscopy. Expansion of the stent to the nominal diameter was carried out by inflating the balloon catheter in the first group to a pressure of 8 atmospheres, in the second one - 16, the third group – 20 and the fourth one - 30.
Results: Analysis of the data showed that there was a difference in the length and height of the measured segments in the marginal regions and the central zone of the stents. In group 1 it was 0.1 mm, in the second - 0.4-0.5 mm, in the third one - 0.1-0.2 mm and in the fourth group - 0.2-0.4 mm.
The diameter of the proximal sections was larger than the distal ones in all groups. The extensibility specified in the factory specifications was exceeded in group 3 in the proximal section and in group 4 - in both

sections. Coating cracking was observed in the area of loop-shaped areas on metal bends.
Conclusion: The greatest stretching of the stents (horizontally and vertically) occurred in the proximal section, the smallest - in the distal section. The diameter of the proximal sections when opened was larger than the distal ones. Uneven opening of the stent cells was noted in the form of skew and displacement of mutually symmetrical loops to the sides. Identified defects in the drug coating can lead to neointimal hyperplasia and cause adverse effects such as local inflammation and thrombosis.

E-PS-08-017
Morphologic spectrum of a heart damage in methadone-toxicity related deaths
A. Malysheva*, E. Romanova, O. Reshetnikova, A. Ermakov
*Immanuel Kant Baltic Federal University, Russia

Background & objectives: Methadone often used in a treatment of heroin dependence for reducing mortality caused by overdose problems. However, the percentage of fatal outcomes of substitution therapy remains at a high level. Present study focuses on pathological heart peculiarities in methadone-related deaths (MRDs).
Methods: One hundred and sixteen cases MRDs were evaluated taking into account epidemiological characteristics, clinical data, toxicological studies, as well as postmortem analysis data. Heart tissue samples were studied microscopically at magnification x100; x200; x400. Clinical and pathoanatomical comparisons were carried out in the following age groups: less than 17; 18-25; 26-35; 36-45 and over 45 years old.
Results: Microscopic investigation has shown pathomorphological features of myocardial damage with varying degrees of intensity. Acute circulatory disorders with signs of stromal edema, foci of blood stasis in the vessels and perivascular haemorrhages were a common histological finding in myocardial tissue samples from methadone users in age groups under 36 years old. Signs of insufficiency of myocardial contractile function were confirmed by fields of ribbon-like deformation, focal swelling and fragmentation of cardiomyocytes. Age group over 36 had pathological features of chronic processes: perivascular sclerosis, stromal lipomatosis, cardiomyocytes' hypertrophy. Inflammatory infiltrates were often found in the stroma. Such changes in the myocardium were detected in 35% of cases of methadone poisoning.
Conclusion: Analysis of our data allows us to conclude that pathomorphological changes in the myocardium in patients who died due to methadone poisoning play an important role in thanatogenesis and can probably serve as a structural basis for arrhythmias and possible sudden death. Further scientific research into the relationship between pathomorphological changes in the myocardium and the possible risk of death during methadone replacement therapy remains relevant.

E-PS-08-018
The study of clinico-pathological predictors for post cardiac transplant rejection
G. Patrichi*, A.I. Patrichi, C. Satala, S. Voidăzan, A.I. Sin
*Pathology Department, UMFST Targu Mures, Romania

Background & objectives: Despite the continuous development of heart transplantation techniques and the success rate due to advancement of immunosuppressive therapy, cardiac rejection remains one of the most worryisome complications that can occur following this procedure.
Methods: This study includes 146 patients between 2010 and 2023, who underwent transplantation within the Cardiovascular Disease and Transplantation Institute and the follow-up of the evolution of myocardial structure and function after surgery based on endomyocardial biopsies in the Pathology Department of Targu Mures Emergency Clinical County Hospital.
Results: 120 men and 26 women were transplanted, with an approximately equal age range under and over 40 years (48.6% and 51.4%). Evaluating the degrees of acute cellular rejection according to the International Society for Heart and Lung Transplantation classification, in 78.8% of cases there were no histological signs of rejection (grade 0), and in cases where there was rejection, it was quantified as mild rejection (17.1%), with small percentages reporting moderate (2.7%) or severe (1.4%) acute rejection. 58.9% of cases that did not show rejection findings were associated with similar non-rejection lesions. While 21.2% of cases (other than ISHLT grade 0) presenting cellular rejection, only 11.7% had associated humoral rejection.
Conclusion: Although almost 80% of the transplanted cases showed ISHLT score 0, non-rejection related lesion like changes were present in 58.9% of the cases, and because more of the non-rejection related criteria are detected, it may be necessary to adjust the grading rejection criteria.

E-PS-08-019
Quantitative assessment of cardiac muscle fibers density depending on cause of death
I.E. Plesea*, M.S. Șerbănescu, V.T. Grigorean, I.D. Avramescu, L. Iovan, L. Eftimie, R.M. Pleșea
*"Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

Background & objectives: Diseases causing death became more and more diverse and myocardial tissue responds to them with structural and functional changes. The authors compared the variations of muscle fibers-MF amount-% between the different cardiac wall regions depending on patients' cause of death.
Methods: Five epicardium-to-endocardium cross sections (left ventricle anterior-LV_AW, lateral-LV_LW and posterior-LV_PW, interventricular septum-IVS and right ventricle-RVW) from 95 patients died with different causes of death (vascular diseases-V_P, non-vascular diseases-NV_P, and suspect/violent cause of death-S/V_Dth) and autopsied, were processed and stained with Picro-Sirius_Red. Slides were digitized. The MF amount was measured with a dedicated software. Average values-AV were compared using Pearson's test.
Results: The FM percentage is the lowest in V_P, increases significantly in NV_P and decreases a little in S/V_Dths.. In NV_P and S/V_Dths, highest values are in LV_W, followed by IVS and RV_W while, in V_P, the highest values are in LV_W and the lowest in IVS. In the LV_W, values are decreasing from anterior to posterior regions in NV_P and S/V_Dths while, in V_P, they are almost the same in all regions. FM have, in both sexes, a decreasing trend from left to right regions, with highest values in NV_P, and lowest in S/V_Dths in men and highest values in S/V_Dths, and lowest in V_P in women.
Conclusion: This remodeling process of the cardiac wall depending on the cause of death is following the same decreasing pattern of FM percentage along its regions in both sexes, more pronounced in women, but with significant differences between men and women regarding the hierarchy of FM values between the three groups of causes of death.

E-PS-08-020
Discovery of ascending aorta dilatation in a male: unravelling the underlying pathology
C. Salzillo*, L. Giovannico, G. Fischetti, A. Marzullo
*Department of Precision and Regenerative Medicine and Ionian Area (DiMePRe-J), Section of Pathology, University of Bari, Italy

Background & objectives: Dilatation of the ascending aorta is a common incidental finding in the imaging of the chest area, especially in middle-aged males. The pathogenesis is not always obvious in the elderly and a histopathological examination of the surgical specimens is recommended.

Methods: We report the case of a 74-year-old man with a family history of aortic dissection submitted to a chest-abdomen CT scan, which showed an "aortic supravalvular diameter of 38 mm, proximal arch diameter of 37 mm, and diameter of the middle third of the ascending aorta of 50 mm".
Results: Eight months later, echocardiography reports "mild aortic regurgitation, aortic root of 41 mm and ascending aorta of 50 mm" were found.
Subsequently, he was hospitalized at the Cardiac Surgery Unit of the Bari Polyclinic and was treated urgently with the replacement of the ascending aorta with a Gelweave straight vascular prosthesis Vaskutek n.30.
Since the cause of the dilation was unclear, the removed ascending aorta was sent to Pathology.
During hospitalization, the patient was subjected to blood tests, ECG, chest x-ray, and echocardiogram che reports: "straight vascular prosthesis in the ascending site, aortic root ectasia with mild aortic valve insufficiency, hypertensive heart disease II, left atrial dilation, ejection fraction 58%".
Conclusion: Pathology report concluded unexpectedly for a giant cell aortitis. The histopathological examination was therefore essential to define the cause of the dilation of the ascending aorta and patient was submitted to further investigations.

E-PS-08-021
Advancements in understanding and managing chagas cardiomyopathy: implications for global health - a scoping review
L. Vasconcelos Cavalcante*, M.d.F. Figueiredo, A.L. Felipe Dias, G. Gadelha Costa, G. Lopes Teixeira, L. Brasileiro Marques, J. Carneiro Melo
*University of Fortaleza, Brazil

Background & objectives: Chagasic cardiomyopathy (CC) is a common complication of patients with chronic Chagas Disease (CD), due to inflammatory processes associated with the infection. The presence of symptoms already indicates damage to target organs.
Methods: Scoping review using the PubMed database, searching for the descriptor “Chagas Cardiomyopathy”. The filters applied were: Free full text, in the last 5 years, Humans, Exclude preprints, Adult: 19+ years. 83 results were obtained, of which 15 were selected for the study.
Results: Chronic Chagas Cardiomyopathy (CCC) is characterized by inflammation, fibrosis, myocytolysis, vasculitis, and parasitic persistence, leading to different degrees of clinical manifestations. The inflammation can be both a cause of T. cruzi infection and a consequence of HF, playing a central role in disease pathogenesis and progression. Hemodynamic stress associated with HF triggers the release of pro-inflammatory cytokines such as TNF-α, IL-6, IL-1β, and angiotensin II. Cardiomyopathy affect 20–40% of individuals with positive serology results. This condition causes substantial disability and early mortality, especially among young people. Prompt and correct diagnosis of CD requires specialized clinical expertise and innovative and intensified disease management.
Conclusion: The primary factor associated with morbidity in patients with CD is the development of CCC. Non-endemic regions, such as the United States and Europe, are now facing new cases, primarily associated with the immigrant population. Therefore, is important to develop more studies to increase the chances of diagnosing it earlier and treat the disease before it evolves to heart events.

E-PS-08-022
Intimal sarcomas of the heart and great vessels
V.M. Virgone*, A. Celi, A. De Martino, M. Levantino, A. Colli, R. Berchiolli, A. Pucci
*Italy

Background & objectives: Intimal sarcomas are extremely uncommon tumours that involve the major vessels, i.e., the pulmonary artery and the aorta, or the cardiac chambers. They usually carry a dismal prognosis, related also to late diagnosis and/or impossible radical excision in most cases.
Methods: In the last ten years, we diagnosed intimal sarcoma in 4 cases, coming from our Cardiovascular Surgery (N=3) or in consultancy. The tumours, involving the left atrium (N=2), the descending aorta (N=1) or the pulmonary artery (N=1), were excised in 3M and in 1F patients (age range 44-74 yrs, mean 57.5) and investigated by routine histology, immunohistochemistry and molecular techniques.
Results: In all cases, histology showed an undifferentiated neoplasia that was mainly constituted by spindle-shaped, atypical and mitotically active cells with stromal myxoid changes and sometimes (N=1) heterologous differentiation. Extensive immunohistochemical analyses showed vimentin positivity, and focal immunoreactivity for caldesmon, smooth musce actin and desmin; markers for epithelial cells, leukocytes, and melanocytes were negative. Fluorescence in situ hybridization (FISH) for MDM2 showed gene amplification. The patients underwent chemotherapy and/or radiotherapy, followed in a case by cardiac transplantation; the tumour relapsed and/or metastasised, first to the lungs, in all cases with a fatal outcome in 3/4 at 1-6 years follow-up.
Conclusion: Primary cardiac sarcomas are rare and, among them, intimal sarcoma represents a diagnostic challenge because of nonspecific histological features. MDM2 amplification is nowadays considered a molecular hallmark of intimal sarcoma. Therefore, MDM2 test is important in high-grade sarcomas to distinguish them from undifferentiated pleomorphic sarcomas (UPS), also because of possible therapeutic implications.

E-PS-09E-Poster Session Electron Microscopy

E-PS-09-001
Alternative use of C4d immunohistochemistry: an electron microscopic study on immunoflorescence negative kidney biopsies
O. Hurdogan*, S. Solakoglu, Y. Ozluk, I. Kilicaslan
*Istanbul Faculty of Medicine, Turkey

Background & objectives: Glomerular C4d deposition is observed in immune complex-mediated diseases. Immunohistochemical C4d positivity is an indicator of complement activation. We aimed to demonstrate potential relation of C4d to electron-dense deposits on electron microscopy(EM) in biopsies without immune complex deposition on immunofluorescence(IFneg).
Methods: We retrospectively identified IFneg kidney biopsies showing immunohistochemical C4d-positivity. C4d-negative and IFneg cases constituted the control group. The presence and localization of glomerular electron-dense deposits were noted on EM. Statistical analyses were performed using Mann Whitney U, Pearson, and Fisher’s exact tests.
Results: Among 56 cases, 31(55.4%) were male. Mean age was 36.43±18.55 years (median:35,[IQR: 21-54]). Thirty-three (58.9%) were C4d positive, 23(41.1%) negative. The presence of segmental sclerosis was significantly higher in C4d-positive group (12[52.2%] vs. 4[12.1%])(p=0.001). C4d-positive group showed significantly increased number of segmental sclerotic glomeruli (1.26±1.51 vs. 0.27±0.88)(p=0.001). The frequency of proteinuria was significantly higher in C4d-positive group (23[100%] vs. 22[66.7%])(p=0.002). There was no significant difference between groups in terms of age, gender, number of global sclerosis, tubular atrophy/interstitial fibrosis, arteriolar hyalinization, and presence of electron-dense deposits. Electron-dense deposits were present in 3(13.0%) C4d-positive cases (mesengial/paramesengial in 2, various glomerular localizations in 1), and 1(3.0%) C4d-negative case (mesengial/paramesengial) (p=0.295).

Conclusion: The presence of electron-dense deposits is very rare in immune complex negative kidney biopsies. Albeit higher number of C4d positive cases showed electron-dense deposits compared to negatives, our results lacked to show statistical significance. C4d positivity without immune complex deposition is highly suggestive of the presence of segmental sclerosis in glomeruli. We believe that C4d immunohistochemistry is a useful tool for the detection of non-immune complex related pathologies, especially segmental sclerosis, and suggest its routine use in practice.

E-PS-09-002

The role of telocytes in the pathogenesis of massive localized lymphedema of the anterior abdominal wall (ultrastructural study)

N. Makarenko*, I. Chekmareva, B. Gogia, O. Paklina
*Moskow Clinical Scientific Center, Russia

Background & objectives: Electron microscopic examination of tissue samples of skin with Massive localized lymphedema (MLL) to identify and evaluate ultrastructural features of telocytes (TC), and their possible effect on the peristaltic contractility of lymphatic vessels.
Methods: Electron microscopy of skin and hypodermal tissue incision biopsy from the anterior abdominal wall of the 50 years old female patient was performed. The mass of the removed lesion accounted 22160 g. Ultrastructural study of the preparations was carried out using an electron microscope JEM 100-CX in transmission mode at an accelerating voltage of 80 KV.
Results: In the dermis, TCs not previously described in MLL were detected. Numerous TC processes were in contact with the SMC of the blood vessels. TC had characteristic ultrastructural features (long processes - telopodes, extended segments - podoms, thin segments - podomeres) (Fig. 1). Single destructively altered TC with pronounced functional insufficiency were observed around the lymphatic vessels (Fig. 2). Ultrastructural analysis revealed destructive changes in endotheliocytes and SMC of lymphatic vessels. Disorders of myo-endothelial and inter-myocytic contacts, collagenization of the vascular wall, fragmentary endothelial detachment, enlargement of the subendothelial space, destruction of cellular organelles in endotheliocytes and SMC were demonstrated in EM.
Conclusion: For the first time, electron microscopic examination of the specimens was carried out, and TCs were detected in MLL. Destruction of TCs, their number decrease up to the complete disappearance and absence, as well intercellular contacts breaking - are factors likely affecting initiation and development of MLL, promoting the lymphatic vessels tone decrease, enhancing lymphatic stasis. TCs population reduction may be an important etiopathogenetic factor for the MLL development.

E-PS-09-003

Chronic pancreatitis: ultrastructural changes of stromal compartment

N. Makarenko*, I. Chekmareva, O. Paklina, D. Kalinin, D. Atyakshin
*Moskow Clinical Scientific Center, Russia

Background & objectives: evaluation of ultrastructural features of telocytes(TC) in pancreas with chronic pancreatitis in context of developing fibrotic tissue and communication between TC, stellate cells (SC) and inflammatory cells.
Methods: electron microscopy (EM) of pancreatic tissue samples from resection material of 23 patients with chronic obstructive pancreatitis and 6 normal pancreatic tissue samples were performed. Ultrastructural study of the preparations was carried out using an electron microscope JEM 100-CX in transmission mode at an accelerating voltage of 80 KV.
Results: In normal TC located between acinar structures, vessels and nerves. TC had numerous homologous cell-to-cell contacts. There were a lot of exosomes in telopodes and in intercellular spaces. In chronic pancreatitis EM study revealed multiple destructive changes of TC and reduce their number in fibrotic fields. Telopodes were shortened with destructive changes. We observed fragmentational destructure of plasmatic membranes of SC which lost glycogen drops. There are a lot of exosomes between collagen fibers. Single mast cells (MS) were degranulated and granules were observed next to fibroblast and between collagen fibers. Also we observed communication between MC and TC. Fibroblasts were increased in size with well-formed granular cytoplasmic reticulum.
Conclusion: TC play leading role in cell-to-cell communication. We assume they control activity of SC and fibroblasts (FB) and their collagen production. In chronical pancreatitis TC's ultrastructural destructive changes and decrease in their number alter organization of the extracellular matrix in the stromal compartment of the pancreas, weaken intercellular signaling. Also, increase of collagen fibers fraction leads to further TC destruction and block exosome transporting in extracellular matrix.

E-PS-09-004

Ultrastructure of multinucleate trophoblastic giant cell in the myometrium of patients with placenta accreta spectrum

N. Nizyaeva*, T. Sukhacheva, A. Milovanov, T. Fokina, T. Patsaev, V. Bochkov
*Petrovsky National Research Center of Surgery, Russian Federation

Background & objectives: Multinucleate trophoblastic giant cells (MTGCs) are described in the area of invasion of placental villi into the myometrium. Aim of the study was to identify and describe the features of the ultrastructural morphology and immunohistochemical phenotype of the MTGCs.
Methods: Myometrial samples from 19 patients (28-42 yy, 32-38 weeks of gestation) diagnosed with placenta increta were studied. The preparations were stained with hematoxylin and eosin. Cytokeratin (CK 5/6/8/18) and CD68 were detected immunohistochemically. Samples were studied using transmission electron microscope also.
Results: MTGCs with a diameter of $14.2\pm3.3\mu m$ were recorded at the border of the decidua and myometrial smooth muscle cells. MTGCs were stained positively with cytokeratin and negatively with CD68. Electron microscopic examination revealed several large, irregularly shaped nuclei in MTGCs and significant number of granular endoplasmic reticulum cisterns located in parallel rows, which indicates the pronounced synthetic activity of these cells. Golgi complex structures, multiple mitochondria, thin filaments and lipid inclusions were also found in the cytoplasm. Multiple invaginations and cytoplasmic projections – microvilli were located along the entire perimeter of the cell. The sarcolemma of MTGCs was often surrounded by a kind of basement membrane, an amorphous electron-dense material.
Conclusion: Thus, the area of placenta invasion into the uterus in patients with placenta accreta is characterized by an accumulation of polymorphic MTGCs. The epithelial phenotype of MTGCs was confirmed by immunohistochemistry. Ultrastructural morphology of MTGCs contribute to the invasion and migration in the uterus.

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E-PS-09-005

Ultrastructural changes of the lungs in coronavirus infection

M. Semko*, Y. Kuzyk
*Lviv National Medical University, Ukraine

Background & objectives: Damage to the endothelium of the lungs is essential in the pathogenesis of the coronavirus infection. The study aimed to determine, ultrastructural changes in the lung tissue of

patients who died as a result of respiratory failure during coronavirus infection.
Methods: The material was dissected with a puncture needle no later than 2 hours after the patient's death. The study group consisted of ten individuals aged 34 to 85 years with a male to female ratio of 1 to 1.5. The disease duration ranged from 9 to 40 days. Research of lung tissue was carried out by the transmission electron microscopy.
Results: There were patients with respiratory failure due to COVID-19 diagnosed with bilateral interstitial pneumonia, progressive diffuse alveolar damage accompanied by the appearance of hyaline membranes, type II pneumocyte hyperplasia, pronounced dyscirculatory changes, and fibroblast activation. In the lung vessels of patients who died on the 14th, 20th, 22nd, and 40th day of the disease, dyscirculatory processes of varying severity were observed in the form of severe hyperemia, stasis, microthrombi, and alternative changes in the endothelium. As a result of alternative changes in the endothelium, vascular permeability was recorded, coagulopathy and endotheliitis with induction of neutrophil infiltration developed.
Conclusion: Transmission electron microscopy of the lungs of patients who died due to respiratory failure caused by COVID-19, pronounced dyscirculatory changes in the microcirculatory channel with the development of hyperemia, stasis, and microthrombosis, pronounced alterative-necrotic changes in the endothelium were revealed. The identified dyscirculatory processes were accompanied by coagulopathy and endotheliitis, which are key aspects of the pathogenesis and thanatogenesis of COVID-19.

E-PS-10E-Poster Session Gynaecological Pathology

E-PS-10-001
Clinicopathological study of leiomyosarcoma of the female genital tract: a single centre experience of 68 cases

K. Adhav*, N. Mittal, J. Ghosh, R. Kulkarni, N. Sable, B. Rekhi, A. Maheshwari, S. Gupta, K. Deodhar, S. Menon
*Tata Memorial Hospital, Mumbai, India

Background & objectives: Leiomyosarcoma (LMS) is a rare, though most common malignant mesenchymal tumour of smooth muscle differentiation involving female genital tract (FGT).This study was done to assess the clinicopathological features, subtypes and immunohistochemical features of LMS diagnosed at our tertiary cancer centre.
Methods: Clinical and pathological data of LMS diagnosed from 2015-2020 were retrieved and reviewed. Demographic data, treatment and follow up details were retrieved from hospital electronic medical record. Various clinicopathological parameters were correlated with clinical outcome. Kaplan-Meier survival plots and Univariate Cox propotional hazard regression model were used to illustrate the prognostically important parameters.
Results: A total of 68 cases were analysed. Histologically, 75% were spindle cell, 16.2% epithelioid and 8.8% were myxoid LMS. Uterus was most commonly involved primary site (n=54, 79.4%). Median age was 49 years. Coagulative tumour necrosis and severe nuclear atypia was observed in 88.2% and 92% cases respectively. The mitotic count ranged 1-20 per mm2. Presence of lymphovascular invasion was found in 22% cases which was statistically associated with worst disease free survival (DFS) (p=0.029). SMA, Desmin and Hcaldesmon were positive in 92%, 82% and 71% respectively. The median DFS was 8.2 months. Loco-regional recurrence was observed in 36% cases. Distant metastasis was observed in 74% cases commonly to lung.
Conclusion: LMS is a rare high grade sarcoma involving FGT with aggressive behaviour. Presence of LVI may portend early recurrences, distant metastasis and shorter DFS. LMS including its subtypes may cause diagnostic challenges and need distinction from mimics by using immunohistochemistry.

E-PS-10-004
Primary ovarian carcinoid tumour: a case series

M. Alzamora*, G. Miranda, A. Coutada, J. Costa, C. Bartosch, R. Dias
*Department of Pathology, Portuguese Oncology Institute of Porto (IPO-Porto), Portugal

Background & objectives: Primary ovarian carcinoid (POC) tumours are rare, accounting for 1% of ovarian tumours, and are often linked with mature cystic teratomas. Average age at diagnosis is 53 years old and around 30% of cases are associated with carcinoid syndrome (CS).
Methods: We report 4 cases of POC identified through a review of internal records ranging from 2008 to 2023. A search for relevant clinicopathological data, such as presence of CS, histologic subtype of carcinoid tumour, and presence of mature cystic teratoma or other carcinomatous components, was performed.
Results: Patient 1 was a 72-year-old patient with a 29cm right-sided tumour diagnosed as a primary mixed neoplasm with mucinous carcinoma and a carcinoid tumour of insular pattern, both components confirmed with immunohistochemistry. The patient died of disease 11 months post-diagnosis. Patient 2 was a 61-year-old patient with an 8cm right-sided tumour diagnosed as insular POC with focal trabecular pattern. The other two patients, an 81-year-old with a 4cm right-sided tumour, and a 32-year-old patient with a tumour of unspecified size and laterality, were diagnosed with insular POC associated with mature teratoma. As of 2024, all three patients are alive and well. None of the patients had CS on presentation.
Conclusion: POC, especially in the isolated form, is a rare occurrence, and warrants ruling out metastasis from other organs. Looking for a teratomatous component is also crucial, as its presence favours a primary ovarian origin. The prognosis for POC is generally favourable, particularly in early stages, yet malignant potential exists. In our series, a patient had an adverse outcome, possibly due to concurrent mucinous carcinoma. Regular follow-ups are recommended despite a typically good prognosis.

E-PS-10-005
Trichorhinophalangeal syndrome type 1 (TRPS1) is expressed in endometrial cancer

G. Karpathiou, T. Amaamri Seebach*, J. Pascal, M. Peoch, M. Mobarki
*CHU of Saint-Etienne, France

Background & objectives: TRPS1 is considered as a highly sensitive and specific immunohistochemical marker to determine breast origin. This could be useful in distinguishing from another primary, such as an endometrial one. We sought to study many endometrial carcinomas for TRPS1 expression.
Methods: TRPS1 expression in endometrial cancer is rarely reported. In this retrospective study, we studied whole slide sections of 76 uterine tumours, including 54 endometrioid carcinomas, 14 high-grade serous carcinomas and 8 carcinosarcomas.
Results: TRPS1 staining was observed in 43% endometrial tumours. Grade and histological type did not correlate with TRPS1 expression but TRPS1 expression was higher (p=0.041) in p53-mutated tumour. No association between TRPS1 expression and MMR or ER and PR was found. Interestingly, TRPS1 was expressed in 40% of normal adjacent endometria.
Conclusion: TRPS1 is common in endometrial tumours and should not be a criterion for diagnosisng a breast over an endometrial primary.

E-PS-10-006
Mutation profiling of central-type primitive neuroectodermal tumour of the uterus: a case report

L.C. Araya Umaña*, K. Romero Figueroa, E. Izquierdo Delgado, A. Escudero López, C. Venegas Mascaró, J. Calzas Rodríguez, M. Cueto Callejón, C. Morante Palacios, B. Muñoz Hernández
*Department of Pathology, Hospital Universitario de Fuenlabrada, Madrid, Spain

Background & objectives: Central-type primitive neuroectodermal tumour of the uterus is a rare malignant with poor outcome. Due to the rarity, there is limited information available on their underlying genetic alterations. We describe the next generation sequencing results from a medical case.
Methods: A hysterectomy with bilateral adnexectomy was performed to an 85-year-old woman due the presence of a intrauterine mass. The tumour showed a neoplastic proliferation of small round blue cell with primitive neuroglial differentiation and lymphovascular invasion. Immunohistochemistry showed positivity with vimentin, cytokeratins, GFAP, synaptophysin, neurofilaments, CD56 and CD99. A 5% rhabdomyosarcoma component was observed.
Results: The NGS found a single nucleotide variant (SNV) of KRAS (p.Gly13Asp) with an allele frequency of 48% and a SNV on PIK3CA (p. Arg115Leu) with an allele frequency of 44%. The fluorescence in situ hybridization with a break-apart probe, did not show EWSR1 (22q12) rearrangement. Our genetic findings in an extracranial location are concordant with those found in intracranial germ cell tumours so that, independently of their histological resemblance to an embryonal CNS neoplasm, the pathogenetic pathway of this type of tumours seems to be different.
Conclusion: Our results suggest that NGS would allow us to categorize this type of neoplasms more accurately and thus better predict their clinical behaviour and the most appropriate molecular therapeutics. To our knowledge this is the first case of central-type primitive neuroectodermal tumour of the uterine corpus reported with its molecular-genetic characteristics.

E-PS-10-007
Uterine leiomyosarcoma with osteoclast-like giant cells: description of two additional cases and literature review
E.M. Ariza Estepa*, T. Cano Barbadilla, N. Maira González, B. Vieites Pérez-Quintela, M. García Rojo
*Hospital Universitario de Jerez de la Frontera, Spain

Background & objectives: Uterine leiomyosarcoma (LMS) accounts for 40-50% of uterine sarcomas and 1-2% of all uterine malignancies. Patients are characteristically older than 50 years. LMS with osteoclast-like giant cells (OLGCs) is an exceedingly rare variant, with only 20 cases reported thus far.
Methods: We describe two LMS with OLGCs cases which presented at an advanced stage in two patients aged 67 years and 53 years. Histological, immunohistochemical and NGS studies were performed. After aggressive local surgery, local recurrence and disease progression took place in both patients, the first of whom died 8 months post-diagnosis, while the second currently exhibits a further local recurrence.
Results: Grossly, the tumours measured 10 cm and 15,5 cm, were poorly circumscribed and showed necrotic and haemorrhagic areas. Microscopically, both revealed multinodular and diffuse growth patterns with a dual cell population: (i) irregularly arranged spindled cells displaying severe atypia, abundant mitoses and necrotic foci and (ii) osteoclast-like multinucleated cells and rhabdoid-looking polygonal cells arranged in sheets. Immunohistochemistry showed positivity for actin, desmin and caldesmon in spindled cells, while giant cells expressed CD10 and CD68. There was negativity for S100, CD34, PLAP, HCG, SALL4, MDM2, EMA, CKAE1/AE3, estrogen and progesterone receptors and myogenin. DNA and RNA-based next-generation sequencing (NGS) was performed, with negative results.
Conclusion: For some authors the presence of OLGCs in LMS seems to portend a poorer outcome, and certainly our two cases' aggressive behaviour would support that claim. No significant differences between LMS with OLGCs and conventional LMS molecular profiles have been identified in NGS studies, the finding of PT53 gene alterations being common in both. Nevertheless, no PT53 changes were detected by NGS in our two cases. More studies are necessary to better understand this rare uterine LMS variant.

E-PS-10-008
Anti-Müllerian hormone receptor II expression in ectopic and eutopic endometrium of patients with deep infiltrative endometriosis
A. Asaturova*, N. Chekeneva, N. Buralkina, M. Dumanovskaya, A. Badlaeva, A. Tregubova, M. Chumakova, T. Serdobintseva, A. Rogozhina, S. Pavlovich
*NMRS for Obstetrics, Gynecology and Perinatology named after V. Kulakov, Russia

Background & objectives: Anti-Müllerian hormone receptors play a significant role in deep infiltrative endometriosis (DIE) pathogenesis and its treatment strategy. The goal of our survey was to analyse AMHR II expression in the eutopic and ectopic endometrium of patients with DIE.
Methods: We recruited 50 patients with DIE(n=20 I-II stage;n=30 III-IV stage according to ASRM classification)and 9 with tuboperitoneal infertility(all patients in reproductive age).A comparative analysis of AMHRII immunohistochemical expression in epithelial and stromal cells of eutopic and ectopic endometrium was performed.We used semiquantative analysis for IHC expression(0-3 scores based on intensity of staining)and Mann–Whitney test was used for statistical analysis.
Results: AMHRII expression in eutopic endometrial stromal cells of DIE patients was significantly higher compared to glandular cells in all study groups ($p<0.05$). AMHRII expression was found to be significantly higher in glandular cells of the eutopic endometrium compared to the ectopic endometrium of pelvic peritoneal foci in DIE patients: 1.60 ± 0.77 and 1.09 ± 0.68, respectively ($p=0.001$). We did not reveal any statistically significant differences in AMHRII expression between patients with I-II and III-IV ASRM stage ($p>0.05$).
Conclusion: We demonstrated AMHRII expression increase in stromal and glandular components of eutopic and ectopic endometrium in patients with deep infiltrative endometriosis proved that AMH-signaling pathway contribute into endometriosis development and its modulation can be a target for treatment strategy in such patients.

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E-PS-10-009
Cross-talk between CD138 and MUM1 plasma cell markers in chronic endometritis diagnosis
A. Asaturova*, A. Badlaeva, A. Tregubova, A. Raksha, G. Tabeeva
*NMRS for Obstetrics, Gynecology and Perinatology named after V. Kulakov, Russia

Background & objectives: The diagnosis of chronic endometritis is challenging due to the poor identification of plasma cells in endometrium. The goal of our study was to assess the reproducibility of plasma cells with CD138 and MUM-1 for accuracy increase of CE diagnostics.
Methods: In this retrospective observational study, 48 samples of formalin-fixed, paraffin-embedded sections of endometrial tissue were immunohistochemically stained for both CD138 (Syndecan 1) and Multiple Myeloma Oncogene 1 (MUM-1) clones following the manufacturer's instructions. The plasma cell counts of all specimens were independently evaluated by three pathologists. Cohen's and Fleiss' kappa coefficients were used to analyse intraobserver and interobserver agreement, respectively.
Results: Intraobserver agreement was fair for plasma cell counting using CD138 (Fleiss's $\kappa = 0.561$) and moderate for MUM-1 (Fleiss's $\kappa = 0.613$), both statistically significant ($p < 0.001$). Interobserver agreement for plasma cell counting using CD138 and MUM-1 ranged from fair to moderate (Cohen's $\kappa = 0.497$ - 0.617 and Cohen's $\kappa = 0.514$ - 0.728, respectively). Observers achieved absolute agreement for plasma cell counting using CD138 and MUM-1 in 15.84% and 16.32% of cases, respectively.

Conclusion: Our findings suggest that MUM-1 and CD138 are valuable for identifying endometrial stromal plasma cells. MUM-1 immunohistochemical staining enhances pathologist agreement rates, aiding morphology examination and averting missed or incorrect chronic endometritis diagnoses.

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E-PS-10-010

TGF-beta signalling components cross-talk in endometrial polyps and endometrial hyperplasia

A. Asaturova*, R. Sarkisyan, A. Badlaeva, A. Tregubova, T. Gavrilova, L. Adamyan
*NMRS for Obstetrics, Gynecology and Perinatology named after V. Kulakov, Russia

Background & objectives: TGF-beta signalling pathway components can be significant to improve either fundamental (pathogenesis) or treatment (target agents) purposes in endometrial pathology. Thus, we investigated TGF-beta and SMAD2 expression in endometrial hyperplasia and polyps in patients with coexisting adenomyosis and leyomioma.
Methods: We reqruited 44 patients (mean age 33,7±4,4 years) with endometrial hyperplasia (1st group,n=9),endometrial polyp (2nd group,n=14), endometrial polyp and leyomioma uteri (3rd group,n=11) and endometrial polyp and adenomyosis (4th group, n=10). We investigated TGF-beta and SMAD 2 expression immunohistochemically (in endometrial stroma (ES) and endometrial glans (EG) (0-3 scores); Kruskal–Wallis test and Spearman's rank correlation were used for statistical analysis.
Results: Expression of TGF-beta in ES before treatment was 2.0(2.0-2.0)(1st group),1.0(1.0-1.75)(2nd group), 2.0(2.0-2.0)(3rd group),2.5(2.0-3.0)(4th group)($p<0.05$);after treatment:1.0(1.0-2.0)(1st group),1.0(1.0-1.0)(2nd group),2.0(2.0-2.0)(3rd group),2.0(1.0-2.0)(4th group)($p<0.01$).Expression of TGF-beta in EG before treatment did not demonstrate significant differences($p>0.05$),after treatment:2.0(2.0-3.0)(1st group),2.0(2.0-2.0)(2nd group),3.0(2.0-3.0)(3rd group),2.0(2.0-2.0)(4th group)($p <0.05$).Expression of SMAD2 in ES before treatment did not demonstrate significant differences($p>0.05$),after treatment:2.0(2.0-2.0)(1st group),3.0 (3.0-3.0)(2nd group),3.0(2.0-3.0)(3rd group),3.0(3.0-3.0)(4th group)($p<0.01$).Expression of SMAD2 in EG before treatment was 3.0(3.0-3.0)(1st group),2.0(2.0-2.0)(2nd group),2.0 (2.0-2.0)(3rd group),3.0(2.0-3.0)(4th group) ($p<0.05$);after treatment:3.0(2.5-3.0)(1st group),2.0(2.0-2.0)(2nd group),2.0(2.0-2.0)(3rd group),2.0(2.0-3.0)(4th group)($p<0.01$).Strong correlation was revealed between TGF-beta expression in ES before and after treatment;between SMAD2 expression in EG before and after treatment.Moderate correlation was revealed between TGF-beta expression in EG before and after treatment.Other correlations were poor or absent.
Conclusion: TGF-beta and SMAD2 expression differs between endometrial pathology and coexistant adenomyosis and leyomioma also contribute. After treatment TGF-beta and SMAD2 expression decrease either in stromal and glansular components so we can suppose that TGF-beta signalling pathway play a significant role in pathogenesis and also can be a target for treatment.

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E-PS-10-011

The impact of the frozen section evaluation for the detection of Lymphovascular Space Invasion (LVSI) and the overall LVSI status in endometrial carcinoma

D. Ates*, A. Oruc, S. Karahan, A. Usubutun
*Hacettepe University School of Medicine Department of Pathology, Turkey

Background & objectives: In daily practice, we observed more lymphovascular space invasion (LVSI) on frozen section slides (FSS) than permanent sections for endometrial carcinoma. We aimed to investigate the effect of frozen section on LVSI status to verify our observation.
Methods: The study included hysterectomies that showed LVSI on final pathology, as well as those that underwent frozen examination. The number of LVSI per piece was recorded in both the FSS(confirmed by CD31) and all other sections.Non-parametric correlations were conducted to determine if there were any differences in the distribution and total number of LVSI between the FSS and the other sections.
Results: The study analysed 57 hysterectomies, 36 of which had LVSI in the FSS and 21 did not. The correlation coefficient was 62.3%, indicating a positive correlation between the number of LVSIs on the FSS and the total number of LVSIs in the final pathology report($p=0.015$). Of the 36 cases with LVSIs identified on FSS, 26(72.2%) had ≥5 LVSIs detected in the final pathology report. There was no statistically significant correlation found between the detection of LVSI on the FSS and the detection of ≥5 LVSI in the final pathology report($p= 0.511$). Out of the 36 cases with LVSI,12 had the slide with the highest number of LVSIs on the FSS.
Conclusion: Detection of LVSI on the FSS indicates that the total number of LVSI in the final pathology report will be higher. When analysed as ≥5 and <5, no statistically significant results were obtained. In terms of distribution, one-third of cases had the highest number of LVSIs on the FSS. Although detecting LVSI during frozen section is technically difficult, it can serve as an indicator of potentially higher numbers of LVSIs in the final pathology report.

E-PS-10-012

Diagnostic challenges in different histological types of ovarian sex cord-stromal tumours - the pathologist's perspective

T.A. Balan*, R.A. Balan, C. Amalinei, S.E. Giuşcă, I.D. Căruntu
*"Grigore T. Popa" University of Medicine and Pharmacy Iasi, Romania

Background & objectives: Ovarian sex cord-stromal tumours (SCSTs) represent a heterogenous group with various clinico-morphological features. Since SCSTs present diagnostic difficulties due to overlapping histopathological aspects, we aimed to present several diagnostic challenges of different ovarian SCSTs and the panel of markers used.
Methods: Our retrospective study included 33 cases of different histological types of sex cord-stromal ovarian tumours, in women between 21-77 years old, during 2001-2023, diagnosed within the Pathology Department of "Elena Doamna" Clinical Hospital of Obstetrics and Gynecology, Iasi, Romania. The surgical specimens were histopathologically assessed by routine histological methods, supplemented with additional immunohistochemical techniques, using a panel of specific markers.
Results: The histopathological examination revealed 25 (75.75%) cases of adult granulosa cell tumour (AGCT), one (3.03%) with thecal component, one case (3.03%) of Sertoli tumour, and 7 (21.21%) cases of ovarian fibroma. For AGCT, the immunohistochemical assessment of ERalpha, Ki67, calretinin, inhibin A, as well as Gordon Sweet stain were used to confirm the histopathological diagnosis, and to differentiate them from other SCSTs, including fibroma. For AGCT with thecal component, the intraoperative consultation diagnosed the thecal area as a thecal or fibromatous component. A wider panel of antibodies was used for the Sertoli tumour, including inhibin, calretinin, AE1/AE3, CK7, CK19, CK20, and CD10, considering that it overlapped morphologically with Wolffian tumour.

Conclusion: The morphological heterogeneity of SCSTs frequently leads to difficulties in histopathological diagnosis. Moreover, the frequent similar morphology, the partial overlap of the immunohistochemical profile shared by these tumours, as well as the existence of different histological mimickers make the antibodies panel often insufficient. In this regard, the assessment of the genetic profile in front of a diagnostic dilemma will be able to improve the accuracy of the histopathological examination, thus contributing to the refinement of therapeutic management and tumour prognosis.

E-PS-10-013

Benign struma ovarii with peritoneal strumosis: a rare case presentation and diagnostic dilemma

L. Barrera-Herrera*, L.F. Jaramillo, A. Saavedra, P. Campo
*Clinica Colsanitas, Colombia

Background & objectives: Struma ovarii (SO), a rare ovarian teratoma subtype, benign SO may exhibit metastasis, termed "peritoneal strumosis," with unclear clinical characteristics and outcomes. We report a case of benign SO with peritoneal strumosis, diagnosed incidentally in a 36-year-old female
Methods: Preoperative CT revealed multiple masses of bilateral adnexa and abdominal-pelvic cavity, suggesting a right ovarian tumour with multiple peritoneal seedings. Laparoscopic right salpingo-oophorectomy, left cystectomy and mesentery mass excision were performed. Preoperative CT suggested ovarian malignancy with peritoneal spread. Serum tumour markers, including TG, CA-125, CA19-9, CEA, AFP were all negative. Thyroid function tests and ultrasound were negative.
Results: Pathological examination revealed SO in the right ovarian tumour, with concurrent cystectomy of the left ovary, and evidence of metastasis to the mesentery. Institutional pathology consultation validated this diagnosis. Immunohistochemical analysis affirmed the presence of TTF-1 and Thyroglobulin, alongside a low Ki-67 index of 2%, consistent with benign SO, observed both in ovarian tissues and peritoneal metastasis. The patient remained asymptomatic following surgery, obviating the need for further therapeutic interventions. This case underscores the importance of accurate histopathological assessment in guiding treatment decisions and highlights the favourable prognosis associated with benign SO with peritoneal involvement.
Conclusion: This case underscores the importance of considering benign SO with peritoneal strumosis, necessitating careful histopathological evaluation for appropriate management decisions. Peritoneal strumosis incidence was reported as 1.31% of cases of SO, exhibiting variable biological behaviours. Despite this, patients typically demonstrate favourable survival rates, regardless of treatment modalities employed. Conservative surgical approaches, coupled with individualized Radioactive Iodine (RAI) therapy, may be favoured, emphasizing the importance of long-term vigilant follow-up.

E-PS-10-015

Uterine tumour resembling ovarian sex cord tumour - a case report

C.A. Batista Batista*, J.G. León Gil, R. Rivas Hernández, A.B. Jiménez Pérez, I. González Morais, J. González Rivero, M.L. Cuesta Martínez, M. Sancho de Salas, L.M. Chinchilla Tábora
*University Hospital of Salamanca, Spain

Background & objectives: Uterine tumours resembling ovarian sex cord tumours (UTROSCT) are rare uterine mesenchymal tumours with unpredictable behaviour. Recurrences and metastases occur. Prognostic morphologic features are not well understood. It represents a challenge in differential diagnosis due to their polyphenotypic immunohistochemical profile.
Methods: A 89-year-old postmenopausal woman complaining of abnormal vaginal bleeding for the last month. Ultrasonography study informs an atrophic uterus occupied by a rounded heterogeneous mass suggestive of an endometrial polyp with ill-defined endometrial-myometrium limits. Adnexal pathology was not observed. Hysteroscopy showed a 5cm mass occupying the entire cavity. A MyoSure resection was performed with a presumptive diagnostic of Leiomyoma.
Results: The biopsy showed a neoplastic proliferation with an epithelioid and vaguely plasmacytoid morphology of tumour cells, replacing the endometrial stroma without endometrial glands alterations. The tumour cells were arranged in solid pattern with trabeculae and cords areas showing an extensive eosinophilic cytoplasm with ovoid nuclei and conspicuous nucleoli. Up to 5 mitoses where found in 10 high power fields. Tumour necrosis was absent. Immunohistochemically a polyphenotypic profile was found with positivity for sex cord markers: Calretinin, WT1, CD56, and CD99; and epithelial markers: CK8/18, ER, PR. Cyclin D1 was focally positive and p53 was wild type. Neuroendocrine markers, CD10, Inhibin, Melan A and BCOR were negative. Ki67 reached 20%.
Conclusion: UTROSCT is a rare neoplasm with uncertain biologic potential. Further studies with a large prospective series are required to improve the knowledge of histological and molecular features that could have a prognostic and a predictive impact. Our case showed an intermediate atypia. No extended disease was found on the whole body PET/CT scan. On a multidisciplinary committee it has been decided to perform a radical hysterectomy.

E-PS-10-016

Histoprognostic factors of survival in vulvar cancer

N. Boujelbene, W. Ben Makhlouf*, I. Zemni, H. Mansouri, A. Khemir, I. Abbes, R. Doghri, L. Charfi, K. Mrad
*Tunisia

Background & objectives: Vulvar cancer is a rare malignant disease of the female genital tract, the prognosis of which depends on several prognostic factors. This study aimed to identify the histoprognostic factors correlated to the overall survival (OS) in patients with vulvar cancer.
Methods: The study included patients treated for vulvar cancer at Salah Azaiez Institute between 2000 and 2020. We considered the following histological parameters: tumour size, depth of invasion, pathological stage(pT), lymph nodes(LN) metastasis, extracapsular LN invasion, histological type and grade of differentiation, vascular involvement, perineural invasion and the presence of vulvar intraepithelial neoplasia. Survival curves were generated by the Kaplan-Meier method.
Results: 134 patients treated for vulvar cancer were included. The mean age was 65.44±13.788 years. The mean tumour size was 41.30±20.69 mm. LN-metastasis was assessed in 45 patients(33.5%). Squamous cell carcinoma was the most frequent histological type (89,6%). Tumours were classified as stage pT1a, pT1b, pT2 and pT3 in 3%, 85.8%, 9.7%, and 1.5% of cases, respectively. With a mean follow-up time of 32.91±37.45 months, the 5-year OS was 87.36%.
On univariate analysis, there was a statistically significant difference(p=0,008) in survival between stage pT1(91,8%) and pT2-3 (29,64%), LN-metastasis (p=0,000449), vascular-involvement(p= 0,000019) and perineural-invasion(p= 0,002). On multivariate analysis, the independent prognostic factor of OS were LN metastasis(HR=2.17; 95%CI=1.30-3.62;p=0,003) and vascular involvement(HR=15.29; 95%CI=1.21-192.8;p=0,035).

Conclusion: lymph node status and vascular involvement impact overall survival significantly and independently in patients with vulvar cancer.

E-PS-10-017

Uterin metastasis of Wilms' tumour in a paediatric patient: a rare presentation

W. Ben Makhlouf*, N. Boujelbene, A. Khemir, G. Sahraoui, E. Jbebli, K. Mrad
*Tunisia

Background & objectives: Wilms' tumour is the most common renal tumour in children, boasting an excellent 5-year survival rate(92%). However, recurrence remains a concern in 15-20%of patients, often affecting the kidney, lung,or liver. we aim to present an exceptional case of uterine metastasis
Methods: This study presents the case of a 4-year-old girl with a history of nephroblastoma diagnosed at the age of 2 years, who underwent left nephrectomy and received chemotherapy. Currently, the child presents with a uterine tumour, necessitating hysterectomy.
Results: Histological examination reveals a tumour characterized by a triad of cellular components: predominantly mesenchymal contingent comprising sheets of rhabdomyoblastic cells with occasional foci of immature mesenchymal tissue, an epithelial contingent consisting of tubular structures lined by regular cubic epithelium, and a blastematous contingent comprised of nodules of small blastic cells with basophilic cytoplasm and rounded nuclei exhibiting fine chromatin. This tumour infiltration extends through the entire myometrial thickness and the cytogenic chorion of the endometrial mucosa, while the cervix remains tumour-free. Consequently, a diagnosis of uterine metastasis originating from her previously diagnosed nephroblastoma is made.
Conclusion: Advancements in treatment modalities have significantly improved survival estimates for recurrent Wilms' tumour, reaching 63.6% at 5 years for all stages. A multidisciplinary therapeutic approach combining multi-drug cytotoxic chemotherapy, targeted radiotherapy, surgical excision, and potential autologous stem cell transplantation demonstrates promising outcomes.

E-PS-10-018
Frequency of intraepithelial lesions in endocervical curettage inrelation to cyto-colposcopic and conization results
I. Benedetti*, C. Gomez, S. Girado
*Universidad de Cartagena, School of Medicine. Histopathology research group, Colombia

Background & objectives: The usefulness of endocervical curettage (ECC) in cervical cancer screening remains controversial because in some cases it does not modify medical behaviour, so it is important to objectively determine its relationship with cytology, colposcopy and cervical conization.
Methods: An observational study was conducted. All patients who underwent ECC for suspected occult lesion during colposcopic evaluation in a Cervical Pathology Unit, during a two-year period, were included. Information was obtained from medical records including age, cytology results, colposcopy, and histopathological study of ECC and conization. Results of cervical conization in patients who underwent it were additional data.
Results: A total of 677 patients with a median age of 39 years (RIC: 31-49) were included. ECC was performed most frequently in the 30-39 years age group (32.9%), followed by the 40-49 years (25.7%) and 18-29 years (18.3%) age groups. ECC increased the likelihood of identifying squamous intraepithelial lesions, with a detection rate of 23.6% for LSIL and 8.7% for HSIL not observed during colposcopic evaluation in patients with suspected occult lesions.
Conclusion: ECC is a minor procedure that, when performed with a precise indication, can provide useful information by identifying occult endocervical lesions early. The use of ECC improved the ability to identify premalignant and malignant lesions located in the endocervix, increasing the detection of HSIL,

LSIL and cervical cancer that would not have been diagnosed without this procedure. The results of the present study provide information that should motivate colposcopists to use ECC in patients with suspected occult lesions.

E-PS-10-019
The prognostic role of osteopontin expression in endometrioid type endometrial cancers (EEC)
H. Berber*, E.D. Serbes, D. Enneli, H.K. Kahraman, C. Cansız Ersoz, C. Ozturk, N.B. Kaplan, S. Taskın
*Ankara University, Medical School, Pathology Department, Turkey

Background & objectives: Osteopontin(OPN) is an extracellular-matrix protein that plays numerous roles in carcinogenesis and progression of various solid organ tumours. Herein, we aimed to determine the possible prognostic role of OPN in endometrioid type endometrial carcinomas (EEC).
Methods: Six tissue-microarray blocks consisting of representative tumour cores of 100 EEC cases(3-4cores/case) diagnosed between 2020-2022 at our institution were constructed. OPN(clone7C5H12) antibody was applied immunohistochemically. The percentage and intensity(1-4) of immunostaining were determined for each core. Staining intensity of >=3 indicated as highOPN. Several histopathological features, P53mutation and mismatch-repair(MMR) status of tumours were noted. Statistical analysis was performed using SPSSversion.
Results: The mean follow-up time of the patients(mean age:61.07, range 38-94 years) was 21.19months(1-199). The prevalence of squamous differentiation and lower uterine segment involvement were found to be significantly higher in tumours with highOPN (p=0,015,p=0,037 respectively). Moreover, highOPN tumours showed greater size(p=0,040), more frequent lymph node metastasis(p=0,047). However, there wasn't any significant relation between tumour grade and OPNexpression. The Kaplan-Meier analysis also revealed no significant association between OPNexpression and survival, tumour recurrence, or metastasis. In terms of MMR and P53 mutation status, MMRdeficient tumours with loss of MSH2 (p=0,044) and MSH6 (p=0,012) were found to show significantly lower OPN expression and all of the 3 p53 mutant EEC cases showed lowOPN.
Conclusion: In conclusion, although OPN expression hasn't shown direct correlation with survival in patients with EEC, our finding that tumours with highOPN tend to show more frequent lymph node metastases suggests its potential role as a prognostic marker for EECs. A striking finding of our study was that MMRdef EECs with MSH2±MSH6 loss showed significantly lowerOPN expression than MSH2-MSH6proficient EECs. Future studies are needed to elucidate this striking correlation of MSH2,MSH6 and OPN protein loss.

E-PS-10-020
Synchronous formation of adult type granulosa cell tumour and benign Brenner tumour in the right ovary and endometriotic cyst in the left ovary: a rare case
H. Bilgi*, I. Ozover Celik
*Prof. Dr. Cemil Tascioglu City Hospital, Turkey

Background & objectives: Ovarian tumours largely consist of pure histological type. While the combination of different tumours of the same histogenetic origin in the ovary is also common, the coexistence of tumours of different histogenetic origin is rare.
Methods: A 53-year-old female patient complaining of spotting bleeding for 2 months applied to the outpatient clinic. USG performed on the patient; 'Multiple myomas were seen in the uterus, the largest of which was 6.5 cm. In addition, it was reported as follows: 'No gross pathology was observed in the bilateral adnexa.' Transabdominal hysterectomy with bilateral salpingo-oophorectomy was performed.
Results: In macroscopic examination, no gross pathology was detected except for multiple myoma in the uterus and two cystic openings in the left ovary. On microscopy, the tumour in the right ovary consisted of two separate components with different histomorphology. Most of the tumour had a solid and partly trabecular insular structure. Tumour

cells had eosinophilic cytoplasm and round to oval nuclei, some with angulated ang groove nuclei. Call Exner bodies were visible. The small area of the tumour had different histomorphology. The tumour had nests of round, oval epithelial cells resembling transitional epithelium dispersed within a dense fibrotic stroma. Endometriotic cyst formation was observed in the left ovary.
Conclusion: In the right ovary, the large area in the tumour showed positive staining with inhibin and SF1 and negative staining with PANCK. Nest-like staining was observed with reticulin. PanCK positivity, inhibin and SF1 negativity were observed in the small area, and the tumour was diagnosed as adult-type granulosa cell tumour and benign Brenner tumour. There were 2 endometriotic cysts in the left ovary. We reported a case of mixed ovarian tumour, which is very rare in the literature.

E-PS-10-021
Ovarian collision tumour, mucinous cystadenoma and adult granulosa cell tumour- a rare case report
P. Bosgana*, E. Geropoulou, M. Gkermpesi, G. Androutsopoulos, V. Bravou
*Medical School of Patras, Greece

Background & objectives: Collision tumour is defined by the presence of two histological distinct tumour components in the same organ.
Methods: We herein report a rare tumour combination of mucinous cystadenoma and an adult granulosa cell tumour (AGCT) in the same ovary of a 63-year-old woman who presented with a unilateral left ovarian mass and underwent a left salpigo-oophorectomy.
Results: Gross examination revealed a multilocular cystic neoplasm, composed of smooth walled cysts and an adjacent solid area with a yellow smooth cut surface. Histologically the cystic component corresponded to a mucinous cystadenoma. The solid area showed a diffuse growth pattern of small, uniform cells, with scant cytoplasm and nuclear grooves and focal presence of Call-Exner bodies. The cells expressed inhibin, calretinin, vimentin, CD56 and focally CD99 and showed low mitotic activity. Collision tumour and heterologous mucinous differentiation within an adult granulosa cell tumour entered the differential diagnosis. However the absence of admixture of the two histologically distinct tumour types favoured the diagnosis of a collision mucinous cystadenoma and AGCT.
Conclusion: Ovarian collision tumours are uncommon and the combination of mucinous cystadenoma and adult granulosa cell tumour reported herein is extremely rare. Pathogenesis of these tumours is unknown and further evaluation is required in order to determine their biologic behaviour.

E-PS-10-022
Plexiform leiomyomatosis: mimicking metastasis in a patient with invazive lobular carcinoma
I. Buldum*, H.E. Peştereli, S.B. Yolburun, D. Durna
*Akdeniz University, Turkey

Background & objectives: Uterine leiomyomas are prevalent benign tumours that develop in the female reproductive system. Our objective here is to highlight the potential for plexiform leiomyomatosis to be misdiagnosed as a metastasis of invasive lobular carcinoma.
Methods: We examined sections of the leiomyoma specimen sent from an external centre using hematoxylin and eosin staining and various immunohistochemical staining methods.
Results: A 53-year-old female patient, who had previously received treatment for invasive lobular carcinoma, presented to the gynecology department with vaginal bleeding. Following investigations, a hysterectomy was performed due to myoma-related cause. Microscopic examination revealed epithelioid cells forming cords and trabeculae within the leiomyoma areas. We conducted further investigations to differentiate invasive breast carcinoma, ultimately diagnosing the patient with plexiform leiomyomatosis.
Conclusion: Plexiform tumourlet, which is an epithelioid variant of leiomyoma, is an exceptionally uncommon form. Its epithelioid appearance requires distinguishing it from other epithelial tumours. The literature documents its findings in patients who have previously been diagnosed with invasive breast carcinoma, emphasizing the potential requirement for additional studies to investigate the correlation between them.

E-PS-10-023
Unveiling the uncommon: a case report of vulvar adenosquamous carcinoma
S. Carralas Antunes*, A. Félix
*Hospital Garcia de Orta, Portugal

Background & objectives: Adenosquamous carcinoma (ASC) is considered a high-grade tumour with uncertain histogenesis, not included in the WHO classification of vulvar tumours. We aim to outline the histopathological features in a vulvar ASC case.
Methods: An 80-year-old woman was referred to an Oncological Center due to a vulvar mass with one-year evolution, with a biopsy compatible with HPV-independent SCC (p16-/p53mut). Physical examination showed a 4.5cm left-median vulvar tumour, extending into the vaginal introitus with palpable left inguinal lymph nodes. Radical vulvectomy with bilateral inguinal lymphadenectomy was performed.
Results: Histologically, an endophytic expansile tumour, composed of squamous elements, with vacuolized clear cells, and glandular differentiation occasionally accompanied by pools of mucin within the centrum of tumour aggregates, at times with signet-ring morphology. Intraepithelial high-grade lesion was present (p53mut). Immunohistochemistry was positive for CK5/6 and p40/p63 peripherally, confirming squamous differentiation. PAS-AB staining highlighted glandular differentiation on the innermost part. A large panel of antibodies was used and both components were p16-, p53mut and ERBB2 expression was 2+ in the glandular component. Lymph-node metastases with extranodal extension revealed both components. An ASC stage IIIC (FIGO2021) was diagnosed. Adjuvant external radiation therapy was performed, and the patient is currently disease-free (Follow-up=1month).
Conclusion: Adenosquamous carcinoma in the vulva contrasts with cervical counterpart by its HPV independence and some areas can morphologically mimic the HPV associated iSMC of cervix. Primary vulvar origin is favoured by the presence of an intraepithelial component (dVIN). The differential diagnosis is broad, including glandular vulvar neoplasms, such as adenocarcinomas of intestinal and mammary gland type, as well as other primary cutaneous tumours such as sebaceous carcinoma and secondary tumours. A large immunohistochemical panel is essential for accurate diagnosis.

E-PS-10-024
Histopathological findings and correlation with ultrasound in a series of cases of invasive mole treated with hysterectomy
D. Cavalcante*, C. Ponte, S. Coelho dos Santos Costa
*Federal University of Ceará, Brazil

Background & objectives: The diagnosis of invasive mole (IM) is clinical, involving serial human chorionic gonadotropin (ß-HCG) and ultrasonography (US). Because no histopathology is needed, IM is uncommon surgical specimen (SS). We analysed the histopathological and US findings in hysterectomy for IM.
Methods: We retrospectively analysed 4 cases of invasive mole treated by hysterectomy from June 2020 to January 2024 at Federal University of Ceará, Brazil.
All patients had previous complete mole and were clinically high-risk.
Results: Patients were 28, 43, 44 and 46 years old. One (44) had very enlarged uterus with perforation on US and SS. Two (43 and 46)

showed moderated enlarged uteri in US with findings suggesting invasion by a mole. This three SS had several molar villi with trophoblastic hyperplasia and marked vascular invasion in one (43).
Patients 28 and 44 underwent monochemotherapy. One of this (28) presented ascending titers of ß-HCG one year after chemotherapy. Her US findings was remarkable different, suggestive of leiomioma. On SS, there was a solid-cystic, circumscribed lesion. On histology, trophoblast infiltrated myometrium along with scattered villi. All patients achieve remission after hysterectomy.
Conclusion: Invasive mole, a subtype of gestacional trophoblastic neoplasia is primarily treated by chemotherapy. Patients who did not desire preserve fertility and are high-risk for life threatening hemorrhage or uterine rupture undergo hysterectomy. When hysterectomy was performed early due to the risk of rupture, the uterus was enlarged on US, which correlated with the finding of abundant villi in the myometrium. One patient who underwent late hysterectomy represented a diagnostic challenge on US and correlated with rare villi on SS.

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E-PS-10-025
HPV-33 and systemic lupus erythematosus: an association for rapidly evolving carcinogenesis in lower anogenital tract? A case report
D. Cavalcante*, R. Verissimo Oliveira, R. Autran Coelho Peixoto, R. Mazon, R.M. Nunes Eleutério
*Federal University of Ceará, Brazil

Background & objectives: Vulvar cancer, accounting for less than 5% of female genital malignancies, is predominantly squamous cell carcinoma (SCC). Carcinogenesis involves high-risk HPV-induced and HPV-independent pathways. Patients with Systemic Lupus Erythematosus (SLE) particularly those on immunosuppressants, show higher HPV infection prevalence.
Methods: A 38-year-old woman with SLE refers to a painless genital wart 6 years ago that after 9 months evolved to multiple condylomatous lesions on vulva, vagina and perianal area. Seven months post local treatment, biopsies of the vulva and perianal region showed high-grade squamous intraepithelial lesion (HSIL). She underwent irregular treatment with imiquimod which was discontinued after adverse reaction.
Results: Three years and 5 months later, she returned with intense vaginal burning and itching, left inguinal adenomegaly, extensive warty, hardened plaques on vulva with ulceration. Histology showed SCC on vulva, and HSIL in the interlabial groove and perianal. The patient underwent radical vulvectomy and bilateral inguinal lymph node dissection. Histology confirmed SCC HPV-associated, multicentric, with extensive HSIL involving surgical margins. Inguinal lymph nodes were negative (stage IB). The p53 was of the wild type in SCC and HSIL. The p16 was strongly positive in the SCC and HSIL. HPV genotyping, perfomed in both vulvar SCC and HSIL, was positive for HPV33. Anal biopsy showed synchronous SCC, superficially invasive.
Conclusion: We report the case of a young patient with SLE and rapid evolution of synchronous vulvar and anal SCC. Both vulvar HSIL and SCC were associated with HPV33 and strong positivity for p16. Despite the rapid evolution and multicentricity, SCC did not present TP53 mutation. This case highlight the potential clinical importance of double positivity for HPV 33 and p16 in precursor lesions, a for close monitoring of patients with lupus and HPV-induced ano-genital lesions.

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E-PS-10-026
Sertoli-Leydig cell tumour with heterologous components: a case report
M.Y. Çelik*, S. Doğan, H.E. Peştereli
*Akdeniz University Hospital, Turkey

Background & objectives: Sertoli-Leydig cell tumour (SLCT) is accounting for 0.5% of all ovarian neoplasms with an average presentation age around 25 years old.The presence of heterologous elements is seen in one-fifth of these already rare neoplasm.We aim to spotlight this uncommon case.
Methods: A 26-year-old female patient with no medical history presented to gynaecology clinic with amenorrhea for one year. AFP in serum was elevated. MRI showed a well-defined lesion measuring 65x48x45 mm in the left ovary and displacing the uterus. Given the suspicion of germ cell tumours, biopsy was recommended. The patient underwent salpingo-oophorectomy and the specimens were sent for histopathological examination.
Results: On gross examination, the cut surface appeared orange-colored with smooth outer surfaces, revealing solid areas measuring 7 cm in diameter along with a 3 cm diameter cystic structure.Microscopic examination revealed a nodular tumour with areas of hypercellularity and loose edematous regions with cystic-adenoid structures.Tumour cells were characterized by minimal cytoplasm, round-oval morphology and monomorphic appearance.22 mitoses/10 HPF were observed. Furthermore, a few Leydig cells and adenoid structures with mucinous epithelium and hepatoid cells were noted.Immunohistochemical analysis revealed no staining with CD30,PLAP,OCT 3/4,glypican 3,WT1 while focal staining was observed with SF1 and inhibin.Positive staining was seen with AFP in hepatoid cells, CK7 and EMA in epithelial areas and MelanA in Leydig cells.
Conclusion: SLCTs are subdivided into well, moderately and poorly differentiated forms based on the degree of tubular differentiation of sertoli cell component and quantity of primitive gonadal stroma. Based on the criteria considered, we have reported our case as a moderately differentiated Sertoli-Leydig cell tumour (SLCT). Adequate sampling and microscopic examination are essential to identify heterologous elements and focal anaplasia as these factors influence treatment decisions. Diligent follow-up of these patients is crucial to detect recurrence early, allowing for prompt intervention.

E-PS-10-027
The importance of PFK-P (Phosphofructokinase-platelet) and PEA-15 (Phosphoprotein enriched in astrocytes-15kDa) expression in cases of endometrioid endometrial carcinoma and endometrial atypical hyperplasia/endometrioid intraepithelial neoplasia
B.B. Cengiz*, D. Arık, T. Öge, Ö.T. Yalçın, A. Özen
*Eskisehir Osmangazi University, Turkey

Background & objectives: To determine the immunohistochemical differences in PFK-P and PEA-15 expression between normal endometrium, endometrial atypical hyperplasia/endometrioid intraepithelial neoplasia (EAH/EIN), endometrioid endometrial carcinoma (EEC) groups and correlation between the expression levels and prognostic factors in carcinoma cases.
Methods: Patients diagnosed with EEC between 2010 and 2015 were included in the study. Hysterectomy materials of 32 patients diagnosed as EAH/EIN in curettage material, EEC in resection and 19 patients operated for non-neoplastic reasons were included as control group. Immunohistochemical analysis with PFK-P and PEA15 was based on the intensity of cytoplasmic staining in tumoural cells.
Results: PFK-P expression intensity was higher in the EEC group compared to EAH/EIN and normal endometrium ($p<0,05$). While 21.1% of the normal endometrium group showed high PFK-P expression, 51.8% of the carcinoma group showed high expression. PEA-15 staining intensity was different in the carcinoma and EAH/EIN materials of 32 patients in the EEC patient group in hysterectomy materials diagnosed as EAH/EIN at curettage ($p<0.01$). Lower PEA-15 expression was observed in EAH/EIN materials compared to carcinoma. PFK-P and PEA-15 expression levels were not associated with clinicopathologic features or survival in EEC cases.

Conclusion: PFK-P and PEA-15 proteins are involved in the carcinogenesis of certain tumours. There are no studies showing the level of PFK-P and PEA-15 expression in the development of EEC and its effect on survival. Our study found that high expression levels of PFK-P and PEA-15 in carcinoma suggest a role in carcinogenesis. Further studies are required to uncover the role of PFK-P and PEA-15 in carcinogenesis and to establish their prognostic significance.

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E-PS-10-028

Targeting exonucleasic region of POLE gene in Tunisian endometrial carcinoma

L. Charfi*, H. Douik, C. El Fekih, A. Khemir, R. Doghri, I. Nasri, G. Sahraoui, O. Azaiez, K. Mrad
*Pathology department Salah Azaiez institute Tunisia / Precision Medicine and Oncology Investigation Laboratory (LR21SP01), Tunisia

Background & objectives: Studies have revealed mutations affecting the catalytic subunit of POLE in human tumours. These mutations cluster in the sequence encoding the exonuclease proofreading domain of POLE and are found in 3% and 8% of colorectal and endometrial carcinomas respectively.
Methods: Our objective was to search for mutations in exonucleasic region of POLE gene in endometrial carcinoma. samples.Forty samples of endometrial carcinoma were collected at the pathology department of Salah Azaiz Institute for POLE exons 9 to 14 screening by Sanger sequencing, after DNA extraction by Qiagen DNA extraction kit.
Results: In the exonucleasic region, eleven patients had POLE mutations: two patients had pG364R mutations, one patient had the silent pL343L mutation, and one patient had a double mutation in exons 12 and 13 (pC407R and pW410G), which were the most common mutations found in three and for patients, respectively.
Conclusion: In conclusion, our findings showed a 27% rate of pole mutations, with one young patient having two double mutations and several metachrone tumours.

E-PS-10-029

PD-L1 expression in serous ovarian carcinoma with calcification

R. Chyzhma*, R. Moskalenko
*Sumy State University, Ukraine

Background & objectives: PD-L1 is an immune response inhibitory factor. At the same time, the expression of PD-L1 in tumour cells contributes to peritoneal dissemination due to inhibition of CTL function. Aim. To study PD-L1 expression in ovarian serous carcinomas with calcification.
Methods: We examined 30 samples of ovarian serous carcinomas with calcification (group 1) and 30 samples without signs of calcification (group 2). An immunohistochemical study was performed using PD-L1 Monoclonal Antibody (clone CAL10, Master Diagnostica) with dilution 1:50.
Results: In the immunohistochemical study, the expression of PD-L1 was established in tumour cells and cells of the tumour microenvironment, and a positive reaction of low intensity was observed in the cells of the inflammatory infiltrate. The expression of PD-L1 in group 1 was 33.97 ± 3.0 cells in the field of view with a diameter of 1 mm. The expression of PD-L1 in group 2 was 30.46 ± 2.82 cells in the field of view with a diameter of 1 mm, without a significant difference according to the Student's test.
Conclusion: Therefore, it was established that calcification of serous ovarian tumours does not affect the level of PD-L1 expression.

E-PS-10-030

Tubulo-squamous polyp of the vagina

I. Čović*, S. Zekić-Tomaš
*University Hospital Center Split, Croatia

Background & objectives: The tubulo-squamous polyp of the vagina is a rare entity. It is thought to be derived from misplaced Skene´s glands which develop from the same cells as the prostate in men. It can share immunohistochemical characteristics with prostatic tissue.
Methods: A 74-year-old woman was admitted to our hospital after a routine gynaecologic examination revealed a polypoid lesion in the upper third of the lateral vaginal wall. A gynaecologic ultrasound showed only sporadic leiomyoma and no other abnormalities. A polypoid lesion measuring 1,2:1 cm was removed and sent for histological examination.
Results: On gross examination, the lesion was smooth, whitish to yellow. Nodularity was observed on the cut surface. Microscopic examination revealed a polyp with biphasic squamous and glandular components. Nests of bland squamous epithelial cells with eosinophilic cytoplasm were randomly distributed and embedded in a highly vascularised hypocellular fibrous stroma. Some of the squamous nests had central spaces filled with necrotic debris and calcification. At the periphery of the squamous nests were tubules lined by low columnar cells. Immunohistochemically, the cells lining the tubules were negative for prostate-specific antigen. Squamous nests were diffusely positive for p-63 and GATA 3. The polyp was removed and a follow-up examination showed no recurrence.
Conclusion: The tubulo-squamous polyp of the vagina is a rare, benign lesion that is usually seen in postmenopausal women. It is likely to be under diagnosed due to the fact that a variety of other lesions may present as a polypoid mass. Differential diagnoses include vaginal adenosis and mixed tumour of the vagina. Prostate-specific antigen staining, indicating the origin of the lesion, may be helpful but it is not crucial for setting the diagnosis.

E-PS-10-031

Gynaecological carcinosarcoma: is it that rare? A series of six cases in a one-year period in a secondary Portuguese hospital

O.M. Da Rocha Moreira Pedro*, D. Almeida, F. Moreira, A. Silva, R. Machado-Neves, M. Honavar, T. Amaro
*ULS Matosinhos; Escola Superior de Saúde - Instituto Politécnico do Porto, Portugal

Background & objectives: To present a series of six cases of gynaecological carcinosarcomas seen in a secondary (group II) hospital over one-year span (December 2022 to December 2023).
Methods: The study examined six cases of gynaecological carcinosarcomas (five uterine and one ovarian), a rare entity, diagnosed in a secondary Portuguese hospital in a one-year span. We investigated the expression of P53 and HER2 to compare with the findings in literature. Immunohistochemistry was performed to determine the expression levels of P53 and HER2 both in the epithelial and mesenchymal components.
Results: The study included six women with gynaecological carcinosarcomas, aged between 52 and 93. Histological analysis revealed serous epithelial components predominated with homologous or heterologous sarcoma. Immunohistochemistry showed P53 positivity in all epithelial components and in the sarcomatous components in two tumours. HER2 expression was 3+ in one case and focally 2+ in two cases, all within the epithelial component. On follow-up, two patients are currently alive, while two died due to surgery complications. One patient succumbed to the disease one month post-diagnosis after receiving palliative chemotherapy. Another patient passed away three months post-surgery due to tumour persistence with hemoperitoneum.

Conclusion: The histological findings align with existing literature, with serous epithelial components predominating and variable sarcomatous components. P53 exhibited 100% positivity in the epithelial component (90% per WHO guidelines) and 2 of 6 cases were positive in the sarcomatous component. HER2 was unequivocally positive in one case (16%), consistent with literature. This underscores the significance of HER2 evaluation. This finding provides additional therapeutic options for this high grade neoplasm.

E-PS-10-032

Vulvar Langerhans Cell Histiocytosis with prominent pagetoid pattern: a diagnostic pitfall

L. De Figueiredo Barbosa*, K.C.K. Prigenzi, M.M.S.e.S. Enokihara, A.M. dos Santos Filho, G.R.d.A. Focchi
*UNIFESP/EPM, Brazil

Background & objectives: Langerhans cell histiocytosis (LCH) is characterized by clonal expansion of myeloid precursors CD1a+/CD207+ and rarely affects the gynaecological tract. We describe below a case report of a vulvar presentation of the disease with an atypical morphological pattern.
Methods: 57-year-old woman with multisystemic LCH following a genital lesion, recentely experienced vulvar itching lesion. Biopsy revealed a dermal proliferation of cells with pale eosinophilic cytoplasm, irregular nuclei, surrounded by some eosinophils, along with intraepidermal spread with pagetoid dissemination. Immunohistochemical analysis confirmed LCH (CD1a and CD68 positive) and ruled out extramammary Paget's disease and melanocytic lesions (CK7 and HMB-45 negative).
Results: Although LCH is most commonly observed in children, with a discrete predilection for males, vulvar involvement can occur at any age and typically precedes multisystemic presentation, as in this case. Morphologically, it is characterized by large, round to oval histiocytes with grooved to convoluted nuclei and expression of CD1a, CD207, CD68, and S100. Due to the pagetoid pattern dissemination of the lesion in our case, additional markers were relevant to rule out possible extramammary Paget's disease (CK7) and melanocytic lesions (HMB-45). MAPK gene mutations are frequently present (around 85% of cases), especially BRAF v.600E mutations, which carry prognostic significance, especially in multisystemic disease.
Conclusion: Vulvar Langerhans cell histiocytosis is a rare disease, with few cases reported in the literature, which can affect any age and is usually early in the multisystemic manifestation of the disease. Knowledge of this lesion is fundamental for the practice of the pathologist and should be widely disseminated.

E-PS-10-033

The evaluation of immunohistochemical research assays in the assessment of folate receptor alpha expression in epithelial ovarian cancer

E. Deutschman*, R. Fulton, C. Sloss
*ImmunoGen, USA

Background & objectives: The VENTANA FOLR1 (FOLR1-2.1) RxDx Assay is FDA-approved to assess folate receptor alpha (FRα) in epithelial ovarian cancer. No reports exist comparing the performance of research-grade assays with the FDA-approved test. We evaluated antibody performance relative to the approved test.
Methods: Six antibodies were evaluated for sensitive and specific FRα staining in normal fallopian tube samples. Only the BN3.2 (Leica) and 26B3.F2 (Biocare) clones could be optimized on the Autostainer Link 48 and IntelliPATH, respectively, and were used to stain ovarian tumour specimens. A pathologist evaluated cases using the VENTANA scoring guide and compared to results obtained using the FDA-approved assay.
Results: Antibodies from Invitrogen (PA5-116453), abcam (ab67422), Proteintech (60307-1-Ig), and LSBio (LS-B5727) displayed high background and/or low specific membrane staining on all autostainers and with all conditions tested in normal fallopian tube specimen. The Leica-Link48 and Biocare-IntelliPATH assays displayed specific membranous staining and were used to evaluate ovarian tumour specimens for comparison to the FDA-approved assay. When employing the clinical cutoff of PS2+ $\geq$ 75% for positivity, overall percent agreements with the VENTANA assay of 71% (Leica-Link48) and 77% (Biocare-IntelliPATH) were observed. While higher agreements were observed on FOLR1-positive specimens (100%-Leica, 86%-Biocare), both assays overpredicted positivity relative to the FDA-approved test, with percent agreements for FOLR1-negative specimens <75% for both assays.
Conclusion: Our data highlight the need for caution in antibody selection when developing immunohistochemical-based assays, as some FRα antibodies failed to cleanly and specifically identify FRα expression. We identified two antibodies appropriate for further investigation; however, as developed, both stain more intensely than the FDA-approved test and may, therefore, over-select patients for treatment with FRα-targeted therapies intended for use with the FDA-approved companion diagnostic. From these data, we advise the use of the FDA-approved assay for patient selection.

E-PS-10-034

Rare variants of malignant vulvar tumours: a 24-year retrospective study

R. Doghri*, W. Ben Makhlouf, A. Khemir, H. Haouari, M. Slimani, N. Hammadi, N. Boujelbene, L. Charfi, G. Sahraoui, K. Mrad
*Pathology department, Salah Azaiez Institute, Tunisia

Background & objectives: Malignant vulvar tumours are infrequent, comprising only 0.3% of all new cancer cases. Squamous cell carcinoma predominates as the most common type, while other histological variants are rare and often poorly understood. We aimed to study these rare histologic variants.
Methods: We conducted a descriptive retrospective study, analyzing 38 cases of malignant vulvar tumours, excluding squamous cell carcinoma. The study spanned 24 years (2000–2024) and was conducted at the pathology department of the Salah Azaeiz Institute.
Results: The average age of patients was 56 years [2 months_78 years]. Among the cases, 37 involved primary vulvar neoplasms, with only one being a metastasis from a primary breast tumour. Melanoma was the most prevalent tumour, identified in 16 cases(42,1%). Malignant epithelial tumourscomprised 14 cases(36,8%), including 5 of Paget's disease, 3 of basal cell carcinoma, 3 of poorly differentiated carcinoma, and 1 each of basosquamous carcinoma, cysticadenoid carcinoma, and Bartholin gland carcinoma. Sarcomas were observedin 6 cases(15,7%), comprising 2 of dermatofibrosarcoma protuberans, 2 of undifferentiated sarcoma, and 1 each of embryonal rhabdomyosarcoma and low-grade myxoid sarcoma. Additionally, one case of mixed tumour, classified as carcinosarcoma, was noted.
Conclusion: Malignant tumours of the vulva are rare, dominated by squamous cel lcarcinoma. Melanoma ranks second, representing 5 to 10% of vulvar neoplasms, with a prognosis darker than its cutaneous counter part. Other entities of vulvar carcinomas and sarcomas remain exceptional and require more exploration.

E-PS-10-035

Extensive intestinal metaplasia associated with severe endometritis: a case report

L. Dragostin*, A. Coman, M. Cioplea, L. Sticlaru
*Department of Pathology, Colentina University Hospital, Bucharest, Romania

Background & objectives: The endometrial epithelium has the capacity to undergo differentiation into several types of epithelium (ciliated,

mucinous, endometrioid, transitional, clear and squamous cell types). However, intestinal metaplasia of endometrium is exceptionally rare, with only a few cases described in literature.
Methods: We report the case of a 73-year-old female who presented with chronic pelvic pain and vaginal discharge. Ultrasound examination revealed several well-defined, solid intramural masses suggestive of leiomyomas, as well as diffuse thickened endometrium. Due to clinical suspicion for carcinoma, the patient underwent hysterectomy and bilateral salpingo-oophorectomy.
Results: Histological examination showed marked and diffuse plasma cell infiltration of the endometrial stroma, as well as several areas rich in neutrophils associated with mucosal ulceration. In addition, lymphoid follicles were observed throughout the uterine wall. However, the most notable finding was extensive areas of complete intestinal metaplasia with goblet cells and even Paneth cells, with intestinal-type glands similar to those present in the lower digestive tract. The enteric phenotype of the lesion was confirmed by immunohistochemical expression of CK20 and CDX2. Other types of metaplasia (pyloric-type and mature squamous) were also observed. No dysplastic or neoplastic lesions were identified. PAX8 stain highlighted only isolated endometrial glands preserved in the endometrium.
Conclusion: We report a very rare case of extensive intestinal metaplasia occurred on a non-neoplastic background. Almost complete replacement of the endometrial glandular compartment with intestinal epithelium underlines the extraordinary plasticity of the endometrium. The etiology of intestinal-type differentiation within the endometrial mucosa is yet unclear. In our case, association with severe chronic active endometritis in the absence of concurrent neoplasia suggests that inflammation can trigger the activation of endometrial stem cells without progression to malignancy.

E-PS-10-036
Prognostic significance of FLOT2 expression in cervical carcinoma
R. Gajanin*, Z. Gajanin, D. Djokanovic, O. Jovic Djokanovic, V. Gajanin, I. Sladojevic, M. Cuk
*University of Banja Luka, Faculty of Medicine, Republic of Srpska, Bosnia and Herzegovina

Background & objectives: Cervical cancer (CC) is the second most common female reproductive organ cancer and the fourth leading cause of tumour death in women. FLOT2 is a protein that belongs to the SPFH protein family and is a receptor for growth factors.
Methods: We determined the expression of FLOT2 in samples of invasive CC and statistically examined the relationship between FLOT2 expression and survival. Aim: to determine the expression of FLOT 2 protein in samples of invasive CC and the impact on survival.
Results: Our research included 98 patients with invasive CC. Moderate and high FLOT2 expression was found in 83.7% of cases, while in 16.3% of cases it was absent. Statistical analysis revealed that CC patients with positive expression of FLOT2 lived longer compared to patients whose cancers were negative for FLOT2 (Log Rank test = 6.178; p = 0.013).
Conclusion: FLOT2 expression in our study was found in 83.7% of invasive CC. FLOT2 expression may be a prognostic biomarker in patients with CC.

E-PS-10-037
Bilateral mucinous ovarian borderline tumours - Krukenberg tumours?
H. Geddert*, M. Friedrich, T. Villena-Ossa, B. Hemmerlein
*Institute of Pathology, Germany

Background & objectives: A 77-year-old female patient developed breast cancer more than 40 years ago, which was treated with mastectomy and radiotherapy. Sclerosing papillomas were excised from the contralateral breast 18 years ago. Benign polyps were removed several times by colonoscopy.
Methods: Large bilateral ovarian tumours have recently been surgically removed.
Histopathologically, there is a 13 cm and 11 cm bilateral ovarian mucinous tumour with atypia. There was also mucinous metaplasia of the tubes including the fimbriae.
Immunohistologically, the tumours express PAX8 and CK7, while CDX2, WT1 and CK20 are almost or completely negative. Proliferation is focally increased up to 10 %
Results: To exclude ovarian metastases of a mucinous carcinoma (Krukenberg tumours), a detailed evaluation of the upper and lower gastrointestinal tract, including the appendix, was performed without significant findings. The presence of a Peutz-Jeghers syndrome was clinically confirmed.
In conclusion, we are therefore concerned with bilateral mucinous ovarian borderline tumours with extensive mucinous metaplasia of the tubes in Peutz-Jeghers syndrome.
The other known lesions (early-onset breast carcinoma, papillomas of the breast, hamartous intestinal polyps) also belong to the spectrum of this syndrome.
Conclusion: The cause is a loss-of-function mutation of the serine-threonine kinase (STK11) on chromosome 19p13.3. The frequency of this autosomal dominant inherited tumour syndrome is assumed to be 1:25,000 to 1:280,000.

E-PS-10-038
Metastatic low-grade appendiceal mucinous neoplasm (LAMN) to the endometrium and fallopian tubes
J. Grujovic*, I. Djordjevic, J. Cvetkovic
*University clinical centre of Nis, Center for pathology and pathological anatomy, Serbia

Background & objectives: Low-grade appendiceal mucinous neoplasm (LAMN) is an appendiceal tumour with a benign morphologic appearance and potentially aggressive biological behaviour. We aimed to report a case of metastatic LAMN mimicking a primary female genital tract mucinous lesion.
Methods: A 57-year-old postmenopausal woman underwent explorative curretage in response to a 3-month history of persistent metrorrhagia. Microscopy discovered a low-grade goblet-cell-rich mucinous neoplasm. The surgical approach was a classical abdominal hysterectomy with bilateral adnexectomy and omental biopsy. Aggregates of mucin were detected in the abdominal cavity during surgery and sampled for cytological analysis.
Results: Grossly, the specimen was unremarkable except the fallopian tubes were coated by "jelly-like" material. Pathohistological analysis revealed a low-grade neoplastic intestinal-type mucinous epithelium replacing the endometrial lining and acellular mucin pool within the myometrium. The same lining was present in both fallopian tubes. Acellular mucins were noticed on the surface of the fallopian tubes. The omental biopsy was without mucins or mucinous epithelium. Tumour cells expressed diffuse strong positivity for CK20, CDX-2, Villin, MUC2, MUC5AC, and focal strong positivity for CK7. The cytological smear was positive for mucins and atypical cells. Regarding the morphology and immunoprofile of the neoplasm, an appendectomy was performed. Microscopic evaluation disclosed the diagnosis of LAMN.
Conclusion: The ovaries are the well-known site of LAMN spreading to the female genital tract. According to this case and literature review, mucinous epithelium growing within the mucosa of the gynaecological system is not undeniable evidence of Müllerian origin. The differentiation between primary gynaecological mucinous lesions exhibiting intestinal differentiation and mucinous metastases to the endometrium and fallopian tubes without ovarian involvement is challenging since both processes share a similar morphology and immunohistochemical profile.

Keywords: endometrium, fallopian tube, mucinous neoplasm, appendix

E-PS-10-039

Clinicopathological and survival analysis of endocervical adenocarcinomas with focus on gastric and invasive stratified mucin-producing carcinomas: a retrospective study of 72 cases

E. Guerra Fernández*, E. Dorca, A. Vidal, R. Taco, A. Esteban, M. Santacana, B. Pardo, M. Gil, J. Ponce, X. Matias-Guiu
*Hospital Universitari de Bellvitge, Spain

Background & objectives: Endocervical adenocarcinoma (EAC) accounts for aproximately 5% of all cervical carcinomas. The aim of this study is to evaluate clinicopathological features of EAC: histological type, Silva pattern, lymphovascular invasion (LVI) and FIGO stage to determine possible associations with clinical outcomes.
Methods: 72 EAC were collected and reviewed from our institution. Clinicopathological features as histological type (predominant and secondary pattern if any), Silva pattern, LVI, FIGO stage, treatment, recurrence, and status were assesed. Immunohistological stanings were performed as p16, ER, p53, MUC6, claudin-18 and HPV testing. Survival and statistical analyses were carried out by using Kaplan-meier, log-rank test and chi squared test.
Results: 72 EAC were recruited: 7 gastric EAC (group 1), 11 invasive stratified mucin-producing carcinoma (i-SMILE) (group 2), 7 mixed predominant i-SMILE and usual EAC (group 3), 4 mixed predominant usual and i-SMILE EAC (group 4), 43 usual EAC (group 5). Mean age was 47.4 years. Usual EAC and mixed predominant usual and i-smile EAC have shown a stadistically significant association with the absence of extensive LVI ($p=0.006$). Statistically significant differences were also found when analyzing mean overall survival ($p<0.005$) and progression-free survival ($p<0.001$) between groups and FIGO stage. Gastric EAC and i-SMILE were associated with worse prognosis.
Conclusion: Histological type and FIGO stage are variables that correlate with clinical outcome. Gastric EAC and pure i-SMILE are associated with worse prognosis, while exhibiting any usual type component is correlated with better clinical behaviour and a lower degree of angioinvasiveness.

E-PS-10-040

Disorder of cellular immunity as a cause of abnormal uterine bleeding

M. Gushchin*, L. Mikhaleva, M. Orazov, S. Mikhalev, R. Vandysheva, D. Masalimova, N. Shakhpazyan, E. Zentsova, R. Mitrelis
*A.P. Avtsyn Research Institute of Human Morphology Petrovsky National Research Center of Surgery, Russia

Background & objectives: Endometriopathy causes increased proliferative potential with a reduced ability to differentiate the endometrium, asynchronous uterine peristalsis, causing abnormal uterine bleeding (AUB) and disruption of the menstrual cycle. Methods for diagnosing the causes of AUB in patients are far from ideal.
Methods: We studied material in the middle stage of the proliferation phase of pipell biopsy or after hysteroscopy of the endometrium of women with a history of AUB and subsequent menstrual irregularities of endometrial origin. The histological sections are stained with H&E, and histochemical to Mallory, and by IHC using sets of monoclonal antibodies markers: CD138, CD56, CD4, CD8, CD20.
Results: we established reliable IHC and histochemical determinants. When examining biopsies in which CD138+ cells were not detected, excess CD56+ values are found in 90%, excess CD20+ values in 9%, excess CD4+ values in 90%, excess CD8+ values in 98%, deviation of the CD4+/CD8+ ratio is detected in 64%, stromal fibrosis - 55%. These changes are regarded as a violation of cellular immunity. Against the background of impaired cellular immunity - the CD4+/CD8+ ratio of the epithelial-mesenchymal compartment, an increase in the expression of CD4+ and CD8+, as well as their ratio in the main group relative to the comparison group, is determined.
Conclusion: Endometriopathy in the form of a violation of cellular immunity is a fundamentally important link for the regulation of reproductive and menstrual function. Accordingly, the identified immunodeficiency in the endometrium in the proliferation phase in patients with chronic endometritis may be one of the leading pathogenetic mechanisms for the development of functional failure of the endometrium and, as a consequence, uterine factor infertility.

E-PS-10-041

The role of VEGF and VWF markers in diagnosing the grade of chronic endometritis in women with abnormal uterine bleeding

M. Gushchin*, S. Mikhalev, R. Vandysheva, R. Mitrelis, M. Orazov, D. Masalimova, N. Shakhpazyan, L. Mikhaleva
*A.P. Avtsyn Research Institute of Human Morphology Petrovsky National Research Center of Surgery, Russia

Background & objectives: One of the causes of abnormal uterine bleeding (AUB) is chronic endometritis (CE), according to the FIGO (PALM-COEN) classification - AUB-E. In vascular dysfunction in CE and recurrent miscarriage, according to modern research, angiogenesis is one of the key factors.
Methods: A complex of pathological examination of the endometrium in the middle stage of the proliferation phase was carried out with histochemical staining according to Mallory and IHC with CD138, VEGF and von Willebrand factor (VWF). An analysis is carried out for the presence of fibrosis,counting the number of CD138+ plasma cells per 1 field of vision at optical zoom 400.
Results: Based on the data obtained on the number of CD138+ plasma cellsand the presence of fibrosis, three degrees of CE grade were identified: severe CE (SCE), medium CE (MCE), low CE (LCE). We concluded that with an increase in the severity of CE, the number of cells produced by VEGF decreases, the activity of angiogenesis and the number of new arterial vessels decreases. Thus, the severity of CE can be determined by the percentage of the number of cells expressing VEGF in the superficial endometrium and in the glands and the number of new vessels by a positive reaction with VWF.
Conclusion: It should be concluded that impaired oxygenation and a decrease in the number of vessels in the functional endometrial compartment are fundamentally important for the regulation of reproductive and menstrual function. Accordingly, the identified imbalance in the endometrium during the proliferation phase in patients with CE may be one of the leading pathogenetic mechanisms for the development of functional failure of the endometrium and as a consequence - uterine factor infertility.

E-PS-10-043

Molecular classification of vulvar squamous cell carcinoma (VSCC) on diagnostic biopsy is highly concordant with final resection specimen: earlier prognostic information to guide personalised medicine

L. Horn*, M. Forberger, M. Alfaraidi, R. Hiller, L. Hoang, B. Gilks, A.K. Hoehn
*University Hospital Leipzig, Germany

Background & objectives: VSCC can be stratified into molecular subtypes based on p16 and p53: HPV-independent /p53abn, HPV-associated, with p16-overexpression and HPV-independent /p53wt. The aim of the study was to correlate the molecular subtype from pre-operative biopsies with subsequent vulvectomy specimen.
Methods: Matched-pairs of 57 VSCC were analysed for immunohistochemical expression of p16 and p53 by performing a three-tiered molecular subtyping to test the accuracy rate.

Results: The overall accuracy rate was 91.2% (52/57) and 97.3% for HPV-independent/p53abn, 94.1% for HPV-associated and 50% for HPV-independent/p53-wt VSCC. Misinterpretation of p53-staining patterns was the reason for the discordance in all cases. Additional molecular workup to define the molecular subtype of VSCC on biopsy was indicated in 3/57 (5.3%).
Conclusion: Molecular subtype of VSCC can reliably be determined on pre-surgical biopsies with a high accuracy rate. Accurate molecular subtyping on diagnostic biopsy is valuable tool for better prognostication, allows more accurate surgical planning, prediction of response to (chemo-) radiation, selection of targeted regimes and planning of the optimal follow-up strategy in the era of personalised medicine.

E-PS-10-044
Nectin-4 expression in vulvar squamous cell carcinoma (VSCC)
L. Horn*, B. Wolf, M. Forberger, R. Hiller, A.K. Hoehn
*University Hospital Leipzig, Germany

Background & objectives: Nectin4 -overexpression is associated with proliferation, angiogenesis, epithelial mesenchymal transition, metastasis, DNA repair and poor prognosis. Nectin4 is a component of antibody-drug conjugate (ADC) enfortumab vedotin (EV). There are no data about expression in VSCC.
Methods: 55 VSCC were immunohistochemically analysed for Nectin-4 expression using a H-score. Staining scores were compared to the 3-tiered molecular subtyping of VSCC: p16+ve/p53wt, p16-ve/p53mut and p16-ve/p53wt VCX. Staining evaluation of Nectin-4 was blinded to the molecular subtype.
Results: All VSCC represented positive immunostaining for Nectin-4, with mean H-score of 4.8 (range 2-9). There were no differences of Nectin-4 expression within the different molecular subtypes of VSCC: mean H-score 5.2 (range 2-9) for p16+ve/p53wt, 4.8 (range 2-9) for p16-ve/p53mut and 2.5 (range 2-3) for p16-ve/p53wt VSCC (p=0.27).
Conclusion: The ADC enfortumab vedotin (EV; nectin4 linked to microtubule inhibitor MMAE) was approved for the treatment of urothelial cancer. Virtually all examined VSCC showed at least weak staining for Nectin-4 within the tumour cells. So, Nectin-4 may represent a potential target for ADC in vulvar cancer. There are no differences of Nectin-4 expression within the different molecular subtypes of VCX.

E-PS-10-045
TROP-2 expression in vulval carcinoma - correlation to molecular subtype
L. Horn*, R. Hiller, M. Alfaraidi, L. Hoang, A. Jamieson, Y. Drew, B. Gilks, J. McAlpine, B. Wolf, A.K. Hoehn
*University Hospital Leipzig, Germany

Background & objectives: TROP-2 is associated with invasiveness and tumour progression and identified as target protein for treatment with antibody-drug conjugates (ADC). Data about the expression profiles of TROP-2 in VSCC are very limited especially with respect to its molecular subtype.
Methods: 55 biopsies from VSCC were immunohistochemically analysed for TROP-2 using H-score. Staining scores compared to molecular subtypes of VSCC: HPV-associated (p16+ve/p53wt), HPV-independent/p53abnormal (p16-ve/p53mut) and HPV-independent/p53wildtype (p16-ve/p53wt) VSCC. Staining evaluation of TROP-2 was blinded to the molecular subtype.
Results: All cases were positive for TROP-2 (7 cases +, 31 cases ++ and 17 cases +++)
Conclusion: The ADC topoisomerase-1-inhibitor irinotecan, coupled via a linker to a humanised IgG-1ntibody hRS7 binding to TROP-2 (i.e. sacitumzumab) represents an effective treatment approach to several carcinomas. All examined VSCC showed staining for TROP-2. So, TROP-2 may represent a potential target for ADC in vulvar cancer. There are no differences of TROP-2 expression within the different molecular subtypes of VCX. Trop2-expression can be determined on diagnostic biopsies.

E-PS-10-046
Immune microenvironment in serous carcinoma of the fallopian tube
N. Hyriavenko*, M. Lyndin, K. Sikora, Y. Lyndina, A. Shamrai, O. Polozhiy, D. Tsepochko, A. Romaniuk
*Sumy State University, Ukraine

Background & objectives: Investigating an interplay between the immune microenvironment in serous carcinoma of the fallopian tube (SCFT) and tumour cells holds promise for unveiling novel diagnostic and therapeutic targets, due to its potential implications in cancer development and progression.
Methods: This study was conducted on 66 samples of SCFT. The qualitative composition of the tumour's immune microenvironment was examined using immunohistochemical staining with antibodies against CD3 (T-lymphocyte marker), CD79α (B-lymphocyte marker), and CD68 (macrophage marker).
Results: The presence of tumour-infiltrating inflammatory infiltrate was detected in 40.9% of SCFT cases. The presence and increased intensity of infiltration depended on the degree of atypia ($p<0.05$). The cellular component of the SCFT microenvironment was predominantly represented by B-lymphocytes (ranging from 30 to 80% of all cells). The number of T-lymphocytes constituted from 10 to 50% of all cells. Decreased levels of T-cell infiltration in tumour tissue were significantly associated with lymph node metastasis ($p<0.001$). The overall number of macrophages ranged from 1 to 20% of the total cell count and was significantly higher in the group of patients with SCFT metastasized to regional lymph nodes ($p<0.001$).
Conclusion: Analyzing the qualitative composition of the tumour microenvironment, it can be concluded that low expression of CD3+ T-lymphocytes is associated with an increased level of CD79α+ B-lymphocytes and CD68+ macrophages, indicating an unfavourable disease course and warranting further investigation.

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E-PS-10-047
Pathological examination of the placenta in COVID-19-positive mothers
A. Ilic*, K. Malešević, T. Lakić, M. Živojinov, M. Stojić, M. Panjković
*University of Novi Sad, Faculty of Medicine, Serbia

Background & objectives: COVID-19 caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) primarily affects the respiratory system, but also has negative effect on other system organs, such as placenta. We analysed the morphological changes of the placenta in SARS-CoV-2-infected pregnant women.
Methods: This was a descriptive retrospective study of 54 pregnant women in the 2nd or 3rd trimester with laboratory-confirmed SARS-CoV-2 infection who delivered between Mart 2021 and December 2021 at University clinical centre of Vojvodina. Demographic, placental, delivery, and neonatal outcomes were collected through medical record review. Histopathologic lesions were categorized according to the Amsterdam criteria by pathologists.
Results: Almost half of examined placentas (43%) showed normal histomorphological characteristics, while the rest mostly showed signs of maternal/foetal vascular malperfusion. Regarding maternal vascular

malperfusion, the most common pathology were chorioamnionitis (37%) and increase in syncytial knots (13.5%), as well as infarction (10%) and fibrin deposition. On the other hand, foetal vascular malperfusion was represented in 8% of cases, such as umbilical vein thrombosis and vascular ectasia. In 4% of cases we found signs of chronic inflammation, such as intervillositis and acute villitis and in 2% of cases placenta increta was present. As for other pathology, dystrophic calcifications were present in several placentas (7%), as well as deposits of hemosiderin.
Conclusion: Our study and literature suggest that placentas from patients with COVID-19 shows no specific pattern of alterations. The limitations of our study and other studies is lacking of control groups which we will aim to improve in future work.

E-PS-10-048
Concurrent papillary thyroid carcinoma in struma ovarii and multifocal serous carcinoma of the fallopian tube: a novel case report
D.G. Iosep*, M. Tanasă, M. Danciu
*Grigore T. Popa University of Medicine and Pharmacy Iași, Romania

Background & objectives: Papillary thyroid carcinoma (PTC) arising in struma ovarii (SO) is an exceedingly uncommon gynaecologic malignancy. Moreover, to our best knowledge, its association with a concomitant primary multifocal serous carcinoma of the fallopian tube has never been previously reported.
Methods: We present the case of a 44-year-old woman who underwent right salpingo-oophorectomy for ovarian torsion owing to a right ovarian cyst. The surgically resected specimen was fixed in 10% formaldehyde and routinely processed. Hematoxylin and eosin staining and immunohistochemical tests were performed.
Results: Gross examination of the ovary revealed a multiloculated cystic lesion with solid components, while the fallopian tube showed an intraluminal mass with papillary projections. Microscopical evaluation of the ovary revealed SO composed predominantly of thyroid tissue, with an area of 0,7cm with solid and microfollicular growth pattern where tumour cells displayed glassy nuclei and nuclear grooves. Immunohistochemistry of the abovementioned area showed positive expression of TTF-1, CK19, HBME-1 and negative expression for CD56 and S100, with a Ki67 index of 1%, consistent with the diagnosis of PTC originating from SO. Additionally, the fallopian tube showed multifocal lesions of serous tubal intraepithelial carcinoma, with a focus of high-grade serous carcinoma.
Conclusion: This is the first documented case of concurrent PTC arising within SO alongside primary multifocal serous carcinoma of the fallopian tube. Malignization of SO, being rare, requires differential diagnosis for the PTC component. While serous tubal carcinoma is strongly associated with BRCA germline mutations, understanding of SO's malignant transformation remains limited due to its scarcity. In the absence of standardized treatment protocols, rigorous postoperative monitoring is crucial to detect and manage potential recurrences or metastasis in these complex cases.

E-PS-10-049
Concurrent loss of SMARCA1 and SMARCA4 in two cases of dedifferentiated endometrioid adenocarcinoma: report of an unusual phenomenon
N.M. Iqbal*, R. Sood, R. Rathore, S. Mathur, J. Meena, R. K.
*Department of Pathology/AIIMS New Delhi, India

Background & objectives: Abnormalities in SWI/SNF chromatin remodelling proteins like SMARCA4(BRG1) define small-cell ovarian carcinoma with hypercalcemia(SCOCHT) and occur in one-third of uterine undifferentiated/de-differentiated endometrial carcinomas(DEC).However,SMARCA4 and SMARCB1 co-deficiency are mutually exclusive.Here, we report two rare DECs exhibiting synchronous BRG1 and INI1 loss.
Methods: Immunohistochemistry (IHC) performed on whole tissue sections for BRG1(1:800; E8V5B), INI1(prediluted, BAF47), BRM(1:2000; D9E8B). Their abnormal expression was defined by an unequivocal complete ("deficient") or patchy loss ("hybrid") with intact Internal control. IHC for PAX8, Caludin-4, and keratin other diagnostic markers was performed along with the mismatch repair proteins. The clinical, radiological and follow-up details of the DEC were analysed.
Results: Case 1:A 34-year-old Indian woman with abnormal uterine bleeding post-right ovarian cystectomy for metastatic adenocarcinoma showed imaging findings of heterogeneous thickening and metabolic activity in the endometrial lining and endocervical canal,with accompanying lymphadenopathy,pleural effusion,and pelvic ascites.Endocervical and endometrial biopsies confirmed dedifferentiated endometrial carcinoma(DEC) with undifferentiated polygonal cells exhibiting rhabdoid morphology and focal glandular differentiation,alongside BRG1 deficiency and hybrid BRM and INI1 expression.
Case 2:A 60-year-old Indian woman with postmenopausal bleeding had a distended endometrial cavity with heterogeneous enhancement in >50% myometrium.Hysterectomy confirmed dedifferentiated endometrial carcinoma(DEC),immunopositive for PAX8 and keratin in the differentiated component,with hybrid loss of BRG1 and INI1.Pelvic lymph node metastasis was detected.Ovarian and fallopian tube histopathology was unremarkable.
Conclusion: This case report underscores the complexity of molecular alterations in DECs. Further research is needed to elucidate the underlying mechanisms driving such rare tumours with synchronous loss of SMARCA4/BRG1 and SMARCB1/INI1.

E-PS-10-050
Overview of genomic alteration in ovarian high-grade serous carcinoma with therapeutic response
J. Jeong*, U. Jo
*Republic of Korea

Background & objectives: High-grade serous carcinoma (HGSC), the most common ovarian cancer, often presents at advanced stages and is characterized by harboring TP53 mutation. We aimed to investigate the association between genetic alteration including TP53 and important prognostic factors.
Methods: We performed targeted next-generation sequencing on 100 ovarian HGSC patients to explore somatic mutations and copy number alterations, investigating the association between genetic alteration, including TP53 and the homologous recombination repair pathway, and prognostic factors such as nodal metastasis status and clinical response score (CRS). Additionally, we analysed the correlation between TP53 genetic alterations and p53 expression patterns through immunohistochemistry.
Results: Among 100 patients, 45 patients received neoadjuvant chemotherapy (neoCTx), and 55 patients did not. There was a significant association between TP53 mutation variants and CRS of neoCTx patients, with missense mutations prevalent in patients with CRS1, while frameshift and nonsense mutations prevalent in those with CRS3 (P=0.035). A significant increase in tumour mutational burden was observed in neoCTx patients lacking lymph node metastasis (P<0.001). In patients not undergoing neoCTx, those with nodal metastasis showed a significantly higher copy number alterations fraction (P=0.001). Additionally, a significant correlation was found between TP53 genetic alterations and p53 expression patterns, with missense mutations correlating with diffuse pattern, and truncated mutations with null pattern (P<0.001).
Conclusion: Assessing TP53 genetic alterations in ovarian HGSC patients who have received neoCTx can provide more precise information about their pathological therapeutic response. Furthermore, the p53 expression pattern may suggest insights into the assessment's results.

E-PS-10-051

An unusual pattern of divergent p57 expression in products of conception with discordant villi

L. Johnston*, A. Snaddon, L. McMahon, L. Christie
*Ninewells Hospital & Medical School, Dundee, United Kingdom

Background & objectives: p57 immunohistochemistry is a useful ancillary technique in identifying complete hydatidiform moles (CHM), which show concordant loss of expression in both villous stroma and cytotrophoblast cells. We present a case with a rare pattern of discordant and divergent p57 expression.
Methods: Ploidy was assessed by flow cytometry. p57 immunostaining was undertaken according to standard protocols. Whilst concordant loss of p57 expression involves loss in both villous stroma and cytotrophoblast cells, rare cases of discordant p57 expression show loss in either the villous stroma or the cytotrophoblast and cases with divergent p57 expression show different staining patterns between villi or within villi.
Results: Histological examination of the products of conception showed grossly abnormal chorionic villi across a range of sizes, with predominantly enlarged, hydropic villi. Occasional large irregular trophoblast pseudoinclusions and deep invaginations were noted, but many villi showed no trophoblast overgrowth. Multifocal or circumferential trophoblast growth with cytological atypia was demonstrated in a minor population of villi.
Ploidy studies indicated a diploid conceptus, prompting p57 immunohistochemistry reflex testing, which demonstrated a discordant pattern with positive cytotrophoblast and negative stroma. Strikingly, regions of atypical trophoblast growth showed incomplete, divergent p57 staining with focal strips of negative cells interrupting the predominantly p57 positive cytotrophoblast, suggesting a diandric cell population was present within these foci.
Conclusion: p57 immunohistochemistry is an important ancillary tool used in conjunction with histology and ploidy studies to aid in diagnosing molar versus non-molar pregnancies, and is invaluable in cases with equivocal histology. We identified a diandric cell line in a small population of cells comprising the atypical cytotrophoblast, which could not be determined by histological analysis alone. The presence of a diandric cell line in the cytotrophoblast prompted registration and follow-up due to undetermined risk of persistent gestational trophoblastic disease.

E-PS-10-052

CD44 and CD133 cancer stem cell markers as indicators for aggressive ovarian tumours

L. Jovanovic*, B. Sosic-Jurjevic, A. Cirkovic, S. Dragicevic, B. Filipovic, S. Milenković, S. Dugalic, M. Gojnic- Dugalic, A. Nikolic
*Serbia

Background & objectives: Cancer stem cells(CSCs) represent significant and not enough explored tumour compartments in many different malignancies. They could have great prognostic and therapeutic potential. In epithelial ovarian tumours(EOT) CSCs are responsible for tumour growth, recurrence, and resistance to standard therapy protocols.
Methods: Our cohort comprised 218 patients with EOT of which 131 were ovarian cancers (OC), 42 atypical proliferative tumours (APT), and 45 benign ovarian tumours (BOT). Immunohistochemical CD44 and CD133 expression were correlated with a set of histopathology parameters and clinical data. Immunohistochemical analysis was performed using the tissue microarray method.
Results: In this study, we analysed CD44 and CD133 expressions considering different EOT histology types and biological behaviours. There was a positive association ($p<0.05$) between CD44 and CD133 markers in all groups. Namely, CD44 showed higher levels ($p<0.05$) in OC than in other groups, while CD133 expression was most prominent in the atypical proliferative tumours. Significant CD44 expression was evident in high-grade serous carcinoma (HGSC) in advanced FIGO stages. CD133 marker did not show an association with these histopathology parameters.
Conclusion: Significant CD44 was demonstrated in ovarian CSC in aggressive types as HGSC, at advanced stages. It indicates the possible benefits of target therapy in patients with HGSC in FIGO III or IV with high expression levels of these markers. CD133 immunostaining was mainly associated with benign tumours.

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E-PS-10-053

p16 and COX-2 expression on the prediction of progression to endometrial cancer and endometrial hyperplasia

M.J. Jurado Rivera*, V. Davila Flores, M.J. Gálvez-Medina, J. Osuna Soto, F. Leiva-Cepas
*Hospital Universitario Reina Sofía, Spain

Background & objectives: Endometrial cancer (EC) is the most commonly diagnosed gynaecological cancer. p16 and COX-2 have a role in EC. The aim of this study is to investigate the expression of p16-COX-2 during the development of EC from endometrial hyperplasia.
Methods: We investigated COX-2 and P16 expressions in patients with proliferative endometrium, endometrial hyperplasia and endometrioid adenocarcinoma.
Results: p16 expression increased in EH and EC ($p<0.012$). COX-2 expression was increased in endometrial cancer compared to other groups without statistically significant. Although p16 and COX-2 expression were increased in patients with advanced grade, >50% of myometrial invasion and lymphovascular invasion, but was not statistically significant.
Conclusion: More detailed studies are needed to investigate the prognostic significance of the COX-2 molecule and might be a potential biomarker for the prognosis.

E-PS-10-054

Non-gynaecological tumours that metastasize to the gynaecological tract: a single centre experience

H. Kandemir*
*Health Sciences University Izmir, Turkey

Background & objectives: To describe non-gynaecologic origin tumours that involve the gynaecologic systemsecondarily and their clinicopathological characteristics.
Methods: Among cases diagnosed or treated at our institution from 2009 to 2020, neoplasms originating outside the gynaecologic region but metastasizing to the gynaecologic system were retrospectively identified through the hospital system.
Results: Metastasis/involvement was observed in a total of 23 cases, aged between 26 and 69 (median: 57). The primary tumour origin was gastrointestinal system (GIS) in 18 cases (79.2%), breast in 2 cases (8.3%), lung in 2 cases (8.3%), and bladder in 1 case (4.2%). Among GIS-related neoplasms, 7 were colorectal (33.3%), 6 were appendiceal (25%), 2 were gastric (8.3%), while the primary site couldn't be determined in 3 cases (16.7%). According to histopathological diagnoses, distribution was as follows: Adenocarcinoma (14; 62.5%), Mucinous adenocarcinoma (6; 25%), low-grade mucinous neoplasm of the appendix (3; 12.5%). Signet ring cell component was present in 3 cases (16.6%).
Conclusion: Among neoplasms causing involvement of the gynaecologic tract, gastrointestinal system-originated neoplasms are the most frequent. The most commonly involved gynaecologic organ is

the ovarian tissue, either single or bilateral. The most common tumours causing secondary involvement in the gynaecologic system have adenocarcinoma and mucinous carcinoma morphology. These findings align with existing literature data.

E-PS-10-055

Enterobius vermicularis induced Bartholin gland abscess

S. Kanoun*, S. Makni, S. Graja, L. Bouzidi, S. Hidouri, T. Sellami Boudawara, M. Zghal
*Department of Pathology, Habib Bourguiba University Hospital, Sfax, Tunisia

Background & objectives: Enterobiasis is a parasitic condition caused by Enterobius vermicularis. Extraintestinal locations are rare. Female genital tract is the most common site. Bartholin gland affection is exceptional. The aim of the study is to discuss clinicopathological features of this rare disease.
Methods: A 27-year-old woman, with no past medical or surgical history, presented to the Obstetrics and Gynaecology Department with a vulvar mass. According to the patient, this mass had been present for more than six months.
Results: Gynaecological examination reveals a cystic mass, painless on palpation, primarily suggestive of a Bartholin gland cyst. A surgical excision was done. Histopathological analysis found a cystic wall containing mucous bartholin gland bordered by inflammatory infiltrate consisting of macrophages, lymphocytes, neutrophils and eosinophils. The lumen contained necrotic material with oval-shaped, asymmetrical parasite eggs, which were approximately 52 µm in size. This size and appearance was typical for Enterobius Vermicularis eggs. Upon retrospective questioning, the patient revealed recurrent episodes of anal and vulval itching exacerbated at night as well as a personal and family history of intestinal pinworm disease. Treatment with Mebendazole 100mg was initiated for the patient and all household members.
Conclusion: Bartholin gland abscesses are typically caused by obstruction of the Bartholin gland duct, leading to an accumulation of fluid and subsequent infection. The most common pathogens associated with Bartholin's gland abscesses are bacteria. E. vermicularis is exceptional. The differential diagnosis includes various parasitic infections. Enterobiasis should be considered as a possible etiology of Bartholin gland abscesses in patients presenting with gynaecological symptoms. Further research and awareness are needed to better understand the pathogenesis, diagnosis, and management of such cases.

E-PS-10-056

Prognostic significance of lymph node involvement and histological reaction patterns in ovarian serous borderline tumours

J. Kim*, K. Kim
*Gil Medical Center, Gachon University College of Medicine, Republic of Korea

Background & objectives: Lymph node involvement (LNI) in ovarian serous borderline tumours (SBTs) is not uncommon, yet it doesn't significantly impact patient outcomes. We examined histological reaction patterns (HRPs) in the lymph nodes of SBT patients to explore their association with prognosis.
Methods: HRPs in lymph nodes were categorised into four patterns based on tumour cell location, adhesion to lymphoid tissues, and desmoplastic reactions. HRP1 and HRP2 indicate non-adherent tumour cells within lymphatics and sinuses, respectively. HRP3 denotes tumour cells firmly adherent to nodal parenchyma without intervening spaces. HRP4 signifies a peritumoural desmoplastic response, regardless of tumour cell location.
Results: In our study, LNI was associated with shorter recurrence-free survival (RFS), yet patients with HRP1 or HRP2—characterized by non-adherent tumour cells within lymphatic lumens or sinuses—had no recurrences. Conversely, HRP3 and HRP4, marked by firm tumour cell adhesion to lymphoid tissues or desmoplastic reactions, were linked to reduced RFS. Additionally, LNI exceeding 1mm significantly impacted RFS negatively. Meanwhile, overall survival remained unaffected by the presence of LNI, HRPs, or the extent of LNI involvement.
Conclusion: The prognosis for SBT patients with LNI is not uniformly favourable, with HRPs around the LNI playing a crucial role in their recurrence risk. Patients exhibiting firm tumour cell adhesion to adjacent lymphoid tissue or presenting with peritumoural desmoplastic reactions have reduced RFS, though this does not significantly correlate with a decrease in overall survival.

E-PS-10-057

Uterine leiomyoma with signet-ring-like cells: a case report

O. Kouroukli*, E.H. Kourea
*Evaggelismos General Hospital, Athens, Greece

Background & objectives: Uterine leiomyomas are common benign mesenchymal tumours that are part of a pathologist's routine and usually do not cause much concern. We present a case of uterine leiomyoma with signet-ring-like morphology aiming to highlight this unusual and alarming feature.
Methods: We received a hysterectomy specimen from a 54-year-old perimenopausal woman. Sections from the intramural tumours, found upon gross examination were taken. On H&E one of these tumours showed signet-ring-like cells and was subjected to immunohistochemical analysis for markers CK8/18, AE1/AE3, PAX-8, ER, PR, SMA, MSA, Desmin, CDX2, SATB2, GATA-3, SOX-10, CD68, CD10 and CyclinD1. PAS-D histochemical stain was also performed.
Results: Multiple intramural tumours measuring 0.5-7 cm were present on gross examination. The typical microscopic appearance of leiomyomas was found in all but the largest tumour. This tumour displayed areas with increased collagen deposition and a disorganized appearance of plump spindle cells, among which some signet-ring-like cells were remarkably present. The immunohistochemical studies confirmed the smooth muscle nature of these signet-ring-like cells and excluded the possibility of a metastatic or primary carcinoma or another malignant tumour. PAS-D stain did not reveal the presence of intracellular mucin. Interrogation of the patient's past medical history and imaging studies was unremarkable.
Conclusion: Cells with signet-ring-like morphology can result from the vacuolization of smooth muscle cells of a uterine leiomyoma. This phenomenon probably represents an involutional change, previously described in apoplectic leiomyomas but not in the usual variant to our knowledge. We conclude that the presence of signet-ring-like cells can happen in a uterine leiomyoma. This finding may be alarming at first sight but the proper diagnostic workup can resolve the concern and reveal the benign nature of these signet-ring-like cells.

E-PS-10-058

Mature teratoma of the ovary with struma and Brenner tumour, attached to ovarian fibroma: a case report

P. Kousidis*, S. Androniadou, G. Karagiannis, V. Christoforidou, S. Mavropoulou, A. Nikolaidou
*Pathology Department, Theageneio Anticancer Hospital of Thessaloniki, Greece

Background & objectives: Coexisting of mature teratoma and fibroma is rare. Brenner tumours are rare tumours categorized into transitional type epithelial ovarian tumours which have been very rarely reported to coexist with other tumour elements.
Methods: A 64-year-old female was admitted to our Gynaecology Department for elective laparoscopic resection of a right ovarian

tumour. She underwent bilateral salipngo-oophorectomy and partial omentectomy with concurrent intraoperative frozen section examination of the right ovary.
Results: Intraoperative frozen section showed an excision specimen with total dimensions of 13.5x10.8x9 cm, with a 10.5 cm cystic and a 5.5 cm solid element. FFPE section examination showed a teratoma, composed of a mixture of mature tissues, ectodermal (squamous cell epithelium, skin appendages), mesodermal (adipose tissue, cartilage, bone formation) and endodermal (struma ovarii and mucous-secretory epithelium). Additionally, a 2 cm Brenner tumour was found within the teratoma. The second, solid tumour, showed features of an ovarian fibroma and was attached to the cystic teratoma (collision tumour).
Conclusion: Coexistence of ovarian teratomas with other ovarian tumours, especially multiple, is a rare occurrence. Our case highlights the importance of clinicians' vigilance in suspecting ovarian tumours with multiple elements and pathologists' need to extensively sample and examine, especially heterogenous, ovarian tumours.

E-PS-10-061
Diagnosis of metastatic disease in patients with borderline mucinous tumour of the ovary
A. Lapa*, M. Alzamora, P. Rodrigues Veiga, R. Dias, C. Bartosch
*Department of Pathology, Portuguese Oncology Institute of Porto (IPO-Porto), Portugal

Background & objectives: Mucinous borderline ovarian tumours rarely metastasise, and mortality is low. We reviewed three patients diagnosed with metastatic disease years after the diagnosis of ovarian tumour and performed immunohistochemistry and genetic analysis.
Methods: All patients were surgically treated including oophorectomy, at the age of 35(PtA), 44(PtB) and 64(PtC). PtA had a bilateral tumour (15cm, 10cm), and the other two were unilateral (28cm, 27cm). All had foci of intraepithelial carcinoma and focal microinvasion. Metastatic disease was diagnosed after 3, 6 and 17 years of follow-up, in the liver (PtA) and lung (all patients).
Results: Clinically, metastases (lung and liver) consisted in multiple small nodules. Morphology and immunohistochemistry profiles were comparable between the ovarian tumours and metastases. All had gastrointestinal differentiation. PtC had PAX8 expression. ER/PR expression was absent in all. Genetic testing showed partially identical profile between primary and metastases. PtA had KRAS (c.437C>T) both in primary and liver metastasis. PtB had KRAS (c.35G>A) both in primary and lung metastasis and the latter also had BRAF (c.1799T>A) and TP53(c.991C>T). PtC primary had KRAS (c.35G>A), but lung metastasis material was insufficient for analysis.
PtA underwent chemotherapy and progressed, perishing within one year. PtB and PtC are currently under systemic chemotherapy.
Conclusion: To safely establish a diagnosis of mucinous borderline tumour metastasis, it is necessary to aggregate clinical, morphological, immunohistochemical and genetic data. Mucinous adenocarcinoma of other locations should be excluded. Careful pathological analysis of the ovarian tumours, with extensive sampling must be performed, given the heterogeneous nature of these lesions. Prognosis of patients with metastatic disease seems dismal with poor response to chemotherapy.

E-PS-10-062
Serous carcinoma with squamous metaplasia in a uterine carcinosarcoma: a case report and literature review
C. Leal*, A. Marques, R. Portugal
*Unidade Local de Saúde de São João, Portugal

Background & objectives: Carcinosarcoma of the uterus is a rare, biphasic, malignant tumour composed of a high-grade epithelial component and a sarcomatous component. We report a case of uterine carcinosarcoma in which the epithelial component is a serous carcinoma with squamous metaplasia.
Methods: A 75-year-old woman presented with abdominal distention and recurrent urinary tract infections. Pelvic ultrasound revealed free fluid in the uterus. Hysteroscopy showed hematometra and an endometrial polyp which was excised. Histological examination showed a high-grade endometrial carcinoma. MRI exhibited a heterogeneous nodular thickening of the endometrium which measured 6,2x4,5cm and invaded >50% of the thickness of the myometrium.
Results: The patient underwent total hysterectomy, bilateral salpingo-oophorectomy and pelvic lymphadenectomy. The specimen showed a white friable tumour, filling the uterine cavity with 8,2x6,2x5,6cm, invading the full thickness of the myometrium and the cervix. Histologically the neoplasia was composed of serous carcinoma with focal squamous differentiation and high-grade sarcoma focally with rhabdomyoblastic differentiation. Immunohistochemical studies revealed aberrant expression of p53, diffuse positivity for p16, and absence of ER and PR in the epithelial component. Areas with squamous differentiation were diffusely positive for p40. The sarcomatous component was diffusely positive for PAX-8 and SMA, and multifocally positive for desmin and CD10. Myogenin was positive in cells with rhabdoid morphology.
Conclusion: Our final diagnosis was carcinosarcoma of the uterus. The patient died seven months post-surgery due to peritoneal carcinomatosis and multiple lung and liver metastases.

This case report highlights the importance of generous sampling on gross examination to determine with utmost precision all the tumoural components. We also aim to emphasize that the presence of squamous differentiation, although more common in endometrioid carcinoma, is not pathognomonic and can also be present in serous carcinoma. We review the literature regarding this topic.

E-PS-10-063
Clinicopathological significance of nucleosome remodeling and deacetylase complex expression in endometrial carcinoma
S. Lee*, J. Chu, S. Do, H. Kim
*Republic of Korea

Background & objectives: Only a few studies have examined the expression of nucleosome remodeling and deacetylase complex in endometrial carcinoma (EC). This study aims to analyse the expressions of histone deacetylase (HDAC1), HDAC2, and chromodomain helicase DNA-binding protein 4 (CHD4) in EC.
Methods: Sixty cases of EC were categorized into two clusters based on the expression levels of the three proteins.
Results: Cluster 1 (C1) exhibited elevated expressions of HDAC2 and CHD4 compared with cluster 2 (C2). Notably, 75% of cases in C2 represented non-aggressive histological types, whereas 37.5% of cases in C1 manifested aggressive types. C2 exclusively comprised pathological tumour stage 1 (pT1) tumours, whereas C1 included pT2 and pT3 tumours. In C1, 25% of cases displayed aberrant p53 expression, contrasting with the absence of such expression in C2. Furthermore, only one patient in C2 experienced disease recurrence, whereas 20.8% of patients in C1 developed recurrent tumours.
Conclusion: High HDAC2 and CHD4 expression may be associated with adverse clinicopathological characteristics in EC. Nevertheless, further studies are needed to validate these results.

E-PS-10-064
Morphological and immunohistochemical approach to the diagnosis of female adnexal tumours of wolffian origin (fatwo) and stk11 adnexal tumour: a study of 6 cases
B. Maghini*, M. Sant'Angelo, A. Municchi, G. Sabetta, A. Bergamini, G. Taccagni

*Pathology Department, IRCCS San Raffaele, Milan, Italy

Background & objectives: FATWO are rare neoplasms arising from mesonephric remnants with indolent behaviour. Nevertheless, metastatic and recurrent cases have been described. The recent identification of STK11 alterations in aggressive tumours with mesonephric appearance introduces the new category of STK11 adnexal tumours.
Methods: We collected 5 cases of FATWO and a case of STK11 adnexal tumour, that were diagnosed between 2018 and 2022. Patients were aged between 35 and 72 years. The tumours were mostly located in the mesosalpinx. Two cases had recurrences in the peritoneum and ovary. Follow up was available for 5 cases. All patients are still alive.
Results: The tumours showed the following patterns: solid (6/6), retiform (6/6), tubular (5/6), cribriform (2/6) and sieve-like (1/6). Atypia were mild in 4/6 cases, mild to moderate in 1/6 and moderate in 1/6 cases. Mitotic count ranged from 1 to 9 mitoses/10 high power fields, with the highest value in relapsed cases. We performed immunohistochemistry (IHC) with the following results: CK AE1/AE3+ (4/4), calretinin+ (6/6), WT1+ (6/6), CD10+ (6/6), androgen receptor+ (5/5), inhibin+ (4/6), PAX8- (3/3), CK7- (5/6) and FOXL2- (2/3). One of the two relapsed cases underwent next-generation sequencing, which revealed a pathogenic variant of STK11. The case was reclassified as STK11 adnexal tumour.
Conclusion: Our results highlight that a IHC panel including WT1, calretinin, CKAE1/AE3, androgen receptor, CK7, CD10 and PAX8, even if not specific, can help rise a suspicion for FATWO, when in the presence of the major morphologic patterns. The number of mitoses and grading of atypia could be useful to suspect more aggressive cases and STK11 adnexal tumours, to avoid misclassification. Molecolar analyses are required to identify STK11 adnexal tumours. Further studies are needed to better classify these neoplasms.

E-PS-10-065
Endosalpingiosis: a histological surprise of unusual location
I. Mallek*, R. Ayadi, E. Brahem, R. Yaiche, K. Mekni, O. Ismail, S. Ben Slama, A. Ayadi
*Department of Pathology, Abderrahmen Mami Hospital, 2083, Ariana, Tunisia

Background & objectives: Endosalpingiosis is the presence of ciliated tubal epithelium in an ectopic location. The clinical features remain uncertain. Endosalpingiosis may correlate with neoplasms and inflammatory diseases of the fallopian tubes. The aim of this study was to describes the clinicopathological characteristics.
Methods: This retrospective study was performed on 34 cases of endosalpingiosis selected from pathology department from 2004 to 2023.
Results: There were 34 female patients with a mean age of 30,47 years (25-73). Reasons for surgery were in most cases ectopic pregnancy (41.18%), uterine leiomyoma (29.41%) and ovarian cysts (17.65%). Surgery for gynaecologic malignancies were associated in 5.88%: 1 case of endometrial cancer and 1case of serous cystadenocarcinoma of the ovary. Adenomyosis was noted in 6 cases. Endosalpingiosis were localized in the fallopian tube (29), mesosalpinx (4), ovary (1). The diagnosis was made on surgical resection in all cases. Microscopic examination showed ectopic glands lined by ciliated tubal type epithelium and absence of endometrial stroma. The final diagnosis of endosalpingiosis was established. The patients had a successful postoperative recovery.
Conclusion: Endosalpingiosis should be included in the list of potential diagnoses, as its benign nature may mask the risks of other concurrent conditions. Diagnosing this condition can be challenging due to its rarity and nonspecific symptoms, particularly in younger patients. Although it may be benign, it's important to recognize these individuals as potentially susceptible to other significant illnesses.

E-PS-10-066
Accuracy of confocal microscopy diagnosis in vulvar biopsies
L. Marimón*, S. Lopez-Prades, I. Matas, L. Sisuashvili, K. Darecka, C. Marti, A. Saco, N. Carreras, M. Del Pino, J. Ordi, N. Rakislova
*Hospital Clínic, Barcelona, Spain

Background & objectives: Ex-vivo fusion confocal microscope (eFuCM) is a morphology-based method designed to generate images reminiscent of hematoxylin and eosin stained sections from fresh tissue specimens by illuminating them with lasers. This study aimed to evaluate FuCM's utility in vulvar pathology samples.
Methods: Prospective study including 83 vulvar biopsies, which were immediately processed (10" in 70º alcohol and 20" in acridine orange) and scanned using a VivaScope 2500-G4 device (Vivascope GmbH, Germany) and were blindly evaluated by a gynaecological pathologist. Subsequently, the specimens were processed for conventional optical microscopy. The eFuCM diagnoses were compared with the diagnoses of the conventional microscopy (gold standard).
Results: The gold standard diagnoses were: 27 high-grade precursor lesions/vulvar intraepithelial neoplasia (HSIL/VIN), 20 inflammatory lesions, 17 LSIL/Condyloma, 10 squamous cell carcinoma, 6 melanocytic lesions, and 3 other lesions. The agreement between eFuCM and the gold standard diagnosis was 51.8% (43/83). The agreement was high for squamous cell carcinomas (9/10, 90%) and HSIL/VIN (21/27, 77.8%), moderate for inflammatory lesions (12/29, 60%) and low for LSIL/Condyloma (1/17, 5.9%), melanocytic (0/5, 0%) and other lesions (0/3, 0%). Most errors in eFuCM were due to technical issues (mainly problems in the orientation of the tissue), the relatively poor quality of the digital images, and absence of immunohistochemical support.
Conclusion: Although eFuCM has been considered a promising tool allowing to provide histological information a few minutes after sampling without altering the tissue for eventual immunohistochemical and/or molecular analysis, its usefulness in vulvar pathology is currently limited. Its performance is relatively high for invasive carcinoma and HSIL/VIN, but very low for other vulvar lesions. Refinement of the tissue processing and improvements in the definition of the digital images would be required before recommending its implementation in pathology laboratories.

E-PS-10-067
STRN3-NTRK3 gene fusion in spleen metastasis by undifferentiated uterine sarcoma: report of a case
S. Marletta*, E. Cavallo, N. Rudini, L. Terracciano, S. Pafumi, M. Caruso, F. Martorana, C. Carnaghi, P. Vigneri, A. Rizzo, P. Colombo
*Division of Pathology, Humanitas Istituto Clinico Catanese, Catania, Italy

Background & objectives: Uterine sarcomas encompass a broad spectrum of malignancies, often behaving aggressively, including leiomyosarcomas, endometrial stromal sarcomas, and so-called undifferentiated uterine sarcomas (UUS). Among these latter, rare tumours harboring rearrangements of the NTRK gene have been recently described.
Methods: Herein we report the exceptional occurrence of a splenic metastasis by a UUS. Comprehensive immunohistochemistry (IHC) and next generation sequencing (NGS)-based molecular analysis were performed for diagnostic purposes and with the aim to eventually identify targetable biomarkers.
Results: A 57-year-old female, who had previously faced hysteroannexectomy for a stromal cervical sarcoma, underwent resection for a 4.5 cm splenic lesion detected during follow-up. Microscopically, the tumour was composed of pleomorphic spindle cells with solid and cystic areas, diffuse coagulative necrosis, and high mitotic index (15/10 HPF). At IHC, neoplastic cells expressed WT1, panTRK, and focally CD34, S100, CD10, and Smooth Actin, while ER, PR, Cytokeratins, DOG1, and desmin were negative. NGS with a

combined DNA and RNA sequencing panel showed a rare STRN3-NTRK3 fusion; no MDM2 amplification was found at FISH. The same profile was documented on the primary tumour, leading to the diagnosis of splenic metastasis by UUS.
Conclusion: UUSs cover morphologically different neoplasms, whose molecular hallmarks keep unfolding thanks to modern sequencing techniques. We describe the first splenic metastasis by an STRN3-NTRK3 fused UUS, whose localization has never been accustomed to pure uterine sarcomas yet. Because the STRN3-NTRK3 fusion is identifiable in rare uterine sarcomas, when a history is on record, a proper panel including pan-TRK and NTRK gene analysis should be performed for its suitability in using targeted therapy with NTRK inhibitors in advanced disease.

E-PS-10-068
HER2 overexpression in uterine serous carcinoma in a tertiary referral centre: a 5 year review
J. Morris*, D. Gibbons
*St Vincent's University Hospital and BreastCheck, Irish National Breast Screening Programme, Dublin, Ireland

Background & objectives: Uterine serous carcinoma is an aggressive endometrial carcinoma subtype with high recurrence rates. Some cases will be HER2 amplified, a target for novel therapies. We analysed cases from our institution for HER2 amplification rates and correlated with disease stage.
Methods: We retrieved from our institution's database all histopathology specimens from the female genital tract that underwent HER2 amplification testing over a five year period (2018 to 2023). All available pathology reports were reviewed and clinical stage, metastatic spread and HER2 amplification status were documented. All cases other than uterine serous carcinoma were excluded from analysis.
Results: 18 cases of uterine serous carcinoma were identified, 12 of which were resection specimens, allowing for accurate clinical staging as per the TNM Classification of Malignant Tumours, 8th Edition. 50% of cases were found to be HER2 amplified, either by immunohistochemistry (IHC) or fluorescent in-situ-hybridisation (FISH). 8 cases were stage T1, 1 was T2 and 3 were T3. We performed Fisher's Exact Tests and found no significant correlation between pathologic stage including metastatic spread and HER2 amplification status.
Conclusion: We did not demonstrate a significant link between HER2 overexpression and clinical stage, nor did we demonstrate a link between HER2 expression and metastatic spread. We did however note that over 50% of cases of uterine serous carcinoma in our institution were HER2 overexpressed which is higher than rates reported in the literature (30-35%). This finding emphasises the importance of assessment of HER2 in all uterine serous carcinomas.

E-PS-10-069
Fumarate hydratase deficiency in uterine leiomyomas: a case report
E. Nardi*, L. Pugliese, M. Pieroni, G. Carignani
*University of Florence, Italy

Background & objectives: Leiomyomas are the most common benign uterine tumours derived from smooth muscle. They occur more often in the fifth decade and they commonly cause abnormal uterine bleeding and dysmenorrhea in reproductive-age women. Around 90% of leiomyomas are of conventional type.
Methods: In 2021 a 20-year-old woman was diagnosed with a leiomyoma with intense vascularization of dubious nature. In 2022 the leiomyoma was increased by about 2 cm and the patient had persistent uterine bleeding refractory to medical therapy. Therefore, she performed a laparoscopic myomectomy. The first histological examination was of a smooth muscle tumours of uncertain malignant potential (STUMP).
Results: However, in consideration of the young age of the patient and of the maternal medical history - the patient's mother performed a hysterectomy at the age of 36, after myomectomy, with histological diagnosis of "leiomyomas with increased borderline cellularity" - the case was re-evaluated and a hypothesis of Fumarate Hydratase (FH) Deficiency was taken into account. Therefore, an additional immunohistochemical investigation was performed. In all sections examined, the tumour had the following immunohistochemical profile: FH -. This result led to the final diagnosis of a uterine leiomyoma with fumarate hydratase deficiency. Then, genomic testing was performed revealing a pathogenic germline mutation of the FH gene.
Conclusion: Patients with germline mutations in the fumarate hydratase gene will more likely develop uterine leiomyomas presenting prominent nucleoli and nuclear atypia. Usually, the patients affected are around 30 years old and the uterine tumour often represents a "sentinel" event that precedes the development of a renal cell carcinoma. The diagnosis of leiomyomas with a FH deficiency at a younger age than the development of renal carcinoma presents a great opportunity for early diagnosis, early intervention and early oncological follow-up.

E-PS-10-070
Membranous dysmenorrhea in a patient with Turner's syndrome: a case report
L. Nazanyan*, P. Khachatryan
*YSMU, Armenia

Background & objectives: Patients with Turner's syndrome usually have low levels of estrogen and progesterone. However, although most patients are diagnosed with primary amenorrhea, some women can spontaneously present with pubertal development and with menarche at 11 to 15 years of age.
Methods: We present a case of a 15-year-old girl with known history of mosaic type Turner's syndrome, who was admitted to the hospital with complaints of severe abdominal pain. An ultrasound was performed, which showed a mass in the uterine cavity. Later, the mass was expelled spontaneously and the abdominal pain subsided. The mass was then sent for histologic examination.
Results: The macroscopic examination showed a large tumour measuring 6.5 x 5.2 x 4.5 cm. Histologic examination showed abundant ill-defined solid areas of spindled-like cell proliferation with abundant eosinophilic cytoplasm and with multiple areas of decidual-like changes with no evidence of chorionic villi. Mitotic activity was infrequent. Based on radiological data, as well as the size of the mass and routine H&E examination immunohistochemical analysis was then carried out to exclude mesenchymal tumours, which showed positive staining of desmin only. SMA, ERG, ALK, HCG, PLAP and p16 stainings were also performed. Together with clinical and pathological correlation a diagnosis of membranous dysmenorrhea was concluded.
Conclusion: Membranous dysmenorrhea is a rare gynaecologic disorder with only a few cases documented. It occurs as a result of a sudden and complete detachment of the decidua during menstruation. Considering that women with Turner's syndrome suffer with abnormal menstrual cycles it islikely that the risk of developing membranous dysmenorrheais higher. Its pathophysiology seems to be related to the estrogen-progesterone imbalance but it is still yet to be understood.

E-PS-10-071
HPV positive cervical squamous cell carcinomas: association with expression of p16, p53 and Ki67
J. Nazarovs*, K. Biserova, D. Krišāne, A. Dudorova, I. Lindenberga, L. Sokolovska, M. Issaguliants, S. Dubencovs
*Riga East Clinical University Hospital, Pathology Centre; Pauls Stradins Clinical University Hospital, Pathology institute; Riga Stradins University, Department of Pathology, Latvia

Background & objectives: Cervical cancer is the fourth most common malignancy in females. Majority of cervical carcinomas (CC) are associated with HPV infection. The aim of this study was to investigate association between morphological features and p16, p53, Ki-67 expression in HPV-positive CCs.
Methods: Biopsy and electroconization histological material of patients (n=75) with primary cervical squamous cell carcinoma diagnosed in 2016-2024 were evaluated histologically, and immunohistochemically for expression of p16, p53 and Ki-67 using Flex kits and Autostainer Link-instrument (Dako) with visualization on Eclipse 55i (Nikon). All were positive for at least one of high-risk HPVs, mainly HPV16 (Anyplex 14, Seegene).
Results: Median age of patients was 49 years (from 23 to 96). Grade 1 carcinomas were diagnosed in 5 (6,6%), Grade 2 in 44 (58,6%), Grade 3 in 26 patients (34,6%). Of 75, 66 (88%) were p16-positive, majority (40; 60,6%) were Grade 2 tumours. Of p16-negative tumours, five were Grade 1 (6,6%), four Grade 2 (5,3%). Interestingly, 8/9 of p16(-)-tumours were positive for HPV16, five with medium, and three, with low virus load. Only four cases (Grade 3) were positive for p53; interestingly, all were HPV16 DNA and p16 positive. Median Ki-67 value was 40% (from 2 to 92). Difference between p16(+) and p16(-) cases (42% and 38%, respectively) was insignificant.
Conclusion: Most of HPV-associated CC cases were p53-negative for p53 , reflecting proteasomal degradation of p53 mediated by E6, with few exceptions. Expression of p16 and Ki-67 varied depending on the tumour grade. High grade tumours were positive for both p16 and Ki-67 which implies diagnostic value of combined p16 and Ki-67 staining in diagnostics of cervical carcinomas. Jointly, these markers represent useful tool for histochemical grading of cervical cancer.
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E-PS-10-072
Carcinosarcoma of the uterus in a 76-year old woman: a case report on a rare and aggressive disease
S. Neves*, F. Sousa Vieira, D. Sá, A.P. Rodrigues, N. Jorge Lamas
*Unidade Local de Saúde de Santo António (ULSSA), Portugal

Background & objectives: Uterine Carcinosarcoma is a rare entity, accounting for <5% of all uterine malignant tumours, comprising both a carcinomatous and a sarcomatous component. It usually presents with pain and bleeding and has a poor prognosis.
Methods: Here we report the case of a 76-year old woman who presented with abundant vaginal bleeding. Ultrasound imaging showed a large nodular lesion in the uterus. She was therefore submitted to total hysterectomy and bilateral salpingo-oophorectomy.
Results: The surgical specimen was an 878g uterus with 18x12x12cm and a cervix with 5x5x5cm. An endometrial vegetating lesion with 5x3x3cm largest diameters was observed, extending through the uterine endocervix and reaching the external cervical orifice. Other polypoid endometrial lesions were also present. The histological analysis revealed a high-grade Carcinosarcoma of the uterine body and cervix with a serous carcinoma component and undifferentiated mesenchymal sarcoma component. Fallopian tubes and ovaries were unremarkable. Metastases were found in 3 out of the 9 pelvic lymph nodes submitted. Cytological analysis of the peritoneal fluid did not show neoplastic cells. The NGS analysis revealed a TP53 p.S241F pathogenic variant with 68% allelic frequency.
Conclusion: This case highlights the main features of the rare uterine Carcinosarcoma, which normally occurs in postmenopausal patients and has a dismal prognosis. Adjuvant chemotherapy with carboplatin and paclitaxel was initiated only a few weeks after surgery due to post-surgical complications. The tumour has locally relapsed in the vaginal dome and metastases were found in the urinary bladder, left ureter and lung. Nearly two years following the initial diagnosis, the patient passed away.

E-PS-10-073
Evaluation of the pathological response of ovarian serous carcinoma to neoadjuvant chemotherapy: a case series
S. Ben Tekaya, Z. Nfikha*, T. Tlili, I. Bahri, D. Chiba, M. Mokni
*Department of Pathology , University hospital of Farhat Hached, Tunisia

Background & objectives: Neoadjuvant chemotherapy (NACT) is considered for patients with advanced-stage ovarian serous carcinoma (OSC) who are not ideal candidates for primary debulking surgery. This study aims to identify the pathological response patterns of OSC to NACT.
Methods: An 8-year retrospective analysis was conducted during the period between 2016 and 2024 at Farhat Hached Hospital's pathology department in Sousse. We identified 15 patients who were diagnosed with OSC based on pathological confirmation from biopsy specimens and who have received NACT followed by total hysterectomy and bilateral salpingo-oophorectomy, with or without omentectomy, appendicectomy, and lymph node dissection.
Results: The mean age was 60.33 years with extremes ranging from 35 to 88. The tumour was bilateral in 13 cases and unilateral in 2 cases. Eleven patients had ovarian gross disease, while 4 had only microscopic disease. Microscopically, 6 cases showed fibrous-hyalin remodeling, while only 5 cases showed necrosis which was focal in 2 cases and extensive in 3 cases. Only 1case showed edematous changes while haemorrhagic changes were found in 2cases. Dense polymorphic inflammatory elements were found in 4 cases. The pathological response grade was CRG3 in 4 cases including 2 cases with a complete response, CRG2 in 6 cases, and CRG1 in 5 cases.
Conclusion: After NACT morphological changes encompass tumour size, cellularity, fibrous-hyalinization, myxoid, edematous remodeling, hemosiderin deposits, microcalcifications, fingerprints of cholesterol crystals, and variable density of polymorphic inflammatory elements. OSC's response to NACT follows a specific pattern that warrants prospective evaluation and prognostic prediction. The microscopic residual disease is seen in 'normal-looking' areas of the ovary as well as metastasis following NACT. Thus, the macroscopic inspection is inaccurate in determining the response to chemotherapy, and a large sampling is required.

E-PS-10-074
New model of immune-mediated model of preeclampsia - experimental research
N. Nizyaeva*, K. Artemyeva, E. Ponomarenko, A. Akhmetshina, I. Stepanova, E. Kuznetsova, A. Stepanov, L. Mikhaleva
*Petrovsky National Research Center of Surgery, Russian Federation

Background & objectives: Based on the well-known model of miscarriage ♀CBA×♂DBA/2, we developed a new preeclampsia model. The bacterial component muramyl dipeptide(C7MDP) stimulated the production of proinflammatory cytokines. Abnormal placental implantation and oxidative stress may play a key role in intrauterine growth retardation(IUGR).
Methods: The aim evaluate the effect of consuming alpha-lipoic acid during pregnancy on the length and weight of the foetuses. The combination of mouse strains ♀CBA×♂DBA/2 was used. On gestation days (GD) 5 and 7, C7MDP was administered intraperitoneally at a dose 1 mg/kg. Morphofunctional studies of the placenta were carried out on 8 and 14 GD.
Results: After birth, the length and weight of the foetuses were estimated. In the placenta with experimental PE model, thinning and disorganization of the layer of giant cells, and in the spongiotrophoblast

numerous large cavities were observed. In the labyrinth the volumetric density of the foetal vessels decreased due to an increase in trophoblast. On 8 GD the production of IL-1α, IL-2, IL-6, IL-17 by splenocytes increases and the production of IFN-γ. At 14 GD the production of proinflammatory cytokines remains high. Moreover, throughout the gestation period, some female pregnant mice were administered alpha-lipoic acid dissolved in drinking water at 10 mg/kg.
Conclusion: Thus, as a result of research the weight and size of the foetuses in cases of experimental PE were up to 20% less compared to the control. But In the group after administered ALA the foetuses were comparable to the control ($p<0.05$). Our data showed that our experimental data showed that ALA administration to pregnant mice effectively prevents intrauterine growth retardation.

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E-PS-10-075
Female pelvic and gynaecological solitary fibrous tumour: case presentation and clinicopathological analysis of cases reported in the literature
D. O'Dwyer*, F. Roberts
*NHS GGC, United Kingdom

Background & objectives: Solitary fibrous tumour (SFT) is an uncommon neoplasm that can arise at any anatomical site. Gynaecological SFT has not been fully characterised in the literature. We present two cases with a review of the literature, including statistical analysis of outcomes.
Methods: Two cases of pelvic and gynaecological SFT with outcome data are described and analysed in conjunction with a review of 82 cases reported in the literature. All cases were stratified according to the modified Demicco risk stratification model. Statistical analysis was performed using Chi square and Kaplan Meier survival graphs.
Results: SFT of the female pelvis and gynaecological tract occurred in women with a mean age of 51 years. Thirty-five cases reported STAT6 immunohistochemistry and 33 were positive (94.3%). Average follow-up was 25 months. Local recurrence and/or metastasis occurred in 14 patients (16.7%) and 3 died of disease (3.6%). Size was associated with local recurrence and/or metastasis ($p=<0.05$) as was mitotic count ($p=0.009$). Older age predicted time to metastasis ($p=0.04$) and mitotic count predicted time to local recurrence and/or metastasis ($p=0.02$). The majority of SFTs were low risk (56.3%) according to the modified Demicco model. Stratification by the modified Demicco model predicted time to local recurrence ($p=0.005$) and to metastasis ($p=0.004$).
Conclusion: We present two new cases of pelvic and gynaecological SFT alongside a statistical analysis of cases reported in the literature. Female pelvic and gynaecological SFT can be reliably diagnosed and stratified according to the modified Demicco model to predict outcomes. Although data is limited with relatively few cases reported in the literature and a paucity of sufficient outcome data, these results are promising.

E-PS-10-076
Pure non-gestational ovarian choriocarcinoma and clear cell adenofibroma, a rare germinal-epithelial coexistence: a case report
A. Ordoñez*, M.Á. Resano Abarzuza, M. Rezola, M. Conde, D.X. Ugás Burranca, M. Carillo Cobarro, I. Ruiz Díaz
*Hospital Universitario Donostia, Spain

Background & objectives: Choriocarcinoma is a gestational tumour that accounts for 0.6% of germinal ovarian lesions. Ovarian clear cell adenofibroma (CCAF) is an infrequent tumour and is associated with endometriosis. We present a case of both neoplasms coexisting with endometriosis.
Methods: A 72 year-old woman without significant past medical history consulted due to pelvic pain. The clinical-radiological examination revealed a suspicious mass of the left adnexa. Macroscopically the mass was 12 cm and presented as a solid-cystic and brownish-white area and another solid, anfractuous and haemorrhagic area. The sections were fixed in 4% formalin, embedded in paraffin and stained with haematoxylin-eosin.
Results: The haemorrhagic area showed an infiltrative cell proliferation, with pleomorphic syncytial areas of syncytiotrophoblast type and other mononucleated areas of cytotrophoblast type.
Immunohistochemistry showed positivity for CKAE1/AE3, beta-HCG and placental lactogen. S100, OCT-4 and CD-30 were negative.
After exhaustive sampling no other germinal components but choriocarcinoma were found and the diagnosis of pure non-gestational ovarian choriocarcinoma (NGOC) was confirmed.
In the solid-cystic area, next to areas of endometriosis, we observed small tubules of simple architecture, non-infiltrating, separated by thin fibrous tracts and lined by a double cell layer without atypia, with eosinophilic luminal secretion (positivity for napsin-A, HFN1-beta and racemase, GATA3 negative). The definitive diagnosis was CCAF, associated with endometriosis.
Conclusion: NGOC are rare, especially in postmenopausal age, but have been documented. Distinguishing the gestational or non-gestational nature and identifying pure or mixed forms are essential for treatment and prognosis. A good clinical history and exhaustive sampling to discard other germinal components are essential. The coexistence of epithelial and germinal tumours is uncommon and understanding their biological association remains under investigation.

E-PS-10-078
Invasive stratified mucin-producing carcinoma of the uterine cervix: comparison of its clinicopathological characteristics and programmed death-ligand 1 expression status with other endocervical adenocarcinomas
C.K. Park*, Y.A. Cho, J. Lee, S. Choi, H. Kim
*Seegene Medical Foundation, Republic of Korea

Background & objectives: Invasive stratified mucin-producing carcinoma (ISMC) is a rare subtype of human papillomavirus-associated mucinous-type endocervical adenocarcinoma (EAC). We investigated differences in clinicopathological characteristics, patient outcomes, and programmed death-ligand 1 (PD-L1) expression status among ISMC, usual-type EAC (UEA), and gastric-type EAC (GEA).
Methods: PD-L1 22C3 immunostaining was performed using 20 ISMCs, 20 UEAs, and 20 GEAs. PD-L1 expression was assessed using combined positive score (CPS). The clinicopathological information was collected from their electronic medical records and pathology slides. Statistical analyses were performed to compare the clinicopathological characteristics and PD-L1 expression status among ISMC, UEA, and GEA.
Results: ISMC was diagnosed at a significantly younger age and showed more advanced stage and shorter survival than UEA. Recurrence-free and overall survival rates of ISMC patients were significantly lower than those of UEA but comparable to those of GEA. All 20 ISMCs showed PD-L1 overexpression with a mean CPS of 43.5 (range, 10–100), which was significantly higher than that of UEA (mean CPS, 8.2) and GEA (mean CPS, 6.5). In spite of PD-L1 overexpression, ISMC patients who treated with pembrolizumab showed no clinical responses.
Conclusion: We confirmed that ISMC exhibits more aggressive behaviour than UEA and that all ISMCs displayed PD-L1 overexpression, which is significantly higher than that of UEA and GEA. Our data suggest that PD-L1 overexpression is associated with poor prognosis of ISMC.

E-PS-10-079

DOCK4 and ISM2 are robust immunohistochemical markers of extravillous trophoblast in placenta accreta spectrum disorders and normal placenta

C. Parra-Herran*, G. Neville, H. Yu, D. Davis, B. Quade, D. Carusi, L. Hsu Lin
*Brigham and Women's Hospital, USA

Background & objectives: DOCK4 is upregulated in placenta accreta spectrum (PAS) trophoblast (PMID:32576693). Likewise, circulating ISM2 is prevalent in PAS patients (PMID:36604494). We document the expression of these biomarkers by immunohistochemistry in trophoblast populations and decidua in both PAS and normal placentas.
Methods: Immunohistochemistry for ISM2 and DOCK4 was performed in 53 PAS cases, 7 placentas with BPMF and 32 normal placentas, including 7 gravid hysterectomies unrelated to PAS. Full-thickness sections of placenta and/or uterus including basal plate were used. Expression was scored as absent, weak/1+, moderate/2+, or strong/3+ in decidua, villous trophoblast, and extravillous trophoblast (EVT, mononuclear and multinucleated).
Results: DOCK4 and ISM2 expression were consistent in each cellular compartment. DOCK4 showed 2+/3+ nuclear and/or cytoplasmic expression in mononuclear-EVT at basal plate and choriodecidual interface and 0/1+ cytoplasmic-only staining in multinucleated-EVT; villous trophoblast showed 1+ cytoplasmic-only staining; decidual cells showed 2+/3+ cytoplasmic-only staining. ISM2 showed 3+ cytoplasmic expression in mono- and multinucleated-EVT; in contrast, decidua and villous trophoblast were consistently 0/1+. Strong/3+ DOCK4 in mononuclear-EVT was more common in PAS (38%) than in placentas without confirmed PAS diagnosis (18%) ($p<0.05$, chi-square & one-tailed Fisher's exact test). DOCK4 and ISM2 expression patterns in decidua, villous trophoblast and multinucleated-EVT were similar in both PAS and normal placentas.
Conclusion: DOCK4 and ISM2 are differentially expressed in trophoblast populations, DOCK4 being stronger in mononuclear-EVT compared to multinucleated-EVT, and ISM2 being strong in EVT but absent/weak in syncytiotrophoblast and decidua. Strong mononuclear-EVT DOCK4 expression occurs more often in the setting of PAS than in normal placentas, which may correlate with the previously documented upregulation of this marker in PAS. Further studies are needed to further determine the utility of DOCK4 and ISM2 in the histopathologic diagnosis of EVT disorders including PAS.

E-PS-10-080

High grade endometrial endometrioid carcinoma: a case report of complete transdifferentiation to pilomatrix-like carcinoma (PiMHEC)

G. Patrichi*, A.I. Patrichi, R. Soslow, S. Stolnicu
*Pathology Department, UMFST Targu Mures, Romania

Background & objectives: Endometrial endometrioid carcinomas are a group of tumours that can show multiple lines of differentiation, including pilomatrix-like high grade endometrioid carcinoma (PiMHEC), a recently described tumour with similarity to cutaneous pilomatrix carcinoma and very aggressive clinical behaviour.
Methods: We present the case of a 56-year-old female with an endometrial tumour associated with secondary involvement of both ovaries, left tubo-ovarian ligament and obturator lymph node metastases. The diagnosis of high grade endometrioid carcinoma in a previously performed curettage was confirmed in the hysterectomy specimen.
Results: Microscopically, the tumour exhibited a solid, nested/insular pattern with basaloid cells, predominantly seen at the periphery, ghost-cell keratinization towards the centre of the nests, and extensive geographic necrosis. No low-grade endometrioid carcinoma component was identified throughout the tumour or metastases after extensive sampling, but the adjacent endometrium showed atypical hyperplasia. Immunohistochemical assessment showed aberrant cytoplasmic and nuclear expression of β-catenin, and focal CDX2 expression. Tumour cells were negative for PAX8, estrogen and progesterone receptors (ER/PR). Focal expression of vimentin, keratin 5/6, synaptophysin, CD56 was observed. Mismatch repair protein staining was retained and p53 showed a wild-type pattern. Based on these morphologic and IHC features, a diagnosis of PiMHEC was established.
Conclusion: The absence of a low-grade endometrioid carcinoma component makes this PiMHEC, a very rare tumour, even more special. This and the absence of PAX8 and ER/PR expression in an unusual morphological context proved to be diagnostically challenging. This patient's presentation at high stage is concordant with the literature's description of this tumour as very aggressive. It is not yet known whether standard adjuvant therapies for high-risk endometrial carcinomas are effective.

E-PS-10-081

Late recurrence of a growing teratoma syndrome-like lesion in a 54-year-old female: a case report

G. Patrichi*, M. Beleaua, A.I. Patrichi, C. Molnar, C. Molnar, R. Soslow, S. Stolnicu
*Pathology Department, UMFST Targu Mures, Romania, Romania

Background & objectives: Growing teratoma syndrome (GTS) is a condition represented by mature teratomas appearing as a retroconversion of immature teratomatous elements to mature elements after administration of chemotherapy. The aim of this paper is to present a peculiar case of GTS-like syndrome.
Methods: We present the case of a 54-year-old female with late recurrent teratomas with ovarian, cervical, endometrial, parauterine and pelvic locations, associated with gliomatosis peritonei.
Results: The patient was first diagnosed with grade 1 endometrial immature teratoma in 2003 in an endometrial curettage, without subsequent adjuvant therapy. The tumour recurred as a mature endometrial teratoma 2 months and then 6 months later, and then presented in the left ovary 8 months after that. 10 years later, she was diagnosed with solid mature teratomas involving the cervix, left parauterine space and gliomatosis peritonei. 20 years later, multiple pelvic recurrences compatible with mature teratomas were diagnosed, in association with gliomatosis peritonei. Molecular genotyping was performed and showed matching DNA in normal and neoplastic tissue providing evidence against a gestational origin for the tumour and recurrences.
Conclusion: To the best of our knowledge, this is the first case of recurrent mature teratomas involving the uterus, ovaries and peritoneum not preceded by chemotherapy, suggesting that a broadening the diagnostic criteria for GTS spectrum could be appropriate.

E-PS-10-082

An epithelioid extragastrointestinal stromal tumour (EGIST) presenting as a peritoneal mass: a case report and current literature review

A.L. Pazmiño Arias*, L. Serrano Munné, N. Juanpere Rodero, M. Iglesias, J. Gimeno Beltrán, C. Fernández Rodríguez, M. Larrubia Loring, A. Herrera Galera, B. Lloveras Rubio
*Department of Pathology at Hospital del Mar, Spain

Background & objectives: Extragastrointestinal stromal tumours (EGISTs) are rare mesenchymal neoplasms. As their gastrointestinal counterparts, they differentiate towards the interstitial cells of Cajal, however they arise extraintestinally. The epithelioid subtype, particularly rare, poses additional diagnostic challenges due to its resemblance to epithelial neoplasms.

Methods: We present the case of a 50-year-old female with abdominal pain. Imaging studies showed two mesenteric masses, the largest measuring 10 cm. The initial radiological diagnostic orientation suggested infectious pseudocollections or a neoplastic origin. After a lengthy and unproductive diagnostic process, an exploratory laparoscopy was performed and the intraabdominal masses as well as the left adnexa were resected.
Results: Macroscopically the masses were soft pseudonodular solid-cystic lesions with haemorragic changes. The ovary showed multicystic morphology. Histologically, the omental lesions were composed of medium-sized discohesive epithelioid cells with expansive growing, abundant cytoplasm and regular nuclei, moderate atypia, and a low mitotic index. Immunohistochemical stains showed positivity for Vimentin, c-KIT, DOG1, Caldesmon, Muscle Specific Actin, CD34, and negativity for broad spectrum Keratins, Calretinin, Inhibin and Desmin. The ovary showed no relevant findings. Molecular studies through an NGS panel revealed the presence of the N848K mutation in exon 18 in PDGFRA gene. The global assessment of these findings suggested the diagnosis of EGIST, having previously excluded a gastrointestinal origin through clinical work-up.
Conclusion: The diagnosis of EGISTs is complex considering their rarity, and especially if they present with an atypical morphology. Because of this, it is important to evaluate positivity for specific immunohistochemical markers (c-KIT and DOG1), along with genetic mutations in KIT or PDGFRA. Our case demonstrates the need of considering EGIST in the differential diagnosis of intraabdominal lesions, even those with an epithelioid morphology, and that clinical correlation, in order to exclude a gastrointestinal origin, is essential to reach this diagnosis.

E-PS-10-083
Ovarian steroid cell tumour: review of this rare entity and its malignant potential in a tertiary university hospital
P. Pérez Montero*, G. Barrios Millán, E.P. Sánchez López, L. Yébenes, A. Berjón, D. Hardisson
*La Paz University Hospital, Spain

Background & objectives: Ovarian steroid cell tumour not otherwise specified (SCT-NOS), is a rare subgroup of sex cord-stromal tumours accounting less than 0.1% of ovarian neoplasms. Most SCTs have a good prognosis but 1/3 may have a malignant behaviour depending on pathological features.
Methods: We reviewed all cases diagnosed as SCT-NOS at our hospital between 1980 and 2024. We revised the histopathological and immunohistochemical slides searching for pathological features that could predict malignant behaviour (size, necrosis, hemorrhage, mitotic activity, and nuclear atypia). We also looked at the clinical records, searching for clinical variables such as age at diagnosis, endocrine manifestations, and outcome.
Results: We identified 8 women with ages between 0 and 68 years at diagnosis (mean 37 years). As described by the published literature, more than a half of our patients had endocrine manifestations, being virilization the most common.
Macroscopic examination disclosed well circumscribed, sometimes lobulated, not encapsulated nodules with brown to yellow color, and a mean diameter of 3,95 cm. Only 1 case showed macroscopic areas of necrosis.
The microscopy findings showed a diffuse growth of round cells with granular cytoplasm from eosinophilic to a more clearly vacuolated appearance (depending on the amount of lipids). Immunohistochemistry was available in 5 patients showing positivity for inhibin and/or calretinin in 100% of them.
Conclusion: Some patients with SCT-NOS have a malignant behaviour. Pathological features that correlate with poor outcome include mitotic activity (2 or more in 10 high power fields), necrosis, hemorrhage, moderate/intense atypia and a tumour diameter above 7cm. In our study, pathological malignancy features were seen in 3 patients including 2 cases with nuclear atypia and 1 with necrosis and tumour size >7cm. As expected, the only patient with 2 malignancy features was the one who developed peritoneal implants and pulmonary metastasis.

E-PS-10-084
Analysis of recurrent endometrial cancer in the last 5 years (2018-2022) at a tertiary level university hospital
F.J. Pérez Rastrollo*, A. Alonso Fernández-Velasco, A.I. Encinas Muñiz, C. González del Rey Rodríguez, A.I. Alonso García, M.I. Palacio Vázquez, M.S. Fidalgo García
*Hospital Universitario Central de Asturias, Spain

Background & objectives: The aim is to establish, within our cases, the prognostic factors shared by recurrent endometrial cancer cases, which constitutes the most common gynaecological cancer in the developed countries and whose incidence is increasing.
Methods: We conducted a descriptive study of recurrent endometrial cancer cases between 1 January, 2018, and 31 December, 2022, by collecting variables from medical records: histology, grade, stage, surgical approach, type of recurrence, and current status, using an Excel database (version 2403).
Results: A total of 240 cases were diagnosed but 11 of those where excluded because they were stage IV at diagnosis. A total of 27 cases recurred. Recurrence occurred in 7.3% of endometrioid cases and 28% of non-endometrioid cases, 4.1% of low-grade cases, and 35.5% of high-grade cases. Regarding stage, recurrence occurred in 6.5% of stage I cases, 28.6% of stage II cases, and 30.23% of stage III cases. The current status of patients who experienced recurrences is described (48.14% of which resulted in death), along with the treatment carried out (13 cases were treated with curative intent, of which 11 are currently alive).
Conclusion: It was observed that, in the total number of recurrences (mostly multiple and distant), non-endometrioid histology, high grade, and stage had a greater influence (with stages II and III being practically comparable). We believe that further studies are necessary to relate prognostic factors and to introduce the molecular classification incorporated in the 2023 FIGO update to tailor adjuvant treatments.

E-PS-10-085
Assessing the expression of PD-L1, tumour-infiltrating lymphocytes and macrophages in newly diagnosed advanced ovarian cancer patients stratified by HR status
A. Piermattei*, G. Anderson, M.C. Cannizzaro, M. Valente, V. Salutari, F. Camarda, V. Ghizzoni, M.T. Perri, E. Giudice, M. Valentini, M.V. Carbone, C. Nero, G.F. Zannoni, G. Scambia, D. Lorusso
*Pathology Unit, Department of Woman and Child's Health and Public Health Sciences, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy

Background & objectives: The role of Tumour Immune Microenvironment (TIME) in advanced epithelial ovarian cancer (AEOC) is still unclear. The purpose of this study is to describe the expression of immunological biomarkers in AEOC patients stratified by homologous recombination (HR) status.
Methods: Tumour-infiltrating lymphocytes (TILs: CD3, CD4, CD8), tumour-associated macrophages (TAMs: CD68) and PD-L1 immunohistochemistry evaluations were performed on prospectively collected FFPE specimens from AEOC chemo-naïve patients. The threshold for positive expression of CD3, CD4, and CD8 was set at over 10% of cells. PD-L1 expression was reported according to combined positive score (CPS, threshold ≥1).

Results: Out of a cohort of 250 AEOC, preliminary results are available for 60 cases (68% HR deficient [HRd] including 18 mutations in BRCA 1/2 genes and 32% HR proficient [HRp]). 52% of patients were CD3pos and 97% of them were also CD8pos. Less HRd/CD3pos patients were observed compared to HRp/CD3pos ones (39%vs79%). HRd/CD3pos patients displayed similar expression of CD8pos and CD4pos (94% and 81%, respectively) while HRp/CD3pos patients showed higher levels of CD8pos compared to CD4pos (100% vs 60%). TAMs expression was higher in HRp compared to HRd patients (50%vs30%). PD-L1 expression was balanced between HRd/CD3pos and HRp/CD3pos (75%vs73%).
Conclusion: HRd patients were found to express lower levels of TILs compared to HRp ones in this convenience cohort. Further analyses are ongoing on the entire cohort, including the better characterization of TAMs subtypes and integration of genomic, transcriptomic and prognostic data.

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E-PS-10-086
The role of cancer genome profiling in distinguishing synchronous endometrial ovarian cancers (SEOCs) from metastatic tumours: the experience of a single referral centre
F. Camarda, C. Nero, A. Piermattei*, I. Marino, T. Pasciuto, S. Duranti, R. Giuseppina, M. De Donato, C. Parrillo, A. Preziosi, M. Manfredelli, A. Santoro, F. Fanfani, A. Fagotti, G. Scambia
*Pathology Unit, Department of Woman and Child's Health and Public Health Sciences, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy

Background & objectives: Synchronous Endometrial Ovarian Cancers (SEOCs), defined according to FIGO 2023 criteria, constitute less than 10% of ovarian (OC) or endometrial cancer (EC). This analysis explores the impact of molecular features integrated with histological findings in the diagnostic definition.
Methods: Patients with a supposed diagnosis of SEOCs were selected between January 1st 2022 and March 1st 2024. Cancer genome profiling (CGP) on matched EC-OC samples was performed within an institutional program (NCT06020625) using TSO500HT (Illumina). The assay identifies single nucleotide variants, insertions/deletions, copy number variations, fusions and splicing variants in 523 and 55 genes for DNA and RNA, respectively.
Results: Fifteen patients had a morphological and immunohistochemical diagnosis of SEOCs. The majority of them had an endometrioid histotype (80% OC, 80% EC) and early FIGO stages (80% OC, 93% EC). Lympho-vascular invasion was substantial in 4 EC samples. Pelvic endometriosis was found in 9 patients (60%). 75% of matched samples had at least 3 overlapping alterations, of which truncating alteration in PTEN was the most common. All patients were addressed to multidisciplinary discussion, and in 3 (20%), diagnosis was changed from SEOCs to EC metastatic to the ovary by integrating molecular data with histopathological features. Adjuvant treatment indications were modified accordingly (chemotherapy plus radiotherapy [n=2], immunotherapy [n=1]).
Conclusion: Despite the small sample size, CGP modified final diagnosis of nearly ¼ of initially supposed SEOCs, implying substantial staging and therefore therapeutic changes. A larger cohort implemented also with additional clinical data such as survival rates, is required to reach a more definitive understanding of the actual impact of molecular matched profiling in SEOCs' differential diagnosis (synchronous early-stage tumours versus singular metastatic entities).

E-PS-10-087
Sebaceous carcinoma in a mature cystic teratoma of the ovary
M. Pinho Fialho*, A. Gradil, C. Ferreira, S. Lérias
*Department of Pathology - Unidade Local de Saude Santa Maria (ULSSM); Instituto Politécnico de Lisboa (ESTeSL), Portugal

Background & objectives: Sebaceous carcinoma originating within an ovarian mature cystic teratoma (MCT) is an extremely rare entity. To the best of our knowledge, less than 14 cases have been reported in the literature.
Methods: We report a case of a sebaceous carcinoma arising within a mature teratoma.
Results: An 83-year-old female presented with urinary retention symptoms. A pelvic MRI scan revealed a left ovary lesion consistent with MCT. The patient underwent a bilateral adnexectomy. Macroscopically a 18cm ovary cystic mass showed partially solid appearance intermixed with soft yellow sebaceous material. Histological examination revealed a MCT with a lobular component containing sebocytes surrounded by basaloid cells with focal squamoid features, nuclear pleomorphism, increased mitosis and associated necrosis. Basaloid cells were immunoreactive to p63 and CK5/6. Sebaceous cells were EMA+ and PRAME+. Mismatch repair protein nuclear expression was intact. A diagnosis of a sebaceous carcinoma arising within a MCT was made. The patient is free of disease at 17 months.
Conclusion: Sebaceous carcinoma within an ovarian MCT is a rare entity. Although ocular sebaceous carcinomas are aggressive, the prognosis of extraocular sebaceous carcinoma is thought to be better since local recurrence or metastasis have not yet been described. Given the paucity of data, the management of these patients remains unclear, however identifying tumour microsatellite instability or germline DNA mutations facilitates further cancer screening and treatment (PD1/PD-L1 inhibitors).

E-PS-10-088
Malignant PEComa of the uterus, review of this rare entity in a case report
P. Puente*, L.C. Araya Umaña, B. Muñoz Hernández, N. Cózar García, R. Khedaoui Smaili
*Hospital Universitario Fuenlabrada, Spain

Background & objectives: Malignant PEComa of the uterus is a rare mesenchymal proliferation with a very low incidence and few published case series. They are tumours that can be confused with smooth muscle tumours due to their clinical-morphological-immunohistochemical overlap.
Methods: The case consists of a diagnostic biopsy of an excrescent lesion of the cervix with subsequent hysterectomy and double adnexectomy and implant resection. A conventional study with hematoxylin-eosin, immunohistochemistry and molecular analysis of the specimen was performed.
Results: A 66-year-old woman with metrorrhagia and abdominal pain of months of evolution came to the emergency department for increased bleeding. On inspection, an outgrowth lesion was identified through the cervix with an irregular endometrial cavity, with numerous lesions not dependent on anatomical structures. The tumour corresponds to a perivascular mesenchymal proliferation composed of cells with intense nuclear pleomorphism, necrosis and abundant mitoses. It presents focal positivity for melanocytic markers and focally muscular with extensive nuclear staining for TFE3 and p53 in a mutated pattern. The specimen showed the same morphology as the diagnostic biopsy with several implants in the abdominal cavity.
Conclusion: Malignant PEComa is a rare mesenchymal lesion that presents positive immunohistochemistry for melanocytic markers and

can express muscle markers, so it is important to take into account due to its differential diagnosis with other mesenchymal lesions. There are specific therapeutic targets depending on the mutation present, so their diagnosis and molecular analysis changes the prognosis of these patients.

E-PS-10-089

High-grade endometrial stromal sarcoma with EPC1-BCOR fusion

C. Ramírez Sánchez*, M.T. Dawid De Vera, M.V. Ortega Jiménez, I. Hierro Martín
*Spain

Background & objectives: Genetic anomalies in BCOR have been linked to the origin of high-grade endometrial stromal sarcoma (HG-ESS). Fusions involving the EPC1 gene have been detected in low-grade endometrial stromal sarcomas (LG-ESS). We present a case of HG-ESS with EPC1-BCOR fusion.
Methods: We describe the case of a 46-year-old woman, with no relevant medical history, who presented with anemic metrorrhagia. An excision of a polypoid formation suggestive of a leiomyoma was performed, resulting in a malignant neoplasia. Imaging tests revealed a thickening in the endometrial cavity without myometrial extension or distant disease. Total hysterectomy and bilateral adnexectomy with pelvic lymphadenectomy was performed.
Results: Hysterectomy revealed a two-cellular-pattern tumour. One component displayed round cells, severe atypia and necrosis. The other one had a spindle morphology, less atypia and greater uniformity. Less than 5% pseudoglandular and myxoid differentiation was observed. The first component showed strong positivity for cyclin D1 and weak for CD10, while the second one was weak for cyclin D1 and strong for CD10. Both were positive for BCOR (70%) and negative for estrogen and progesterone receptors, desmin, actin and CD117. NGS study detected an EPC1-BCOR fusion (BCORex6::EPC1ex11, EPC1ex10::BCORex7). The final diagnosis was HG-ESS, stage IC. The patient remains disease-free after 9 months without adjuvant treatment and is under oncological surveillance.
Conclusion: Chromosomal translocations involving the EPC1 gene have been associated with LG-ESS, while those affecting the BCOR gene are linked to HG-ESS. EPC1-BCOR fusion is uncommon, with only one previous case reported in the literature. That tumour exhibited prominent myxoid stroma and aggressive clinical course. Contrarily, our case lacks such features. Due to the rarity of this fusion, it is necessary to report more cases to characterize its morphology and biological behaviour. This discovery might influence endometrial stromal sarcoma classification.

E-PS-10-090

Prognostic value of L1CAM and ß-catenin in endometrioid endometrial carcinoma

M. Rezola*, M. Moreno, A. Val-Carreres, A. Ordoñez, D.X. Ugas, M.A. Resano, I. Bernal, Y.P. Rodriguez, A. Juaristi, J. Kutz, A. Meizoso, I. Sarasola, E. Hurtado, I. Ruiz
*Spain

Background & objectives: The aim of this study is to evaluate the expression of L1CAM and ß-catenin in Endometrioid Endometrial Carcinoma (EEC).
Methods: A retrospective study was performed on 144 EEC diagnosed at the Pathology department of Hospital Universitario Donostia. The inclusion criteria were histologically confirmed EEC and availability of endometrial tumour tissues, between January 2017 and December 2022. Immunohistochemical analysis of L1CAM and ß-catenin was performed and related to the following parameters: lymphovascular space invasion (LVSI), myometrial infiltration and metastases event.
Results: Of all samples studied, based on the presence of LVSI, there were 25 (17.4%%) cases with LVSI . Myometrial invasion equal or more than 50% was found in 44 (30.5 %) cases. There were 20 (13.8%) cases of metastasis: in lymph node, peritoneal implants and ovary. L1CAM positivity rate was 15/144 (10%; all cases). 4 of them associated with LVSI , 8 to myometrial infiltration and 4 with metastatic disease. ß-catenin positive rate was 8/144 (5,5%; all cases): 3 of them associated with LVSI, 3 to myometrial infiltration and 2 with metastatic disease.
Conclusion: L1CAM could be a strong biomarker for the prognosis of EEC. There is a relation with myometrial infiltration, lymphovascular invasion and metastases. In our study, there was no evidence of both L1CAM and ß-catenin positive in the same case.

E-PS-10-091

Peritoneal melanosis associated with mucinous ovarian cystadenoma: a rare case report

P. Rodrigues Veiga*, R. Rocha, M. Alzamora, R. Dias
*Department of Pathology, Portuguese Oncology Institute of Porto (IPO-Porto), Portugal

Background & objectives: Melanosis is a condition where there is accumulation of brown to black pigment in various organs, the most common site being the gastrointestinal tract. Peritoneal melanosis is a rare and benign entity, although it might be associated with other conditions.
Methods: We describe a case of a 66-year-old woman that presented with abdominal distension for a month. Physical examination revealed a pelvic mass with fibroelastic consistency. A transvaginal ultrasound was performed, and showed a bulky cystic adnexal lesion, confirmed by computer tomography, measuring 17cm in greatest dimension. She underwent surgery.
Results: Grossly, the left ovary measured 18cm and was transformed into a cavitated lesion with a smooth and integrate external surface. The lesion presented thin wall with a smooth internal surface and incomplete septa, presenting areas of black colour, the largest measuring 3cm with brownish content inside. An intraoperative frozen section was performed and showed a cystic lesion covered by simple mucinous epithelium, without cytological atypia. The definite result was of mucinous cystadenoma. The cyst subepithelial stroma presented histiocytes (CD68 positive) with granules of brownish pigment, positive for Masson-Fontana coloration. Immunohistochemically, the cells were negative for HMB45 and MelanA. A large sampling was carried out and no teratoma component was identified.
Conclusion: Peritoneal melanosis is a rare condition, with the most common sites affected being the peritoneum, ovary, and omentum. Although its pathogenesis is not yet fully understood, peritoneal melanosis appears to be associated with ovarian lesions like mucinous or serous cystadenoma, mucinous carcinoma, teratoma. In these cases, it is important to exclude other differential diagnoses, the most important being metastatic melanoma. Physical examination with skin inspection, histochemical and immunohistochemical staining are useful in distinguishing these.

E-PS-10-092

Challenges in the morphological and molecular diagnosis of primary fallopian tube cancer

A. Romaniuk*, N. Hyriavenko, D. Sumtsov, G. Sumtsov, Y. Lyndina, K. Sikora, M. Lyndin
*Sumy State University, Ukraine

Background & objectives: Significant challenges arise in the diagnosis of primary fallopian tube cancer (PFTC) due to its histological and molecular diagnosis. Hence, this study aimed to investigate the

overall morphological pattern of PFTC using molecular markers to establish the neoplasm's origin.
Methods: This study involved 105 postoperative specimens from PFTC patients were used for histological and molecular study. The expression of pan-cytokeratin (cytokeratin AE1/AE3), leukocyte common antigen (CD45), CD7, CD20, CK 5/6, CDX-2, chromogranin A, CD56, thyroid transcription factor 1 (TTF-1), Wilms tumour protein 1 (WT-1), and p53 was determined through immunohistochemical analysis.
Results: Histological examination of postoperative specimens, coupled with immunohistochemical techniques when necessary, revealed that out of 105 cases, 87 (82.8%) neoplasms were serous adenocarcinomas (CK7+/CK20−, WT-1+, p53+80%), mostly of high malignancy grade (90.8%). Additionally, there were 12 (11.4%) cases of endometrioid adenocarcinomas (CK7+/CK20−, WT-1−, p53+30%), 2 (1.9%) cases of mucinous adenocarcinomas (CK7+/CK20+, CDX-2−, p53−), and one case each of carcinosarcoma, clear cell (CK7+/CK20−, WT-1+, p53+70%), squamous cell carcinoma (CK 5/6+, CK7−/CK20−, WT-1−, p53−), and neuroendocrine tumour (chromogranin A+, CD56+, CDX-2−, TTF-1−). AE1/AE3 was employed in cases suspected of non-epithelial origin and was positive in 100% of such observations.
Conclusion: Analysis of the above findings underscores the histological diversity of tumours in the fallopian tubes. Identifying the tumour allows for a more differentiated approach to treatment, particularly after determining additional prognostic markers.

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E-PS-10-093
Relationship between the level of expression of ERα and COX-2 in endometrial hyperplasia depending on the genotype of the PvuII polymorphism of the ESR1 gene
A. Romaniuk*, N. Tsyndrenko, M. Lyndin, I. Diadiura, O. Romaniuk
*Sumy State University, Ukraine

Background & objectives: The relationship between the PvuII polymorphism of the ESR1 gene and the histological variant of endometrial hyperplasia and the levels of estrogen receptor alpha and cyclooxygenase-2 expression was studied.
Methods: The rs 2234693 polymorphism was investigated in 95 patients by polymerase chain reaction followed by restriction fragment length analysis (PCR-RFLP). We determined the expression of estrogen receptors and cyclooxygenase-2 on tissue samples obtained after hysteroresectoscopy in the same patients. Statistical data analysis was performed using the SPSS Statistics 29.0 for Windows software package.
Results: The distribution of genotype variants according to the PvuII polymorphism of the ESR1 gene in patients with hyperplastic processes of the endometrium revealed that 30 (31.6%) women were homozygous for the T/T allele, 47 (49.5%) heterozygotes T/C, and homozygous carriers minor allele C/C – 18 (18.9%). Among patients with endometrial hyperplastic processes, 29 cases were with atypical endometrial hyperplasia (30.5%), 11 cases with glandular endometrial polyps (11.6%), 55 cases with glandular-fibrous endometrial polyps (57.9%).
Conclusion: Dependence between the genotype variant according to the studied polymorphism and the histological variant of hyperplastic processes of the endometrium and the degree of expression of estrogen receptors alpha and cyclooxygenase-2 in the epithelial and stromal components was not revealed.

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E-PS-10-094
Bilateral ovarian steroid cell tumour
F.G. Salman*, E.C. Ulukus
*Memorial Hospitals Group, Turkey

Background & objectives: Steroid cell tumours are a rare subgroup of sex cord-stromal tumours, accounting for less than 0.1% of all ovarian tumours. They are usually unilateral, about 5% of them are bilateral. Patients often present with endocrine manifestations, most commonly androgenic symptoms.
Methods: A 65-year-old female presented with hirsutism and male-pattern baldness. Biochemically, high levels of free testosterone were found. A left adnexal mass was detected on magnetic resonance imaging, and total hysterectomy with bilateral salpingooophorectomy was performed.
Results: A solitary, brown-colored, well-circumscribed tumour was seen within the left ovary on gross examination. Tumour dimensions measured 15x12 mm. Microscopically, 2 tumours with the same morphology were observed in both ovaries with a 4 mm diameter focus on the right ovary. Tumours showed diffuse growth, nests and follicle-like arrangements, composed of large polygonal cells with abundant, granular eosinophilic cytoplasm. Reinke crystals and tumour necrosis were absent. Focal intratumoural haemorrhage, mild nuclear atypia and 1 mitosis /10 high power fields were seen. Stromal hypertechosis was observed in both ovaries. Immunohistochemically, tumours were positive for inhibin, calretinin, melan-A, and negative for FOXL2 and EMA.
Conclusion: Given that approximately 1/3 of steroid cell tumours exhibit malignant behaviour, differentiation from benign tumours is critical. Although predicting malignant behaviour based on pathological features is difficult, but predictive factors of malignant behaviour should be evaluated and mentioned in the pathology report. Immunohistochemistry can be helpful in distinguishing from other sex cord-stromal and metastatic tumours.

E-PS-10-095
Evaluation of BRCA status in ovarian carcinoma patients: comparison of fresh frozen tissue (FFT) and formalin-fixed paraffin embadded samples (FFPE)
A. Salvador*, A. Mangogna, P. Visentin, A. Tulisso, M. Orsaria, C. Di Loreto, D. Cesselli, L. Mariuzzi
*Institute of Pathological Anatomy, University Hospital of Udine, Italy

Background & objectives: In the era of precision oncology, early assessment of BRCA mutational status plays a crucial role in predicting the likelihood of response to PARP inhibitors.In this study, we assessed the mutational status of BRCA1/BRCA2 comparing FFT and FFPE tumour samples.
Methods: We enrolled 170 ovarian carcinoma patients who underwent surgery between 2004 and 2022. DNA was extracted from FFPE in 114 cases and from FFT in 56 cases to evaluate BRCA status. Tumour MASTR Plus Dx (Devyser) was used to detect sigle nucleotide variants (SNV) and small insertions and deletions (In/Dels), while MLPA (MRC Holland) to assess large genomic rearrangements (LGRs).
Results: Germinal and/or somatic alterations were identified in 63 cases, accounting for 37% of analysed samples. The frequency of BRCA mutations was significantly higher in FFT (62.5%, 50.0%

somatic vs 12.5% germinal) than in FFPE ones (21.9%, 8.8% somatic vs 13,1% germline) (Fisher's exact test p=0.0015). FFPE and FFT significantly differed in the type of identified variants: SNV and small In/Dels represented 92.9% of the mutations identified in the FFPE-samples, but only 16.7% of those identified in FFT (Fisher's exact test p<0.0001). In this latter, LGRs represented 83.3% of somatic mutation and were detected only by MLPA.
Conclusion: This study suggests that the possibility to evaluate BRCA1/2 status on FFT increases the likelihood of detecting somatic BRCA1/2 abnormalities. Compared to the formalin-fixed tissues used in most available NGS tests, fresh-frozen tissue samples allow to better identify large genomic rearrangements. In our opinion, it is crucial to implement FFT, which we have shown to be feasible and reliable, to enlarge the BRCA mutated population that might receive PARP inhibitors with the greatest benefit.

E-PS-10-096
Mesonephric-like adenocarcinoma of the ovary: a propos of two cases
E.P. Sánchez López*, P. Pérez Montero, M. De Uribe Viloria, L. Yébenes, D. Hardisson, A. Berjón
*La Paz University Hospital, Spain

Background & objectives: Mesonephric-like adenocarcinoma of the ovary is a rare tumour that resembles mesonephric differentiation and exhibits various histological patterns. Studies show its tendency to manifest at an advanced stage suggesting adverse behaviour. We present two cases diagnosed at our centre.
Methods: We searched our files for diagnosed cases of mesonephric-like adenocarcinoma and found only two cases. The histology, immunohistochemistry slides and molecular studies were reviewed, along with the medical records to obtain personal history, age at diagnosis, symptomatology and radiological studies.
Results: We present a 76-year-old woman and a 50-year-old woman with complex adnexal masses, the second one with metastases at the moment of diagnosis.
Histologically, both tumours were composed mainly of glands with complex growth, presented foci of necrosis, nuclei with open chromatin and frequent mitosis. The second case also showed papillary pattern, and solid areas of spindle cells.
Immunohistochemically, the first case was positive for PAX8, GATA3 (weak), TTF1 and CD10 (luminal). The second case showed positive stain for PAX8 and GATA3, while TTF1 and CD10 were negative. Both tumours were ER-negative and expressed a p53 wild-type pattern of stain. A KRAS mutation was detected in the second case.
Conclusion: These findings are consistent with those reported in the literature. Mesonephric-like adenocarcinoma is an uncommon neoplasm that should be considered in an ER-negative, p53 wild-type adenocarcinoma of gynaecological origin. Morphological features such as papillary thyroid carcinoma-like nuclei, eosinophilic intraluminal secretions and spindle cell areas may help to guide the diagnosis, but the most useful feature is the positivity for GATA3 and/or TTF1. These cases also demonstrate the tendency of this tumour to present at an advanced stage.

E-PS-10-097
Pseudocarcinomatous hyperplasia of tubal epithelium associated with acute and chronic salpingitis: a case report
I. Savic*, M. Vekic, D. Opric
*Institute of Pathology, Faculty of Medicine, University of Belgrade, Belgrade, Serbia

Background & objectives: Pseudocarcinomatous hyperplasia of the tubal epithelium is a rare condition. A 21-year-old nulliparous woman was admitted to hospital for surgery due to an ultrasound-proven cyst of the right ovary. The patient reported abdominal pain and pressure during urination without urgency.
Methods: Tumour markers CA-125 and CA19-9 were 380.1 U/ml and 62.47 U/ml, respectively. Clinical diagnosis was ovarian tumour with thick and fibrous adhesions around both adnexal structures. Left salpingectomy and right adnexectomy were performed.Both tubes were enlarged (37×16-18mm, 60×5-25mm) and with adhesions. The right ovary was enlarged and presented a 23mm cyst.
Results: Histopathological examination showed plicae of the fallopian tube in papillary, cribriform or gland-like pattern, lined with cylindrical cells with cilia, showing mild cytological atypia with focal pseudostratification, crowding and loss of polarity. Mucosa and muscle layer were diffusely infiltrated with mononuclear infiltrate (lymphocytes, plasma cells) admixed with polymorphonuclear infiltrate, narrowing the lumen due to increased cell growth. No visible masses in fallopian tubes and no mitotic figures were found. Diagnosis of pseudocarcinomatous hyperplasia of tubal epithelium was made. Her CA-125 was 18.1 UI/L one month after surgery. She has experienced no recurrence 3 months after diagnosis and feels well.
Conclusion: Pseudocarcinomatous hyperplasia of the tubal epithelium is benign and reactive condition associated with acute and chronic inflammation of the fallopian tube. It is very important having in mind this entity and differentiating it from tubal carcinoma. Younger age, absence of mitotic figures, chronic inflammation, and lack of cytologic atypia favour reactive condition over carcinoma. It is important to escape overtreatment in these patients.

E-PS-10-099
Clinical and morphological features of endometrial cancer at the regional level
I. Sertakov*, A. Filin, I. Gusev, A. Sotnikov, A. Goryacheva, E. Verbitskaya, E. Ulitina, A. Bobrovskikh, M. Bobrovskikh, A. Tishchenko
*Voronezh State Medical University, Russia

Background & objectives: Endometrial cancer ranks 4th among the female part of the population, in Russia it ranks 3rd among women oncopathology. The aim of the work is to analyse the incidence of regional endometrial cancer in the period from 2011 to 2018.
Methods: Histologically confirmed cases of endometrial cancer were selected for the study in patients who were registered at the regional oncological dispensary of the Voronezh region of Russia. The patients' belonging to age groups, disease staging categories and patient survival after diagnosis were analysed.
Results: 3,832 cases of newly diagnosed endometrial cancer were selected for the period from 2011 to 2018. The largest group of patients was aged 56-74 years, reflecting global trends. In second place is a group aged 35-55 years, followed by a group of 75-90 years. An increase in morbidity was noted in the group of 21-35 years old. When studying the incidence of endometrial cancer by stage, it was revealed that the majority of patients had stage I and II of the disease (89.6% of the total number of cases. During the period from 2011 to 2018, 375 patients died, of which 212 people (56.5%) died before a year after diagnosis.
Conclusion: In the Voronezh region, the problem of endometrial cancer incidence is still relevant. Although the pathology is diagnosed in a timely manner in 80% of cases, attention should be paid to the rejuvenation of the disease and the high percentage of mortality of patients up to a year after diagnosis. Obviously, prognostic criteria for endometrial cancer outcomes based on the stage of the disease are insufficient and additional search for such is needed.

E-PS-10-101
Dysregulation of CEACAM1 expression in the endometrium under microelementosis conditions
K. Sikora*, Y. Lyndina, N. Hyriavenko, N. Tsyndrenko, A. Shamrai, D. Tsepochko, M. Lyndin, A. Romaniuk

*Sumy State University, Ukraine

Background & objectives: The carcinoembryonic antigen-related cell-adhesion molecules (CEACAMs) play a crucial role in various pathologies, including in the uterus, mediating cell-cell communication, adhesion, and immune responses, highlighting its significance as a potential diagnostic and therapeutic target.
Methods: In this study, we collected uteruses from Wistar rats, which were assigned to two groups: untreated (control) animals and experimental animals, orally administered by heavy metals (HMs) mixture (Zn,Cu,Fe,Mn,Pb,Cr) during 30 and 90 days. Immunohistochemical and immunofluorescent investigations of CEACAM1 expression in uterine sections was conducted using mouse anti-rat mAb 11-1H) antibodies, kindly provided by B.B.Singer.
Results: Immunohistochemical and immunofluorescent analysis of CEACAM1 in rat endometrium revealed moderate apical expression on the apical surface of luminal epithelium and weak focal expression in glands, as well as in single stromal leukocytes. After 30 days of HM exposure, CEACAM1 expression on the surface of the endometrium significantly increased, together with the amount of positively stained leukocytes in the surrounded inflamed tissues. Conversely, on day 90, weak-to-negative CEACAM1 immunoreactivity was observed on both luminal and gland endometrial epithelium. Some areas lacked protein expression, notably in atrophied epithelium.
Conclusion: Our findings demonstrate significant upregulation of CEACAM1 expression in rats endometrial epithelium on day 30 under HMs exposure compared to controls, which might reflect enhanced protein manifestation in response to stress and activation of protective signaling pathways. Concurrently, on day 90, pronounced deregulation of CEACAM1 in endometrial epithelium may be attributed to atrophic changes in epitheliocytes and depletion of defensive mechanisms.

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E-PS-10-102
Confusing histopathological features and HPV testing results in vulvar squamous cell carcinoma arising in a young woman: a case solved using next generation sequencing
L. Sisuashvili*, A. Saco, N. Carreras, C. Celada, L. Marimon, C. Montironi, J. Ordi, N. Rakislova
*Hospital Clínic, Barcelona, Spain

Background & objectives: A small subset of vulvar squamous cell carcinomas (VSCC) show overlapping features not allowing to determine human papillovirus (HPV) status. We report an unusual, surgically treated VSCC, in a 21-year-old woman who recurred after 1 year of follow-up.
Methods: An unusual case of VSCC in a 21-year-old woman is described. HPV testing, and immunohistochemistry (IHC) for p16 and p53 were performed in a primary and recurrent tumour, and DNA and RNA sequencing in a primary tumour.
Results: Histological examination revealed a keratinizing VSCC and associated high-grade squamous intraepithelial lesion (HSIL). Comparing IHC profiles between the primary and the recurrent tumour, a consistent overexpression of p53 was observed in both components, but the results of the HPV testing and p16 were variable (positivity in the primary tumour and negativity in the recurrence). Molecular analyses revealed TP53 mutation and overexpression, in addition to overexpression of cell cycle-regulating genes (including CCND1) and collagen-coding genes (such as COL1A2 and COL6A1), all of which have previously been reported in HPV-I VSCC. These molecular features supported an HPV-independent etiology for the tumour.
Conclusion: This case demonstrates that molecular analysis may help to correctly classify challenging VSCC showing puzzling clinical, morphological and IHC characteristics.

E-PS-10-103
A case report of steroid cell tumour of the ovary: endocrine manifestations of a rare tumour
S. Soni*, S.A. Xu, T. Childs, G. Gray
*Queen's University, Canada

Background & objectives: Steroid cell tumours (SCT) are uncommon sex cord-stromal tumours of the ovary with potential endocrine manifestation mimicking other conditions. This case report emphasizes the necessity of considering SCT in the diagnostic spectrum for patients displaying hyperandrogenic symptoms.
Methods: A 63-year-old woman presented with hyperandrogenic symptoms including male pattern baldness, hirsutism, and clitoral enlargement, persisting for twenty years, initially diagnosed with congenital adrenal hyperplasia based on elevated levels of 17-hydroxyprogesterone and testosterone. Abdominal CT scans showed no evidence of adrenal abnormality. Treatment options were limited due to cost, inefficacy, or side effects, and testosterone levels remained significantly elevated.
Results: More recently, she presented with abdominal distension. A subsequent CT scan revealed a large adnexal mass accompanied by ascites and pleural effusion, with unremarkable adrenal glands. Following total abdominal hysterectomy with bilateral salpingo-oophorectomy, examination of the sections from the 21cm ovarian mass revealed sheets of monotonous polygonal cells with round nuclei containing central nucleolus, and abundant foamy or eosinophilic cytoplasm lacking Reinke crystals. The morphological features were consistent with steroid cell tumour, further supported by immunohistochemical analysis showing expression of SF1, calretinin, inhibin, and estrogen and androgen receptors. The ovarian surface was also involved. Postoperatively, testosterone levels normalized completely.
Conclusion: SCT can present with androgenic, estrogenic, or rarely, Cushing syndrome-like symptoms. This case underscores the importance of considering this exceptionally rare diagnosis in the workup of hormonally active lesions. Prompt and accurate diagnosis is crucial to prevent irreversible endocrine manifestations and associated medical and psychosocial comorbidities.

E-PS-10-104
Mesenchymal stem cell-conditioned medium influences wound healing and MMP9, TIMP1, and FGF2 expression in the rat uterus
N. Tikhonova*, V. Aleksankina, A. Milovanov, T. Fokina, A. Aleksankin, M. Aksenova, A. Akhmetshina, A. Sklifas, A. Temnov

*Petrovsky National Research Center of Surgery, Russia
Background & objectives: Preventing and treating cesarean scar defects is important task to decrease pregnancy complications. Conditioned medium (MSC-medium) obtained by culturing mesenchymal stem cells with low oxygen content(10%) was evaluated for its effects on expression of extracellular matrix(ECM) components in rat uterine wound.
Methods: MSC-medium was used to treat uterine surgical incision on Sprague-Dawley rats (treated group=17, untreated=10). The mRNA expression of MMP9, TIMP1, FGF2, Col1a, and Col4a in wound healing zone was measured at 5th and 15th days after surgery. At the same samples, there were performed the histological examination with Mallory staining and with aSMA and CD34 immunohistochemical staining.
Results: By 5th day, there were smaller Col1a expression (p=0.04) and CD34+cells (p=0.001) in treated group like the area of wound healing zone (p=0.012). At 15th day, there were lower expression

of MMP9 (p=0.047), TIMP1 (p=0.019), FGF2 (p=0.013), Col1a (p=0.017), but more CD34+cells (p=0.001) and the area of healing zone (p=0.003) in untreated group. In both groups, the healing area from the 5th to the 15th day increased unreliability (p=0.120; p=0.951) unlike significant increased number of CD34+cells (p=0.01; p=0.046) and significant decrease MMP9 (p=0.008), TIMP1 (p<0.001), FGF2 (p=0.04), Col1a (p=0.002) expression only in untreated group. There were no significant differences in ratio of MMP9/TIMP1 for any groups or periods.
Conclusion: MSC-medium obtained under a reduced content of O2 (10%), significantly influences on size of healing area and expression of ECM components in uterine wall after full-thickness surgical incision. Strong performance the indicators from 5th to 15th days in untreated group and absent significant differences in treated group may indicate about faster and better healing with MSC-medium. Moreover, levels of MMP9, TIMP1, FGF2, Col1a expression in treated group for both monitor points were close to parameters of intact uterine horn.

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E-PS-10-105
Metaplastic atypical endometrial hyperplasia/endometrioid intraepithelial neoplasia: an endometrioid precancer variant associated with KRAS mutations
A. Travaglino*, S. La Rosa, G.F. Zannoni
*Italy

Background & objectives: The classification of complex endometrial lesions with metaplasia different from squamous morules is still controversial. Our aim was to perform a molecular characterization of complex metaplastic lesions in order to improve their classification.
Methods: Consecutive cases of complex mucinous, tubal, eosinophilic, squamous (non-morular) and papillary endometrial lesions from 2 institutions were retrieved. A centralized histological review was performed. Immunohistochemical expression of estrogen receptor, progesterone receptor, p53 and mismatch repair proteins was assessed. Molecular analysis of KRAS was performed.
Results: Twenty cases were included. All cases showed dilated glands with pseudopapillary intraluminal projections and coexistence of two or more metaplasia types; 60% of cases showed coexistence of three or more metaplasia types. Metaplastic areas (especially eosinophilic and squamous) showed decreased expression of estrogen and progesterone receptors. All cases showed wild-type p53 immunohistochemical pattern and retained mismatch repair expression. KRAS mutation was identified in 85% of cases and showed no association with a specific type of metaplasia.
Conclusion: Complex endometrial metaplastic lesions with metaplasia different from morules share morphological similarities and are associated with KRAS mutations. We suggest to classify these lesions under the umbrella term "metaplastic atypical hyperplasia/endometrioid intraepithelial neoplasia" to simplify the interpretation of pathology reports.

E-PS-10-106
Adrenoreceptors ARB1 and ARB2 expression in different forms of adenomyosis
A. Tregubova*, A. Asaturova, A. Badlaeva, A. Sokolov, A. Arakelyan, A. Rogozhina, V. Suhoparova, I. Dyadishcheva, L. Adamyan
*FSBI «National Medical Research Center for Obstetrics, Gynecology and Perinatology named after Academician V.I.Kulakov», Russia

Background & objectives: Adrenoreceptors were demonstrated to correlate with pain syndrome in patients with adenomyosis and to contribute into its pathogenesis. We goal of our investigation was to compare ARB1 and ARB2 in different forms of adenomyosis for fundomental and treatment purposes.
Methods: We recruited 90 patients with diffuse adenomyosis(1st group,n=30,mean age 46.7+-4.3 years),nodular adenomyosis(2nd group,n=30,mean age 34.4+-5.2 years) and benign ovarian cysts(control group,n=30,mean age 27.8+-6.8 years).Ectopic foci from study groups as well as eutopic endoemtrium from control group were assesed immunohistochemically with ARB1 and ARB2.Hscore (0-12 score) was used for semiquantative assesment;Kruskal–Wallis test and Spearman's rank correlation were used for statistical analysis.
Results: Expression of ARB1 was 9.5(9.0-10.0)(1st group), 8.0(7.0-9.0)(2nd group), 4.5(2.25-4.75)(control group) (p2nd group –1st group= 0,007;pcontrol group – 1st group<0,001;pcontrol group – 2nd group < 0,001); Expression of ARB2 was 7.0(7.0-8.0)(1st group), 6.0(5.0-7.0)(2nd group), 3.0(2.0-4.0)(control group) (p2nd group –1st group=0,006;pcontrol group – 1st group< 0,001;pcontrol group – 2nd group < 0,001); we detected strong correlation between ARB1 and ARB2 expression (ρ=0.689, p<0.001). ARB2 expression depends on ARB1 expression is described by the equation of pair linear regression YARB2 = 0,503 × XARB1 + 2,002: with ARB1 expression increases by 1 score ARB2 expression increases by 0,503 scores.
Conclusion: Adrenoreceptors ARB1 and ARB2 differently express in different forms of adenomysis demontrated more prominent expression in diffuse adenomyosis. Moreover, ARB1 and ARB2 expression differs from eutopic endoemtrium in control group. Thus, wew can suggest that adrenoreceptors play role in adenomyosis pathegenesis and contribute into more prominent pain syndrome in diffuse adenomysis patients. Expression ARB1also correlates with ARB2 expression and demonstrates the cross-talk of these G-Protein-Coupled Receptor signalling pathway components.

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E-PS-10-107
BCL-6 expression for presurgical triage of the patients with superficial and deep endometriosis
A. Tregubova*, A. Asaturova, A. Badlaeva, A. Rogozhina, M. Dumanovskaya, N. Buralkina
*FSBI «National Medical Research Center for Obstetrics, Gynecology and Perinatology named after Academician V.I.Kulakov», Russia

Background & objectives: It was shown that bcl-6 expression in endometrium can predict endometriosis in patients with unexplained infertility. The goal of our survey was to reveal whether this marker can be used to differentiate deep and superficial endometriosis in endometrial biopsy.
Methods: We recruited 45 patients (mean age 32.5+-3.2 years) with superficial endometriosis (1st group, n=15), deep endometriosis (2nd group, n=15) and control group(with leiomyoma, n=15).We detected Bcl-6 expression in endometrial samples semi-quantitatively. The data are presented as M ± SD, where M is the mean value, and SD is the standard deviation. Multivariate analysis of variance analysis was used for statistics.
Results: BCL-6 expression was assessed with HSCORE = $\sum$ Pi (i + 1)/100, where i=intensity of staining (weak (1), moderate (2),strong (3) and Pi is the percentage of stained epithelial cells for each intensity(0% to 100%). BCL-6 expression was 1.8±0.4 in the 1st group, 2.6±0.3 in the 2nd group and 1.3±0,3 in the control group (p< 0,001 between 1st

group and control group; p < 0,001 between 1st and 2nd groups, p < 0,001 between 2nd group and control group).
Conclusion: We concluded that BCL-6 expression can be used not only for endometriosis prediction on the basis of endometrium assessment but also can help to differentiate superficial and deep of endometriosis for more personalized triage before surgical treatment.

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E-PS-10-108
Crosstalk between steroid hormone receptors and retinoid metabolism in rudimentary uterine horns
A. Tregubova*, A. Badlaeva, Z. Batyrova, A. Asaturova, Z. Kumykova, J. Kessler, T. Aksenova, T. Ivanets, V. Chuprynin, E. Uvarova
*FSBI «National Medical Research Center for Obstetrics, Gynecology and Perinatology named after Academician V.I.Kulakov», Russia

Background & objectives: Several studies strongly support that steroid hormones play an important role in retinoid metabolism in human endometrial disorders, so we aimed to investigate the interaction between estrogen, progesterone receptors, and retinoid X receptors alpha and beta in rudimentary uterine horns.
Methods: Formalin fixed, paraffin embedded samples of normal cycling human endometrium (n=20) and endometrium in rudimentary uterine horns (n=20) were immunohistochemically examined for retinoid X receptor (RXR) alpha, beta, estrogen (ER) and progesterone receptors (PrR) using H-score. A blood serum level of retinol metabolites was also estimated. Statistical analysis was made using Mann-Whitney test, Spearman's rank correlation.
Results: Endometrium in rudimentary uterine horns was decreased in H-score of RXR alpha, beta, as well as ER, PrR. Additionally, H-score for PrR in normal endometrial glands was 1.9-fold higher as compared with those in uterine horns, for ER - 29-fold higher ($p<0.001$). There was a significant positive correlation between hormone receptors and RXR alpha both in endometrial stroma and glands ($p<0.05$). Similarly, a positive correlation was found between hormone receptors and RXR beta. When the blood serum for healthy controls and patients with uterine horns were compared, the latter group was found to have a significantly lower level of retinol metabolites.
Conclusion: Overall, this study strengthens the idea that in situ estrogen and testosterone metabolism is possible associated with retinoic acids in both normal human endometrium and endometrium of rudimentary uterine horns through RXRs.

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E-PS-10-109
A large polypoid adenomyoma of the endometrium - a potential pitfall
H. Trihia*, P. Bafaloukos, C. Iavazzo
*Metaxas Cancer Hospital, Greece

Background & objectives: Polypoid adenomyoma (PA) of the uterus is a rare endometrial polyp in which the stromal component is made up of smooth muscle. We describe an unexpected finding of a PA, in a woman with long-lasting abnormal vaginal bleeding.
Methods: A 75-year old woman, with abnormal vaginal bleeding of three years duration was diagnosed with a mass, filling the uterine cavity. Endometrial curettings were non-diagnostic. She underwent hysterectomy with bilateral oophorectomy and omentectomy.
Results: Macroscopically, the endometrial cavity was filled with a 5cm circumscribed, homogeneous mass with spongy, microcystic appearance which was abutting on the endometrium, with a broad base of 2,5cm. Microscopically, there were cysts, endometrial glands, crowded in areas with lobulated architecture, without atypia, embedded in a fibrous stroma with prominent leiomyomatous component, positive in smooth muscle actin (SMA) and desmin. Estrogen and progesterone receptors were typically positive in glands. The diagnosis was of a benign adenomyomatous polyp of the endometrium.
Conclusion: Endometrial polypoid adenomyoma, accounts for 1,3% of all endometrial polyps, with incidence higher in women >50 years, maybe related to unopposed prolonged estrogenic stimulation and represents a benign neoplasm of unknown histogenesis. It is a uterine space-occupying lesion. On imaging, it may be confused with prolapsed leiomyomas or malignancy. Cystic spaces in a prolapsed uterine tumour should raise the suspicion of a PA. Diagnosing polypoid adenomyoma is vital because it can potentially be managed by hysteroscopic resection or avoid overtreatment.

E-PS-10-110
Ovarian leiomyoma: a rare cause of virilization
M.I. Ttito Condori*, G. Gonzalez Lopez, M. Martinez Lopez
*Hospital Universitario Doce de Octubre, Spain

Background & objectives: Smooth muscle tumours of the ovary, particularly leiomyomas, are rare, accounting for less than 1% of ovarian neoplasms . This case details an ovarian leiomyoma presenting with virilization, adding to fewer than 80 documented cases, emphasizing its rarity.
Methods: A 74-year-old woman presented with a 3-year history of hirsutism and abnormal uterine bleeding. Laboratory analysis revealed elevated serum testosterone levels (146 ng/dl), while dehydroepiandrosterone sulfate and cortisol levels remained within normal limits, suggesting ovarian androgen overproduction. Bilateral laparoscopic oophorectomy was performed based on these findings. The surgical specimen was sent to the pathology department.
Results: The macroscopic analysis revealed an ovary with a rounded morphology and a smooth, grey surface. Histological examination showed stromal hyperplasia with hypertecosis. At the hilum, a nodular proliferation of smooth muscle cells without atypical features was observed, consistent with a leiomyoma with a maximum measure of 1 cm. The lesion was surrounded by a thick layer of Leydig cells (hilus cells), suggestive of ovarian Leydig cell hyperplasia. Due to a change of residence, there is no available data for clinical and laboratory follow-up on the patient.
Conclusion: Ovarian leiomyoma is a rare entity with varied clinical presentations, ranging from asymptomatic to virilization, and even seizures. Leiomyomas associated with androgen production may originate from hilus cells, inducing theca cell luteinization. Published cases suggest that these lesions are mostly benign and unilateral. Following their removal, testosterone levels typically decrease dramatically, resulting in the resolution of virilization. Given the limited number of reported cases, information on these hormone-producing lesions remains scarce.

E-PS-10-111
Synchronous endometrioid carcinomas in the endometrium and the ovary with a distinct molecular profile
A. Zarrou, D. Karagkiozidis, K. Mesiakaris, G. Androutsopoulos, V. Zolota, V. Tzelepi*
*Department of Pathology, School of Medicine, University of Patras, Greece

Background & objectives: Recent reports have shown that synchronous endometrial and ovarian carcinomas are clonally related, representing spread from one location to the other. Herein we report a case of endometrioid carcinoma in the ovary and the endometrium with a distinct MMR phenotype.

Methods: A 43 year old woman presented with an ovarian mass and unremarkable serum tumour-markers. A total abdominal hysterectomy with bilateral salpingo-oophorectomy and pelvic lymph node dissection was performed. A partially cystic white tan mass was seen in the right ovary measuring 8cm. Also, a polypoid mass, measuring 0.7cm, was seen protruding in the endometrial cavity, along with increased endometrial thickness.
Results: On microscopic examination both the ovarian and the endometrial mass showed features of endometroid carcinoma, FIGO grade I, with adjacent hyperplasia without atypia in the endometrium and foci of endometriosis in the ovary. On immunohistochemistry, both tumours expressed CK7, ER, PR, wild-type p53 and (focally) p16, and were negative for WT1, SATB2, napsin and CK20. Interestingly, loss of MSH6 expression was seen in the endometrial tumour, but not in the adjacent hyperplasia or the ovarian carcinoma. Ion amplisec analysis showed the presence of MSI in the endometrial tumour (MSI score 47). Genetic analysis revealed that the patient did not have Lynch syndrome. POLE analysis is pending.
Conclusion: A diagnosis of two independent primary carcinomas in the endometrium and the ovary, each staged pT1aN0 (AJCC 8th Edition) (IA, FIGO) was made. The simultaneous presence of two separate carcinomas in the female reproductive tract can be a manifestation of a metastatic carcinoma or a result of two primary tumours arising independently. Careful evaluation of the gross, microscopic and molecular features of the tumours is necessary for establishing an accurate diagnosis.

E-PS-10-112
Malignancy in mature cystic teratomas: is it really rare? A single centre experience.
A. Üzümcü*, A. Bayram, H. Sozen, S. Onder
*Istanbul University, Istanbul Faculty of Medicine, Turkey

Background & objectives: Mature cystic teratoma is the most common ovarian germ cell neoplasm. Malignant transformation is a rare event accounting for 1.5%-2% of the cases. We searched our pathology archive to reveal the malignancy in ovarian teratoma cases.
Methods: In our archive, we identified 721 cases diagnosed as ovarian teratomas between 2006 and 2023 and analysed their demographic and histopathological features. We also searched for the cases that showed somatic neoplasia in the background of teratoma. The malignancy rate as well as the details of the malignant tumours were also exhibited.
Results: Of 721 cases, 676 (94%) were diagnosed as mature cystic teratoma (MCT) and 40 (5%) as immature teratoma. Sixty four patients had bilateral MCTs.
Thirty one (5%) patients developed somatic neoplasia in the background of MCT. Of these 23 (74%) were malignant, 3 (10%) were borderline whereas 5 (16%) were benign. The distribution of malignant cases was as follows: 9 cases of squamous cell carcinoma (SCC) (39%), 7 neuroendocrine tumours (31%), 3 papillary thyroid carcinomas (13%), 3 mucinous adenocarcinomas (13%) and 1 mucinous cystadenocarcinoma (%4).
The mean age of patients with MCT with neoplasia was 46,1 (±13,5 years) whereas the mean age of those without neoplasia was 33,06 (±14,91 years).
Conclusion: Mature cystic teratomas are usually benign tumours but rarely show malignant transformation. In our series, the malignancy rate of MCTs was 3% as well as SCC was the most common malignant tumour arising in MCTs in accordance with the literature. The mean age of the patients with neoplasia was higher than the patients without neoplasia as expected. Therefore ovarian teratomas must be carefully examined to not to overlook malignancy especially in elder patients due to poor prognosis.

E-PS-10-113
Rare and unusual case of primary ovarian angiosarcoma
S. Vidhale*, K. Surnare, N. Oza, S. Kane
*Tata Memorial Hospital, India

Background & objectives: The incidence of Angiosarcoma occurring primarily in the ovary is 1 in 1000,000 cases of ovarian malignancies. We hereby report this case of ovarian angiosarcoma considering the rarity of this entity occurring in the female reproductive organ.
Methods: We report a case of a 55 years old female patient with a right adnexal mass which was subjected to excision. The right ovarian mass was diagnosed as primary ovarian angiosarcoma based on histology and immunohistochemistry.
Results: A 55 years old female presented with pain in the abdomen along with ascites. Serum CA125 levels were raised (1394U/ml). She underwent right salpingo-oophorectomy followed by total hysterectomy. The adnexal mass was externally well encapsulated, measuring 5.5x5.0x2.5cm. Cut surface showed a solid, brown coloured lesion, with areas of haemorrhage. Microscopic examination revealed a well encapsulated tumour displaying a diffuse and lobular type of architecture, composed of florid vascular proliferation. The dilated vascular spaces were lined by atypical flat to plump endothelial cells. The atypical endothelial cells showed strong and diffuse cytoplasmic expression for immunohistochemical stains CD31, CD34, and nuclear expression for ERG.
Conclusion: Despite its rarity, ovarian angiosarcomas are identifiable histologically and should be subjected to thorough screening along with a vigilant eye for vascular neoplasms in order to entail an appropriate diagnosis in the initial stage followed by surgical clearance, as this increases the chances of survival that may be reduced in the later stage as chemotherapy is palliative.

E-PS-10-115
Villous adenomatous neoplasm of the vagina – a case report highlighting diagnostic issues
S.L. Wong*
*Singapore General Hospital, Singapore

Background & objectives: Villous adenomas of the vagina are rare lesions. In large lesions, a curative excision may be preceded by a biopsy. When there is high grade dysplasia, the possibility of associated adenocarcinoma is considered. Primary versus metastatic lesions are also considerations.
Methods: Biopsy of a vaginal tumour was obtained from a 68 year old lady, consisting of 3 pieces of tissue measuring from 0.5 to 0.6cm. Immunohistochemistry CK7, CK20, CDX2, SATB2, PX8, ER, WT1 and p16 were performed. Subsequently, a vaginectomy was performed, which consisted of a piece of mucosa covered tissue containing a polyp measuring 1.2cm in extent.
Results: Biopsy showed superficial fragments of a villous neoplasm lined by pseudostratified cells with adenomatous change amounting to high grade dysplasia. On immunohistochemistry, the tumour cells showed positivity for CK7, CK20, CDX2 and SATB2. They display patchy heterogenous staining for p16, and were negative for PAX8, ER and WT1. The biopsy was reported as 'superficial fragments of an intestinal-type adenomatous neoplasm with high grade dysplasia', with a recommendation for complete excision and exclusion of a primary tumour from the intestinal tract. The subsequent vaginectomy specimen showed a villous adenoma with high grade dysplasia. No definite stromal invasion was seen.
Conclusion: Villous adenomas of the vagina with high grade dysplasia can mimic adenocarcinoma, either primary adenocarcinoma or metastasis from the uterus or intestinal tract. Complete excision is

recommended if an adenomatous neoplasm is diagnosed on biopsy, in order to exclude an underlying more severe lesion and to obtain clear margins.

E-PS-10-116

Histopathological features and clinical findings in HPV-associated and non-HPV-associated squamous precancerous lesions of the lower genital system

S. Yağcı*, Ö. Özen, H. Örün, E. Yağcı, A.N. Haberal Reyhan, A. Ayhan
*Department of Pathology, Baskent University, Faculty of Medicine, Ankara, Turkey

Background & objectives: In our institution, a designated reference centre for Gynaecologic Oncology, we explored the correlations between clinicopathological features and outcomes of recurrence and progression to malignancy in patients diagnosed with HPV-associated and non-HPV-associated vulvar squamous precancerous lesions.
Methods: This retrospective cohort study included 115 patients diagnosed with high-grade squamous intraepithelial lesion (HSIL), vulvar intraepithelial neoplasia (VIN), vulvar carcinoma in situ, and differentiated VIN (dVIN) between 2007 and 2023. Cases of vulvar condyloma and concurrent vulvar squamous cell carcinoma were excluded. Risk factors for recurrence and clinical worsening (recurrence and/or progression) were investigated through binary logistic regression.
Results: The median age was 40 years (range 17-84), with most (93.9%) diagnosed with HSIL and a smaller group (6.1%) with dVIN. Metachronous cervical HSIL occurred in 24.6% of cases, and 53% had multifocal lesions. Excisional treatment was used in 61.7% of patients, with 43.6% showing positive surgical margins. Recurrences and progression were observed in 19% and 6.2%, respectively. Metachronous cervical HSIL was linked to a 3.7-fold increased risk of recurrence, while multifocality and smoking history increased risks by 7.9 and 3.2 times, respectively. Including progression, metachronous cervical HSIL and positive margins were linked with 3.6-fold and 3.2-fold increased risks of clinical worsening.
Conclusion: This study underscores the importance of assessing risk factors in HPV-associated HSIL cases and considering them in treatment planning. Our findings have identified specific risk factors that can predict recurrence and clinical worsening.

E-PS-10-117

Lignous endometritis: a gynaecological presentation of congenital plasminogen deficiency

S. Yağcı*, A. Ok Atılgan
*Department of Pathology, Baskent University, Faculty of Medicine, Ankara, Turkey

Background & objectives: Ligneous disease is a rare chronic, non-infectious pseudomembranous inflammation characterized by widespread subepithelial fibrin deposition. It predominantly affects mucosal membranes. Plasminogen deficiency is commonly observed. Diagnosis relies on both laboratory findings and histopathological examination.
Methods: A 28-year-old female patient, who was being monitored for fertility reasons, presented to our hospital with complaints of discharge. Her menstrual periods were regular, and both Pap smear and HPV tests were negative. A hysterosalpingography revealed linear filling defects at the level of the uterine corpus, suggestive of adhesions. Subsequent hysteroscopy confirmed these adhesions and an endometrial biopsy was taken.
Results: Histopathological examination showed a dense exudate rich in polymorphonuclear leukocytes and a significant eosinophilic accumulation beneath the surface epithelium of the endometrium. Trichrome histochemistry confirmed this accumulation as fibrin. The findings were reported as ligneous endometritis, and it was recommended to check the patient's serum plasminogen levels and monitor her accordingly. The patient was treated with antibiotics for endometritis and referred to haematology. Her serum plasminogen level was found to be low (43%). Treatment with intrauterine alteplase (thrombolytic) and fresh frozen plasma (FFP) was initiated. After one year, the patient underwent in vitro fertilization, successfully conceived, and gave birth to a healthy child at 39 weeks.
Conclusion: In the literature, 33 cases of ligneous disease in the female genital system have been reported. Of these cases, 24 (72.7%) were found to have a deficiency in serum plasminogen. Plasminogen levels were not evaluated in the remaining 9 cases. Plasminogen deficiency can be either acquired or congenital, and it is a chronic and rare condition. While there is no definitive treatment currently available, concentrated plasminogen replacement therapy appears to be a promising option for these patients in the future.

E-PS-10-118

F-actin regulators are implicated in human endometrial cancer

E. Zarogianni, P. Bosgana*, C. Geramoutsou, G. Androutsopoulos, V. Bravou
*Medical School of Patras, Greece

Background & objectives: Reorganization of the actin cytoskeleton is fundamental to cancer cell invasion and metastasis. This study aims to address the role of N-WASP, LIMK1, LIMK2 and SSH1 important regulators of actin filament turnover in endometrial endometrioid carcinoma.
Methods: N-WASP. LIMK1, LIMK2 and SSH1 protein expression was evaluated by immunohistochemistry in 110 FFPE human endometrial endometrioid carcinoma in relation to clinicopathological parameters.
Results: N-WASP, LIMK1, LIMK2 and SSH1 a were expressed in 86.4%, 92.5%, 71.6% and in 67.6% of endometroid carcinomas cases respectively with cytoplasmic and nuclear localization. Iimmunoreactivity score of all proteins was higher in carcinomas compared to adjacent non-neoplastic endometrium. N-WASP expression was significantly higher in cases with lymph node metastasis and adnexa involvement and nuclear SSH1 expression was significantly higher in cases with cervix invasion, isthmus involvement and in tumours of advanced stage. There was also a significant positive correlation between SSH1 and LIMK1 in endometrioid carcinomas.
Conclusion: Our study provides novel evidence that regulators of actin dynamics N-WASP and SSH1 are implicated in human endometrial endometrioid carcinomas progression and represent promising novel therapeutic targets.

E-PS-10-119

Primary carcinoid tumours of the ovary arising in mature cystic teratomas: a clinicopathological study of 5 cases

M. Zghal*, W. Ghribi, I. Bahri, S. Makni, C. Chaari, T. Sellami Boudawara, S. Graja
*Department of Pathology, Habib Bourguiba University Hospital, Sfax, Tunisia

Background & objectives: Primary carcinoid tumours of the ovary (PCTO) are rare tumours, accounting for 0.3% of all carcinoid tumours. They usually accompanied mature cystic teratomas (MCT). We aimed to investigate the clinical and pathological features of this rare entity.
Methods: This is a retrospective and descriptive study of 5 cases of PCTO within a MCT, registered at the department of pathology of the university hospital of Sfax in Tunisia, during a period of 12 years from 2013 to 2024. Their epidemiological, clinical, and pathological characteristics as well as their outcome were retrospectively reviewed.
Results: The mean age was 40.8 years (28-56 years). The tumour was discovered by abdominal pain in 4 patients and incidentally in one patient. Macroscopic examination revealed solido-cystic masses

containing sebaceous material and hairs, with mean size of 5.3 cm. Histological examination showed mature squamous and respiratory epitheliums, as well as mesenchymal tissue. Area of uniform polygonal cells, arranged in insular (4 cases) or trabecular (1 case) pattern was notable in the cyst wall with a mean volume of 0.3 cm. These cells displayed abundant eosinophilic cytoplasm and small round nuclei without atypia or mitotic activity. Immunohistochemical study was positive for chromogranin and synaptophysin to varying degrees. No recurrence was observed.
Conclusion: PCTO are rare tumours representing 0.1% of ovarian neoplasms. 85% of POCT accompanied MCT. The most common form of malignant transformation from ovarian MCT are squamous cell carcinomas, followed by adenocarcinomas then carcinoid tumours. POCT are almost unilateral with solid yellowish cut surface, varying from microscopic foci to 30 cm in size. The most common histological subtype is insular, followed by trabecular, strumal and mucinous. PCTO have low malignant potential with good outcome. Diagnosis relies on histopathological and immunohistochemical characteristics.

E-PS-10-114
Significance of immunoreactivity and morphometric analysis of HPV-induced cervical dysplasia
B. Vukomanovic Djudjevic*, S. Glumac, S. Radojevic Skodric, K. Durdevic, B. Jovanović
*Serbia

Background & objectives: Cervical epithelial dysplasia, High-grade (HSIL) and Low-grade (LSIL) is group of interconnected morphological changes in the histological architecture of the cervical mucosa. The main ethiological factor is Human papiloma viruses family.
Methods: This retrospective study included 99 patients examined at the Department of Gynecology of the Military Medical Academy, Belgrade, in the period of four years in patients with a verified presence of high-risk HPV infection by polymerase chain reaction. Morphometric analysis was performed on H&E and PAS stained slides at 400 x magnification,and we performed immonhistochemical marker Survivin.
Results: It is shown high statistical significance by morphometric analyses in patients with HSIL and LSIL than in control group without dysplasia, as well as survivin expression.
Conclusion: Using morphometric methods for analyses of dysplastic nuclei in cervical dysplasia, as well as using immunochistochemistry marker survivin make significance methods in analyses cervical HPV-induced dysplasia.

E-PS-11E-Poster Session Haematopathology

E-PS-11-001
Extreme variation on an ontogenic sequence – massive plasma cell differentiation in a primary thyroidal, extra-nodal marginal zone lymphoma
A. Abrari*, U. Mukherjee, K. Akhtar
*The Rotherham NHS Foundation Trust, United Kingdom

Background & objectives: Plasma cell differentiation is not a rare feature of extra-nodal marginal zone lymphomas, including primary thyroid lymphomas. However, extreme plasma cell differentiation, is not very common and may raise the possibility of other morphologically overlapping conditions with management implications.
Methods: A 68 year old lady, was referred to a major referral hospital in north India, with a fairly rapidly enlarging, asymmetric, firm, right thyroid mass, accompanied by neck pain and difficult breathing, provoking consideration of an aggressive neoplasm, including an anaplastic carcinoma. Imaging, largely non-committal, reported no extra-thyroid spread or lymphadenopathy. An ultrasound guided core biopsy was comprehensively evaluated histologically.
Results: The biopsy cores were overrun by confluent and densely cellular infiltrates of plasma cells. There was a subsidiary population of small lymphocytes, intimate with residual oxyphilic follicles, forming lympho-epithelial lesions. Stray lymphoid follicles with reactive germinal centres were also noted. No sheets of mitotic, blastoid cells were seen. Comprehensive immunohistochemistry (LCA, Cam5.2, CD20, CD 79a, CD138, CD38, CD56, CD43, IgM, MUM1, cyclin D1, Bcl2, Bcl6, CD5, CD10, CD3, CD23, Ki67, kappa and lambda light chains, and ancillary testing were performed. The results interpreted in the light of haematological, radiological and clinical findings, were then construed as a primary, extra-nodal marginal zone lymphoma of the thyroid with extreme plasma cell differentiation.
Conclusion: The present case illustrates an extreme exemplar of the ontogenic oddity of large-scale plasma cell differentiation, engendering exclusion of divergent entities, including de novo plasma cell neoplasms and lympho-plasmacytic lymphoma.
Careful appraisal of morphological and immunohistochemical nuances, considered conjointly with haematological and clinical inputs leads to a precise diagnosis.

A case may also be made for reflexing to core biopsy, if the usually first-line, fine needle aspiration cytology of any thyroid mass, should yield a significant proportion of plasma cells.

E-PS-11-002
Histiocytic sarcoma: an unusual presentation of a rare entity
K. Adoke*, S.H. Mohammad
*Federal Medical Center Birnin Kebbi, Nigeria

Background & objectives: Histiocytic sarcoma (HS) is a rare non-Langerhans histiocytic disorder accounting for less than 1% of all hematolymphoid disorders, it has an aggressive clinical course with limited treatment options. Has a male predominance with extranodal sites also affected in some cases.
Methods: A 22 year old woman presented with 3 weeks history of fever and two months history of abdominal pain and distension. Ultrasound revealed multiple mesenteric lymph nodes measuring 4x4cm. All the other base line investigations were normal. A diagnosis of Non-Hodgkin's lymphoma was made by the clinician and a biopsy of the mesenteric lymph node was taken for histology.
Results: Histology showed total effacement of lymph node architecture by diffuse sheets of round to oval cells with prominent nucleoli and abundant cytoplasm with some displaying epitheloid morphology. Hemophagocytosis and necrotic areas were also seen. Immunohistochemistry showed CD 163 and CD 68 positive while CD 5, CD15, CD 30, CD 23, S-100 and Pan-cytokeratin were all negative. A diagnosis of HS was made and patient was placed on cyclophosphamide, doxorubicin, vincristine and prednisolone (CHOP). Was discharged after a remarkable improvement and subsequently lost to follow up.
Conclusion: HS is an uncommon non Langerhans histiocytic disorder with numerous differential diagnosis, hence immunophenotyping including molecular studies are necessary for both establishment of a diagnosis and therapy in some cases.

E-PS-11-003
Hydroa vacciniforme lymphoproliferative disorder, systemic subtype
C.T. Alfaro Cazon*, F.N. Figueroa
*Department of Anatomic Pathology, Hospital Nacional Prof. Alejandro Posadas. Anatomic Pathology, Argentina

Background & objectives: Hydroa vacciniform lymphoproliferative disorder (HV-LPD) is a cutaneous form of chronic active Epstein-Barr virus (EBV) disease, encompassing a variety of behaviours, from the

classic form with self-limited photodermatosis to the systemic form with extensive skin lesions and multiorgan involvement.
Methods: We present a clinical case Hydroa vacciniforme lymphoproliferative disorder, systemic subtype, with unfavourable clinical evolution. To summarize this entity, we summarize the histomorphological and immunophenotypic characteristics.
Results: A 4-year-old male patient, native of Bolivia, presents clinical features characterized by chronic dermatitis of one year of duration, which includes fever, vomiting and diarrhea. Presents papulovesicular eruptions that evolve into blisters and ulcers, leaving varioliform atrophic scars and hepatomegaly. Bone marrow aspirate and biopsy shows hemophagocytosis.The histology of the skin evidence dense infiltrate of small to medium sized lymphoid cells of atypical appearance, with a perivascular, periadnexal and interstitial distribution, with foci of angiocentricity. Positive expression for CD3 with co-expression of CD2,CD7 and CD8,showing partial deletion for CD5.TIA-1, Granzime-B,CD56, and of LMP-1 (EBV) is observed focally.Ki67 of up to 20%. In situ hybridization EBER in 5% of proliferation.
Conclusion: Hydroa vacciniforme lymphoproliferative disorder it is a rare entity, mainly in children and adolescents from Asia and indigenous populations from South and Central America. Is a challenge at the time of diagnosis, with highly variable clinical course, prognosis and prediction. It is important to distinguish HV-LPD from systemic chronic active EBV disease without HV-LPD, because the latter is invariably fatal in the absence of haematopoietic stem cell transplantation. Its multidisciplinary study is essential.

E-PS-11-005
Incidental angiomyomatous hamartoma of the lymph node with adipose component: a rare cause of an inguinal mass
A. Alpsoy*, S. Boztekin, G.O. Elpek
*Afyonkarahisar State Hospital Department of Pathology, Turkey

Background & objectives: Angiomyomatous hamartoma (AMH) is a rare lesion primarily affecting the inguinal lymph nodes. AMH represents the proliferation of smooth muscle and blood vessels. We present a rare case of AMH including adipose tissue component in the inguinal lymph node.
Methods: A 75-year-old male presented with a mass and discomfort in his right inguinal area. Ultrasonography revealed findings consistent with the hernia in the right inguinal area. A surgical procedure was conducted to repair the inguinal hernia. During the surgery, enlarged lymph nodes were detected and subsequently excised. Microscopic examination was performed with H&E staining and immunohistochemical application.
Results: Macroscopically, one of the five lymph nodes exhibited a diffuse mass that appeared white in the centre. Microscopically, the capsule was thickened and the lymph node consisted of a proliferation of smooth muscle, blood vessels, and adipose cells starting at the hilum and extending through the medulla, and cortex. Benign spindle cells and vascular proliferation without a palisaded nature were highlighted by SMA, Desmin, CD31, and CD34. The adipose cells within the lesion were stained with S100. A differential diagnosis was made for lymphangioleiomyomatosis with the help of a negative HMB45.
Conclusion: AMH was first presented by Chan et al. in 1992 as a rare hamartoma of inguinal and femoral lymph nodes. Since then, there have been fewer reported cases involving an adipose cell component. It is imperative to note that this case is of utmost importance, as it is one of the few cases ever reported to have an adipose cell component in AMH.

E-PS-11-006
Sarcoma myeloid mimicking a perihilar cholangiocarcinoma
A. Alves*, J. Pimentel, R. Pina, M.A. Cipriano
*Unidade Local de Saúde de Coimbra, Portugal

Background & objectives: Sarcoma myeloid is a tumour mass of myeloid cells, usually diagnosed in the context of acute myeloid leukemia or as its relapse, rarely preceding the leukemia diagnosis. It commonly affects the skin, lymph node, bone and soft tissues.
Methods: A male patient in his 50's presented with right upper quadrant abdominal discomfort and mucocutaneous jaundice persisting for two weeks. Imaging studies revealed a thickening of the common biliary duct and left hepatic duct wall, suggesting a diagnosis of perihilar cholangiocarcinoma. He was submitted to embolization of the left branch of the portal vein followed by left hepatectomy.
Results: On gross examination, there was a thickening of the common biliary duct wall, reaching 0,6cm, with indistinct borders but appearing to extend throughout its length to the left biliary duct. Histologically, there was a diffuse infiltration of the biliary wall by hematopoietic intermediate-sized cells, with scant cytoplasm and round nuclei, with light chromatin and absent nucleoli. These cells exhibited diffuse immunopositivity to myeloperoxidase and multifocal positivity to CD117 while CD3, CD20, CD34, CD138 and CD163 were negative. No evidence of epithelial neoplasia, either in situ or invasive, was found. A diagnosis of sarcoma myeloid was rendered.
Conclusion: Sarcoma myeloid, although rare, can appear in the biliary ducts, causing bile flow obstruction, with clinical and radiological signs similar to those of inflammatory or neoplastic conditions of the biliary path and only histological assessment or bone marrow or peripheral blood evaluation for acute myeloid leukemia could lead to the accurate diagnosis. This patient exhibited immature myeloid blast in peripheral blood but because of the unusual symptoms and radiological findings, the correct diagnosis and management was delayed.

E-PS-11-007
Fluid overload-associated large B-cell lymphoma: a case report and literature review
B.B. Ardaya Lopez*, H. Galindo Guzman, C. Martinez-Laperche, D. Monzon Diaz, M.B. Bastos Oreiro, F.J. Menarguez Palanca, F.J. Díaz Crespo
*Hospital General Universitario Gregorio Marañon, Bolivia

Background & objectives: Fluid Overload-Associated Large B-cell Lymphoma (FO-LBCL), a novel and rare entity in the latest (WHO) Classification of Hematolymphoid Tumours, with fewer than 100 reported. Our case, involving a woman with pericardial effusion, adds to the limited literature on this condition.
Methods: We present a case of a 59-year-old woman referred to our hospital with dyspnea and pericardial effusion, who underwent pericardiocentesis due to signs of hemodynamic compromise on echocardiography. Cytology revealed abundant lymphoid cellularity with high nuclear atypia and an immunophenotype consistent with large B-cell lymphoma. Extension studies ruled out primary tumour masses. Subsequent follow-up revealed no evidence of tumour recurrence.
Results: Histopathological assessment of the effusión revealed abundant large cells with marked nuclear atypia and prominent cytoplasm in a hematic background. The atypical cells exhibited positivity for lymphoid B-cell markers CD45/CD20/CD79, and central germinal origin, with CD10/MUM1 negativity and BCL6 positivity. Stains for HHV8 and VEB(EBER) were negative, while Ki67 was high (70%). These findings are consistent with Large B-cell lymphoma, supported by monoclonal proliferation demonstrated in B cell clonality study (IGH). In the absence of primary tumour masses in extension studies, the diagnosis meets FO-LBCL criteria. Additionally, MYC rearrangement was detected via Fluorescence In Situ Hybridization (FISH). The follow-up supports this diagnosis, with the patient alive and without tumour masses.
Conclusion: In conclusion, this rare and relatively new entity affects immunocompetent elderly individuals, often expressing at least one pan B-cell marker and presenting clinical features similar to Primary

Effusion Lymphoma (PEL), yet KSHV/HHV-8 negative. Prognosis, based on limited follow-up data, appears favourable compared to PEL. However, further research into genomic landscape and molecular oncogenesis through additional cases and thorough analysis is warranted due to the scarcity of cases reported.

E-PS-11-008

Primary bilateral ovarian Burkitt's lymphoma: report of two cases of this extremely infrequent presentation

M. Arias Duart*, P.J. Armijos González, F.J. Menarguez Palanca, Y. Martín Guerrero, M.d.C. Viñuela Benéitez, E.M. Pena Burgos
*Hospital General Universitario Gregorio Marañón, Spain

Background & objectives: Burkitt's Lymphoma (BL) is a non-Hodgkin B-cell lymphoma with aggressive but curable outcome. Primary presentation of the ovary represents less than 1.5% of all ovarian lymphomas. Our aim is to report two new cases of primary bilateral ovarian BL.
Methods: We present two patients, the first one was a 32-years-old woman who debuted with an increased abdominal circumference and elevated serum LDH levels. The second one was a 30-year-old woman that noticed a mass in her iliac fossa. Radiological images revealed bilateral adnexal masses in both cases. No other lesions were detected (PET-TC). Bilateral adnexectomy was performed in both patients.
Results: The same gross and histopathological findings were observed in both specimens. The adnexes were increased in size (10 and 20 cm) with hard consistency and homogeneous whitish appearance. They were histologically composed by large cells with a sheet-like growth pattern with a ''starry sky" image. Abundant mitosis, haemorrhagic areas and necrotic foci were present. These cells showed diffusely immunoreactivity for CD20, CD10, BCL6 and C-MYC. BCL2 was negative. Cell proliferation index was 99% approximately. EBER CISH was negative. Molecular studies (FISH) demonstrated MYC gene rearrangement. No infiltration was identified in bone marrow. BURKIMAB-14 was administered in both patients. Metabolic complete response was objectified with PET-TC and they are actually disease-free.
Conclusion: There are only less than 30 reported cases of primary ovarian BL. Half of the cases arise in paediatric population and most cases are bilateral masses. BL need to be thought in a bilateral adnexal tumour with rapid progression and high serum LDH levels, especially in adolescents and young adult women. Gross, histopathological, immunohistochemically and molecular data are requested to reach the correct diagnosis to provide an adequate treatment for these localized and curable tumours.

E-PS-11-009

Pathological study of endoplasmic reticulum stress in Kikuchi-Fujimoto Disease (KFD)

S. Asano*, K. Shikano, K. Yamazaki, K. Mori, Y. Sogame, Y.H. Hashimoto, S. Kawana, M. Kashimura
*Iwaki City Medical Center, Japan

Background & objectives: At the previous conference, we reported that in Kikuchi-Fujimoto Disease (KFD, unfolded proteins (UP) accumulate in the endoplasmic reticulum (ER) and induce ER stress, which results in apoptosis.This time, we will report on the stress sensors and immune responses.
Methods: Using KFD electron microscopy specimens, paraffin-embedded tissues, and frozen samples, we investigated the UPR signal transmitted from ER stress histopathologically, immunohistochemically, and molecularly. Main antibodies used: PERK, ATF6, IRE1, CHOP, bcl-2, p-53, GRP78 (BiP).
Results: Stress sensors (PERK, ATF6, and IRE1) were all expressed simultaneously, and CHOP was induced at the same time as BiP transcription and induction.
PERK+ cells were found here and there at the edge of the lesion, but ATF6+ and IRE1+ cells were mainly found in histiocytes and dendritic cells, especially around small blood vessels and within the vessels.
Bcl-2+ and p-53+ cells were rarely seen within the lesion.
The relative mRNA ratios of PERK, ATF4, BiP, and CHOP differed between cases, and the ratios did not correlate with histological type.
Conclusion: In this disease, when ER stress is induced, the UPR quickly functions, and proteins such as IFNα are actively synthesized, and homeostatic mechanisms come into play. However, it was suggested that CHOP-induced apoptosis is triggered early as a result of long-term intense stress.

E-PS-11-010

Hashimoto-Pritzker reticulohistiocytosis: a rare case with an unusual course

K. Ben Lazreg*, S. Ben Hammouda, S. Mabrouk, N. Ellouze, A. Ben Mabrouk, A. Bellalah, M. Njima
*Fattouma Bourguiba University Hospital, Monastir, Tunisia

Background & objectives: Hashimoto-Pritzker reticulohistiocytosis (HPRH) is the benign variant of the Langerhans cell histiocytosis (LCH) group. It is very rare and characterized by multiple skin lesions appearing in newborns without systemic manifestations. Herein We report another rare observation of this entity.
Methods: A female neonate born at term after an uneventful pregnancy, presented with dry, scaly erosive cutaneous lesions on trunk, limbs, and face. Ichthyosis, bullous epidermolysis, Kaposi sarcoma, and LCH were suspected. Therefore, a biopsy was performed.
Results: Microscopic examination showed that the papillary dermis is often filled with a dense cellular infiltrate. This infiltrate consists of round cells with pale or eosinophilic cytoplasm and sometimes foamy cytoplasm. The cells have eccentric nuclei, sometimes with nuclear grooves. Immunochemistry findings revealed positive expression of these cells with CD1a and PS100 and no expression of CD117 (to rule out the diagnosis of mastocytosis). The diagnosis of LCH was retained. The absence of systemic involvement is consistent with HPRH. The patient died of severe sepsis due to infectious complications of the skin lesions.
Conclusion: HPRH is a rare presentation of LCH occurring at birth or during the first days of life without systemic manifestations, and with spontaneous resolution in days to months. The newborn presents usually with Blueberry muffin rash. Multiple differential diagnoses are clinically suspected including dermatological, hematological, and infectious (TORCHES) causes. A biopsy is needed to confirm the diagnosis. HPRH has a benign course with spontaneous regression. However, a near follow-up is needed to avoid complications.

E-PS-11-011

Unveiling molecular insights in lymphoma-like lesions of the lower genital tract: a comprehensive six-patient study

G. Caballero*, G. Frigola, A. Saco, M. López, D. Colomer, I. Luzón Vazquez, M. Marginet, M. Gomà Gallego, F. Climent, E. Campo, B. Gonzalez-Farre
*Hospital Clínic Barcelona, Spain

Background & objectives: Lymphoma-like lesions of the lower genital tract (LLLLGT) are highly proliferative benign lesions composed of large atypical cells, sometimes with clonal immunoglobulin rearrangements. This study aims to provide insights into molecular features to help in the differential diagnosis with lymphoma.
Methods: Six cases of LLLLGT in a five-year span were recruited and reviewed. Immunohistochemistry (IHC) for lymphoid markers and for Human Papilloma virus (HPV), in situ hybridization for Epstein-Barr virus (EBV) and BCL2, BCL6 and MYC FISH were performed in selected cases. Analysis for IGH gene rearrangement

and mutational status of 60 lymphoma-related genes with Next-Generation-Sequencing (NGS) were carried out.
Results: The median age of the patients was 45 years (32-61yr). Five patients had cervical polyps and one a clitoral lesion. Histologically, five cases showed a diffuse subepithelial inflammatory infiltrate, while one exhibited a nodular pattern. Lesions were composed predominantly of plasmablasts (2/6), centroblasts (2/6), anaplastic cells (1/6), or a mixture of large cells (1/6). Mitoses were frequent and Ki67 was high (60%-90%). Two cases showed lambda light chain restriction, two exhibited clonal IGH rearrangement. FISH were normal. EBV and HPV were negative. No mutations were observed in five cases studied, besides a CREBBP nonpathogenic germinal variant in one case. Follow-up from 1.5 to 11 years showed no recurrences.
Conclusion: LLLLGT are infrequent, highly proliferative and morphologically atypical but benign lymphoid lesions that can resemble lymphomas such as the recently recognized follicular centre lymphoma of the lower female genital tract. Although they may exhibit light chain restriction or clonal IGH rearrangement, these do not necessarily mean malignancy. The absence of oncogenic alterations in these cases, even in those with clonal IGH or monotypic light chain expression, supports the diagnosis of reactive lesions.

E-PS-11-012
A fibroblastic reticular cell tumour as unexpected diagnosis
I. Catalina-Fernandez*, A. Caro Romero, J. Sanz Repetto, R. Ávila Polo, D. Corrales Mateo
*Hospital Universitario Puerto Real, Spain

Background & objectives: Male of 69 years old, with surgically resected condyloma acuminatum of penis. During follow-up, a 3 cm right inguinal lymphadenopathy is identified and resected with suspicion of metastasis from squamous cell carcinoma. Testis ultrasound is negative.
Methods: Histological examination with hematoxylin-eosin staining, immunohistochemical techniques, and molecular techniques (EWSR1 and IGH rearrangements, CDKN2A/2B deletion and fusion of 63 genes by next-generation sequencing (NGS) FusionPlex Sarcoma S2 panel).
Results: Lymph node with architectural distortion, atypical germinal centres with irregular contours, composed of large-sized cells with pleomorphic nuclei, conspicuous nucleoli, and many mitoses. Variable-sized cytoplasms without secretory vacuoles and images of emperipolesis. Some inflammatory cells accompanying these cells. The cells only show immunohistochemical expression for Cam5.2, vimentin, SALL4, and weakly for EMA and BCL6. The rest are negative: CD35, CXCL13, CK20, CK7, CK5/6, p63, p40, CD4, CD1A, ALK, CD20, PAX5, CD3, BCL2, CD10, CD123, CD38, CD30, CD117, OCT3/4, PSA, PAX8, p16, PLAP, CD43, s100, MUM1, inhibin, HHV8 CD68, EBER. All molecular tests are unremarkable.
Conclusion: Fibroblastic reticular cell tumour (FRCT) is a rare tumour with 21 cases reported in the literature. FRCTs are characterized by cells arranged in a whorls, fascicles or sheets accompanied by lymphoplasmacytic infiltrate. FRCT shows overlapping morphological features with follicular dendritic cell sarcoma (FDCS) and interdigitating dendritic cell sarcoma (IDCS). Shows positivity for vimentin. Cytokeratin and EMA are often positive. FRCT should lack markers of FDCS (CD21 and CD35) and IDCS (S100). Metastatic carcinoma should be considered in the differential diagnosis.

E-PS-11-013
Sclerosing extramedullary hematopoietic tumour of gallbladder - a case report
I. Catalina-Fernandez*, N. Maira González, D. Corrales Mateo, A. Hens Perez, A. Caro Romero
*Hospital Universitario Puerto Real, Spain

Background & objectives: Sclerosing extramedullary hematopoietic tumour (SEMHT) was described by Beckman and Oehrle in 1982. It is an uncommon lesion associated with chronic myeloproliferative disorders, mainly chronic idiopathic myelofibrosis. SEMHT typically presents as retroperitoneal masses but it can occur in other organs.
Methods: We present a case of a 52-years old man with a medical history of post-polycythemia vera myelofibrosis and splenomegaly. During the follow-up of his disease, an abdominal computerized tomography revealed a gallbladder with a thickened wall. A cholecystectomy was performed with suspicion of carcinoma.
Results: Grossly, the surgical specimen was found to measure 11 x 6 cm. The luminal diameter of the gallbladder was decreased and a marked thickening of the wall with a multinodular appearance was identified. Histologically, the mucosa showed a chronic inflammatory infiltrate of the chorion. Most of the wall was replaced by a dense fibrous stroma with polymorphic cells including scattered large atypical cells, myeloid and erythroid precursors, lymphocytes, eosinophils and plasma cells. Immunohistochemically, the giant cells were positive for CD31 and CD61 and the granulocytic precursors were positive for myeloperoxidase. Numerous small cells positive for CD15 were also identified. Inmmunohistochemical staining for cytokeratin, desmin, ALK and CD34 yielded negative results.
Conclusion: SEMTH is a rare tumour-like condition generally associated with chronic myeloproliferative disorders that, as we can see, can affect the gallbladder. Morphologically, these tumours may be mistaken for sarcomas, carcinomas or another lymphoid malignancy, because of the presence of large atypical cells. The use of an adequate panel of antibodies and the awareness of clinical history is essential to prevent misdiagnosis.

E-PS-11-014
Fatal outcome in idiopathic multicentric Castleman disease with TAFRO syndrome: case report
M. Cerbu*, A. Birceanu, I.M. Mergeanu, T. Turcu, R.G. Grigore, G. Halcu
*University Emergency Hospital Bucharest, Romania

Background & objectives: TAFRO syndrome is a rare subtype of idiopathic multicentric Castleman disease characterized by thrombocytopenia, anasarca, myelofibrosis, renal dysfunction and organomegaly. Idiopathic multicentric Castleman disease is a benign lymphoproliferative disorder characterized by generalized lymphadenopathy, systemic inflammatory symptoms with organ dysfunction.
Methods: We report the case of a 56-year-old male who presented with enlarged lymph nodes (axilla, cervical, supraclavicular and inguinal), fever, thrombocytopenia, anaemia, hypoalbuminemia, pleural effusion, ascites and renal failure. Biopsy from the right axillary lymph nodes were sent to our department. The blocks were sectioned and stained with Haematoxylin–Eosin, and blank slides were cut for immunohistochemical stains.
Results: The lymph node had a disorganized architecture with frequent atrophic germinal centres (grade 3), focally showing slight hyperplasia of the mantle zone with an "onion skin" appearance and proliferation of blood vessels forming the so-called "lollipop lesion". CD20 and CD79a showed the B cell within the remnant follicles; pan T-cell markers (CD2, CD3, CD5 and CD7) showed regular expression in the T lymphocytes. CD21 and CD23 were positive in the meshwork of proliferative dendritic follicular cells. HHV8 was negative.
The patient's condition deterioreted rapidly, this episode being the second one in the last three months. Unfortunately, he became comatose, and a few days later, he succumbed to the disease.
Conclusion: TAFRO syndrome is a very rare subtype of Castleman's disease, which was described for the first time in 2010, with acute symptoms, rapid progression and fatal without urgent treatment.

Correct and prompt diagnosis is possible with a close collaboration between the clinician and pathologist, thus giving a better prognosis to these patients.

E-PS-11-015

Leukaemia cutis preceding circulating blastic-phase-spread in chronic myelomonocytic leukaemia: a case report

S. Charfi*, O. Boudaouara, I. Dammak, R. Mallek, H. Turki, T. Sellami Boudawara, L. Bouzidi
*Department of Pathology, Habib Bourguiba University Hospital, Sfax, Tunisia

Background & objectives: Leukaemia cutis (LC) is a rare occurrence in patients with chronic myelomonocytic leukaemia (CMML). The diagnosis is particularly challenging when CMML is priorly unknown. We aim through this report to outline the importance of interprofessional-teamwork in establishing the accurate diagnosis.
Methods: We report on a case of a LC revealing the diagnosis of a CMML, diagnosed in pathology, dermatology and haematology departments of Sfax Hospital.
Results: A 58-year-old man presented with a unique violaceous-plaque-like-lesion of the leg. The lesion grew rapidly in size within few weeks and became ulcerated. There was no lymph node enlargement at diagnosis. Skin-lesion-biopsy showed a dense dermal infiltrate composed of medium-sized blast-like cells. These cells expressed myeloid markers (i.e. myeloperoxidase, CD68 and CD33) and CD4 while CD56, B and T-cell-markers were negative. Given this myelomonoblastic dermal proliferation, further haematological investigations were conducted. A granulocytic hyperplasia with striking dysgranulopoiesis and less than 2% blasts were demonstrated in both peripheral-blood-smear-sample and bone-morrow-biopsy. These findings were consistent with the diagnosis of a LC revealing a CMML, with no acute leukaemic spread.
Conclusion: CMML is a haematological malignancy showing both features of myeloproliferative neoplasm and myelodysplastic syndrome. Once diagnosed in a patient with a CMML, LC might be the first sign of transformation to acute myeloid leukaemia and is associated with poor outcomes. Prior to leukaemic spread, LC may be misdiagnosed as a blastic plasmacytoid dendritic cell neoplasm, which shows the greatest overlap on histologic sections. Staining of tumour cells with myeloperoxidase favours the diagnosis of a LC.

E-PS-11-016

Piringer Kuchinka lymphadenitis: shall we go till histology to suggest the diagnosis of toxoplasmosis?

S. Charfi*, O. Boudaouara, L. Bouzidi, S. Makni, T. Sellami Boudawara, M. Bouhamed
*Department of Pathology, Habib Bourguiba University Hospital, Sfax, Tunisia

Background & objectives: Piringer-Kuchinka-lymphadenitis is one of the most common presentations of toxoplasmosis in immunocompetent-hosts. However, histology is rarely needed since diagnosis is usually achieved by serology. This report highlights the pathologist's role in suggesting the diagnosis of toxoplasmosis even if unsuspected clinically.
Methods: We report a case of an acquired toxoplasmosis revealed by a histologically-diagnosed-Piringer-Kuchinka-lymphadenitis in an immunocompetent-woman.
Results: A 24-year-old woman presented with a one-month-history of a mildly-painful non-tender lateral neck swelling. No general symptoms were reported. PET-scan showed hypermetabolic cervical lymph nodes. Fine needle lymph node aspirates found clusters of epithelioid histiocytes. Cervical adenectomy was subsequently accomplished. Histopathologic analysis of the lymph node revealed lymphoid follicular hyperplasia, monocytoid B-cell proliferation, and small non-necrotizing epithelioid microgranulomas. This histologic triad is characteristic of Piringer-Kuchinka lymphadenitis. Toxoplasmic serology, performed retrospectively, confirmed the diagnosis of an acute-acquired-toxoplasmosis. The patient recovered spontaneously within few weeks.
Conclusion: The histologic triad gathering reactive follicular hyperplasia, small clusters of epithelioid histiocytes and monocytoid-B-cells hyperplasia is definitional of Piringer-Kuchinka lymphadenitis. Even though not diagnostic of toxoplasmosis, it is considered highly suggestive of toxoplasmic infection. In fact, Piringer-Kuchinka lymphadenitis may be encountered in several infectious and neoplastic diseases. Thus, Toxoplasmic serology is needed to confirm the diagnosis as it is exceedingly rare to find toxoplasma cysts in histological specimens.

E-PS-11-017

Erdheim-Chester disease: about two cases and review of the literature

D. Chiba*, I. Bahri, S. Ben Tekaya, W. Mokni, N. Ouini, A. Benabdelkader, H. Hamchi, B. Sriha, M. Mokni
*Department of Pathology, Tunisia

Background & objectives: Erdheim-Chester disease(ECD) is a rare potentially fatal multiorgan myeloid neoplasm, occurring in adults. Clinical and radiological presentations aren't specific. Histological examination is essential for the diagnosis.
Methods: Two men diagnosed with ECD in our pathology department were retrospectively reviewed.
Patient1:
A 46-year-old man presented with hepato-splenomegaly and retroperitoneal adenopathy. He was explored by bone marrow biopsy.
Patient 2:
A 35-year-old man presented with nodular facial skin lesions. He had a biopsy for this lesion.
Results: Histological examination showed in these two cases xanthomatous and foam histiocytes infiltration with Touton giant cells, lymphoplasmacytic infiltrate, and surrounded by fibrosis. Necrosis was absent. The immunohistochemical study revealed positivity for CD68 and PS100 and negativity for CD1a. ECD was first described by William Chester and Jakob Erdheim in 1930 and reclassified by the World Health Organization as a hematopoietic neoplasm of histiocytic origin. It frequently affects adults in the fifth decade.
Conclusion: It is a systemic disease with frequent involvement of bone, retroperitoneum, nervous system, and lung. Clinical features depend on the site involvement. It is characterized by the accumulation of foamy macrophages, chronic inflammation, fibrosis, and organ failure. Histological examination with an immunohistochemical study is essential for the diagnosis and discrimination of differential diagnosis such as Langerhans cells histiocytosis, Rosai Dorfman disease, and reactive histiocytic proliferation.

E-PS-11-018

Indeterminate dendritic cell tumour: case report with literature review

D. Chiba*, S. Ben Tekaya, I. Bahri, W. Mokni, N. Ouini, A. Benabdelkader, B. Sriha, M. Mokni
*Department of Pathology, Tunisia

Background & objectives: Indeterminate dendritic cell tumour (IDCT) is an extremely rare neoplastic dendritic disorder that tends to be neglected in differential diagnosis. Its physiopathology, etiology, and prognostic features are poorly understood due to its rarity.
Methods: Herein, we report a case of a 79-year-old male patient, with a medical history of lichenified eczema, who presented with multiple axillary lymphadenopathies. A lymphadenectomy was performed.

Results: The microscopic examination of 3 lymph nodes showed the same histological aspect, with a histiocytic proliferation organized in clusters focally destroying the normal nodal architecture. These histiocytes were large, with pale eosinophilic cytoplasm. The nuclei were vesicular and reniform with small nucleoli. The background contained reactive lymphocytes plasma cells and melanin deposits but no eosinophilic infiltrate. There was no capsular rupture. Immunohistochemical study was performed, the tumour cells were diffusely positive for PS100 and CD1a and focal positive for CD163; they are negative for Langerin, CD68, CD23, CD21, CD117, Sox10, HMB45 and CK. The diagnostic of IDCT was retained.
Conclusion: To our best knowledge, approximately 102 cases have been documented in the literature. Generally, it is restricted to the skin or less common lymph nodes. Few other locations were reported. IDCT might be mistaken for Langerhans cell histiocytosis (LCH) due to their similar morphologic and immunohistochemical features. However, the negative immunostaining for Langerin and the ultrastructural lack of Birbeck granules in IDCT allow the distinction between them and avoid an overly aggressive treatment of an IDCT erroneously diagnosed as LCH.

E-PS-11-019
ALK positive histiocytic proliferation with a DCTN1::ALK fusion
Y. Choe*, D. Peker, M. Horwath, S. Gjorgova Gjeorgjievski
*Emory University Hospital School of Medicine, USA

Background & objectives: *ALK*-positive histiocytosis is a clinicopathologic spectrum of histiocytoses that occur in infants to young adults as a localized or multisystemic disease. The *ALK* expression by immunohistochemistry correlates with efficacy of *ALK* inhibitor therapy in patients with unresectable or disseminated disease.
Methods: A 10-month-old girl presented with a 4-month history of a red, firm scalp lesion that gradually increased to 1 cm in size. The lesion was excised and submitted for histopathologic evaluation, showing a dermal infiltrative spindle cell proliferation, with focal subcutaneous extension. The cells have abundant eosinophilic and granular cytoplasm, oval nuclei with finely granular chromatin pattern, and inconspicuous nucleoli.
Results: Mitotic activity and tumour necrosis were absent. By immunohistochemistry, the cells were positive for CD68, CD163, ALK, and EMA (focal). SMA, Desmin, S100, SOX10, CD30, CD34, CD1a, CD45, AFB, and GMS were negative. Next-generation-sequencing fusion panel identified a *DCTN1::ALK* fusion transcript. Differential diagnosis included epithelioid fibrous histiocytoma (EFH) and *ALK*-positive histiocytosis. EFH histologically is characterized by a well-circumscribed dermal epithelioid lesion with an epidermal collarette and exophytic growth, features absent in this case. Based on this, we favour this lesion to represent an *ALK*-positive histiocytosis with a rare *ALK* fusion partner, which is only the third case of *DCTN1::ALK* fusion reported, and the first in the infant demographic.
Conclusion: In infants with *ALK*-positive histiocytosis, hematologic and liver abnormalities are most common, compared to neurologic involvement in older patients. Localized proliferations commonly occur in bone, lungs, or skin as in this case. This patient did not express symptoms of systemic disease commonly reported in infants, and was treated with local excision without reported recurrence on 6 month follow up. Identification and evaluation of novel molecular targets remains important due to its implication on diagnosis and treatment.

E-PS-11-020
Plasmacytoid dendritic cells in breast implant-associated seroma fluid: a potential pitfall in workup for anaplastic large cell lymphoma
Y. Choe*, M. Horwath, D. Jaye, S. Asakrah, D. Peker
*Emory University Hospital School of Medicine, USA

Background & objectives: Breast seromas are a common late side effect of breast implant surgery, and may require aspiration to help exclude a malignant process In particular, it is important to exclude breast implant-associated anaplastic large cell lymphoma (BIA-ALCL), a rare T-cell neoplasm.
Methods: An otherwise healthy 30-year-old female with a history of placement of silicone breast implants 9 years prior presents with swelling and discomfort of the right breast. An MRI of the right breast was indeterminate for implant rupture. A 140 cc, cloudy orange fluid specimen was aspirated and cytospin, cell block, thin-prep, and flow cytometry analyses were performed.
Results: Cytomorphology was significant for a mixed population of abundant small lymphocytes, histiocytes, and occasional eosinophils. There were occasional larger lymphoid cells with eccentric nuclei and pale amphophilic to vacuolated cytoplasm. Immunohistochemical stains performed on the cell block revealed abundant CD3+ small T-cells which were mostly CD4+. The larger cells expressed CD4 and CD123 and were negative for CD56 and CD30, a marker for anaplastic large cells lymphoma. Flow cytometry immunophenotypic analysis revealed a distinct cell population (5%) that expresses CD4 (bright), CD36, CD38, CD123, HLA-DR (dim), and CD45 without expression of surface CD3, CD34, and CD56, characteristic of reactive plasmacytoid dendritic cells.
Conclusion: In this unusual case, an expanded population of reactive pDCs shared some phenotypic characteristics with BIA-ALCL (i.e. larger CD4+ cells negative for most lineage-specific markers). Additional immunophenotypic markers, especially CD30, CD123, and CD56, helped exclude BIA-ALCL as well as to exclude blastic plasmacytoid dendritic cell neoplasm (BPDCN). The finding of pDC-rich inflammation in breast-implant-associated seroma fluid has not been previously reported in the English literature, and awareness of this phenomenon may help avoid a potential diagnostic pitfall.

E-PS-11-021
Study of myeloid cell nuclear differentiation antigen (MNDA) in primary cutaneous marginal zone lymphoma and primary cutaneous follicular lymphoma
A. Córdoba*, I. Fernandez, A. De Oliveira, L. Ruiz, C. Llanos, D. Guerrero
*Hospital Universitario de Navarra, Spain

Background & objectives: Myeloid cell nuclear differentiation antigen (MNDA) is normally expressed on myelomonocytic cells and a subset of B lymphocytes. It was found to be differentially expressed between nodal marginal zone lymphoma (MZL) and follicular lymphoma (FL).
Methods: We want to test whether this difference in expression occurs in primary cutaneous marginal (13 cases) and follicular zone lymphomas (11 cases). All of them were therefore stained for MNDA by immunohistochemistry (IHC) and the results correlated with other clinicopathologic findings.
Results: We have observed that MNDA is expressed in all cases analysed in both MZL and FL. The positive lymphocytes are located around the reactive follicles or in the periphery of the nodules in MZL; and similarly in the periphery of the nodules that make up LF. The percentage of positive lymphocytes varies with higher expression in MZL (20%), while it does not exceed 5% in LF.
Conclusion: Differentiating PCMZL from PCFL is sometimes a challenge in dermatopathology. Previous studies have shown that MNDA can be useful in the differentiation of nodal MZL and FL. Some studies have shown that 61% to 95% of MALT lymphomas are MNDA+; however, the majority of FL are negative. We have analysed 24 cases of primary cutaneous lymphomas and observed MNDA expression in all of them. We observed a difference in the expression of 20% in PCMZL and 5% in PCFL.

E-PS-11-022

A case report of pyoderma gangrenosum as an initial cutaneous manifestation of multiple myeloma

M. Cristian*, K.M. Hebeda, A. Amir
*Center for Research and Development of the Morphological and Genetic Studies of Malignant Pathology - CEDMOG, "Ovidius" University of Constanta, Romania

Background & objectives: Multiple myeloma (MM) is a clonal plasma cell disorder in which a paraneoplastic syndrome with skin changes may be the initial presentation. We report a patient who presented initially with pyoderma gangrenosum, being subsequently diagnosed with MM.
Methods: A 66-year-old female with a clinical history of ductal carcinoma of the left breast and melanoma in situ of the left dorsal trunk, presented with two progressive, nonhealing, progressive ulcers on the right lower leg and the right forefoot with 3 months duration and pancytopenia. Screening for an underlying cause revealed increased IgA type kappa M-Protein, and an increased Kappa/Lambda ratio.
Results: Skin biopsy of lower right leg showed an epidermis without interface inflammation, exocytosis or spongiosis but with a dense neutrophilic infiltrate in the dermis with also areas of abscessation. No other morphological specific features and no demonstrable microorganisms. After excluding other causes of ulceration, a diagnosis of pyoderma gangrenosum was made. The bone marrow biopsy revealed diffusely increased kappa positive plasma cells, approximately 30% of the cellularity. Congo red stain was negative for amyloid. Immunoflowcytometry on the bone marrow aspirate identified a clone of plasma cells with expression of CD45- CD19- CD20-CD38++ VS38c+ CD138+ cytIgKappa+ cytIgA+, confirming the diagnosis of IgA positive plasma cell myeloma in combination with neutrophilic dermatosis.
Conclusion: Indeed, a strong association between IgA and neutrophilic dermatoses has been shown, probably in part related to the activation of neutrophils by the IgA receptors on their surface [1,2]. This case illustrates an additional dermatological manifestation as the presenting feature of plasma cell neoplasia, expanding the spectrum of the plasma cell neoplasms with associated paraneoplastic syndrome as defined by WHO5 [3].

E-PS-11-023

Blastic plasmacytoid dendritic cell neoplasm (BPDCN) – a diagnostic challenge

M. Cristian*, L. Șeicaru, R. Polimaru, G. Baltatescu, E. Calin, A. Caloian, L. Mazilu, S. Deacu
*Center for Research and Development of the Morphological and Genetic Studies of Malignant Pathology - CEDMOG, "Ovidius" University of Constanta, Romania

Background & objectives: BPDCN is a rare, aggressive haematological neoplasm consisting of immature cells with plasmacytoid dendritic cell differentiation, characterized by a high frequency of cutaneous involvement and systemic dissemination. The current report describes clinical and biological data focusing on morphology and immunophenotype.
Methods: We present a case of a 67-year-old male patient presenting with skin lesions, which vary in size, color and form multiple patches and plaques, that involve the head, the upper posterior thorax and lumbar region, followed by punch biopsies. The cutaneous specimens were morphologically evaluated and immunohistochemically stained.
Results: Histopathological examination revealed a diffuse monotonous infiltrate of medium-sized lymphocytes with immature blastic morphology, centred in the dermis with extension to subcutaneous tissue, while sparing of the epidermis and adnexal structures. Immunophenotypically, BPDCN cells are positive for pDC-associated markers, including CD123, plus CD4 and CD56 and, the absent expression of lymphoid or myeloid lineage markers, along with absence of CD34 expression and a high Ki-67 proliferation index, whereas specific markers (myeloperoxidase, CD19) were not expressed.
Conclusion: The diagnosis of BPDCN remains challenging for both clinicians and pathologists, since most will only encounter it once a year or less. Although the criteria are well defined by the WHO classification, its presentation is quite heterogeneous, and cytogenetics and mutation profiles are not specific. The current report highlights the critical importance of the prompt referral of the patient to a specialist and encourages the communication among the various specialists involved, in achieving the best possible outcomes for the patient.

E-PS-11-024

Unusual bone tumour: primary bone lymphoma, 3 case reports and literature review

H. Erdoğan*, N.S. Şeker
*Turkey

Background & objectives: Primary bone lymphoma is a rare neoplasia that affects only the skeletal system and consists of malignant lymphoid cells. Since this type of lymphoma is rare, it is not initially considered in the differential diagnosis.
Methods: Between 2010 and 2023, 30 cases diagnosed with bone lymphoma in our centre, and 3 cases were evaluated as primary bone lymphoma when evaluated with clinical data.
Results: Of the 3 cases we present, two are male and one is female. All our cases were B-cell lymphoma, and all but one were in the DLBCL category. When we look at case series and reviews in the literature, we see that T-cell lymphomas are very rare, and DLBCL is frequently observed among B-cell lymphomas. Morphologically, the cases have a high-grade appearance, and proliferation indexes are high. After diagnosis, the cases were followed up after R-CHOP treatment. No recurrence was detected in any of them.
Conclusion: Our aim with these case reports is to draw attention to this rare type of lymphoma and make it come to mind. Our longest follow-up case was 13 years, and during this period, no recurrence was detected, no matter how high-grade the lymphoma itself was. In these cases, multidisciplinary work is very important to confirm the diagnosis of primary bone lymphoma and is also very important for the prognosis of the patients.

E-PS-11-025

A novel JAK2 fusion in T-cell prolymphocytic leukemia

O.C. Eren*, R. Stuver, T. Zhou, M. Zaidinski, A.J. Moskowitz, S.M. Horwitz, M.D. Ewalt, Y. Zhang, M. Lim
*Memorial Sloan Kettering Cancer Center, Turkey

Background & objectives: T-cell prolymphocytic leukemia (T-PLL) is a rare and aggressive mature T-cell malignancy characterized by marked lymphocytosis, B symptoms, lymphadenopathy and hepatosplenomegaly. There is no standard treatment approach and in the absence of allogeneic transplant the prognosis remains poor.
Methods: Disease-defining cytogenetic abnormality in T-PLL is juxtaposition of the TCL1-family oncogene to the TCR gene enhancer locus. Application of next generation sequencing technologies led to the discovery of highly recurrent gain-of-function mutations in JAK1/3 and STAT5B in over 70% of T-PLL, providing opportunities for therapeutic intervention using small molecule inhibitors. However, additional genetic mechanisms contributing to disease pathogenesis remain unknown.
Results: Herein we describe the identification of a novel gene fusion SMCHD1::JAK2 resulting from a translocation between chromosome 9 and 18 involving SMCHD1 exon 45 and JAK2 exon 14 (t(9;18)(p24.1;p11.32)(chr9:g.5080171::chr18:g.2793269)), a previously

undescribed genetic event in a patient with T-PLL harboring the key disease defining inv(14) resulting in rearrangement of TCL1 and TRA/D.

Conclusion: In this report, we describe the distinct clinical and genetic features of the patient's disease course over a 24-month duration post-treatment using ruxolitinib (JAK 1/2 inhibitor) and duvelisib (selective PI3K gamma/delta inhibitor).

E-PS-11-026

Chronic myeloid leukemia presenting as extramedullary T- lymphoblastic crisis and extramedullary hematopoiesis

K.T. Galvis Castro*, D.L. Martinez Baquero, C.E. Saavedra Andrade, R.E. Andrade Perez, M.L. Romero Prieto
*Hospital Universitario Fundación Santa fe de Bogotá. Universidad de los Andes, Facultad de Medicina, Colombia

Background & objectives: Chronic myeloid leukemia (CML), BCR-ABL1-positive is a myeloproliferative neoplasm arising from hematopoietic stem cells with translocation t(9,22 (q34.1;q11.2). CML is usually present in a chronic phase followed by accelerated and/or blast-phase (BP) transformation.
Methods: A 29-year-old male presented with weight loss, soft tissue infection, generalized lymphadenopathy, hepatosplenomegaly, leukocytosis, and thrombocytosis. Cervical lymph node (LN) and bone marrow (BM) biopsies were submitted for evaluation.
Results: Flow cytometry of the LN revealed a predominant population of T lymphoblast expressing CD45+dim, nTdT+, cyMPO-, CD34+, CD56-, CD117-, CD7+, sCD3-, cyCD3+, CD4-, CD8-. Also, a small myeloblast population CD45+dim, CD34+, sCD3-, cyCD3-, CD7+, CD117+ was observed. LN setions showed architectural effacement with sheets of lymphoblast and areas of extramedullary hematopoiesis with abnormal hypolobulated megakaryocytes. BM biopsy was hypercellular with megakaryocytic and granulocytic expansion and mild reticulin fibrosis. By Flow cytometry 1% of myeloblast and 0.3% of T-lymphoblast was detected. Molecular analysis revealed BCR-ABL1 p210 transcript at 49%IS by PCR. FISH analysis in LN confirmed the presence of BCR-ABL1, with fusion signal observed at lymphoblast and extramedullary hematopoietic component.

Conclusion: T-lymphoblastic leukemia/lymphoma (T-ALL/LBL) presenting as BP of CML is rare, in most BP cases, the blast lineage is myeloid, and few cases of T-lymphoblastic transformation have been reported. In patients without history, its crisis may be challenging and of clinical relevance. In this case, the BCR-ABL(p210) positivity in the bone marrow and lymph node supports an undiagnosed CML, presenting with novo T-LBL. This case highlights the importance of broad tools for precise diagnosis in hematopathology.

E-PS-11-027

Composite lymphoma with a methacronic presentation showing the same clonal immunoglobulin heavy chain (IGH) gene rearrangements

K.T. Galvis Castro*, A. Rozo Cruz, M.A. Forero Rivera, M.L. Romero Prieto, R.E. Andrade Perez, C.E. Saavedra Andrade, D.L. Martinez Baquero
*Hospital Universitario Fundación Santa fe de Bogotá. Universidad de los Andes, Facultad de Medicina, Colombia

Background & objectives: Composite lymphoma, characterized by the coexistence of two distinct lymphomas within the same organ or tissue site, is rare and poses a complex diagnostic challenge. A monoclonal origin involving a common precursor cell undergoing divergent differentiation pathways has been described.

Methods: We present an unusual case of composite lymphoma. A 52-year-old male presented with abdominal pain, B-symptoms, and generalized lymphadenopathy. Radiologically, a large conglomerate of mesenteric lymphoid nodes, with retroperitoneal extension, was dominant. Despite treatment, disease progression occurred at two different times, prompting further investigation and subsequent diagnosis. All biopsies, multiple and from the same mesenteric location, underwent thorough evaluation
Results: The initial lymph node biopsy revealed architectural effacement by a nodular mixed inflammatory infiltrate, with scattered large and atypical cells, some exhibiting Reed-Sternberg morphology. Positive for CD30, PAX5(weak), and CD15(subset), and negative for CD20, LMP1 and CD3, leading to a diagnosis of classical HL, nodular sclerosis subtype. Subsequent biopsies, performed 5 months later, displayed a diffuse proliferation of medium to large lymphoid cells expressing CD20, CD10, BCL-6, BCL2, and c-MYC, with negativity for MUM1, CD30, and Ki-67 index of 95%. These findings were consistent with DLBCL with GC phenotype. A relapse occurred 10 months after, with new biopsies showed similar findings to the initial biopsy, confirming a relapse of cHL.

Conclusion: The PCR-B clonality testing performed on the last two biopsies revealed clonal rearrangements of IGH displaying identical clonal peaks, indicating a shared clonal origin. The coexistence of cHL and DLBCL in the same patient and anatomical site, with a metachronal presentation, represents an exceptional phenomenon with significant challenges. Further research into the molecular mechanisms underlying these lymphomas is warranted to advance understanding and improve patient outcomes.

E-PS-11-028

Hepatosplenic T-cell lymphoma diagnosis in a children through histopathology and flow cytometry - a case report

K.T. Galvis Castro*, M.A. Forero Rivera, A. Rozo Cruz, D.L. Martinez Baquero, M.L. Romero Prieto, C.E. Saavedra Andrade
*Hospital Universitario Fundación Santa fe de Bogotá. Universidad de los Andes, Facultad de Medicina, Colombia

Background & objectives: Hepatosplenic T-cell Lymphoma (HSTCL) is a rare, aggressive lymphoma, mainly impacting young adults. It presents extranodal involvement in the spleen, liver, and bone marrow, characterized by a proliferation of cytotoxic T cells, often of the gamma delta T-cell receptor type.
Methods: We report a paediatric case referred to our institution with clinical impression of refractory idiopathic thrombocytopenic purpura. An 11-year-old male presented with B-symptoms, abnormal bleeding, fever, hepatosplenomegaly (spleen 23cm), anemia, and severe thrombocytopenia. Treatment with steroids, antibiotics, and immunoglobulin yielded no response. Upon admission, a reassessment was performed, and a new bone marrow biopsy was conducted.
Results: Flow cytometry of BM aspirate demonstrated 14% of abnormal T cells expressing sCD3, TCRγδ, CD45, CD2 and CD16. They were negative for CD4, CD8, CD56, CD34 and CD30 and, exhibited loss of CD7 and CD5. The BM biopsy showed an extensive infiltration by a T lymphoid neoplasm with a sinusoidal pattern highlighted by CD3 staining. CD4, CD8, TDT, CD56, granzyme B stains were negative. The atypical lymphocytes displayed intermediate size, clear and agranular cytoplasm, inconspicuous nucleoli and irregular nuclear contours. Hematopoiesis was predominantly erythroid, with dyserythropoiesis. In situ hybridization analysis for EBER was negative.

Conclusion: The diagnosis of HSTCL is challenging because it is uncommon and rarely encountered in paediatric clinical practice. Here, we report one case from our hospital, highlighting its clinical and pathological features and emphasizing the significance of considering

the neoplasm in children with splenomegaly and cytopenia without lymphadenopathy. The typical immunophenotype and sinusoidal BM involvement in this case provided the criteria for the appropriate diagnosis.

E-PS-11-029

Blastic plasmacytoid dendritic cell neoplasm (BPDCN) as a development of chronic myelomonocytic leukaemia (CMML-1)

S. Gamba Torrez*, S. Rubio Mediavilla, A. Hogeboom Gimeno, T. Zudaire Fuertes, A. Esteban Figuerola, J. Alberdi Ballina, J.J. Sola Gallego
*Spain

Background & objectives: BPDCN is an aggressive haematological malignancy derived from plasmacytoid dendritic cells. It accounts for less than 1% of acute leukaemias and 0.7% of primary cutaneous lymphomas. Its relationship to other haematological malignancies is unclear.
Methods: An 80-year-old male with a history of untreated CMML-1 with monocyte phenotypic aberrancies (CD56+, HLA-DR+/-) presented with acute onset dyspnoea and a truncal erythematous macular eruption. Laboratory tests, peripheral blood smear, skin biopsy and bone marrow aspirate (BMA) with subsequent next generation sequencing (NGS) were carried out.
Results: Immunophenotype of peripheral blood showed 56% of blastoid morphology cells positive for HLA-DR, CD123, CD4, CD7, CD38, CD9 (50%), CD56 (50%), CD45 (low), NG2 and CD33 (dim). They were negative for CD34, MPO, CD117, CD19, CD3, CD13, CD11, CD15, and CD203. This was similar to the immunophenotype observed in BMA.
Skin biopsy showed a diffuse lymphoid proliferation occupying the superficial dermis and subcutis, consisting of monomorphic intermediate-sized blastoid cells. The epidermis was spared. Immunohistochemistry (IHC) revealed positivity for CD123, TdT, CD56, CD4, CD43 and BCL2 and negativity for CD3, CD20, CD34 and CD117. Ki67 was 70%. NGS detected a clonal linkage of LMMC-1 and BPDCN.

Conclusion: BPDCN may present as isolated disease (80%) or in association with other myeloid neoplasms, including myelodysplastic syndromes and CMML (20%). The nature of the relationship between BPDCN and underlying myeloid neoplasms is unclear. In the present case, the clonal linkage evidenced between BPDCN and CMML-1 may be indicative of disease progression rather than a secondary development. Furthermore, BPDCN should be differentiated from mature plasmacytoid dendritic cell proliferation, which characteristically shows CD56 negativity.

E-PS-11-030

CD30 negaive T-cell lymphoma with ALK rearrangements: a first case of CD30 negative ALK positive anaplastic large cell lymphoma?

J. García-Gómez*, A. Muñoz, G.A. Martín-Small, K. Matute-Molina, A. Martín Franco, L. Varo Navarro, C. Sanz, A. Hernández, J.L. Mate, G. Tapia
*Hospital Universitari Germans Trias i Pujol, Spain

Background & objectives: ALK-positive anaplastic large cell lymphoma (ALCL) is a mature T-cell lymphoma with ALK gene rearrangements and mandatory expression of CD30. It is a rare disease representing 10-15% of non-Hodgkin's lymphomas in children and 3% in adults.
Methods: We present a case of a 50-year-old woman who presented a soft tissue mass in the right psoas and pectineal muscles, associated with massive edema in the right leg. PET-TC showed the mass to be hypermatobolic, and several lymphadenopaties in the right inguinal region and retroperitoneum. A trucut-biopsy of the muscular mass and inguinal lymph node were performed.
Results: Hematoxylin-eosin sections showed a proliferation of discohesive neoplastic cells infiltrating the muscle, and the lymph node, the latter with a sinusoidal pattern. In the immunohistochemistal study, the cells were diffusely positive for CK CAM5.2 and ALK1, weakly positive for CD45, CD43 and CD4, and negative for other queratins, lymphoid markers (CD3, CD2, CD20, CD79a) and EBERs. Importantly, CD30 was negative in both biopsies, performed with Roche and Dako plattforms.
FISH confirmed ALK translocation, and the study of TCR-gamma and TCR-beta chains found a clonal rearrangement. The IgH and IgK chains were non-clonal.
A NGS panel (Oncomine Comprehensive Assay) was performed, detecting NPM1::ALK fusion, and mutacions in SETD2 and NOTCH1 genes.

Conclusion: This is a unique case of ALK-rearranged T-cell lymphoma, consistent with ALCL, However, as CD30 expression is considered mandatory, a definite diagnosis of ALCL could not be provided. As far as we know, this is the first case of ALK-rearranged, CD30 negative T cell lymphoma described.

E-PS-11-031

T-Cell lymphoma with CD20 expression and presence of Reed-Sternberg cells: a unique and challenging case

B. Garzón*, M. Villar Espada, M.D. Suárez Sánchez, L. Pérez Ortega, J.J. Borrero Martín
*Juan Ramón Jiménez University Hospital (Huelva), Spain

Background & objectives: Peripheral T-cell lymphomas (PTLC) are complex. The immunophenotype may be ambiguous, existing examples with aberrant expression of CD20 so molecular studies are necessary. Cases of PTLC have been observed with Reed-Sternberg-like cells. This case highlights potential pitfalls in diagnosis.
Methods: 43-year-old female, under observation for neutropenia and the presence of pathological cervical lymphadenopathy, with suspicion of lymphoproliferative syndrome. Paraffin sections of the lymph node were studied using conventional staining techniques as well as immunohistochemistry to characterize the lymphoid populations in our sample. Additionally, flow cytometry and molecular studies were conducted.
Results: The studied sections revealed a blurred architecture consisting of medium-sized cells, areas of necrosis and a larger-sized population with Hodgkin-like morphology. Immunohistochemical analysis demonstrated expression of both T (CD2+/CD3+/CD5+/CD7+/PD1+) and B (CD20+) antigens in the neoplastic population, showing an alpha-beta T phenotype without loss of pan-Ts (CD8+/CD4-). No helper markers expression were observed. The large-sized population was CD30+/EBER+/PAX5+ weak nuclear, confirming its Hodgkin nature. The proliferative index was estimated at 15%. Molecular analysis revealed a clonal TCRG rearrangement. Flow cytometry revealed a T phenotype with partial expression of CD20. Final diagnosis was a CD8+/CD20+ alpha-beta peripheral T-cell lymphoma with Reed-Sternberg-like cells, without reaching a complete histological picture of Hodgkin lymphoma.

Conclusion: Peripheral T-cell lymphomas (PTCL) with aberrant CD20 expression and Reed-Sternberg-like cells present a significant diagnostic challenge, as they can be mistaken for Hodgkin lymphoma. The importance of flow citometry, molecular and immunohistochemical

studies for accurate identification is highlighted. This case underscores the complexity in evaluating and classifying PTCLs, emphasizing the need for a comprehensive approach to ensure appropriate clinical management and determination of effective therapeutic strategies.

E-PS-11-032
Kimura's disease: a case report
M.A. Gil Galvín*, M. Veras Lista, E. Revilla Sanchez
*Hospital 12 de Octubre, Spain

Background & objectives: We describe the case of a 53-year-old man from China with a clinical presentation of pruritus, urticarial skin lesions and peripheral blood eosinophilia. The CT scan reveals inguinal lymphadenopathies, and a core needle biopsy of the largest one were done.
Methods: After fixation in formalin and embedding in paraffin, we analysed histological sections stained with hematoxylin and eosin, as well as additional immunohistochemical study and molecular clonality analysis. A literature search was conducted for published cases up to the present date.
Results: In the histological sections, the lymph node showed hyperplastic follicles with reactive germinal centers surrounded by mantle zones. The paracortex was expanded due to an infiltrate mainly composed of non-atypical eosinophils, which converge to form large aggregates and microabscesses. There was a proliferation of high endothelial venules. There are no signs of lymphoproliferative process. The immunohistochemical study showed a conserved distribution of B and T cells. Eosinophils stained positive for MNDA and CD15. The study of T cell receptor (TCR) and immunoglobulin heavy chain (IgH) clonality reported polyclonal results.
Conclusion: The findings suggests, firstly, Kimura's disease, a rare entity considered a chronic inflammatory disease of unknown cause. It is more common in middle-aged asian males and typically presents as a solitary mass, although it can also present with generalized lymphadenopathy. It is associated with eosinophilia, increased IgE and acute-phase reactants in peripheral blood. It is an indolent process evolving over years. Treatment involves surgical excision, which may be accompanied by radiotherapy, corticosteroids, immunosuppressants or targeted therapy.

E-PS-11-033
Variants of unknown significance: are they the answer to the clinicopathologic evolution of plasma cell neoplasias?
C.A. Gomez Gonzalez*, M. Hekimgil, N. Ozsan, A. Gunes, N. Soyer, S.D. Bozer, B. Durmaz, H. Akin, M. Tobu, D. Demir
*Department of Pathology, Ege University Faculty of Medicine, Turkey

Background & objectives: Plasma cell neoplasms, predominantly multiple myeloma (MM),manifest a broad clinical spectrum. Understanding molecular profiles,including variants of unknown significance(VUS),could enhance risk stratification and personalized treatment.This study aims to elucidate the clinical implications of genetic variants in the evolution of plasma cell neoplasias.
Methods: Retrospectively, patients with NGS evaluation and biopsy diagnosed with MM and plasmacytoma were included between 2023-2024. Demographic information, laboratory values, treatment, clinical evolution,and survival were recorded. Bone marrow biopsy findings as cellularity, percentage and morphology of plasma cells, bone marrow description,and immunohistochemical profile were evaluated. Genetical findings (FISH, karyotype), NGS analysis (DNA/RNA based-NGS), pathogenic variants,and variants of unknown significance(VUS) were recorded.
Results: Twenty cases were analysed male:female distribution was 11:9; the median age of presentation was 62.6 years-old. MM group consisted of 18 cases, within this group concurrent diagnosis of amyloidosis (n=4), and chronic lymphocytic leukemia (n=1); the two remaining cases only presented plasmacytoma. The average plasma cell percentage was 30%, kappa:lambda light chain=12:8; IgG, IgA, and only light-chain cases 14, 2 and 4, respectively. We identified two cases with del17p and one case with del17p and del1p (high-risk MM). Pathogenic variants in the MM group involved KRAS, KLF2, NRAS, and ETV6; in plasmacytoma EVT6. The spectrum of likely pathogenic variants was wider, including JAK2, CTLA4, CDKN2A, TET2, DNMT3A, NOTCH1, and IKZF1 genes.
Conclusion: The NGS analysis identified VUS numbers over 50, affecting genes located in 17 different chromosomes, with the most common VUS being on chromosomes 9, 19, and 11, respectively. The molecular landscape of MM is remarkably diverse. The clinical significance of mutations of unknown significance—potentially influencing treatment response and progression to secondary malignancies—is underscored by global genomic instability. Addressing this complexity necessitates rigorous pathology-molecular correlations, presenting critical challenges for advancing patient care.

E-PS-11-034
The importance of histopathological features of bone marrow aspirate smear and trephine biopsy in myelodysplastic sendrome
I. Guvendir Bakkaloglu*, I.E. Zemheri, A.H. Kaya, E. Kilicaslan
*Kartal Dr. Lütfi Kırdar City Hospital, Department of Pathology, Turkey

Background & objectives: Examination of bone marrow(BM) aspiration and biopsy can provide clues for prognosis of Myelodysplastic Syndrome(MDS).Our aim is to reveal detailed histomorphological features,to investigate the superior tecnique for the exact blast count and to indicate importance of the microenvironment in MDS.
Methods: The diversity of dysplasia, and their relationship with cytogenetic mutations and overall (OS) were examined. Blast rate in aspiration were compared with CD34 and CD117 positivity in biopsy. Microvessel density (MVD) and abnormal localization of immature progenitors (ALIP) were evaluated. The effects of histomorphological findings and clinical parameters on OS and prognosis were interpreted.
Results: In 130 (93.5%) of 139 cases, aspiration slides were evaluated and detailed dysplasia diversity was examined.By regression analysis, presence of hyperlobulation in megakaryocytic series (p:0.014, odds ratio:3.485 (confidence interval: 1.289-9.424)) and presence of ALIP(p:0.010, odds ratio:2.206 (confidence interval: 1.210) -4.020)) were significantly associated with poor prognosis.Aspiration blast rate correlates with CD34 and CD117 in the biopsy (p<0.001, <0.001, respectively).Amongst microenvironmental cells, while CD3 T lymphocytes and CD61 megakaryocytes increases,survival time is significantly getting shorter (p: 0.003, 0.003, respectively).In addition, an increase in MVD was found to be associated with poor prognosis (p: <0.001). When these parameters were analysed by multiple regression analysis,the most significant was MVD among them (p: <0.014).
Conclusion: The detailed diversity of dysplasia in the BM may provide clues in the diagnosis and OS in MDS. ALIP and MVD can be included in the hematopathology reports of patients. Moreover, these parameters can provide important information about the course of the disease as well as contributing to the diagnosis.

E-PS-11-035
Pathohistological and clinical correlation in patients with multiple myeloma
S. Ivić*, I. Stanišić, Z. Milić, V. Trivunović, J. Baljak, T. Lakić
*Faculty of Medicine Novi Sad, University of Novi Sad, Serbia

Background & objectives: Multiple myeloma is a malignant immunoproliferative disease mainly characterized by clonal proliferation and accumulation of pathologically plasma cells in the bone marrow. Our

goal was to assess the correlation between the pathohistological finding and the clinical presentation of the disease.
Methods: Retrospective study conducted at University clinical centre of Vojvodina in Novi Sad, Serbia that evaluated a total of 166 patients diagnosed with multiple myeloma following a pathohistological examination of bone marrow biopsies, during the six year period (2018-2023). Archival medical documentation from Center of pathology and histology were analysed.
Results: Multiple myeloma occurs more often in elderly population (mean age 62) and men (53%). Mean value of bone marrow infiltration with atypical plasma cells was 53%, while atypical kappa monoclonal plasmacytic proliferation was detected in most cases (58%). Most patient were diagnosed in 3rd stage of disease, using ISS (54%) and Durie-Salmon staging system (60%). Osteolitic lesions were detected in 64%, presence od light chains in urine in 74%, and renal insufficiency in 35% of patients. A correlations were found between the percentage of bone marrow infiltration and the Durie-Salmon stage of the disease (+0.27), anaemia (-0.37), M-protein (+0.20) and beta-2 microglobulin values (+0.22), but were not proven statisticaly significant.
Conclusion: Multiple myeloma is a disease that affects older population, mostly in 6th and 7th decade of life. Men are slightly more affected than females. Most of the patients are diagnosed in the third stage of the disease, no matter which staging system is being used. Although not proven statistically significant, a higher percentage of bone marrow infiltration by monoclonal plasma cells is associated with a more severe clinical picture and a higher stage of the disease in multiple myeloma patients.

E-PS-11-036
Follicular lymphoma of the ocular adnexa: a clinicopathological study of 15 cases
B. Kaliullayev*, J. Martinez, P. López, N. Fullana, M. Cortés, M. Gomà Gallego, M. Abia, H. Iliev, M.J. Paúles, J. Azcarate, J. Bosch, F. Climent
*Hospital Universitari de Bellvitge, Spain

Background & objectives: Follicular Lymphoma [FL] of the Ocular Adnexa [OA] accounts for up to 23% of OA lymphomas and may be primary or secondary; the former ones have not been widely studied lacking, among others, data on their genetic profile.
Methods: We searched for cases of FL involving the OA from January 2008 to March 2024. Clinicopathological and diagnostic data, including next-generation sequencing [NGS] results were collected and retrospectively analysed.
Results: Fifteen patients were identified; eleven of them were female. The median age was 65 years (range: 35-82). Ten (66%) presented the eye involvement [EI] at the time of diagnosis, and five (50%) of them had primary lymphoma (Stage IE Ann-Arbor). The other five (5/15, 33%) presented EI during a relapse of the FL. The growth pattern of lymphoma of those ten cases was diffuse (2), nodular and diffuse (1) and nodular (6). Immunohistochemically, eight cases were CD10+, six CD23+ and nine BCL2+. FISH detected BCL2 rearrangement [BCL2-R] in four cases; other four were BCL2-R-negative. In BCL2-R-negative cases, NGS revealed mutations in TNFRSF14, TNFAIP3, KMT2D, CREBBP, FOXO1, EP300 and SOCS1 genes.
Conclusion: EI as the initial clinical presentation of FL occurs in 66% of our series, and 50% of them correspond to primary FL of the OA. The current case series complements the existing scarce data on extranodal and OA FL lacking BCL2-R, yet demonstrating its genetic diversity involving mutations in STAT6-different genes, such as TNFRSF14, TNFAIP3, KMT2D, CREBBP, FOXO1, EP300 and SOCS1.

E-PS-11-037
Tissue involvement followed by exsanguination - an unexpected complication of chronic lymphocytic leukemia
S. Khan*, H. Sanchez
*Yale University, USA

Background & objectives: Chronic lymphocytic leukemia (CLL) is regarded as an indolent disease with a course most associated with comorbidity rather than acute fatality. This study sought to investigate both in-house and literature cases of tissue infiltration by CLL leading to fatal hemorrhage.
Methods: Analysis of in-house autopsy records going back over two decades revealed approximately thirty cases of hemorrhage due to CLL related blood dyscrasia. We focused on identifying exsanguination cases with direct causality. Exclusion Criteria: Cases that lacked histologic slides for assessment, DLBCL transformation and cases that did not overtly describe CLL as a major contributing factor in the cause of death.
Results: Extensive search of in-house autopsy cases where CLL was directly implicated in the cause of death yielded three definitive cases of exsanguination. Tissue infiltration and compromise was histologically confirmed by reviewing the slides. Immunohistochemical work-up demonstrated that the neoplastic hematologic process observed in these three fatal cases were indeed typical CLL. Of the three cases, two of the fatal hemorrhage events occurred spontaneously and one occurred intraoperatively as a procedural complication. Our study found that superimposed focal tissue infection may have contributed to the intraoperative death. This association was not clearly evident in the other cases. The haemorrhages were pulmonary and intestinal in origin, echoing many of the literature findings.
Conclusion: CLL is clearly capable of causing compromise to tissue integrity although exact mechanisms are yet to be elucidated. Exploration of this type of morbidity and its potential to cause death via acute exsanguination may have significant clinical implications. Literature search has revealed numerous instances of spontaneous hemorrhage of tissue involved by CLL although predisposing factors and associated clinical outcomes are not often specified. Our findings suggest the fatal potential of CLL may be underrepresented in the pathophysiology of the disease.

E-PS-11-038
Anaplastic lymphoma kinase (ALK)-positive histiocytosis with ALK-EML4 fusion – presentation as a pulmonary lesion
O. Kuczkiewicz-Siemion*, M. Ruskań-Bakun, K. Seliga, A. Tysarowski, P. Wołoszyn, D. Pierzchała, A. Wojewódzka, A. Szumera-Ciećkiewicz
*Department of Pathology, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland

Background & objectives: ALK-positive histiocytosis is a rare entity. It was recently considered a separate condition from other histiocytosis characterized by positive immunostaining for ALK and recurrent KIF5B-ALK gene fusion. The less common partner genes include CLTC, TPM3, TFG, EML4, DCTN1, COL1A2, TRIM33.
Methods: We present a 37-year-old female referred to our Institute for histopathological consultation. The patient presented with a polypoid/nodular lesion in the right upper lobe bronchus suspected of pulmonary endometriosis. A histopathological, immunohistochemical, and molecular assessment was performed.
Results: The lesion comprised spindle-shaped cells with slight cytological atypia without visible mitotic figures or necrosis. Immunohistochemical profile of the lesion showed: CD68(+), CD163(-/+) weak, BRAF(-), Langenin(-), ALK1(+), CD10(+), Vimentin(+), CD4(+/-) weaker than on lymphocytes T, LCA/CD45(-/+), CD14(-/+), ER(-), PGR(-), HBME(-/+), Calretinin(-/+), Mesothelia(-), S100(-), SOX10(-), MelanA(-), CD30(-), CD25(-), CD3(-), CD20(-), CD1a(-), CD34(-), CD31(-), ERG(-), SMA(-), Desmina(-), CK Pan(-), CK5/6(-), p63(-), EMA(-), TTF1(-), Bcl-2(-), WT1(-), STAT6(-), CD117(-), EBER(-), Ki67(+) low (1-3%). Molecular assessment by Targeted Next Generation Sequencing using the FusionPlex Comprehensive Thyroid and Lung (CTL) KIT (ArcherDx) detected in-frame fusion: [NM_004304.4]:ALK [20] - [NM_019063.4]:EML4 [2].

Conclusion: The microscopic image, together with the results of immunohistochemical and molecular evaluation, confirms the diagnosis of ALK-positive histiocytosis. The reported case with ALK-EML4 rearrangement seems preferentially documented in lung location, as other reported cases so far have been confirmed.

E-PS-11-039
CD5-negative and CD10-positive mantle cell lymphoma: a clinicopathologic and gene expression study
S. Li*, J. Xu
*MD Anderson Cancer Center, USA

Background & objectives: Mantle cell lymphoma (MCL) is typically CD5+, CD10- and with CCND1::IGH. CD5-/CD10+ MCL cases are exceedingly rare but may pose significant diagnostic challenges. It is unclear if these cases are MCL with germinal centre origin.
Methods: We analysed 10 cases of CD5-/CD10+ MCL with CD5 and CD10 expression assessed by immunohistochemistry (IHC) and/or flow cytometry (FC). CCND1::IGH was detected by Fluorescence in situ hybridization (FISH). Targeted RNA -Sequencing for B cell lymphoma analysis was performed in 3 cases. Clinicopathologic features and outcomes were extracted from electronic medical records.
Results: Three cases were diagnosed in lymph nodes and the other 7 in extranodal sites. Eight of 8 (89%) patients presented with high stage disease with frequent extranodal involvement. Eight cases were blastoid and 2 were classical MCL. All cases were positive for cyclin D1 and CCND1::IGH. 57% cases were positive for SOX11, and Ki-67 proliferation rate was ≥30% in 7/9 (78%). After rituximab-based immunochemotherapy, 7 (7/9, 78%) patients achieved complete remission. After a median follow up of 165 months (range 1-229 months), 5 (50%) patients died. The median overall survival was 71 months. All 3 cases undergoing for RNA-seq showed a gene expression signature in between GCB and ABC subtypes.
Conclusion: CD5-/CD10+ MCL cases frequently have blastoid morphology, a high proliferation rate and extranodal involvement. Although these cases are CD10 positive, gene expression profile showed they do not have a GCB gene expression signature. Their unusual immunophenotype makes it critical to distinguish these tumours from follicular lymphoma, high-grade B-cell lymphoma or diffuse large B cell lymphoma. A complete workup, especially immunohistochemistry for cyclin D1 and SOX11 and FISH for CCND1::IGH, is important for reaching the correct diagnosis.

E-PS-11-040
The impact of molecular testing on Large B-cell lymphomas in a regional referral centre
R. Lockhart*, L. McKenna, O. O'Brien
*Beaumont Hospital, Dublin, Ireland

Background & objectives: Large B-cell lymphomas are heterogenous - while DLBCL, NOS is most common, molecular analysis to exclude MYC, BCL2 and BCL6 rearrangements is required. Currently, cases for molecular analysis are sent off-site. This audit aims to assess the impact on diagnosis.
Methods: A keyword search was performed on the laboratory IT system "WinPath" for all cases over a five year period. Cases for MDT review only, other histological lymphoma diagnosis and recurrences were excluded. Reports were then analysed for histological diagnosis, presence of rearrangements and final diagnosis. Turnaround times to initial diagnosis and final molecular diagnosis were calculated.
Results: In total, 132 cases were identified over the 5-year period. Of these, 57% were sent for NGS. 13% of cases were subsequently diagnosed with High-grade B-cell lymphoma with MYC and BCL2 and/or BCL6 rearrangements (9 "double hit", 1 "triple hit").
The RCPath recommends an average of 10-14 days for initial lymphoma diagnosis. The total average turnaround time for these cases was 37 days from day of receipt of case to the final molecular report. The initial morphological and histological report had an average turnaround of 17 days from receipt. There was a turnaround time of 20 days for molecular reports from being sent off-site to publication of the final report.
Conclusion: This data shows that the incidence of "double/triple hit" lymphoma is in line with other studies. As these categories have significant prognostic implications for patients, optimising turnaround times is essential. This audit shows prolonged turnaround times both for the initial and molecular report. Lymphoma NGS is being introduced to allow for timely reporting. In addition, outside institutions will be asked to send relevant blocks upfront as required. This will be re-audited 12 months after the implementation of these changes.

E-PS-11-041
Kikuchi Fujimoto and COVID-19
A. López Prieto*, J. Machuca Aguado, R. Rendon, J.L. Villar, J.J. Ríos
*Spain

Background & objectives: The Kikuchi-Fujimoto disease (KF) is a rare self-limiting subacute necrotizing lymphadenopathy usually associated with fever. Currently, the etiopathogenesis of KF remains unknown. We have collected 3 cases, all of them women, in our centre during the period between 2020-2023.
Methods: The patients were between 21-30 years old and presented with unilateral cervical lymphadenopathy accompanied by B symptoms. They were diagnosed with COVID-19 infection two months prior. Excision of the cervical lymph node was performed. Sections stained with hematoxylin-eosin were studied, and the antibody CD123 and others were used. Additionally, in situ hybridization for EBV and PCR for COVID-19 were conducted.
Results: Macroscopically, they consisted of whitish nodular formations measuring 2.5 cm in diameter. Histologically, it was a lymph node with clear areas of precise boundaries, located in the subcapsular and paracortical regions. They were composed of a heterogeneous cellular population with karyorrhectic remnants and areas of necrosis, without polymorphonuclear cells. In these areas, the predominant cells had abundant vacuolated clear cytoplasm and an irregular nucleus with a crescent shape. Additionally, there were large activated lymphoid cells and a third type of CD123-positive cells in aggregates corresponding to plasmacytoid dendritic cells. The rest of the lymph node maintained a preserved architecture. In situ hybridization for EBV and PCR for COVID-19 were negative.
Conclusion: The two main etiopathogenic theories of Kikuchi-Fujimoto disease involve infectious and autoimmune factors. It is postulated that this condition may arise as a result of an exaggerated immune response by T cells to viral antigens in genetically susceptible individuals. The temporal relationship between COVID-19 infection and the onset of Kikuchi-Fujimoto disease, supported by observed findings and existing literature, suggests a potential causal relationship.

E-PS-11-042
Clinicopathological analysis of splenectomy's role in splenic lymphoma management: a two-decade retrospective study
V. Macarrón*, M.A. Abad, M. De Uribe Viloria, E. García Fernandez, G. Olmedilla
*La Paz University Hospital, Spain

Background & objectives: The spleen can serve as a location for primary or secondary involvement by lymphomas. Splenectomy has been an optional treatment but has decreased in the past years. Our study investigates the therapeutic role of splenectomy for lymphomas involving the spleen.

Methods: We have documented all splenectomies performed due to a splenic lymphoma at our hospital in the past 20 years. We searched for the following features in patients' medical records: age, gender, intervention date, symptoms, histological diagnosis, place of initial diagnosis, bone marrow status, clinical stage, primary/secondary origin, additional treatments, and clinical evolution.
Results: Among the 55 cases identified, only 7 (12,7%) occurred within the past 5 years. The mean age was 60,4 years and 58,2% were men. B symptoms and cytopenia were present in 30,4% and 39,1% respectively. In 49% of cases, bone marrow was affected. Stage IV was the most prevalent (60%). B lymphomas constituted 90% of the cases, being marginal zone lymphoma the most prevalent histology (30,1%). 67,2% were primary cases. Twenty patients received neoadjuvant chemotherapy, showing histologic response in 100% of high-grade lymphomas and in 20% of low-grade ones. In total, 37 patients received any chemotherapy (64,8% achieved complete response) while 17 patients did not (41,7% achieved complete response).
Conclusion: The decline in splenectomy rates reflects the advancement in new treatments approaches and highlights its modest oncologic results. Furthermore, chemotherapy response is highly variable among different types of lymphoma, with high-grade B lymphomas being the most benefited. However, combining splenectomy with neoadjuvant or adjuvant chemotherapy increases complete response rates. In conclusion, splenectomy should be considered as an alternative for the treatment of these patients, emphasizing the importance of individualized care.

E-PS-11-043
Unveiling the MYD88 V217F mutation: a diagnostic challenge in low-grade B-cell lymphomas with plasmacytic differentiation
J. Machuca Aguado*, F.J. Diaz de la Pinta, M. Quintero, R. Manso Alonso, J.C. Caballero Hernáez, R.N. Salgado Sánchez, S.M. Rodríguez-Pinilla
*Virgen Macarena University Hospital

Background & objectives: Low-grade B-cell lymphomas with plasmacytic differentiation comprise lymphoplasmacytic lymphoma (LPL) and splenic marginal zone lymphoma (SMZL) usually involving bone marrow and requering differential diagnosis. Previously, MYD88 V217F mutation has been sparsely reported in 2 LPL cases and 6 SMZL cases.
Methods: Morphological and immunohistochemical analysis of two bone marrow biopsies was conducted. We also reviewed clinical, molecular and cytogenetic findings for integrated diagnosis. Next generation sequencing (NGS, Ilumina Next Seq) study was performed in bone marrow material of both cases. In second case, cytogenetic analysis was performed after cell culture together with FISH studies for 6q deletion and 17p deletion (TP53).
Results: First patient is a 57-year-old male presenting IgG monoclonal peak of 2.5 g/dl, lymphadenopathy and splenomegaly. Second patient is an 81-year-old female with IgG monoclonal peak of 4.3 g/dl, lacking other symptoms.
Bone marrow of both revealed intrasinusoidal and intertrabecular infiltrates forming follicles of CD20+/MNDA+ B-cells and lambda-restricted plasma cells around these follicles, preserving FDCs meshwork with CD23.
In first case NGS study identified pathogenic mutations at MYD88 (V217F) and CCND3. Additional studies could not be performed due to lack of material, so it was considered suggestive of SMZL. At second case, cytogenetic analysis did not detect any alteration and NGS identified MYD88 (V217F) and CXCR4 mutations, favouring LPL diagnosis.
Conclusion: MYD88 L256P is present in 90% of LPL, although it may occur in SMZL. Other MYD88 mutations have been identified in both entities, including V217F, lacking specific details of these cases. We analyse for first time 2 cases of B-cell lymphomas with plasmocytic differentiation carrying V217F mutation, both being IgG-lambda restricted and presenting a SMZL-like pattern of bone marrow infiltration. We emphasize that these may pose a diagnostic challenge, requiring integrating clinical, morphological, cytogenetic and molecular data for definitive diagnosis.

E-PS-11-044
Myeloid sarcoma (MS) presenting as skin tumour in paediatric acute myeloid leukemia (AML)
J. Madeira*, S. Reis, R. Pina
*Pathology department, Hospitais da Universidade de Coimbra, Unidade Local de Saúde de Coimbra, Portugal

Background & objectives: MS is a rare extramedullary tumour composed of myeloid blasts, with or without maturation, reported in 2–9% of patients with AML. Rarely, MS can precede the onset of AML. Skin and orbits are the most common sites in childhood.
Methods: Male patient, 2-months-old, admitted to the Paediatric Unit due to vomiting and irritability. The laboratory tests results were for white blood cells 10.2×109/L, hemoglobin 6.4g/dL, and platelets 77×109/L. On the physical examination, an exuberant edema of the right hand and multiple nodular lesions in both forearms were observed, with redness and pain, hard-elastic consistency, measuring approximately 1cm in diameter.
Results: A biopsy of the skin lesions was performed and revealed a mass in the dermis and hypodermis that diffusely replaced the tissue architecture. The neoplastic cells were mid to large, with scant and pale cytoplasm, round to oval or folded nuclei, and blastic chromatin. The mitotic figures were numerous. Immunohistochemistry: diffuse CD45, CD43, lysozyme and CD4, focal myeloperoxidase and glycophorin A, and negative CD117 and CD34. The diagnosis of MS was made. Subsequent studies revealed AML with t(8;21)(q22;q22.1), a balanced translocation that results in the fusion of RUNX1 and RUNX1T1, established by real time PCR. The patient is undergoing chemotherapy according to the CHIP-AML22 protocol, despite having no leukemia.
Conclusion: MS can occur at any age (median age: 46-59-years) with a slight male predominance. The clinical manifestations are diverse, and depend on whether the bone marrow is involved by AML with associated cytopenias. The presence of MS at diagnosis of AML does not seem to influence prognosis. AML with t(8;21)(q22;q22.1) has a relatively favourable outcome and is associated with a high rate of complete remission. The recommended therapy is AML-type chemotherapy, and surgery/radiotherapy for symptomatic tumoural masses may be considered.

E-PS-11-045
ALK-positive large B-cell lymphoma with abberant expression of CD4 and cytokeratins: a case report
M. Matanie*, L. Dubouis, E. Poullot, C. Robe, E. Lechapt, P. Gaulard
*Henri-Mondor University Hospital, APHP, France

Background & objectives: Anaplastic lymphoma kinase-positive large B-cell lymphoma (ALK+LBCL) is a very rare subset of aggressive B-cell lymphoma and a diagnostic challenge (184 cases reported). We report one additional case of ALK+LBCL with a plasmablastic immunophenotype and CD4 and cytokeratins expression.
Methods: A 43-year-old patient presented with a gradual deterioration in general condition. The PET scan showed multiple adenopathies associated with splenic and multiple bone involvement. Lymph node biopsies revealed a diffuse proliferation composed of large, monomorphic cells with an abundant eosinophilic cytoplasm and eccentrically located nuclei. Brisk apoptosis and numerous mitosis were observed. The neoplastic cells showed weak expression of PAN-Cytokeratins.

Results: However, owing to the plasmablastic cytology, further investigations were performed: the neoplastic cells were positive for CD138, OCT2, MUM1 and CD45 and negative for CD20, PAX5, CD79A and CD19 and showed lambda monotypic expression (in situ hybridization). They also expressed EMA, c-MYC, CD30, and aberrant CD4. Furthermore, they were negative for all the additional T markers. The ALK staining was nuclear and cytoplasmic suggesting a t(2;5) translocation. There was no evidence of infection by EBV or KSHV/HHV8. By PCR, B-cell clonality was demonstrated. FISH analysis did not reveal a rearrangement of the MYC gene. A targeted NGS sequencing using a 36-gene panel dedicated to B-cell lymphomas disclosed no pathogenic mutations.
Conclusion: ALK+ LBCL can affect individuals of any age, with a male predominance, and is not associated with any immunodeficiencies. The CD4 and cytokeratins expression, along with the absence of mature B cell–associated markers as observed in our case, can create some diagnostic difficulty. The prognosis is poor, with a > 30% 5-year survival rate. Treatment typically involves the CHOP regimen, but ALK inhibitor agents could be valuable in the future.

E-PS-11-046
Breast implant-associated anaplastic large-cell lymphoma (BIA-ALCL): case report and diagnostic and therapeutic approaches
S. Mcgrath*, L. McKenna, O. O'Brien, K. Pilson
*Beaumont Hospital, Ireland

Background & objectives: Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) is a rare variant of ALCL, typically presenting as unilateral seroma approximately 8 years after implant placement. There is a reported 100% 5-year survival with early disease, however, prognosis worsens with later stage.
Methods: We present the case of a 46-year old woman with a right chest wall lump 8 years after having bilateral breast implants inserted. Ultrasound revealed an 18mm mass suspicious for malignancy. Core biopsy showed inflammatory infiltrate with admixed large, atypical cells. These cells were immunoreactive for CD30 & CD3. ALK1 & PAX5 were negative. The profile was consistent with BIA-ALCL.
Results: PET/CT demonstrated FDG-avid nodules in the right breast and right pectoralis major and a right subpectoral node. The right capsulectomy specimen contained multiple tumour masses within the capsule cavity, some of which were free floating, with others adherent to the breast implant and the fibrous capsule. It focally extended through the capsule into muscle. A clonal T-cell receptor gamma chain gene rearrangement was identified by PCR. All lymph nodes received at the time were negative. However, given the pre-operative FDG-avid subpectoral node the decision at MDM was to monitor with serially imaging. Subsequently, lymph nodes were identified which contained the patient's known lymphoma. Systemic chemotherapy was commenced.
Conclusion: BIA-ALCL is a rare entity, however, the rate is set to increase, given the growth in numbers of implants placed for both cosmesis and reconstruction. As this is a relatively recently described disease challenges exist regarding indications for treatment and duration of follow-up. Given the unusual presentation, staging and progression we believe that this case presents unique learning opportunities for this type of lymphoma and its management.

E-PS-11-047
Extra-nodal lymphomas of the head and neck: demographic, clinical and pathological characteristics in a moroccan serie
S. Moqran*, F. Harmouch, S. Aitbrahim, N. Elouatassi, G. Berradi, L. Tahiri, L. Chbani, N. Hammas
*Pathology department, University hospital Hassan II, Morocco

Background & objectives: Head and neck lymphomas represent a common malignant tumour group. However, extra-nodal lymphomas are a rare occurrence and represent a distinct entity with a different presentation and evolution from lymph node lymphomas. Our aim is to describe their distinctive characteristics.
Methods: A retrospective study was conducted over a period of 12 years (2013-2024), including all extra-nodal lymphomas of the head and neck diagnosed in the Department of Pathology, University Hospital Hassan II of Fez, Morocco. The histological study was performed on formalin-fixed and paraffin-embedded tissue sections. An immunohistochemical complement was systematically used.
Results: A total of 23 cases were collected, with a slight male predominance and a sex ratio of 1.3. The mean age was 53 years (2yrs-79yrs). The two most common sites were the tonsils and the nasosinus with 7 cases each. B-cell lymphomas were the most common, represented by diffuse large B-cell lymphoma in 48% of all recorded cases, followed by mantle cell lymphoma (4 cases), marginal zone lymphoma (2 cases), then follicular lymphoma (1 case). T lymphomas were in the minority, represented by 2 T/NK and 2 T lymphoblastic lymphomas. Hodgkin's lymphoma is represented by one case. Knowing that the majority of patients received chemotherapy, 10 deaths were recorded.
Conclusion: Extranodal lymphomas of the head and neck are rare. The rare series reported in the literature agree with our results regarding the predominant histological type, which is diffuse large B-cell lymphoma. Regarding the localisation, no case of oral localisation was recorded in this series, knowing that this localisation has a poor prognosis compared to extra-oral lymphomas in the majority of series in the literature.

E-PS-11-048
A complex presentation of Langerhans cell histiocytosis in adult with BRAF V600E mutation: a case report
N. Moulai*, R. Bennoui, M. Guermi, S. Ahmed Allal, W. Ouahioune
*Faculty Of Medicine of Blida, Algeria

Background & objectives: Langerhans cell histiocytosis (LCH) in adults presents with severe systemic involvement, challenging diagnostics and management. This report details a complex adult LCH case with neurological and systemic manifestations, emphasizing the role of BRAF V600E mutation.
Methods: We describe a 56-year-old male patient with a one-year history of neurological disorders, including encephalitis and diabetes insipidus, alongside maxillary bone lesions and mediastinal and hilar lymphadenopathy. Diagnostic procedures included skin biopsy, immunohistochemistry for CD68, CD1a, S100, Langerin, and BRAF VE1, and molecular analysis for the BRAF V600E mutation via RT-PCR.
Results: Skin biopsy showed Langerhans cell proliferation with CD68, CD1a, S100, Langerin and Braf VE1 expression, and a significant BRAF V600E mutation impacting the MAPK signaling pathway. This mutation typically contributes to LCH pathogenesis, exacerbating systemic manifestations. The patient's complex symptoms, including central nervous system and skeletal involvement, categorized his condition as multisystem LCH. Treatment adjustments were informed by molecular profiling, focusing on targeted therapies to address specific pathogenic drivers.
Conclusion: This case highlights the diagnostic and therapeutic challenges of adult LCH with extensive organ involvement. It underscores the necessity for a multidisciplinary approach, integrating advanced molecular diagnostics and targeted therapies such as BRAF inhibitors. Such strategies are crucial for managing severe manifestations and improving outcomes in adult LCH patients, advocating for personalized treatment plans based on genetic profiling

E-PS-11-049
A rare case of ureteral diffuse large B-cell lymphoma emerging in a patient with Polycythemia Vera JAK2 V617F mutation: a unique presentation

N. Moulai*, M. Amtout, M. Guermi, R. Bennoui, G. Ifaidi, W. Ouahioune
*Faculty Of Medicine of Blida, Algeria

Background & objectives: Diffuse large B-cell lymphoma (DLBCL) rarely develops in patients with polycythemia vera (PV), especially within the ureter.This case report aims to detail such a unique clinical presentation, discuss diagnostic challenges, and explore potential pathophysiological links between these two hematological disorders.
Methods: A 71-year-old woman with a known history of JAK2 V617F-positive PV for a year under treatment with hydroxyurea, who presented with acute abdominal pain. Computed tomography (CT) scans revealed a right pelvic ureter tumour with associated lymphadenopathy without peripheral tumoural syndrome or splenomegaly. The patient underwent a right nephroureterectomy and extensive lymph node dissection.
Results: The patient underwent successful surgical resection of the right nephroureterectomy and iliac and obturator lymph node dissection.The ureteral tumour measured 28x7 mm, and histological examination showed extensive infiltration by large B-cells with a diffuse architecture, primarily composed of centroblasts. Three out of fifteen dissected lymph nodes were also infiltrated by lymphoma confirmed DLBCL non-germinal centre B-cell type (non-GCB) phenotype with 30% of cells expressing CD30. The involvement of the JAK-STAT pathway, commonly activated in PV through JAK2 mutations, may suggest a mechanistic link to the DLBCL pathogenesis given its role in lymphoid cell proliferation and survival.
Conclusion: This case highlights the rare occurrence of DLBCL in a PV patient, with an unusual extra-nodal presentation in the ureter. The case underscores the importance of considering secondary hematological malignancies in patients with PV. Further research is necessary to explore the underlying mechanisms of lymphomagenesis in PV and the potential role of JAK2 mutations in the co-development of lymphoma.This case contributes to the limited literature on the association between these two complex conditions and suggests a potential shared pathogenic pathway.

E-PS-11-050
Epidemiological and pathological profiles of T/NK cell lymphomas: a retrospective study
N. Moulai*, I. Benameur, R. Bennoui, M. Guermi, S. Ahmed Allal, G. Ifaidi, W. Ouahioune
*Faculty Of Medicine of Blida, Algeria

Background & objectives: T/NK cell lymphomas are rare and aggressive malignancies with variable clinical presentations and outcomes. This study aims to assess the epidemiological and histopathological aspects of T/NK cell lymphomas diagnosed over four years at the Pathology Department Blida in Algeria.
Methods: This descriptive retrospective study analysed 102 cases of nodal and extra-nodal T/NK cell lymphomas from January 2018 to December 2021. Inclusion criteria were biopsy-proven diagnoses of T/NK cell lymphoma with complete histological and immunohistochemical examinations performed. Exclusion criteria included patients diagnosed with T-cell leukemia.
Results: The study population was predominantly male (63.7%), with a median age of 46.6 years. Nodal involvement was noted in 52.94% of cases. Extra-nodal manifestations were primarily in cutaneous (20.6%), bone marrow (6.9%), mediastinal (6.9%), and nasal (5.9%) sites. The most common histological subtype was Anaplastic Large Cell Lymphoma (ALCL), constituting 34.3% of cases, predominantly ALK-negative (62.9%). The T Lymphoblastic Lymphoma (LTL) subtype affected younger males and represented 18.6% of cases. Other significant subtypes included Mycosis Fongoides (MF) (13.73%), nodal T Follicular Helper Lymphoma (nTFHL) (10.7%), extranodal NK/T-cell lymphoma nasal type (9.8%) typically nasal and affecting mostly males under 65 years, Peripheral T-cell lymphoma NOS (5.8%) and Enteropathy-associated T-cell lymphoma (1%).
Conclusion: For the first time, we have reported clinical and pathological data on precursor and mature T-cell and NK-cell lymphomas in our regionT/NK cell lymphomas demonstrate varied clinical and histopathological profiles, influenced by both subtype and tissue involvement. The ALK-negative subtype of LAGC was the most prevalent in our study.

E-PS-11-051
Impact of Epstein-Barr virus status on microenvironment profiles in diffuse large B-cell lymphoma: a prospective study
N. Moulai*, M. Guermi, R. Bennoui, G. Ifaidi, W. Ouahioune
*Faculty Of Medicine of Blida, Algeria

Background & objectives: Our study aimed to compare the microenvironment profiles of EBV-positive and EBV-negative diffuse large B cell lymphoma (DLBCL) to understand the role of EBV in modulating immune checkpoint expressions and other immunological features within the tumour milieu
Methods: Our prospective study analysed 78 DLBCL cases, including 67 EBV-negative with ABC phenotype, 11 with GCB phenotype, and 13 EBV-positive ABC phenotype cases. We assessed expressions of PD-L1, PD-1, cytotoxic markers (CD8, Granzyme B, Perforin), and regulatory T cell markers using immunohistochemical assays. Mann-Whitney U tests and Pearson's correlation evaluated the association between EBV status and these immunological markers.
Results: EBV-positive DLBCL cases showed significantly higher PD-L1 expression (100% of cases) than EBV-negative cases (24.4%). A pronounced difference in the expression of immune checkpoints and cytotoxic markers was observed, with the EBV-positive group exhibiting enhanced cytotoxicity, highlighted by elevated CD8, Granzyme B, and Perforin levels. Regulatory T cell markers, including FOXP3 and CD25, did not differ significantly between groups. Statistical analysis revealed a strong correlation between EBV status and a more suppressive immune microenvironment, underscoring the impact of EBV on the immunological dynamics within DLBCL.
Conclusion: EBV status defines distinct immunological profiles in DLBCL, enhancing immune checkpoint expression and cytotoxic responses. These findings underscore the potential of EBV as a prognostic factor and therapeutic target, suggesting that tailored treatment strategies considering EBV status could improve patient outcomes. Further investigation is required to elucidate EBV's mechanistic roles in modifying the tumour microenvironment and to develop targeted therapies for EBV-associated DLBCL.

E-PS-11-052
Myeloid sarcoma: a rare presentation of myeloid neoplasm - a case report
M. Nadia*, M. Hamdani, M. Walha, K. Bel Haj Ali, A. Khabir
*Habib Bourguiba University Hospital of Medicine,Tunisia

Background & objectives: Myeloid sarcoma, also known as Granulocytic sarcoma is a rare extramedullary tumour of immature granulocytic cells, most commonly seen in acute myeloid leukaemia.However, this tumour is rarely reported.Here we report a case of granulocytic sarcoma associated with acute monoblastic leukaemia.
Methods: A 34-year-old female with a history of monoblastic leukaemia who underwent allogeneic stem-cell transplantation at the age of twenty-four and was treated for tuberculous lymphadenitis at the age of twenty-six, presented with a protruding tibial mass measuring six centimeters in diameter which developed over a period of seven months. Her complete blood count test was normal.A surgical biopsy was performed.

Results: Histopathological study of the specimen revealed a dense tumour proliferation of scattered mononuclear neoplastic round cells. Nuclei were hyperchromatic with irregular and prominent nucleolus. Tumour cells showed high mitotic activity with some atypical mitosis. The tumour infiltrated the surrounding tissues including bone.
On immunohistochemistry, tumour cells were positive for CD45 and CD117(C-kit), they were negative for keratin, CD3, CD20, CD68, CD79a and CD138. This profile was consistent with myeloid sarcoma.
Conclusion: Although myeloid sarcoma of bone is rare, it should be suspected in patients with history of acute-myeloid-leukaemia (AML) developing bone tumour. The diagnosis can be more challenging in absence of AML history.

E-PS-11-053
TCF3::PBX1 fusion paediatric B acute lymphoblastic leukaemia in disguise behind the eyes – an unusual clinicopathologic presentation with hyperdiploid clone
S. Naskar*, T. Paul, J. Kulkarni, D. V, A. K C, H. Rambhojun
*Sri Shankara Cancer Hospital & Research Centre, India

Background & objectives: Paediatric acute lymphoblastic leukaemia/lymphoma (ALL/LBL) is the most common childhood blood cancer. Extramedullary B-LBL often affects central-nervous-system (CNS), testis, spleen, and liver. Primary orbital involvement indicates poor prognosis. We describe a rare case of B-ALL presenting with a retro-orbital mass.
Methods: A 4-year-old boy presented with progressive proptosis of the right eye for 2 weeks. Magnetic resonance imaging (MRI) of the orbit showed a large ill-defined lobulated mass with intracranial/sphenoid extension. There was no previous treatment history. The patient's haemoglobin and platelet count were normal with leukopenia. Peripheral blood, bone marrow examination and biopsy of the orbital mass were performed.
Results: The peripheral smear revealed about 21% blasts showing dot and block cytoplasmic staining with Periodic acid Schiff. Bone marrow was hypocellular, with 25% blasts and 45% small lymphocytes. Flow cytometry identified 25% blasts positive for CD79a and CD10, and negative for Tdt and myeloid markers. A diagnosis of B-cell lymphoblastic leukaemia with CNS involvement was conferred. CSF cytology was negative. A biopsy from the retro-orbital mass confirmed B-cell lymphoblastic lymphoma, with a Ki67 index of ~90% and weak Tdt positivity. Karyotyping showed a hyperdiploid male karyotype with chromosomal gains and TCF3::PBX1 gene rearrangement. Treatment followed BFM 2002 protocol. He achieved complete remission with a relapse-free 26 months post-remission (till date).
Conclusion: Pre-B-ALL/LBL typically presents with a marrow full of leukaemic blasts. Our case showed a unique bone marrow picture with 25% blasts and 45% mature lymphocytes. Primary orbital manifestations are rare in B-ALL, with our case being the first reported with TCF3::PBX1 gene rearrangement presenting as a retroorbital mass. Hyperdiplod clone and increased lymphocytes in the marrow niche can indicate good prognosis. A bone marrow/peripheral-smear analysis is essential for diagnosing and managing cases with retro-orbital mass, even without suspicious blood parameters.

E-PS-11-054
Follicular lymphoma and chronic lymphocytic leukemia, 10 years, single institution
Z. Nikin*, T. Ivkovic Kapic, N. Solajic, T. Vasiljevic, L. Popovic, M. Popovic
*Oncology Institute of Vojvodina, Serbia

Background & objectives: Follicular lymphoma (FL) and chronic lymphocytic leukemia (CLL) represent the most frequent small B-cell lymphomas in the World. The aim was to find out concordance of our hospital`s results in a 10-year material with international data.
Methods: All biopsies of follicular lymphomas and chronic lymphocytic leukemias diagnosed at the Oncology Institute of Vojvodina from January 2010 to March 2020. Demographic and medical data were taken from the hospital information system. HE staining and immunohistochemistry were performed according to standard procedures. Microsoft Excel and IBM SPSS Statistics were used for data analyses.
Results: There were 184 CLL patients, 115 males and 69 females. Males were on average 64.23 years old, median 65 and females 67.16 years old, median 69. There were 187 FL patients, 82 males and 104 females and 1 patient without data. Males were on average 57.28 years old, median 57 and females 58.72 years old, median 59. CLL was more frequent in males and FL in females, and males got ill younger for both lymphomas, with statistical significance. Distribution through decades was the same among sexes for each lymphoma. FL were grade 1 in 38.51%, grade 2 in 29.05%, grade 3a in 28.38% and grade 3b in 4.06%.
Conclusion: Distribution of patients through decades was as expected, mostly in 7th and 6th decade for CLL and FL respectively. Distribution between males and females was concordant with WHO data, CLL was more frequent in males and FL in females. Surprisingly, the incidence of FL was much lower and the incidence of CLL was somewhat higher compared to western results and similar to some regional and Asian results. Distribution of grades in FL is concordant with WHO data.

E-PS-11-055
Primary uterine T-cell lymphoblastic lymphoma: an uncommon localization-about a case
L. Njim*, A. Ben Mabrouk, M.M. Hamzaoui, M. Njima, A. Bellalah, A. Zakhama
*Fattouma Bourguiba University Hospital, Monastir, Tunisia

Background & objectives: Extranodal primary non-Hodgkin's lymphomas genital form represents 0.5% of all malignant genital diseases.To the best of our knowledge, only four previous case of primary uterine T-cell lymphoblastic lymphoma(PUTLL) have been described.We report a case of PUTLL with review of literature.
Methods: It was about a 55-year-old patient. She had no personnel or family history of cancer. She complained of chronic pelvic pain. On Imaging, an uterin mass measuring 20.6 ×14cm was identified. The diagnosis of a large sub mucosal myoma was proposed. The patient underwent an hysterectomy with bilateral adnexectomy.
Results: Grossly, the uterine corpus measured 28x16x6 cm. On the section, the uterine body is completely occupied by a yellow mass which showed haemorrhagic and necrotic changes. Histologically, this mass was made of discohesive, monomorphic and small size cells with numerous mitosis. These celles were admixed with macrophages and apoptotic bodies. The tumour infiltrated all layers of the uterus body, parameters, and adnexa. Immunohistochemically, tumour cells were positive for CD3, CD4, CD5 and Tdt while they were negative with CD20, Myeloperoxydase, granzym B, ALK, and cytokeratin. The proliferation index was 90%. The diagnosis of T-cell lymphoblastic lymphoma was made. As part of an extension assessment, a bone marrow biopsy was negative.
Conclusion: T-cell lymphoblastic lymphoma is a highly aggressive tumour. It often arises as a mediastinal mass with bone marrow involvement. Presentation at other sites without nodal or mediastinal localization is uncommon. Its occurrence as a primary tumour of the uterus is very rare. Due to the morphology of neoplastic cells, a challenging differential diagnosis with all small round blue cell tumour category is mandatory. In ambiguous cases, molecular biology may represent an adequate tool to confirm diagnosis.

E-PS-11-056

PseudoRichter-transformation in patients with small lymphocytic lymphoma after ibrutinib interruption - a case report

E. Oliva Domínguez*, I. Orbegozo Arrizabalaga, K. Gonçalves Villarreal, I. García Miranda, M.L. Ramírez Feliz, J.I. Iparraguirre Santiago, A. Fernández de Larrinoa Santamaría, L. Zaldumbide Dueñas, M. Vázquez Peraita
*Hospital Universitario Cruces. Basque Country. Spain

Background & objectives: Small lymphocytic lymphoma (SLL) shows an indolent course, however, 5% of cases undergo a Richter-Transformation (RT). Ibrutinib is a drug approved for SLL treatment. The term PseudoRichter-Transformation refers to a SLL with clinical/pathology features of RT originated after ibrutinib interruption.
Methods: A new case is described: an 84-year-old woman with a previous diagnose of SLL and stable disease treated with ibrutinid for six years. The patient underwent an elective surgery due to an inguinal hernia. Ibrutinib was stopped one week before the surgery to mitigate bleeding risk. During the surgery, an abnormal-appearing lymphadenopathy was identified, excised and sent to the Pathology-Department.
Results: Histologically, the lymph node architecture was totally effaced by medium-large sized lymphoid cells arranged in a diffuse or vaguely nodular pattern. These cells were relatively uniform with vesicular nuclei, prominent nucleolus and scant cytoplasm. They expressed CD20+, CD5+ and CD23+; prognostic markers p53 and ZAP70 were negative and the proliferative index (Ki67) was high (60%). Currently, four months after the surgery and with the treatment reintroducction, the patient is asymptomatic and a subsequent radiological test showed no signs of disease progression. However, a following biopsy was not performed.
Conclusion: Few cases of PseudoRichter-Transformation have been reported. This entity clinically simulates a RT which develops after ibrutinib interruption and remits once restarted. Histologically, after ibrutinib interruption biopsy demonstrates a diffuse large-B-cell lymphoma morphology consistent with RT with immunophenotype similar to a SLL; when the treatment is resumed the biopsy shows a residual SLL. It is indispensable to know this entity and differentiate it from a true RT, as this one requires aggressive treatment and has a poor prognosis.

E-PS-11-057

Immunohistochemical expression of p53 in adult Burkitt lymphomas

E. Özoğul*, B. Sayınalp, A. Üner, A. Saglam Ayhan, S. Akın, İ. Barista, Y. Büyükaşık
*Hacettepe University Faculty of Medicine, Department of Pathology, Turkey

Background & objectives: Burkitt Lymphoma (BL) affects primarily children, but also rarely adults and with a worse prognosis. Genetic insights emphasize the dysregulation of the MYC-ARF-p53 pathway. This study explores p53 immunostaining in adult BL and its potential as a prognostic marker.
Methods: Thirty-two adult BL cases (diagnosed 2009-2020) were analysed. Tissue sections underwent p53 immunostaining using clone DO7 antibody (Leica) at 1:200 dilution on an automated immunostainer. Nuclear p53 staining was semiquantitatively scored for percentage (0-3) and intensity (0-3). A multiplicative staining score (H-score) was calculated (range 0–9). TP53 mutational analysis was not performed; survival data was collected from clinicians.
Results: The median age was 39, ranging between 20 and 76, with an F/M ratio of 8/24. In 31 out of 32 cases, p53 was extensively positive, ranging from 75% to 100% (scores 2-3). Six cases had a staining intensity score of 1/3, 14 cases had 2/3, and 11 cases had 3/3. Overall survival did not show a statistically significant difference by H-score ($p=0.066$), intensity, or distribution of p53 staining. In one case, p53 was totally negative without any internal control, where staining was considered unsuccessful.
Conclusion: We found extensive positivity with p53 immunostaining in most cases, but no significant correlation with overall survival. Despite the known role of TP53 mutations in both paediatric and adult BL in prognosis; the absence of statistically significant associations between p53 staining parameters and survival may suggest a complex interplay of factors in outcomes. Additional inquiry, merging genetic investigations with immunohistochemical analyses, is essential to reveal the intricate molecular pathways responsible for the overexpression of p53 in adult BL.

E-PS-11-058

Primary hepatic extranodal marginal zone lymphoma: an extremely rare entity presented in a colonic adenocarcinoma patient

B. Pamuk*, B. Özbek, N. Alhan, O. Salim, I. Kuzu
*Ankara University School of Medicine, Turkey

Background & objectives: Primary hepatic extranodal marginal zone lymphoma (PH-EMZL) is an extremely rare malignancy. It is an indolent B-cell lymphoma that comprises around 5/1.000.000 of all non-Hodgkin's lymphoma. Here we aim to present a case and review current literature.
Methods: A 74-years old man who had right hemicolectomy due to colon adenocarcinoma with no chemotherapy or radiotherapy treatment history, presented with a liver mass measuring 1.5 cm after 2 years of his diagnosis. Wedge biopsy of liver was examined with immunohistochemistry and IgH clonality analysis.
Results: Microscopical examination showed nodules composed of monotonous small mature monocytoid B lymphoid cells with round or slightly irregular nuclei colonising germinal centres in some areas. Infitrating cells were strongly immunohistochemically positive with CD20, BCL2, and IgD antibodies. CD21 and CD23 showed FDC meshwork of residual germinal centres and also revealed positive neoplastic B cells palely. LEF1, SOX11, CD10, MNDA and CyclinD1 were all negative. Immunoglobulin heavy chain evaluation was demonstrated by PCR and fragment analysis and showed clonality.
Conclusion: PH-EMZL is an extremely rare disease. Majority of reported cases were asymptomatic with median age around 60 years. Chronic antigenic stimulation is an important etiology for MZL. Most probable chronic antigenic stimulation agent is hepatitis virus but HBsAg, anti-HCV antibodies, HBV DNA and also anti-HIV antibodies were all negative. However, HBc IgG was found positive, adressing a previous infection. Pemphigus foliaceus history of the patient might indicate an autoimmune background. More data is required for PH-EMZL's etiology, prognosis and treatment.

E-PS-11-059

Follicular lymphoma with diffuse growth pattern and CD23 expression: a series of 15 cases diagnosed in our hospital during the 2014-2024 period

Y. Rey Fanjul*, E. Mateo Álvarez, C.J. Grau Polo, D. Rodriguez Villar, P. Gonzalvo Rodríguez, J. Cuevas Fernández, E. Asensi Miranda, R. Rodríguez Aguilar
*Sespa, Spain

Background & objectives: Follicular lymphoma showing diffuse growth pattern are rare, with features leading them to be currently recognized as a provisional entity within ICC-22 classification, and a follicular lymphoma (FL) subtype within WHO22, referred to as FL with predominantly diffuse growth pattern.
Methods: We reviewed all FL cases diagnosed in our hospital during the 2014-2024 period and selected those with diffuse growth

pattern and/or CD23 expression. We analysed the resulting 15 cases to study their epidemiological, clinical, pathologic and immunophenotypic characteristics, and contrasted them with those described in the literature.
Results: The majority occurred on female patients (10), with ages ranging from 33 to 86 and an average of 64 years old. Most showed inguinal location (9), followed by cervical, mesenteric, and axillary. They were mostly low graded (14), with 7 showing mixed pattern, 5 entirely diffuse and 3 follicular. Only 4 cases presented at early stage (I-II) and 3 showed marrow bone extension. Response was complete on 10 cases, and 5 recurred with an average of 60 months. All expressed CD23, BCL6 and CD10, and were negative with CD21 and CD5. Although 13 cases showed BCL2 expression, fluorescence in situ hybridization (FISH) for t(11;14) proved negative on 10 of them.
Conclusion: We report a series of 15 cases diagnosed as FL with predominantly diffuse growth pattern and/or CD23 positive. The histology showed a diffuse infiltrate composed by centrocytes and interspersed centroblasts. Most of their features were consistent with those described in literature, with predominantly female patients, inguinal location, low histological grade, and good clinical response. However, we found mostly advanced stages, unlike literature's descriptions. They were CD23 positive, and FISH proved t(11;14) negative on most of them, despite BCL2 marker expression.

E-PS-11-060
Composite classic Hodgkin lymphoma and follicular lymphoma: case report of a rare and poorly characterized entity
D. Sá*, S. Neves, I. Araújo, F.E. Costa, J.R. Vizcaíno
*Anatomic Pathology Service, Pathology Department, Unidade Local de Saúde de Santo António, Portugal

Background & objectives: Composite lymphoma is defined as the simultaneous occurrence of more than one type of lymphoma in the same organ/tissue. To our knowledge less than 30 cases of Composite classic Hodgkin lymphoma and follicular lymphoma have been reported in the literature.
Methods: We herein report a case of a 77-year-old man presenting with B symptoms, abdominal dilation, and dyspnoea. A CT scan revealed multiple adenopathies and a 6 cm pelvic conglomerate mass that compressed the bladder and caused renal hydronephrosis. Lymph node biopsy was performed and it showed a B-cell lymphoma compatible with the diagnosis of follicular lymphoma.
Results: The patient was then submitted to an inguinal lymph node excision and we received three fragments of lymph node parenchyma which had a pink-white and homogenous cut surface. Histologic examination showed two different components, one composed of small lymphocytes with centrocyte morphology and follicular pattern that on immunohistochemistry showed expression of CD20, BCL6, CD10 and BCL2 and no expression of CD3, CD5, CD21, CD23, LEF1 and CyclinD1. Intermixed, there was another component measuring 0,3cm composed of large Hodgkin and Reed-Sternberg cells scattered on a T-lymphocyte background. Immunohistochemistry was positive on the large cells for CD20, PAX5, MUM1, CD30, CD15 and EBER and negative for CD45, BOB1, CD3, Myc and p53.
Conclusion: Composite Hodgkin lymphoma and follicular lymphoma (CHLFL) is a rare entity that most often occurs in older adults, involves lymph nodes, and mostly presents de novo. Most cases display a distinct zonal distribution of each component and the two components are usually clonally related. In the cases reported the CHL component was either of mixed cellularity or nodular sclerosis type.The 5-year overall survival in these patients was 48% and our patient is still alive 3 years after the diagnosis.

E-PS-11-061
Beyond the unusual: a trifecta of vascular transformations
A. Santos*, R. Oliveira, P. Lupi
*Centro Hospitalar de Lisboa Ocidental, Portugal

Background & objectives: Sclerosing angiomatoid nodular transformation (SANT) is a vascular splenic lesion of uncertain aetiology. While benign, the nonspecific symptoms and the inconclusive results of diagnostic modalities make the differential elusive, with iatrogenic risks for the patient.
Methods: We report the case of a 30-year-old woman with left upper quadrant pain, fatigue, asthenia, anorexia and early satiety. On physical examination, she presented splenomegaly and bilateral inguinal adenopathies. Analytically she presented with iron deficiency anaemia. An ultrasound showed splenomegaly with hyperechoic nodules. The investigation carried out did not document etiology. A splenectomy was performed for diagnosis and symptomatic relief.
Results: The macroscopic examination showed an enlarged spleen, with pale, firm, spiculated nodules, with a central scar in a "spoke-wheel" pattern. An accessory spleen and four lymph nodes were also documented. Histologically, the spleen showed multiple nodules, with haphazard vessels, surrounded by fibrosclerotic stroma. The immunohistochemistry markers CD34, CD31 and CD8 showed these nodules to have three types of vessels: central sinusoids, peripheric capillaries, and ubiquitous venules. The accessory spleen showed similar changes, with faintly delineated nodules, which had a similar staining pattern with CD31, CD34 and CD8. Moreover, the lymph nodes present in the splenic hilum showed exuberant vascular transformation of sinuses, with ample ectatic vessels.
Conclusion: SANT is a rare lesion with a fairly benign evolution, whose definitive diagnosis can only be done through histological examination. Further research into the aetiology, presentation and results of diagnostic modalities may improve patient outcomes by adopting an expectant attitude, and avoiding the risks associated with splenectomy. The concurrent presentation in an accessory spleen and the vascular transformation in the hilar lymph nodes may indicate that the same event triggered these changes.

E-PS-11-062
Myelomastocytic leukemia: an understated entity, a case report
A. Sifre-Ruiz*, M.M. Buda, A.M. Cordovilla Morneo, C. Esquina Rodriguez, I. Etxebarria Fernandez, M.V. Alarcón-Amaya, V. Moreno-Nieto
*Clinical Department Unit of Pathological Anatomy, OSI Araba, Araba University Hospital, Vitoria-Gasteiz, Alava, Spain

Background & objectives: Myelomastocytic leukemia (MML) is a rare type of leukemia defined by the increase of immature mast cells (MC) and metachromatic blasts in presence of an evolved myeloid neoplasm. We present the case of a 67-year-old male with a thoracic mass.
Methods: Our patient underwent two big aspiration needle biopsies, taken from the thoracic mass and bone marrow; both samples were processed. Histological examination with haematoxylin-eosin, different immunohistochemistry techniques and molecular analysis was performed. External consultation was made, which coincided with our diagnostic orientation. A brief literature review was also conducted.
Results: We received two tissular cylinders. In the microscopic study of the thoracic mass sample, we found a pleomorphic, mononucleated cell population, with an admixed multinucleated and pleomorphic population. The other sample represented an hypercellular bone marrow, at the expense of a diffuse infiltrate of large cells with an immature appearance, blastic chromatin and minimal differentiation. Both tumours seemed to be the same malignancy. Immunohistochemistry

techniques demonstrated positivity for CD43, CD56, CD117 (intense), CD300 (partial) and tryptase (partial and weak). Expression of CD34, CD79a, CD2, CD25, CD99, Pax5, TdT, e-cadherine, MPO, S100, CD61, OCT3/4, CD45 and CD68 was not observed. KIT gene analysis showed no alterations.
Conclusion: MML is an understated malignancy, defined by concrete histological features and molecular alterations. It's a challenging diagnosis, due to its rarity and similarities with other neoplasms. Its differential diagnosis from mast cell leukemia appears to be the most conflicting, however, immature MC lacking CD25 expression and wild-type KIT gene, supports MML diagnosis. Tryptase-positive acute myeloid leukemia, forms of systemic mastocytosis (especially those with associated haematologic neoplasms), and basophilic leukemias should be taken into account in the differential diagnosis process, too.

E-PS-11-063
Plasmablastic lymphoma of the oral cavity in an immunocompetent elderly patient-case presentation and review of literature
S. Simion*, D. Buteică, L. Banias, D. Smaranda, H. Emőke
*Mures County Clinical Hospital, Târgu Mureș, Romania

Background & objectives: Plasmablastic lymphoma (PBL) is a rare and aggressive large B-cell lymphoma that often presents as a tumour mass in the oral cavity of human immunodeficiency virus (HIV)-positive patients. Few cases have been reported in immunocompetent patients, usually involving extraoral sites.
Methods: We report the case of a 63-year-old chronic smoker with an irregular, rapidly growing, grey-white, ulcerated tumour mass of the anterior mandible extending to the floor of the mouth and tongue. An excisional biopsy fragment was sent for histopathological examination.
Results: Microscopically, the tumour was composed of large cells resembling immunoblasts/plasmablasts with plasma cell differentiation forming cohesive clusters with focal necrosis. Immunohistochemically, these cells expressed CD138, MUM1 and lambda light chain, and were negative for common B-cell markers. Ki67 proliferation index was over 90%. The anatomical site, histological appearance and immunophenotype of the tumour cells were compatible with plasmablastic lymphoma. Testing for HIV and EBV infection was recommended, both tests proved negative. Plasmablastic plasma cell myeloma was excluded in the absence of lytic bone lesions and bone marrow involvement. After 5 treatments, the tumour showed a favourable response to chemotherapy (V-EPOCH) with a significant reduction in tumour mass.
Conclusion: Plasmablastic lymphoma, a rare subtype of diffuse large B-cell lymphoma, is a diagnostic and therapeutic challenge due to its aggressiveness and poor prognosis. Until 2024, in english literature oral cavity involvement of PBL in HIV-negative and EBV-negative patients has been reported in 18 cases. Our case highlights an exceptionally rare occurrence in an HIV-negative, EBV-negative and immunocompetent individual, underscoring the heterogeneous nature of this haemolymphoid neoplasia.

E-PS-11-064
Relapse of acute lymphoblastic leukemia limited to the uterine cervix: a case report
S. Ben Tekaya*, T. Tlili, O. Bado, N. Ouini, I. Bahri, W. Mokni, H. Hamchi, B. Sriha, M. Mokni
*Department of pathology, Farhat Hached University Hospital, Sousse, Tunisia

Background & objectives: In spite of advances in treatment of acute lymphoblastic leukemia (ALL), 15% of children patients still relapse. We aim to report a very unusual case of a patient with a uterine cervix mass as the unique manifestation of B-ALL relapse.
Methods: A 17-year-old female patient, with a 2-year history of B-ALL in remission, presented with vaginal spotting. Gynaecologic examination revealed a 4 cm mass in the uterine cervix. A biopsy was performed.
Results: Microscopic examination showed a lymphoid proliferation made of small-sized monomorphous cells with scant cytoplasms. The nuclei were round with dispersed hromatin. Immunohistochemical study showed diffuse staining for CD79a, CD34, and TdT. The Ki67 proliferation index was high (80%). The bone marrow smear was normal with no lymphoblasts.
Conclusion: Most of the cases of B-ALL relapse include infiltration of the bone marrow. Isolated extramedullary relapse is rare, occurring in 8% of cases. The most commonly involved organs are the central nervous system, lymph nodes, spleen, liver, ovary, and testis. Involvement of the uterine cervix is extremely rare and should be considered in case of abnormal uterine bleeding in the setting of B-ALL.

E-PS-11-065
Systemic amyloidosis associated with chronic lymphocytic leukemia: clinical and pathological study
O. Sudareva*, E. Ignatieva, S. Lezhenina, E. Guryanova
*I.N.Ulianov Chuvash StateUniversity, Russia

Background & objectives: We highlight an autopsy observation of a patient with systemic amyloidosis associated with chronic lymphocyticleukemia. The peculiarity of this case is the initially unverified nosological form of proven amyloidosis with damage to the heart and leading syndrome of heart failure.
Methods: The results of clinical and laboratory studies were studied in a 80-years-old-patient, who underwent 3 courses of chemotherapy. To type the form of hemoblastosis, a punctate with an IHC study of CD5, 19, 23, BcL-2, Ki-67 was evaluated. Histological preparations of internal organs were stained using standard hematoxylin-eosin, van Gieson and Congo red techniques to detect amyloidosis.
Results: Posthumously, hemoblastosis was confirmed and typed in the patient with trebanobioptate cellularity up to 80% due to clonal mature lymphocytes with coexpression of CD5, 19, 23, BcL-2 up to 100%. Macroscopically, the endocardium of the left ventricle is thickened, with a greasy sheen; atherosclerotic lesion of the coronary arteries, stage IV, degree 3. In the internal organs - congestive plethora, general edematous syndrome, brown atrophy. Histologically: infiltrates in the interstitium from mature lymphocytes in the internal organs are determined. Abundant deposits of eosinophilic masses were found along the vessels and in the mesenchyme of the liver, kidneys, myocardium, and spleen, stained with Congo red.
Conclusion: The peculiarity of this clinical observation of a patient with chronic leukemia in the progression stage is that the leading syndrome in the clinical picture was heart failure against the background of paraneoplastic syndrome with the development of multiple organ failure. This form of AL amyloidosis, taking into account the patient's age and repeated courses of specific chemotherapy, can also be attributed to a therapeutic pathomorphosis with a violation of parenchymal-mesenchymal relationships in parenchymal organs.

E-PS-11-066
Clinicopathological insights into primary breast diffuse large B-cell lymphoma: a case series
A. Syrnioti*, K. Boulogeorgou, S. Chatzileontiadou, C. Frouzaki, A. Fola, I. Xenidis, T. Koletsa
*Department of Pathology, School of Medicine, Aristotle University of Thessaloniki, Greece

Background & objectives: Primary breast lymphoma (PBL) constitutes 0.04%-0.5% of all malignant breast neoplasms. Primary breast diffuse large B-cell lymphoma (PB-DLBCL) is the most common histopathological subtype (40%-70%). We aimed to highlight clinicopathological issues that arise in PB-DLBCL through a case series.

Methods: We retrospectively collected cases of PB-DLBCL from the archives of our Pathology Department over a period of 10 years (2014-2024). Finally, three cases with adequate tissue material and available clinical information were included in the study. Core biopsy of the breast mass was examined on hematoxylin-eosin and immunohistochemical stained sections.
Results: The patients were female (mean age 68.3 years). Imaging revealed solid, lobulated masses, ranging from 1.62 to 2.6 cm in greatest diameter. Axillary lymph node involvement was detected in 2 patients. Histological and immunohistochemical evaluation set the diagnosis of DLBCL, with a non-germinal centre (non-GCB) phenotype (Hans algorithm). Two cases displayed c-myc positivity, whereas the third had a double-positive phenotype. The Ki67 proliferative index ranged from 70 to 90%. No evidence of bone marrow infiltration was present. The patients underwent R-CHOP immunochemotherapy, achieving complete remission. Nevertheless, one of the patients presented with central nervous system (CNS) involvement one year post-diagnosis.
Conclusion: PB-DLBCL is a rare extranodal NHL, commonly presenting as lobulated mass. The use of core biopsy is crucial to avoid unnecessary mastectomy. PB-DLBCL displays aggressive histopathological features; however, prognosis varies, deteriorating notably in cases with CNS involvement. The pathogenesis and the reason for its relatively frequent recurrence in CNS, an immunoprivileged site, remain largely unknown, urging the need for prospective multi-centre studies, due to its rarity. Establishment of specific therapeutic guidelines is needed to ensure optimal management of this lymphoma.

E-PS-11-067
Extranodal Burkitt's lymphoma presented as an epidural mass of the thoracic spine - a rare case
Z. Tatsiou*, K. Chatzidimitriadis, M. Apostolidou, S. Stamatiou, A. Orfanidou
*Greece

Background & objectives: Lymphoma involvement of the spine is usually a late manifestation of systemic disease. Primary extranodal lymphomas in this region are extremely rare, accounting for only 0.1% of all lymphomas, and may present with spinal cord compression as the first symptom.
Methods: Our case concerns a 54-year-old man who presented with worsening chest pain and progressive paraparesis. The imaging test showed an epidural mass in the area of the th7-th9 thoracic vertebrae, with epidural compression of the spinal cord, infiltration of the vertebral processes as well as lung and liver infiltrations. Excision of the tumour was performed by petalectomy and spinal fusion.
Results: Microscopic examination showed diffuse infiltration by a monotonous population of medium-sized lymphoid cells with high proliferative and apoptotic activity with "starry sky" appearance and tingible body-laden macrophages and presence of necrosis. The Immunohistochemical examination was positive for CD20, CD79a and CD10, while it was negative for pancytokeratins, CD3, CD99, S100 protein, SOX10, p63 protein, synaptophysin and chromogranin. Cell proliferation index ki67 was positive in >85%. Subsequently, the diagnosis of Burkitt's lymphoma was made. The patient received chemotherapy and 5 months later is in stable condition with minimal neurological improvement.
Conclusion: In conclusion, we present a rare case of extranodal Burkitt's lymphoma presenting as an epidural mass and paraparesis as the first manifestation of the disease. Although it is extremely rare, it should be included in the differential diagnosis of a high-grade malignancy of the spine, the accurate diagnosis of which, requires the application of appropriate immunohistochemistry.

E-PS-11-068
Crystals and chains: a symphony of neoplastic plasma cells
A.E. Teles*, F. Soares Nogueira, S. Carralas Antunes, A. Galzerano, D. Gomes Pinto
*Hospital Garcia de Orta, Portugal

Background & objectives: Plasma cell neoplasms, associated with histiocytosis and crystal deposition, are rare and present an intricate diagnostic challenge in bone marrow biopsies. The primary aim of this case report is to expand upon its histopathological attributes, exploring nuances.
Methods: We present a case report of a 72-year-old man with hypogammaglobulinemia, undergoing clinical investigation for suspected malignancy. He underwent a bone marrow biopsy procedure conducted at the right posterosuperior iliac crest, which was followed by histopathological analysis.
Results: Histopathological examination showed a hypercellular bone marrow secondary to a marked histiocytic and plasma cell infiltration, the latter comprising around 25% of all nucleated cells present. These cells were mildly atypical. On immunohistochemistry, they expressed CD56, compatible with an aberrant phenotype, and showed Kappa light chain restriction on in situ hybridization. Histiocytes were positive for CD68. Accompanying the plasma cells, there were elongated deposits of a birefringent material, which stained on PAS, was resistant to diastase, and didn't stain on Congo red. These features enabled a final diagnosis of "Plasma cell neoplasm associated with histiocytosis and crystal deposition".
Conclusion: The coexistence of atypical plasmacytosis and histiocytosis with crystal deposition is an atypical presentation for a plasma cell neoplasm, adding a layer of intricacy to this diagnosis. It is important to be able to recognize these features, not to overlook a diagnosis of malignancy. Our findings align with the known subtypes of monoclonal immunoglobulin deposition disease (MIDD) and are illustrative of this rare presentation. Further research is warranted to elucidate the underlying etiology and pathogenesis of MIDD.

E-PS-11-069
Plasmablastic lymphoma of thyroid in an HIV-negative patient: a case report
G. Pazarlis, C. Roumbas, G. Kakiopoulos, C. Paschalidi, N. Tepelenis*, T. Choreftaki
*Department of Pathology, General Hospital of Athens "Georgios Gennimatas", Athens, Greece

Background & objectives: Plasmablastic lymphoma (PBL) is an aggressive B-cell non-Hodgkin's lymphoma with plasmacytic differentiation, posing diagnostic challenges due to overlaps with myeloma and lymphoma. PBL progresses rapidly, often resisting chemotherapy, warranting comprehensive discussion on causes, presentation, diagnosis, and interprofessional management.
Methods: A 73-year-old Caucasian male with hypothyroidism, hypertension, deep vein thrombosis, and benign prostatic hyperplasia presented with an enlarged neck mass. Over five months, the mass enlarged causing dysphagia and dyspnea. Evaluation: thyroid function tests, neck CT (showing enlarged thyroid), and FNA biopsy. Additionally, CMV: IgG (+), EBV: IgG (+), HBV: HBcore(+) Ab, Hbe(+)Ab, and HIV(-).
Results: Histopathology of the specimen disclosed a proliferation of neoplastic cells with plasmablast and immunoblast-like morphology, abundant cytoplasm, without recognisable nucleoli compatible with plasmablastic lymphoma (PBL). In view of the morphological features, immunohistochemical stains were performed: Ki67 stain is positive approximately to 50% of neoplastic cells. B lineage marker

CD79a is positive, while CD20 and PAX5 is negative. CD30 antibody, which is associated with anaplastic large cell lymphoma, shows negativity. Epithelial markers such as KerAE1/AE3, ThG and TTF1 found to be negative. Plasma cell-associated marker CD138 is negative. CMYC accounts for 35% positivity. Also, LCA (+), CD3(-), CD10(-), CyclinD1(-), SOX11(-), BCL2(+), BCL6(-), EBER(-), CD56(-),EMA(-).
Conclusion: PBL is a challenging disease, both to diagnose and to treat. This case shows a lymphoid proliferation with histomorphological features and immunophenotype of plasmablastic lymphoma (PBL). The patient is in our Haematology-Oncology Clinic for further treatment.

E-PS-11-070
Acute erythroid leukaemia, analysis of two cases
E.M. Vázquez Tarrio*, A. Diez Fernández, L. Astilleros Blanco de Cordova, E. Revilla Sanchez
*Hospital 12 de Octubre, Spain

Background & objectives: Acute erythroid leukaemia represents less than 1% of all cases of AML. It is a neoplastic proliferation of immature cells committed to the erythroid lineage (usually >80% of the bone marrow cells are erythroid, and at least 30% proerythroblasts).
Methods: We aim to describe the immunophenotypic, cytogenetic and clinical features of two cases. Clinical history and results of bone marrow aspirate, trephine specimens, immunohistochemistry, flow cytometry and molecular studies were collected. We also reviewed the existing literature on acute erythroid leukaemia.
Results: Both patients were men over 60 years. Bone marrow smears shhowed increased immature erythroid cells with dysplastic signs. Bone marrow core biopsy were hypercellular and erythroid lineage were 80% and 70% of bone marrow elements respectively, and showed sheets of immature erythroblasts (over 50% and staining CD71, glycophorin, e-cadherin, CD117). CD34 stained a 18,7% and 5,7% of myeloid blasts respectively. Both cases showed immunohistochemical overexpression of p53. Molecular studies confirmed the presence of a complex karyotype and mutations in TP53 by NGS. One patient is currently under treatment with azacitidine and venetoclax, four months after the diagnosis, and the other one passed away three months after the diagnosis.
Conclusion: Acute erythroid leukaemia is a rare and aggressive form of acute leukaemia with deleterious clinical course and a median survival of 2-4 months. The differential diagnosis is broad, including both reactive and neoplastic conditions associated with erythroblast proliferation. Detection of mutant p53 patterns by immunochemistry is a useful surrogate marker for TP53 gene mutations and the presence of a complex karyotype.

E-PS-11-071
Study of three cases of follicular variant of peripheral T cell lymphoma (PTCL) - a rare and aggressive subtype of nodal lymphomas of T follicular helper (Tfh) phenotype
S. Vidhale*, N. Oza, S. Gurjal, S. Kane
*Tata Memorial Hospital, India

Background & objectives: Follicular T-cell lymphoma (FTCL) accounts for less than 1% of all T-cell lymphomas. FTCL develops predominantly in lymph nodes; however, it may involve the skin, bone marrow and peripheral blood also. Here, we delineate three cases of FTCL.
Methods: We report a series of 3 cases of Peripheral T cell Lymphoma with Follicular T helper phenotype. Excision Biopsy performed was subjected to adequate tissue fixation and processing followed by staining with hematoxylin and eosin preparation. All cases were further subjected to immuno-histochemical stains. We present our detailed findings and interpretations that led to the diagnosis of this rare entity.
Results: Case 1: 65 years old female presented with fever and weight loss accompanied by generalized lymphadenopathy with splenomegaly. CASE 2: 35 years old male with neck swelling since two years. On imaging, multiple discrete and conglomerate left cervical and supraclavicular nodes were noted. Case 3: 70 years old male presented with fever and generalized lymphadenopathy. Microscopically, all 3 cases revealed more or less similar features comprising of vague nodules with expanded paracortical zone composed of small to intermediate-sized atypical lymphoid cells admixed with histiocytes, plasma cells, and eosinophils. On immunohistochemistry, the atypical cells in the nodules and the paracortical zone were positive for CD3, CD2, CD7, CD4, PD-1, and ICOS.
Conclusion: The rarity of this follicular variant of PTCL raises the concern of misdiagnosing these lesions considering the complexity in the morphological features and the immunohistochemical phenotype expressed by the different subgroups of PTCL. This variant of PTCL maybe considered as a differential in a lymph node displaying a follicular or a nodular pattern, as this entity of T-cell lymphomas have a worse prognosis. A thorough histopathological examination supported by immunohistochemical stains and molecular studies is necessary for an accurate diagnosis.

E-PS-11-072
A case of adult T-cell leukemia/lymphoma with HTLV-1–infected Hodgkin and Reed-Sternberg–like cells
D. Yamashita*, S. Bamba, K. Karube, T. Ishikawa, S. Hara
*Department of Pathology, Kobe City Medical Center General Hospital, Japan

Background & objectives: Classic Hodgkin lymphoma must be distinguished from a variety of T and B-cell proliferations, both reactive and neoplastic, that mimics HRS cells. Here, we present a case of adult T-cell leukemia/lymphoma with HRS cells which was diagnosed by HBZ-RNA scope.
Methods: A 68-year-old man was referred to our hospital with swelling of the left neck 4 months prior to the visit.A biopsy of the left cervical lymph node showed a small number of HRS-like cells in a diverse inflammatory background. Immunohistochemistry, tumour cells were CD4+CD30+EBER-ALK-CM-.
Results: Patient serum was positive for HTLV-1 antibodies, and we tentatively diagnosed as adult T-cell leukemia/lymphoma(ATLL). HTLV-I proviral DNA monoclonality was not detected. Next, we performed HBZ-RNA scope on paraffin sections, and observed that HRS-like tumour cells expressed HBZ. We finally confirmed the diagnosis of ATLL. The patient had no relapse in 6 months with 2 courses of modified LSG15, haplo-PBSCT.
Conclusion: ATLL has a poor prognosis among T-cell lymphomas, and early diagnosis and treatment are desirable. Proof of HTLV-I proviral DNA monoclonality by Southern blotting is necessary to confirm the diagnosis of ATLL, but the large amount of DNA, and need for unfixed specimen are major limitations. We believe that the HBZ-RNA scope method, which can detect HBZ expression under direct observation using pathology specimens, is useful in challenging cases, and is expected to provide more rapid and accurate therapeutic intervention.

E-PS-11-073
Follicular lymphoma nomenclature according to the WHO 2022 classification: How much has changed in the daily routine?
N. Yeldir*, A. Cakir
*Istanbul Medipol University, Turkey

Background & objectives: Follicular lymphoma (FL) was traditionally graded(1,2,3a,3b) based on the number of centroblasts. In theWHO2022revision, the follicular lymphoma classification was renewed, the obligation to specify the degree was removed and the following morphological groups were defined:(1) classical FL(cFL),(2) follicular large B-cell lympho ma(FLBL),(3)FL with uncommon features.
Methods: Cases diagnosed with FL between 2014 and 2024 were screened from the hospital patient system. These cases, originally named according to the WHO2016 classification, have been reclassified according to the ICC and WHO2022 criteria.
Results: Of the 111 cases diagnosed withFL, M/F was 49/52. The mean age was 57.1 years.Sixty-six cases diagnosed with low-gradeFL, grade1-2 according to WHO2016,were reclassified as classicalFL according to WHO2022.Twenty-two of the 23 grade3AFL cases were also reclassified as cFL, while one of them was classified as FLBL.Four grade3BFL cases and one high-gradeFL case were classified as FLBL. Six of the 7 grade3AFL and diffuse large B-cell lymphoma (DLBCL) cases were reclassified as cFL, while one case was classified as FLBL. Five grade 3B FL and DLBCL cases were classified as FLBL.As a result, 12 cases were reclassified as FLBL.Eight of these cases were initially diagnosed withFL and DLBCL in the WHO2016 classification.
Conclusion: In 2022, WHO and ICC revised the classification of myeloid and lymphoid neoplasms at similar times. While the nomenclature of all FL changed according toWHO2022, there was no change according to ICC. WHO2022 finds the distinction between 3A and 3B important, the ICC emphasizes this distinction less. In our study, when WHO2016 and WHO2022 were compared, it was found that there was a diagnostic change in only 10.8% of the cases.

E-PS-11-075

Atypical lymphocytic lymphoma transitioning into dendritic cell sarcoma after bruton's tyrosine kinase inhibitor treatment

J.T. Zúñiga Gaitán*, M. Bosch Schips, A.M. Montaña Ramirez, J. Castellvi Vives
*Vall d'Hebron University Hospital, Barcelona, Spain

Background & objectives: Dendritic cells can originate from myeloid and lymphoid progenitors, but transdifferentiation from mature B-cell to an interdigitating dendritic cell is not well understood. We present a B-cell lymphocytic lymphoma transforming into interdigitating dendritic cell sarcoma after Bruton's tyrosine kinase inhibitor(BTKis).
Methods: A 63-year-old woman, previously diagnosed with lymphocytic lymphoma and having undergone more than 10 lines of treatment without response, was admitted at our institution. The diagnosis of lymphocytic lymphoma was confirmed through lymph node excision. After the initiation of BTKis, the patient experienced progressive worsening, suggesting a potential transformation to Richter's syndrome. Therefore, a new biopsy was performed.
Results: The initial lymph node excision showed small atypical lymphocytes with immunohistochemistry supporting lymphocytic lymphoma. However, it presented an atypical phenotype characterized by negative CD5, strong positive CD23, and weakly positive LEF1, along with trisomy of chromosomes 7 and 12 with deletions of 3p and 9q mutations but not in inmunoglobulin gene. Additionally, TP53 mutation was observed in peripheral blood. The sample after clinical-radiological worsening, exhibited a significant number of large pleomorphic cells. These cells showed positivity for S100, HLA-DR, CD4, CD45, CD68, and negativity for specific markers of Langerhans cells, follicular dendritic cells, cytokeratins, and melanocytes. BRAF(p.V600E) mutation and IGH gene clonal rearrangements were identical in both components.
Conclusion: As we are aware, three similar cases have been documented in the literature. However, our case initially presented as an atypical lymphocytic lymphoma. Trisomies 12 and 7, along with the IGH rearrangement and BRAF(p.V600) mutation, were identical in both tumour components, supoporting a transdifferentiation from the same clonal cell origin. Similar cases have been reported post BTKis treatment, the role of which remains unclear. Understanding these cases is crucial for potentially developing new therapeutic strategies.

E-PS-12E-Poster Session Molecular Diagnostics Pathology Symposium

E-PS-12-001

Molecular aberrations in non-high risk neuroblastoma progressing to high-risk neuroblastoma

R. Bruinsma*, M. Dierselhuis, W. de Leng, L. Kester, M. van Noesel, L. Tytgat, K. van de Ven, M. Wijnen, R. de Krijger, L. van der Steeg
*Prinses Maxima Centrum, The Netherlands

Background & objectives: After relapse a significant fraction of non-high-risk neuroblastomas is re-classified as high-risk. Only 20% of these patients survive. We aim to determine whether molecular aberrations in non-high-risk neuroblastoma might predict future progression to high-risk neuroblastoma.
Methods: All patients treated in the Princess Máxima Center between 2014 and 2023 with a non-high risk neuroblastoma, which later reclassified as high-risk, were included. Gene mutations, amplifications and copy number variations were detected using fluorescence in situ hybridization (FISH), targeted next generation sequencing, single nucleotide polymorphism array and/or whole exome sequencing. All molecular data were obtained from the primary tumour.
Results: We included 12 cases primarily diagnosed as non-high-risk neuroblastoma (according to the DCOG NBL 2009 treatment protocol), but were reclassified after progression (n=4) refractory disease (n=3), relapse (n=3) or metastases (n=2). Eight tumours presented with a MYCN gain (2-4 gene copies) at FISH analysis. Furthermore, one neuroblastoma harbored an ALK mutation. Combined MDM2 and CDK4 amplifications were detected in two tumours. Copy number analysis yielded segmental chromosomal aberrations in nine cases, including three 1p deletions, three 11q deletions and four 17q gains.
Conclusion: Non-high-risk neuroblastoma that progress to high-risk neuroblastoma often present with MYCN gain and/or segmental chromosomal aberrations. Furthermore, ALK mutations or combined MDM2 and CDK4 amplification might indicate a more aggressive tumour. The data from this small cohort indicate that the stratification criteria for LR-neuroblastoma may need to be revised.

E-PS-12-002

mRNA expression level of ALK in neuroblastoma is associated with histological subtype, ALK mutations and ALK immunohistochemical protein expression

R. Bruinsma*, M. Fiocco, W. de Leng, L. Kester, K. Langenberg, L. Tytgat, M. van Noesel, M. Wijnen, L. van der Steeg, R. de Krijger
*Prinses Maxima Centrum, The Netherlands

Background & objectives: *ALK* mutations, amplification and immunohistochemical expression are related to poor survival in neuroblastoma patients. We investigated the prognostic relevance of ALK mRNA expression levels and their relationship with histological subtype of neuroblastomas, ALK immunohistochemical expression and genetic aberrations of *ALK*.
Methods: Whole transcriptome sequencing data of diagnostic biopsies were available from 54 patients, with ALK mRNA expression level as continuous variable. Overall survival (OS) and event free survival (EFS) were estimated with Kaplan-Meier's methodology. ALK protein expression was analysed by immunohistochemistry. *ALK* aberrations were detected using whole exome sequencing, single nucleotide

polymorphism array, next generation sequencing and/or fluorescence in situ hybridization.
Results: OS was 74.8% (SE 6.6) and EFS was 60% (SE 7.6), respectively, by the end of follow up. mRNA expression was not associated with OS (HR 1.127, 95% CI (0.812-1.854) and adjusted EFS (HR 1.134, 95% CI (0.783-1.644). ALK mRNA expression levels were associated with histological subtype of neuroblastoma (OR 1.914, 95% CI (1.083-3.382)) and with ALK immunohistochemical protein expression (negative versus weak: OR 2.829, 95% CI (1.290-6.204)) (negative versus moderate/strong: OR 2.934, 95% CI (0.889-9.679)). Furthermore, *ALK* mutated tumours had a significantly higher mRNA expression level than neuroblastomas without an *ALK* mutation ($p<0.001$).
Conclusion: mRNA expression levels of ALK are higher in *ALK* mutated neuroblastomas and are associated with poorer differentiation degree and higher immunohistochemical protein expression. ALK mRNA expression is not associated with OS and EFS in children with a neuroblastoma.

E-PS-12-003
Prognostic value of molecular aberrations in low- or intermediate-risk neuroblastomas: a systematic review
R. Bruinsma*, C. Lekkerkerker, M. Fiocco, M. Dierselhuis, K. Langenberg, M. van Noesel, L. Tytgat, M. Wijnen, L. van der Steeg, R. de Krijger
*Prinses Maxima Centrum, The Netherlands

Background & objectives: Prognosis of non-high risk neuroblastomas is quite good (70-90% survive). However, some children still succumb to their disease. We aim to identify molecular aberrations (not already incorporated in the risk stratification) associated with overall survival (OS) and/or event-free survival (EFS).
Methods: We conducted a systematic search for Pubmed, Embase, Cochrane and Google Scholar. Two reviewers independently and blindly screened titles/abstracts, reference lists of protocols and reviews, and read full texts. Risk of bias and applicability were assessed using a specified Quality in Prognosis tool and an applicability tool designed by the researchers. GRADE criteria were used to determine quality of evidence.
Results: Sixteen studies (4718 patients) were included. Thirteen investigated single molecular aberrations. 1p loss of heterozygosity (LOH), 1p deletion, 17q gain and number of chromosomal breakpoints were associated with poorer OS and EFS. Furthermore, 1q gain, 2p gain and 4p deletion were associated with inferior OS, but not with EFS. Loss of the entire X chromosome was associated with poorer EFS (OS was not reported). *ALK* mutations and 3p deletion were not associated with poorer outcome. Seven studies showed an association with, or a trend towards, inferior outcomes in tumours with a segmental chromosomal aberration (SCA) profile. Quality of evidence for both single molecular aberrations and genomic profile was rated moderate.
Conclusion: 1p LOH/deletion, 1q gain, 2p gain, 4p deletion, 17q gain, loss of whole chromosome X and number of chromosomal breakpoints were associated with poor outcome. Neuroblastomas with an SCA profile seem to be associated with inferior outcomes as well. Quality of evidence was rated as moderate.

E-PS-12-004
BRAF-mutated tubular eccrine adenoma
A. Córdoba*, I. Fernandez, M.R. Mercado, C. Llanos, J.I. Yanguas, D. Guerrero
*Hospital Universitario de Navarra, Spain

Background & objectives: Tubular adenoma (TA) are benign sweat gland tumours that can exhibit apocrine (tubular apocrine adenoma, TAA) and eccrine differentiation (tubular eccrine adenoma,TEA). However, morphologically they are very similar. The molecular pathogenesis of either tumour is poorly understood at present.
Methods: We present a case of TEAwith immunohistochemical expression of BRAF and BRAFV600E mutation.A 48 years old man, with a solitary keratotic nodule in his left arm. The lesion was surgically removed.
Results: Histologically, a circumscribed tumour composed of tubular glands in the dermis, and epidermal hyperplasia is observed. The glands are lined by cuboidal luminal epithelial cells, which have eosinophilic cytoplasm and round nuclei with small nucleoli. There is also a layer of myoepithelial cells around the luminal cells. Occasionally a micropapillary growth is observed. The stroma is sclerotic with a mild mononuclear cell infiltrate. Decapitation secretion is absent. All neoplastic cells were diffusely positive for CK14.The inner (luminal) layer was positive for CK7 and CEA. The cells of the outer layer (myoepithelial cells) were positive for p63. Immunohistochemical staining specific for BRAFV600E was positive. Activating mutations of BRAFV600E were identified.
Conclusion: Tubular adenoma is a rare neoplasm. In 1977, Rulon and Helwig described a new neoplasm called papillary eccrine adenoma. TAAs are most frequently seen in the head, especially on the scalp, whereas TEAs are more frequent in the extremities. We concluded that BRAF activating mutations were frequently present in TEAs, indicating that, in addition to a morphological resemblance between TAAs and TEAs, they are closely related genetically. Therefore, they could be considered to be linked as a single entity.

E-PS-12-005
Immunological changes in gut barrier function by pro-inflammatory biomarkers linked ROS-cell death mechanisms by flow cytometry methods in Romanian liver cirrhosis patients
E. Matei*, A. Dumitru, G. Cozaru, A. Chisoi, L. Alexandrescu, R.C. Popescu, M. Pundiche Butcaru, E. Dumitru, S. Rugină, C. Tocia
*CEDMOG, Ovidius University, Constanta, Romania

Background & objectives: The gut barrier is a morphological, functional mechanism that includes epithelial, immunological, vascular, and liver barriers.
Methods: Immune changes by pro-inflammatory biomarkers in the gut–liver-axis-linked ROS-cell death mechanisms in chronic and acute inflammation (CII; AII) when gut cells are exposed to endotoxins in patients with hepatic cirrhosis (HC) were analysed by flow cytometry methods.
Results: Late apoptosis is a chronic response to injury induction by gut immune barrier dysfunction, oxidative stress, and liver-dysregulated barrier in duodenal tissue samples recovered from patients with hepatic cirrhosis with A-B child (CII:41.32 ± 6.71 vs. AII: 0.27 ± 0.77, $p<0.01$) or C child stages (CII: 42.16 ± 17.63 vs. AII: 0.41 ± 0.69, $p<0.01$). Necrosis is an acute and severe reply to endotoxin action in gut cells when the innate and adaptive functional immune system reacts to pro-inflammatory Th1 and Th2 cytokines in patients with hepatic cirrhosis with A-B child (AII: 11.74 ± 2.21 vs. C: 1.78 ± 0.29, $p<0.05$) or C child stages than controls (AII: 17.73 ± 2.60 vs. C: 1.78 ± 0.29, $p<0.01$).
Conclusion: Our study highlighted ROS-cell death mechanisms in chronic or acute inflammation when gut cells are exposed to endotoxins and immune changes in the gut–liver axis.

E-PS-12-006
The effect of isocitrate dehydrogenase 2 (IDH2) gene variation and tert gene variation in prostate cancer
F. Özkan*, S. Güleç Yılmaz, T. Akdeniz, T. Isbir
*Yeditepe University Medical Faculty, Department of Pathology, Turkey

Background & objectives: Prostatic carcinoma is a heterogeneous disease with metastatic potential so identifying the molecular characteristics may contribute to new therapy regimens We aimed to use next-generation sequencing technology to identify variations in the IDH2 and TERT target genes in prostatic cancer.
Methods: In our study, blood samples from 27 patients at Yeditepe University Hospital who had been diagnosed with prostatic carcinoma were usedThe IDH2 and TERT genes were examined using next-generation sequencing and confirmed by Sanger sequencing.
Results: One of these mutations was discovered in the IDH2 gene and four others within the TERT gene. One variant detected in IDH2 was seen in 2 heterozygous patients. Four variants located in the exonic region of the TERT gene have been identified. Of these, c.2850 C>T heterozygous was determined in 6 patients, c.1392 C>T heterozygous in 1 patient, c.915 G>A in 18 patients, 4 of which were homozygous and 14 heterozygous, and c.261 G> T was determined in one patient. Among these five variants, one was identified as potentially harmful. It was confirmed by Sanger sequencing that the patient carrying the potentially harmful variant was a TERT c.261G>T heterozygous mutant.
Conclusion: All of these variations except TERT rs2736098 were not known to exist in prostate cancer. For the first time, rs1033845124 missense mutation in the TERT gene (CADD score > 10, no ExAC frequency) was identified as possibly pathogenic for prostate cancer. It is possible to bring these variations to the clinic and determine new treatment modalities.

E-PS-12-007
Molecular diagnostic characteristics in non-small cell lung carcinomas (NSCLC) and its relationship with the PD-L1 expression
A. Sert*, A. Sadioğlu, Ö. Ekinci, B. Öğüt, M.A. Inan, N. Akyurek
*Gazi University Faculty of Medicine, Turkey

Background & objectives: Programmed death ligand-1 (PD-L1) expression is a predictive biomarker of response to immune checkpoint blockade in NSCLC. However, there is limited evidence of the relationship between PD-L1 expression, and their association with driver mutations in NSCLC patients in Turkey.
Methods: A total of 1364 patients with advanced NSCLC were analysed using the FISH analysis and NGS system. PD-L1 expression was estimated by immunohistochemistry (IHC) using the PD-L1 clone SP263 and was defined as negative if TPS was < 1%, low if TPS was 1-49% and high if TPS was ≥ 50% of tumour cells.
Results: In the total population, 63.6% had negative PD-L1 expression, 12.6% had low expression (1%-49%), and 18.8% had high expression (≥50%). The PD-L1 positive rate was 33.5% in squamous cell carcinomas and 30.9% in adenocarcinomas. Of the overall patient population, 26.7% *KRAS*, 20.2% *EGFR*, 3.2% *HER2,* 1.2% *BRAF V600E*, 0.3% *MET* exon 14 skipping mutations, 4.7% *ALK* and 1.2% *ROS1* rearrangements were detected. Patients carrying *ROS1* ($p = 0.006$), *ALK* ($p= 0.041$) rearrangements, *KRAS* ($p < 0.021$), *BRAF V600E* ($p < 0.001$), and *MET* ($p= 0.001$) mutations had significantly elevated expression of PD-L1, while those harboring *EGFR* ($p < 0.001$) and *HER2* ($p < 0.04$) mutations had lower PD-L1 expression.
Conclusion: Our study showed the heterogeneity in PD-L1 expression with respect to major oncogenic drivers in Turkey. *KRAS, BRAF, MET* mutations and *ALK* and *ROS1* rearrangements were more frequent, while *EGFR* and *HER2* mutations were less frequent compared with the overall PD-L1 expression levels.

Molecular testing of non-small cell lung carcinomas (NSCLC) for oncogenic driver mutations has become standard in pathology practice.

E-PS-12-008
Comprehensive pan-cancer analysis of FRS2 gene alterations and protein expression in the TCGA (The Cancer Genome Atlas) cohort – a genome database study
M. V M*
*Jipmer, Puducherry, India

Background & objectives: FRS2, a signal-transducing adaptor protein, is proven to be overexpressed in a few tumours, and its role is still under investigation in many others. In the TCGA cohort, pan-cancer analysis of FRS2 gene alterations and protein expression is studied.
Methods: Frequency and mutation data of FRS2 gene alterations in TCGA dataset are evaluated using cBioPortal. Comparative analysis between FRS2 gene expression in tumour and adjacent normal tissue, and role of the gene in tumour microenvironment (as assessed by correlation between gene expression and cancer-associated fibroblasts and CD8+ T cells) are done using TIMER2. Survival analysis is done using GEPIA2 software.
Results: Amplification is the most common alteration involving FRS2 gene in the TCGA cohort, which occurs in the highest frequency in dedifferentiated liposarcoma (72.8% cases). 42 cancer cohorts showed FRS2 gene alterations. A comparative analysis between tumour and adjacent normal tissue gene expression revealed significantly higher expression in tumour tissue in 13 cancer cohorts, including gastric and colorectal adenocarcinomas and head and neck SCC. A higher gene expression tumour also correlated with cancer-associated fibroblasts in 8 cancer cohorts, which again included colorectal adenocarcinomas and head and neck SCC ($p <0.5$). A higher expression showed a significant association with better OS in Clear cell RCC, indicating a prognostic role for the gene.
Conclusion: This study evidences that FRS2 gene alterations, besides their well-established diagnostic utility in dedifferentiated liposarcoma, may also play a significant role in the pathogenesis of colorectal, gastric, and renal cell carcinomas. A higher frequency of gene amplification in these tumours can have diagnostic and prognostic implications. In addition, a significant association of gene expression with cancer-associated fibroblast in a few tumours indicates a potential role in the tumour microenvironment, further evidencing this gene's role as a potential therapeutic target.

E-PS-13E-Poster Session Neuropathology

E-PS-13-001
Clival IgG4-related hypertrophic pachymeningitis
T. Al-Halouly, M. Bafaqeeh, M. Tashqandi, M. Mohajry, S. Al-Dandan*
*King Fahad Medical City/King Fahad Hospital Hofuf, Saudi Arabia

Background & objectives: IgG4-Related Disease (IgG4-RD) is an autoimmune multi-organ chronic fibro-inflammatory disorder. Hypophysitis and rarely hypertrophic pachymeningitis are the two cardinal presentations in the central nervous system. Only 14 cases of clival IgG4-related hypertrophic pachymeningitis (IgG4-RHP) are reported in the English literature.
Methods: A 26-year-old male presented with a one-year history of dysarthria and neck pain associated with blurred and double vision of one month's duration. On physical examination, he had dysarthria with drooping of saliva and cranial nerve XII fasciculations. The MRI revealed a well-defined, intensely enhancing retro-clival lesion. The patient underwent resection of the lesion by endoscopic trans-nasal trans-clival approach.
Results: Histopathological examination of the lesion demonstrated marked dural thickening, dense storiform fibrosis, and prominent

lymphoplasmacytic cellular infiltrate. The plasma cells were primarily IgG4+ by immunohistochemistry (>40 per HPF). The lymphoplasmacytic infiltrate was polytypic with no kappa or lambda restriction. The negative ALK1 immunostain argued against inflammatory myofibroblastic tumour. The special stains were negative for acid-fast bacilli and fungi. There was no angiofollicular hyperplasia to suggest Castleman disease. The absence of leukocytoclastic vasculitis and necrotizing granulomas ruled out ANCA-associated vasculitis.
Conclusion: Clival IgG4-related hypertrophic pachymeningitis is a rare disease. The clinical presentation and imaging are indistinguishable from meningioma. Histologic assessment and ancillary studies are necessary to rule out other diagnostic considerations, such as lymphoproliferative disorders, infections (mycosis and tuberculosis), Castleman disease, and ANCA-associated vasculitis.

E-PS-13-002
Fatal invasive rhinocerebral aspergillosis with Hülle cells in a young immunocompetent male
D. AlGhamdi, M. Bafaqeeh, A. AlSawadi, F. Alkhureeb, S. Al-Dandan*
*King Fahad Medical City/King Fahad Hospital Hofuf, Saudi Arabia

Background & objectives: Hülle cells are specialized cell types unique to Aspergillus species. They can germinate and reinitiate both asexual and sexual development. Identifying Hülle cells in Aspergillus rhinocerebritis is rare, with only four cases reported in the English literature.
Methods: A 36-year-old male presented with a three-month history of headaches, weight loss, and visual disturbances. He had sinus surgery for nasal polyps eight months before his presentation. On physical examination, he had unequal pupils, right eye ptosis, and 3rd cranial nerve palsy. The MRI revealed a destructive lesion involving the right sphenoid sinus, skull base, and right temporal lobe.
Results: Microscopic examination of the lesion demonstrated marked angioinvasive chronic necrotizing pyogranulomatous cerebritis. There were fungal hyphae with frequent septations and dichotomous branching. There were also many Hülle cells with globose and pear-shaped morphology and thick, hyaline walls. The fungal hyphae and Hülle cells were positive for PAS and GMS stains. Additionally, Hülle cells showed alternating parallel apple-green and fire-orange birefringence in a Maltese-cross pattern with the Congo red stain. Ultrastructural examination revealed several Hülle cells of variable sizes (4.0-6.0 μm) with thick lamellar walls (0.5-1.5 μm). Microbial culture showed heavy growth of Aspergillus flavus. The condition of the patient rapidly deteriorated following decompressive craniotomy and debulking, and he died.
Conclusion: Different species of the genus Aspergillus produce Hülle cells. However, A. nidulans and A. ustus are the only ones reported with sinus infections. The presence of Hülle cells among culture-proven growth of Aspergillus flavus indicates mixed infection. The formation of Hülle cells might have contributed, in whole or in part, to the microorganism's pathogenicity and virulence by evading the host's defensive mechanism. Herein, we characterize Hülle cells by morphology, special stains, and ultrastructure.

E-PS-13-003
Spinal ependymoma with eosinophilic hyaline droplets and rounded globular bodies
S. Al-Dandan*, J. Al-Obeid, J. Majrashi, A. Almalki, A. AlHussain, I. AlAhmad
*King Fahad Medical City/King Fahad Hospital Hofuf, Saudi Arabia

Background & objectives: Eosinophilic inclusions in brain tumours are categorized into eosinophilic hyaline droplets (EHD) and rounded globular bodies (RGB). They are rare in ependymomas and have been described only in paediatric supratentorial ependymomas.
Methods: A 54-year-old female patient presented with progressive lower limb weakness, decreased sensation, and urine and stool incontinence. Motor examination revealed severe bilateral lower limb spastic weakness. Magnetic resonance imaging of the thoracic spine demonstrated a heterogeneous T2 hyperintense intramedullary lesion. The patient underwent T4-T7 laminectomy and debulking of the tumour.
Results: Microscopic examination revealed a well-circumscribed glial neoplasm with prominent perivascular pseudorosette formation and occasional true ependymal microrosettes. The tumour comprises uniform cells with round to oval nuclei with stippled chromatin patterns embedded in a fibrillary background. We could detect two types of eosinophilic material/deposits. The rounded globular bodies (RGB) were rounded, extracytoplasmic, faintly eosinophilic on H&E, and green-blue on Trichrome stain. The eosinophilic hyaline droplets (EHD) were irregular, intracytoplasmic, brightly eosinophilic on H&E, and fuschinophilic on Trichrome stain. Immunohistochemical staining for GFAP and EMA was strong for RGB and faint for EHD. Ultrastructurally, RGBs were heterogeneous with electron-dense and electron-lucent deposits, while EHDs were homogeneous, dark, and electron-dense.
Conclusion: Eosinophilic hyaline droplets (EHD) and rounded globular bodies (RGB) are extremely rare in ependymal tumours and have not been described in adult spinal ependymomas. An imaging review demonstrated no radiological feature that correlates with RGBs or EHDs. The rarity of these deposits in ependymomas makes establishing the correct diagnosis challenging. We characterized these eosinophilic inclusions by morphology, special staining, immunohistochemistry, and ultrastructure.

E-PS-13-004
Contribution of immunohistochemistry in the diagnosis of brain metastases
R. Aouadi*, A. Zehani, A. Ayari, A. Khadhar, I. Chelly, H. Azouz, K. Bellil, S. Haouet
*La Rabta Hospital, Tunisia

Background & objectives: Brain metastases account for 15 to 25% of intracranial tumours. Along with histological examination, immunohistochemistry is essential to identify the primary tumour. We aimed to study brain metastases's histological features and to evaluate immunohistochemistry's contribution to the etiological investigation.
Methods: We gathered 105 cases of brain metastases diagnosed in our department over an 8-year period (2016-2024). An immunohistochemical study was carried out in all cases to characterize the primary tumour. For each case, different antibodies were used depending on the clinical and histological orientation.
Results: Patients were 73 men and 32 women with a mean age of 55,51 years. Histological types comprised adenocarcinoma (55 cases), poorly differentiated carcinoma (18 cases), neuroendocrine carcinoma (11 cases), epidermoid carcinoma (9 cases), papillary carcinoma (4 cases), sarcomatous carcinoma (2 cases), lymphoma (2 cases), synovial sarcoma (1 case), germ cell tumour (1 case), urothelial carcinoma (1 cases) and clear cell carcinoma (1 case). In men, pulmonary origin was identified in 47 cases, followed by digestive tract, bladder, thyroid, kidneys and breast. In women, the primary site was mainly the breast, followed by lungs, ovaries, parotid gland, colon, thyroid, endometrium, and soft tissue. The primary site was unknown in 16 cases.
Conclusion: Adenocarcinoma is the most common histological type of brain metastases. Immunohistochemistry is often required to determine the origin. Pulmonary and mammary origins are the most frequent in men and women respectively. However, in some cases, determining with certainty the primary site may be challenging and the final diagnosis is limited to a group of tumours with a comparable profile.

E-PS-13-005

Histologically heterogeneous paediatric glioneuronal tumour with FGFR1::TACC1 fusion

E.B. Balaban*, C. Sönmez, F. Aker
*University of Health Sciences Haydarpaşa Numune Training and Research Hospital, Department of Pathology, Turkey

Background & objectives: Paediatric-type low-grade gliomas (pLGG) account for approximately 30% of all childhood brain tumours. In pLGG, there are well-defined entities as well as tumours with overlapping morphology. Here we report a case that has heterogeneous morphology with *FGFR1::TACC1* fusion.
Methods: An eleven-year-old boy was admitted to the hospital with complaints of headache, nausea and balance disorder. He had an operation for a right lateral intraventricular mass 6 years ago. Brain MRI revealed an intraventricular mass located in the centre of the right lateral ventricular body. The patient underwent a craniotomy for resection of the tumour.
Results: Histopathological examination revealed a circumscribed glial/ glioneuronal tumour with different morphological components. These components include rosette-forming glioneuronal tumour-like areas consisting of smooth papillae and rosette structures formed by small round neurocyte-like cells without atypia; a pilocytic astrocytoma-like area consisting of cells with elongated nuclei, bipolar piloid processes and eosinophilic granular bodies, dysembryoplastic neuroepithelial tumour-like areas consisting of microcystic structures on a myxomatous background, a fine vascular capillary network, pleomorphic xanthoastrocytoma-like areas consisting of thick-walled vascular structures, multinucleated giant cells. No mitosis, necrosis and vascular endothelial proliferation were observed. GFAP was positive in all components to varying degrees . IDH-1, BRAFv600E and EMA were negative. Next Generation Sequencing revealed *FGFR1::TACC1* fusion.
Conclusion: In conclusion, although there are well-defined entities and tumours with overlapping morphology in pLGG, the diagnostic, prognostic, and predictive significance of these fusions in CNS tumours and pLGG has not yet been established. Considering the recurrence of our case, we can say that close follow-up is necessary.

E-PS-13-006

Connecting the dots: molecular pathology contribution in brain tumours of young patients

R.A. Barna*, A. Lamy, S. Vautier, C. Lazureanu, D. Herman, A. Dema, J. Sabourin, F. Marguet
*Victor Babes University of Medicine and Pharmacy, Romania

Background & objectives: The latest WHO classification of the central nervous system (CNS) tumours marks a significant change, incorporating histological findings with molecular characterization. This case series examines how the new classification contributes to diagnosing challenging brain tumours in young patients.
Methods: We report four CNS tumour cases in young patients with discrepant histologic features, where achieving a precise diagnosis proved difficult with hematoxylin-eosin and immunohistochemistry (IHC), especially when IHC staining differed among laboratories. All cases underwent analysis via next-generation sequencing (NGS), using an Archer NGS custom assay (ArcherDX, USA) for library creation, and the MiSeq System (Illumina, USA) for sequencing.
Results: A 34-year-old male had a glial tumour with IDH1 and ATRX positive immunohistochemically. NGS revealed ATRX, IDH1 and TP53 pathogenic variants, and CDKN2A deletion, diagnosing as Astrocytoma G4.
A 47-year-old male displayed a high-grade glioma with primitive/ embryonic areas and IDH1 negative immunohistochemically. NGS revealed TERT promoter, PTEN, RB1 and TP53 pathogenic variants, and wild-type IDH1, diagnosing as Glioblastoma.
A 35-year-old male had a polymorphic glial tumour, ATRX positive and IDH1 negative immunohistochemically. NGS identified TERT promoter, KRAS, and PIK3CA pathogenic variants, diagnosing as Pleomorphic Xanthoastrocytoma.
A 3-year-old male, suspected of atypical teratoid/rhabdoid tumour (ATRT), had homozygous loss of SMARCB1 and aberrant-cytoplasmic IHC expression for INI1. ATRT was confirmed eventually.
Conclusion: In conclusion, the diagnosis of CNS tumours in young patients which might have particular morphological aspects, can be challenging, especially when relying solely on traditional morphologic diagnostic methods. However, the integration of molecular pathology methods has proven useful in overcoming diagnostic uncertainties and achieving more accurate diagnoses, which is underscored by this case series. Furthermore, the latest WHO classification of CNS tumours has brought some level of clarity to the diagnostic processes, providing a structured framework for establishing accurate diagnoses.

E-PS-13-007

Diagnosis of toxoplasmosis in brain biopsy

I. Blazquez*, B. Kaliullayev, M. Gomez, J. Martinez, N. Vicente, J. Rodriguez, A. Domingo, N. Vidal
*Hospital Universitari de Bellvitge, Spain

Background & objectives: Toxoplasma gondii is an intracellular protozoan parasite that causes subclinical manifestations in immunocompetent patients but can cause severe manifestations in immunocompromised ones , such as toxoplasmic encephalitis, whose clinical presentation is very varied.
Methods: Review of biopsy cases diagnosed as cerebral toxoplasmosis at the Bellvitge University Hospital (HUB) in the last 10 years . We include clinical, morphological and immunohistochemical data.
Results: Three patients have been diagnosed with cerebral toxoplasmosis in the last 10 years. All were immunosuppressed patients, one of them had liver transplant and another one multiple myeloma. The third one was diagnosed with HIV following a biopsy diagnosis of toxoplasmosis. The clinical presentation was different between them: one with headache for weeks and the other two with aphasia. They showed multiple space-occupying, hyperenhancing and oedematous brain lesions on MRI, some of which were ring-shaped. All three cases were clinically and radiologically classified as neoplasms: one as lymphoma and two as metastases. Biopsies showed necrosis and brain parenchyma with dense lymphoplasmacytic and histiocytic inflammatory infiltrate, identifying cysts filled with bradyzoites.
Conclusion: It is important to consider toxoplasmosis in biopsy of patients with multiple brain lesions even if the clinical-radiological orientation is neoplasia, especially if the patients are immunosuppressed. Morphologically, the presence of bradyzoite-filled cysts should be sought in order to reach the diagnosis. This diagnosis has prognostic implications, and may even be the first sign of unknown immunosuppression.

E-PS-13-008

Neuropathological features of non-diffuse midline "neuroepithelial" tumours H3K27-altered: a single centre experience

A. D'amati*, A. Mastronuzzi, A. Olivi, F. Vegni, C. Mazzarella, L. Massimi, M. Gessi
*Department of Pathology, Neurosurgery and Paediatric Oncology, Fondazione Policlinico Universitario "A.Gemelli" IRCCS, Università Cattolica del Sacro Cuore, Roma, Italy

Background & objectives: Diffuse midline glioma (DMG), H3 K27-altered, is an infiltrative glioma with loss of H3K27me3 and either H3K27M mutation, EZHIP overexpression or EGFR alteration. However, H3K27M mutation may occur in other non-infiltrative midline tumours. Classification of such tumours is still controversial.

Methods: Between June 2016 and March 2024, 43 cases of H3K27-altered midline tumours were diagnosed in the Pathology Department of Fondazione Policlinico Universitario "A.Gemelli" IRRCS, Rome, Italy. These tumours affected 20 adults and 23 children. The series encompasses 10 pontine, 4 spinal, 5 brain stem, 19 thalamic, 1 multifocal tumours. Clinical course, imaging, histopathology, immunohistochemical profile, and molecular alterations were collected.
Results: Along with 40 DMG H3K27-altered cases, we identified 3 midline tumours showing unusual histology lack of infiltrative growth pattern, loss of H3K27me3 expression and harboring H3K27M mutation. Patient #1, a 37-years-old man, displayed a brain stem lesion, histologically consistent with pilocytic astrocytoma. After incomplete resection and chemoradiotherapy, remained stable for 12 months, showing afterwards neuroradiological progression. Case #2, a 6-years-old girl, and case #3, a 9-years-old boy, had thalamo-mesencephalic and cervical location, respectively. The histology was consistent in both cases with ganglioglioma. Case #2 relapsed after 15 months and the histopathological analysis after second surgery showed tumour progression. Patient #3, after surgery and chemoradiotherapy, remained stable at 22-month follow-up.
Conclusion: The cases herein reported underline the peculiar, probably less aggressive, clinical behaviour of these tumours, in comparison with standard DMG H3K27-altered. As the identification of such tumours is mandatory by pathologist, the careful discussion of such cases in multidisciplinary tumour board is pivotal.

E-PS-13-009
RB1-altered pineoblastoma presenting as diffuse leptomeningeal lesion in a familial retinoblastoma patient
A. D'amati*, A. Ruggiero, E. Miele, F. Vegni, G. Attinà, S. Mastrangelo, L. Massimi, M. Gessi
*Department of Pathology, Neurosurgery and Paediatric Oncology, Fondazione Policlinico Universitario "A.Gemelli" IRCCS, Università Cattolica del Sacro Cuore, Roma, Italy

Background & objectives: Pineoblastoma (PB) are rare and aggressive tumours arising in the pineal region. Recent advances demonstrated that PB encompasses different molecular types, including the RB1-altered subgroup. In this subgroup are also cases occurring in patients with familial retinoblastoma syndrome.
Methods: We report an unusual paediatric RB1 altered pineoblastoma presenting as a diffuse leptomeningeal lesion without any intraparenchymal central nervous system (CNS) involvement or presence of a mass lesion in pineal region. Clinical course, imaging, histopathology, immunohistochemical profile, and molecular alterations were collected.
Results: The patient was a 28-month-old girl, that underwent clinical examination for tremors, headache and gait disturbances. MRI revealed diffuse leptomeningeal enhancement, with solid tissue encasing L3-L5 cauda equina roots. The pathologic tissue obtained from an open neurosurgical biopsy revealed an undifferentiated round cell tumour, expressing neural markers and showing high proliferative activity index. The DNA methylation profiling analysis was indicative of a pineoblastoma, RB1 subtype (score 0.99). Genetic counseling revealed that the patient and her relatives harbor a germline RB1Arg661Trp mutation in the clinical settings of a familial retinoblastoma syndrome. After the diagnosis the patient received high-dose chemotherapy and radiation therapy.
Conclusion: Although RB1-altered pineoblastomas usually display very aggressive clinical behaviour in young children, the patient showed stable disease 19 months after the diagnosis.

E-PS-13-010
Clinical and pathological features of solitary fibrous tumours in the central nervous system: a series of 14 cases
Y. Dhouibi*, A. Zehani, A. Ayari, A. Khadhar, I. Chelly, K. Bellil, S. Haouet
*Department of Pathology, Rabta University Hospital, Tunisia

Background & objectives: Solitary fibrous tumours (SFTs) within the central nervous system (CNS) are rare neoplasms characterized by diverse clinical presentations. This study aims to present 14 cases with SFTs of CNS and to campare our results to the published data.
Methods: A retrospective analysis of 14 cases of CNS SFTs diagnosed at our institution was conducted, involving the examination of clinical, radiological, and histopathological data, along with a review of histopathological slides. Additionally, a re-evaluation of slides was performed, and tumours were reclassified according to the latest WHO classification of CNS tumours.
Results: In our series, the median age was 56 years, with a male predominance (male-to-female ratio 1.8). Clinical signs included generalized seizures , frontal syndrome (2 cases) and contralateral motor impairment. MRI consistently depicted meningioma-like features, predominantly Dural (12 cases) and spinal (2 cases). Intraoperatively, all tumours appeared encapsulated, haemorrhagic, and friable. Upon slide re-evaluation, most patients exhibited WHO grade 1 SFTs (7 cases), with 3 cases classified as grade 2 and 5 as grade 3. Immunohistochemical analysis showed intense and diffuse positivity for CD34, with EMA negativity in 12 cases and focal positivity in 2 cases. Excision was complete except for 2 patients.
Conclusion: This series highlights the clinical and pathological heterogeneity of CNS SFTs, emphasizing their diagnostic challenges. Our findings corroborate previous literature regarding the male predominance and meningioma-like radiological features of CNS SFTs.

E-PS-13-011
Primary isolated central nervous system lymphomatoid granulomatosis
Y. Dhouibi*, A. Zehani, k. ghedira, i. dhkhil, A. Ayari, A. Khadhar, I. Chelly, H. Azouz, K. Bellil, S. Haouet
*Department of Pathology, Rabta university hospital, Tunisia

Background & objectives: Lymphomatoid granulomatosis (LYG), a rare lymphoproliferative disorder associated with Epstein-Barr virus (EBV), predominantly affects the lungs but can also involve the skin, kidney, liver, and central nervous system (CNS). Primary isolated CNS LYG is exceptionally rare, with few cases reported.
Methods: We reported the case of a woman with isolated CNS LYG confirmed by pathological examination in our institution. The clinical and pathological, radiological and therapeutic aspects of this unusual presentation are discussed.
Results: A 51-year-old woman with a history of systemic lupus. The patient presented with headache and a right hemi-body heaviness. MRI showed a left parietal and occipital lesion. The patient had a complete excision of the lesion. Histopathological examination with immunohistochemical study revealed an angiocentric and angiodestructive lymphoid proliferation accompanied by extensive areas of necrosis. Atypical large-sized cells with hyperchromatic nuclei expressing CD20 were observed. Additionally, reactive T lymphocytes with CD3 positive staining were present. Notably, 50 cells positive for EBV were identified per high-power field. The diagnosis of grade 3 CNS LYG was concluded. The presence of EBV was detected using the FISH technique. Chemotherapy followed by radiotherapy were decided.
Conclusion: LYG is a rare systemic lymphoproliferative disorder with diverse clinical presentations and variable outcomes. Our case report highlights the importance of considering LYG in the differential diagnosis of patients presenting with neurological symptoms, particularly in the context of immunodeficiency or systemic autoimmune diseases. Furthermore, the multidisciplinary approach involving neurologists, oncologists, radiologists, and pathologists is essential for comprehensive patient care.

E-PS-13-012
Unveiling prognostic significance: Ki67 and CD44 expression in grade 2 meningiomas
Y. Dhouibi*, A. Zehani, A. Ayari, A. Khadhar, I. Chelly, K. Bellil, H. Azouz, S. Haouet
*Department of Pathology, Rabta University Hospital, Tunisia

Background & objectives: Meningiomas, prevalent in adult central nervous system (CNS), originate from arachnoid cells. WHO grades, based on histological features, correlate with recurrence risk. Our aim was to assess Ki67 and CD44 expression in grade 2 meningiomas, exploring their prognostic significance.
Methods: The study conducted a retrospective analysis of grade 2 meningioma cases over four years and three months. The cases were surgically treated at the Neurosurgery Department of Tunis and histologically confirmed at the Rabta Hospital. Data collection involved epidemiological, clinical, radiological and evolutionary aspects, with statistical analyses correlating these variables with immunohistochemical markers. Ethical considerations were observed throughout the study.
Results: In our study of 30 patients (median age: 61 years, male predominance), common clinical manifestations included headaches, visual acuity decrease, and motor disturbances. MRI revealed tumour locations: 50% on convexity, 30% parasagittal, and 13.4% at the skull base. Subtotal resection in 4 cases necessitated postoperative radiotherapy. Ki67 ranged from 1 to 10%, and CD44 immunostaining showed varying expression. Tumour recurrence occurred in 8 cases, with 2 patients experiencing a second recurrence. Two patients progressed to grade 3 anaplastic meningioma. Ki67 expression correlated with male gender, age over 55, and glial tissue infiltration, as well as tumour recurrence and progression. CD44 expression correlated significantly with meningioma grade.
Conclusion: In conclusion, our study provides insights into the clinical and radiological features of grade 2 meningioma, along with their management. The identified correlations between Ki67 and CD44 expression and clinical outcomes underscore the potential relevance of these biomarkers in predicting tumour behaviour and guiding treatment strategies.

E-PS-13-013
Paediatric intracranial angiomatoid fibrous histiocytoma with ESWR1::CREB1 gene fusion: a case report
P.M. Dy*, K.S. Wahing, J.G. Bañez, E.M. Yturralde, E. Muñoz, S.J. Aw, K.T.E. Chang, G. Ozoa
*Department of Laboratories, Philippine General Hospital, Philippines

Background & objectives: Angiomatoid fibrous histiocytomas (AFH) are rare mesenchymal neoplasms accounting for 0.3% of all soft tissue tumours. Rarer still are AFH located intracranially. We report a case of a 10-year-old boy with an exophytic intracranial mass.
Methods: A 10-year-old boy presented with a 6-month history of neck stiffness and progressive bilateral lower extremity weakness. MRI showed an avidly enhancing extra-axial mass on the infrapontine and anteromedullary region with significant compression of the cervicomedullary region. He subsequently underwent excision of the tumour.
Results: Microscopic sections show cellular sheets of fairly monomorphic round to spindle cells with abundant cytoplasm and indistinct cytoplasmic borders. Bands of interstitial collagen and dilated thin-walled vascular channels were present. Angiomatoid and lymphoid areas were not identified. Immunohistochemistry studies with SSTR2, cyclin D1, desmin, EMA, and CD99 were positive. Molecular studies using next-generation sequencing assays showed EWSR1 (exon 7) and CREB1 (exon 6) gene fusion. The case was eventually diagnosed as angiomatoid fibrous histiocytoma with EWSR1::CREB1 gene fusion. Tumour recurrence and an intratumoural bleed one month post-surgery further complicated the clinical course of the patient, which ultimately resulted in mortality three months post-surgery.
Conclusion: Paediatric intracranial AFH are exceedingly rare, with these tumours currently classified under the provisional entity known as intracranial mesenchymal tumours with FET::CREB fusion in the current 2021 WHO classification of central nervous system tumours. This case highlights the difficulty in diagnosing these tumours given the variable histomorphologic features, the absence of a characteristic immunohistochemical marker, and the unusual infrapontine location. A combination of molecular methods and conventional immunohistochemical techniques will aid in establishing the diagnosis of this rare entity.

E-PS-13-014
Comparative analysis of histopathological features in grade 2 meningiomas with and without brain invasion
S. Ekmekci*, İ. Eraslan, Y. Adalı, B.G. Özamrak, M. Bozdağ, D. Ayaz, E.E. Pala
*Izmir Provincial Health Directorate, Izmir City Hospital, Department of Pathology, İzmir, Turkey

Background & objectives: Meningiomas,the most common primary brain tumours,originate benignly from meninges.Despite controversies,the 2021 WHO classification includes brain invasion(BI) as a criterion for atypical meningioma due to its negative prognostic impact.This study compares histopathological features of grade 2 meningiomas with and without BI.
Methods: From 264 meningioma cases diagnosed between 2019 and 2023, we selected 67 Grade 2 cases. We analysed Hematoxylin and Eosin-stained sections from formalin-fixed paraffin blocks for histopathological features, including brain and dural invasion, necrosis, and mitotic frequency. This study included patients meeting the latest WHO criteria for atypical meningioma, with comprehensive clinical, pathological, and follow-up data collected.
Results: Among the 67 Grade 2 meningioma cases analysed, 35 were female and 32 male, with ages ranging from 1 to 88 years. Histopathological findings revealed necrosis in 37 cases (55.2%), hypercellularity in 44 cases (65.7%), prominent nucleoli in 19 cases (28.4%), small cell change in 15 cases (22.4%), and a patternless growth pattern in 27 cases (40.3%). Dural invasion was present in 15 cases (22.4%), and brain invasion was observed in 33 cases (49.3%). The majority of tumours were located intracranially (65 cases), while 2 cases located in spine. Brain parenchymal invasion was noted in 33 cases.
Conclusion: The debate surrounding the prognostic value of brain invasion versus histological grading in grade II meningiomas remains a contentious issue within the field of neuro-oncology. Identifying brain invasion as a standalone diagnostic marker could shift the paradigm of postoperative decision-making, traditionally guided by broader histological scores. This focus on brain invasion might enable the development of more individualized treatment plans, specifically tailored to combat the unique progression risks associated with brain invasion in grade II meningiomas.

E-PS-13-015
Central nervous system tuberculosis: a single-institution experience over 15 years
O. El Mnif*, A. Zehani, A. Ayari, A. Khadhar, I. Chelly, H. Azzouz, K. Bellil, S. Haouet
*La Rabta University Hospital Tunis, Tunisia

Background & objectives: Central Nervous System tuberculosis, a very rare manifestation of TB has presented diagnostic challenges. Although the diagnosis of tuberculosis is traditionally bacteriological, its cerebral localization frequently leads to an incidental histologic diagnosis following open brain biopsies or complete excisions.
Methods: We present a retrospective study of 9 cases of CNS tuberculosis diagnosed at our department of pathology between 2009 and 2023.Both clinical and radiological findings have led to either open brain biopsies or excisions of specimens, which were studied in our department using H&E staining.

Results: There were 4 male and 5 female patients,aged between 3 and 63 years with a mean age of 36. Headaches persisting for more then 2 months were the most common presenting complaint. One patient experienced a decrease in visual acuity,while another presented with status epilepticus.None of the patients exhibited general tuberculosis symptoms. A brain CT scan were suggestive of a parenchymal tumour in 6 cases,meningioma and two giant pituitary adenomas.All patients underwent surgery, with surgical resection performed in 7 cases and open biopsies in 2cases. Microscopic examination revealed epithelioid granulomas cases, characterized by central necrotic caseum surrounded by fibrotic cells and lymphocytes. All patients received after diagnosis anti-tuberculosis treatment.
Conclusion: CNS tuberculosis is a formidable diagnostic challenge causing significant morbidity and mortality even in the setting of appropriate antitubercular therapy. Keeping this diagnosis in mind, especially in endemic countries, is essential for an appropriate, early management.

E-PS-13-016
Diffuse hemispheric glioma H3G34–mutant: a review of a case series
F.D.A. Gallardo Chamizo*, E. Rivas Infante, R. Ávila Polo, E. Montijano Pozas, R.N. Rodríguez Rodríguez, L. Mosteiro González, L. Zaldumbide Dueñas
*Hospital Universitario San Cecilio, Spain

Background & objectives: Diffuse hemispheric glioma H3G34–mutant (DHGH3G34) is a new paediatric-type diffuse high grade glioma, recently recognized in the 2021 WHO classification of the CNS. The aim of this study is to review the clinicopathological features of DHGH3G34 diagnosed in our centre.
Methods: Six patients with DHGH3G34 were retrospectively identified in our hospital between 2019 and 2023. Clinical, radiological, histological, and molecular characteristics were reviewed and compared to the cases published in the literature.
Results: The median age was 22 years (12-29 years), and all cases were hemispheric, with high-grade MRI features in 4 patients. Only one patient was alive after 35 months and the median overall survival of the 5 remaining cases was 6 months. A diffusely infiltrating astrocytoma with necrosis and/or vascular proliferation was observed in all cases, a PNET-like morphology in 5 cases. Scattered giant cells were found also in all cases. In the immunohistochemistry (IHC) study, all cases were IDH-negative, ATRX-negative, and p53-positive, and only one case was clearly positivity for G34R. H3-3A molecular analysis revealed G34R mutation in 4 cases and G34V mutation in the other 2.
Conclusion: No significant differences were observed when we compared G34R and G34V cases. Our results also confirmed that a PNET-like pattern is a frequent morphology in this entity and the G34R antibody is not a reliable IHC tool for screening. DHGH3G34 present a very short life expectancy and the only case with a longer survival was observed in the patient who underwent more aggressive surgical treatment.

E-PS-13-017
Solitary fibrous tumours: a case series
H. Kandemir*
*Health Sciences University Izmir, Turkey

Background & objectives: Solitary fibrous tumour is a spindle cell tumour primarily composed of fibroblastic elements. The most common sites of metastasis are the lung. Brain metastases are rare. Immunohistochemical findings are crucial for histopathological diagnosis. WHO states that molecular confirmation of NAB2/STAT6
Methods: Between 2014 and 2023, data from 15 cases diagnosed with SFT were retrospectively evaluated. Clinical, morphological, and prognostic indicators such as patient age, tumour localization, tumour size, mitotic index, tumour necrosis, recurrence, etc., were analysed. Immunohistochemical staining with Desmin, DKA, CD34, CD31, S100, bcl2, CD99, STAT-6, and Ki67 was performed on all cases.
Results: The ages of the patients ranged from 9 to 74, average age was 45.6.Out of 15 cases, 9 were female, 6 were male.Tumour localization included retroperitoneum (3),abdominal/peritoneal (2), cerebellum (2), spinal intradural (4),kidney (1), atrium (1), and head/neck (scalp/nasal area) (2).The average tumour size was 6.4 cm.The average mitotic count was 5. Less than 50% necrosis was detected in 3 cases.Four of the cerebellar and spinal cases were classified as Gr1, and 1 as Gr3.All cases were positive for STAT-6. Following surgery, chemotherapy was administered to 2 cases, and radiotherapy was administered to 1 case.In postoperative follow-ups, local recurrence was not observed in 11 patients, while 4 patients experienced recurrence.
Conclusion: Our archive includes a paediatric case of SFT as well as very rare localizations such as the atrium, kidney, and central nervous system. The importance of considering SFT in the differential diagnosis of spindle cell mesenchymal tumours, especially in atypical localizations, and adding STAT6 to the panel were highlighted. Additionally, the need to consider extra-axial masses in the differential diagnosis of CNS tumours, albeit rare, was emphasized. The cases exhibited benign or aggressive behaviour associated with tumour grade.

E-PS-13-018
Idiopathic granulomatous hypophysitis: a challenging diagnosis
S. Kanoun*, M. Bouhamed, F. Kolsi, I. Dammak, S. Hidouri, C. Chaari, T. Sellami Boudawara, S. Makni
*Department of Pathology, Habib Bourguiba University Hospital, Sfax, Tunisia

Background & objectives: Idiopathic granulomatous hypophysitis (IGH) is a rare inflammatory disorder of the pituitary gland. It often mimics pituitary adenoma clinically and radiologically. The aim of this study is to report an observation about IGH and discuss its differential diagnoses.
Methods: IA 23-year-old woman presented with menstrual disturbance, galactorrhea and blurred vision.
MRI scan revealed a large sellar mass with parasellar and suprasellar extension. The mass appeared hyperintense on T1- and T2-weighted images with homogeneous enhancement after administration of gadolinium. Laboratory work-up revealed hypothyroidism, hyperprolactinaemia and hypocortisolism. The diagnosis of pituitary macro-adenoma was made. she underwent transsphenoidal excision of the mass.
Results: Histopathological examination of the specimen showed pituitary tissues containing multiple noncaseating granulomas composed of epithelioid histiocytes, multinucleated giant cells and mononuclear inflammatory cells. No viral inclusion or infective pathogen was seen. Additionally, no eosinophils or features of Langerhans cell histiocytosis were reported. Tuberculosis was ruled out in our patient by a negative tuberculin skin test, chest X-ray (CXR), and polymerase chain reaction of cerebrospinal fluid. She did not present any pulmonary symptoms and a normal CXR and angiotensin-converting enzyme levels ruled out sarcoidosis as well. Serologic studies for Wegener's granulomatosis and syphilis came back as negative. Therefore, our patient was diagnosed with IGH.
Conclusion: IGH, though rare, may be underdiagnosed due to nonspecific symptoms, necessitating histological confirmation particularly when radiologic findings deviate from typical hypophysitis or suggest a tumour, as in our case.
Precise incidence and etiology remain unclear; elimination of related systemic inflammatory disorders is crucial such as sarcoidosis, tuberculosis, Wegener granulomatosis and Langerhans cell histiocytosis. Early diagnosis is essential for optimal management including corticosteroid

replacement, preserving pituitary function. Further research is crucial for understanding the pathogenesis and optimizing diagnosis and treatment strategies.

E-PS-13-019

An unusual polyphenotypic cerebral tumour: where does the fifth-edition of the WHO Classification of Tumours of the CNS stands?

R. Khazen*, C. Kesrouani
*Hotel Dieu de France hospital, Saint Joseph University, Lebanon

Background & objectives: The fifth-edition of the WHO Classification of Tumours of the CNS introduces major changes that emphasize the importance of integrated molecular studies into definitive diagnosis. However, some cases fail to be classified even when proper and extensive testing is performed.
Methods: We here present the case of a fronto-temporal lesion in a 52 y.o. patient, who presented with a five-month history of dizziness. Cerebral imaging revealed a right fronto-temporal nodular mass. The lesion was resected, and the specimen was submitted to the pathology laboratory. Histological examination, immunohistochemisty and molecular studies were performed.
Results: Histological examination revealed a well-circumscribed, non-infiltrating tumour composed of a mixture of spindled and epithelioid cells, gland-like structures, and areas of necrosis. Immunohistochemistry reveals a polyphenotypic pattern, with positivity for glial (GFAP, Olig2) and epithelial markers (Cytokeratin AE1/AE3, EMA), including specific markers (CK7, CK20), unusual for glial tumours. BRG1, NUT and INI1 expression was conserved. FISH with ZFTA and MN1 break-apart probes was non-conclusive. The overall findings did not differentiate between poorly differentiated well-circumscribed, high grade glial tumour and metastatic carcinoma of unknown origin. A PET Scan showed no other suspicious lesions. The tumour was classified as poorly differentiated high grade malignant tumour and treated as a high-grade glial tumour.
Conclusion: Despite adequate pathological workup, the tumour could not be classified within a standard WHO diagnosis. In this case, the use of layered integrated reports including combined tissue-based histological and molecular diagnosis including broad panel genetic testing is strongly encouraged. Furthermore, methylome profiling was proposed as it may be the most effective way to characterize some diagnostically challenging neoplasms, and the only way to identify some rare tumour types and subtypes.

E-PS-13-020

Beyond morphology: paediatric central nervous system tumours with NTRK fusions

G. Kolak Gözüküçük*, T. Söylemez Akkurt, F. Kuşku Çabuk, B. Koçak, A. Erşen Danyeli
*Pathology Department, Istanbul Basaksehir Cam and Sakura City Hospital, Turkey

Background & objectives: We present three paediatric patients diagnosed with central nervous system (CNS) tumours harboring neurotrophic tyrosine receptor kinase (NTRK) gene fusions, highlighting the diverse clinical and histopathological characteristics of these rare entities.

Methods: We retrospectively examined three paediatric patients with NTRK fusions detected through next-generation sequencing (NGS), conducting histopathological and immunohistochemical analyses to better observe their morphological differences. Additionally, we assessed their current clinical statuses and the treatments they received.
Results: Initial case was an eight-month-old male patient presenting with a mass lesion. Microscopic examination revealed a hypercellular tumour with an astrocytic phenotype, including areas of microvascular proliferation and palisading necrosis. Subsequent NGS identified a fusion involving the ETV6::NTRK3 genes. Our subsequent case was a two-year-old male. Magnetic Resonance Imaging (MRI) revealed a peripheral enhancing mass. Microscopic examination of the tumour revealed bipolar hair-like cells with round-oval nuclei dispersed within a microcystic stroma. Morphological features suggested a diagnosis of pilocytic astrocytoma. NGS was identified a NOS1AP::NTRK1 fusion. Our last case was a one-year-old male. Morphological and immunohistochemical findings suggested pilomyxoid astrocytoma. NGS analysis identified a GIBC1::NTRK1 fusion.
Conclusion: Chromosomal rearrangements of NTRK1, NTRK2, and NTRK3 genes lead to oncogenic fusions across a wide spectrum of tumours. In gliomas and other primary CNS tumours, NTRK fusions are observed in 0.55% of cases. Detecting this fusion is of great importance as it will guide towards targeted treatment with TRK inhibitors rather than diagnosis. If confirmed in larger trials, such agents could offer appealing alternatives to mitigate the long-term complications of chemotherapy and radiotherapy while preserving the generally favourable prognosis.

E-PS-13-021

The relationship between primary organ and location in brain metastases: a 10-year experience of a single institute

D. Kose*, S. Nalbant, M. Karakus, C. Tanik, F. Kabukcuoglu
*Sisli Hamidiye Etfal Research & Training Hospital, Turkey

Background & objectives: Brain metastases (BM) are the most common neoplasms of the central nervous system in adults and have a very poor prognosis. We aimed to investigate the frequency of brain metastases and the localization of primary organs for different organ tumours.
Methods: Parameters such as age, gender, primary tumour, and brain localization in cases of brain metastasis were evaluated in this study. This monocentric study includes a total of 221 cases with BM diagnosed in the Pathology Department of Şişli Etfal Training and Research Hospital between 2014 and 2024.
Results: 221 cases of brain metastasis were reported. Of these cases, 150 (67.8%) were male, and 71 (32.1%) were female. The average age of the patients was 58 years. Brain metastases were predominantly caused by lung carcinomas (134 cases/60.6%), breast (33 cases/14.9%) and renal cell cancer (8 cases/3.6%). The primary tumour could not be detected in 17 patients (7.7%). The least common tumours were ovary (1/0.5%), thyroid (1/0.5%), and adenoid cystic carcinoma of the salivary gland (1/0.5%). The most common localization of metastasis in the brain was the cerebellum (55 cases, 24%), and the second most common location was the frontal lobe (43 cases, 19.4%).
Conclusion: Our study statistically evaluates the relationship between the anatomical locations and pathological findings of brain metastases and their corresponding primary tumours in the Marmara Region, Turkey. The incidence, survival, and treatments of BM vary greatly depending on the specific histology of the primary tumour. Once the disease reaches the CNS, the prognosis is usually relatively poor. Common causes of BM are lung cancer, breast cancer, melanoma, and RCC in adults and our series is consistent with the literature.

E-PS-13-023

Atypical presentation of a meningioma

L. Leon*, M.d.C. Gómez Mateo, N. Marínez Arnau, N. Estrada Mallarino, S. Hakim Alonso, J. Alfaro Torres, M. Guerrero
*Spain

Background & objectives: Meningiomas with extracranial extention are extremely rare and may be even clinically mistaken for cutaneous lesions. Histological evaluation and immunohistoquemistry stainings are needed to make a proper diagnosis.
Methods: We present the case of a 55-years-old male with a frontal lesion that has evolved over a period of two months. A benign cyst

subcutaneous lesion was suspected and a partial excision was performed. Initially, a provisional diagnosis of sarcoma was done, and the sample was sent to our centre for further diagnostic investigation.
Results: Histological examination revealed a malignant tumour characterized by a solid growth pattern with tendency to form short bundles with whirls. This proliferation consisted of ovoid cells with mild pleomorphism. Numerous mitosic figures and areas of geographical necrosis were observed. The initial immunohistochemical study only showed positive expression of vimentin. Although EMA and progesterone receptors were negative, patchy staining of SSTR2A was demostrated. Proliferative index Ki67 was 45%. With the suspicious of meningioma, radiological studies were conducted revealing the presence of an extra-axial lesion protruding through the cranial structures, inducing an epidural prominence. The final diagnosis of anaplastic meningioma grade 3 was established and an extended surgical intervention was performed.
Conclusion: Anaplastic meningiomas can mimick carcinomas or sarcomas. Clinical presentation due to extracranial spread is extremely rare and turns its diagnosis into a challenge for the entire medical team.

E-PS-13-024
Primary desmoplastic round cell tumour of the central nervous system with EWSR1::WT1 rearrangement: a case report
E. Montijano Pozas*, E. Rivas Infante, C. Ramírez Sánchez, F.D.A. Gallardo Chamizo, P. Solano Páez, M. Rivero Garvía
*Hospital Universitario Virgen Rocío, Spain

Background & objectives: Desmoplastic round cell tumour (DSRCT) is a frequently abdominopelvic localized small round cells sarcoma defined by the EWSR1::WT1 gene rearrangement.The intracranial location is extremely rare. We present a case of intracranial DSRCT located in the cerebellum with molecular confirmation
Methods: We describe a case of an 8-year-old male with a 3-month history of headache. Imaging studies revealed an intra-axial lesion in the right cerebellar hemisphere with midline deviation, heterogeneity, calcifications and no bone involvement.The radiological diagnosis was medulloblastoma. Surgical total resection was performed successfully.
Results: The histopathological study revealed an undifferentiated tumour with a diffuse pattern, composed of medium-sized cells with scant cytoplasm and atypia.No desmoplastic areas or rhabdoid cells, were observed. Immunohistochemical study revealed intense diffuse positivity for muscular markers (actin and desmin) and focal positivity for CD99. Glial and neural differentiation markers (GFAP, NeuN, NF, synaptophysin, and SOX10), as well as NKX2.2, BCOR and epithelial markers (EMA and CKpan) were negative. The cellular proliferation index was 80%. FISH study demonstrated a EWSR1 rearrangement and the NGS study identified the EWSR1::WT1 fusion, resulting in the definitive diagnosis of a primary cerebral DSRCT.
Conclusion: DSRCT of the central nervous system are extremely rare, with less than 20 cases previously reported in the literature. We report anintracranial primary DSRCT that typically displays muscular differentiation but lacks epithelial markers. Given the undifferentiated morphology, the differential diagnosis in children has to include other small round cellsarcomasand embryonal tumours. Despite desmin immunostaining can be a useful screening approach, a precise molecular characterization is necessary to confirm the diagnosis.

E-PS-13-025
Predictive value of digital analysis of ki-67 in schwannomas with relapses after gross total resection
D. Murzaeva*, N. Matiashina, A. Musikhina, A. Bunyat, D. Matveeva, A. Sufianov, Y. Zabrodskaya
*Almazov National Medical Research, Tyumen State Medical University, Russia

Background & objectives: Relapse rates following total removal of schwannomas range from 0.05% to 9.2%. There are currently no methods or criteria for determining the risk of relapse. We propose the potential use of Ki-67 for predicting relapse in schwannomas.
Methods: The study included adult patients diagnosed with "schwannoma" who underwent surgical treatment: 14 patients who remained relapse-free over the past 10 years, 20 patients with primary tumours, and 27 with recurrent tumours. Ki-67/MIB1 slides (n=61) were investigated by a pathologist with using Aperio ImageScope (12.4 ver., Leica Aperio AT2). Statistical tests included the Mann-Whitney criterion, Wilcoxon criterion, and ROC analysis.
Results: In our study, Ki-67 values were most reproducible when calculated per 1 mm², which included the arithmetic mean of four values: Ki-67 values in the "hot spot," two mean Ki-67 values, and the minimum value of Ki-67. In relapse tumours, the Ki-67 value is statistically higher than in tumours without relapse. The identified threshold Ki-67 values at cut-off points were as follows: > 5.5% in Antoni B or the entire slide, > 4.5% in Antoni A, and > 3.5% in mean Ki-67 values. A Ki-67 value equal to or greater than these thresholds indicates a high risk of schwannoma recurrence, with a sensitivity of 84.2% and specificity of 71.4% ($p<0.001$).
Conclusion: Based on the results of our study, Ki-67 can be used as a potential prognostic marker of schwannoma recurrence. The progression of schwannomas appears to involve both schwannocytes and immune cells. Further studies are necessary to find potential targets for targeted therapy and to determine the threshold values of Ki-67 in other nerve tumours.

E-PS-13-027
Correlation of histopathology, electromyography and laboratory findings in non-specific myositis
F. Nozzoli*, L. Tei, E. Nucci, G. Baroni, M. Capassoni, F. Galluccio, D. Massi, S. Guiducci
*Section of Anatomic Pathology, Department of Health Sciences, University of Florence, Italy

Background & objectives: Non-specific myositis (NSM) refers to a rare idiopathic inflammatory myopathy subset with heterogeneous clinicopathological features. Herein, we provide a histopathological characterization of a NSM patients cohort and analyse whether laboratory markers and electromyography (EMG) severity correlate with muscle biopsy findings.
Methods: We identified 36 patients who underwent muscle biopsy due to the clinical suspicion of NSM. Hematoxylin and eosin and Gomori's trichrome stains were assessed for morphology. Immunohistochemistry for endomisial infiltrates was performed with the following antibodies: CD4, CD8, CD20, CD68 and HLA-ABC. Statistical analysis was performed to explore correlations between EMG severity, serum markers, myositis-specific, myositis-associated autoantibodies and immune biomarkers.
Results: Thirty-three patients were female (91.6%) and the mean age at diagnosis was 55 (range 22 – 76). Fiber's size and shape changes were present in 18/36 (50%), internal nuclei in 6/36 (16.6%), endomisial connective tissue alterations in 12/36 (33.2%) and necrosis in 3/36 (8.3%). CD4+ cells were present in 18/36 (50%), CD8+ in 7/36 (19.4%), CD20+ in 1/36 (2.7%), CD68+ in 6/36 (16.6%), and HLA-ABC overexpression in 7/36 (19.4%). Creatine phosphokinase (CPK) serum levels correlated with CD4+ ($p=0.006$), CD8+ ($p=0.003$) endomisial infiltrates and HLA-ABC overexpression ($p=0.003$); anti-tRNA synthetase with CD4+ ($p=0.018$) and CD8+ ($p=0.005$), while EMG severe alterations correlated with the presence of CD8+ infiltrates ($p=0.011$) and HLA-ABC overexpression ($p=0.001$).

Conclusion: Our study showed that morphological alterations in muscle fiber's size and shapes together with CD4+ endomisial infiltrates were the most frequent findings in muscle biopsies of NSM patients. Among laboratory and instrumental diagnostic tools, CPK serum levels, anti-tRNA synthetase and EMG emerged as the most useful diagnostic tool to predict histologically proven inflammation in NSM. Furthermore, our findings showed that EMG severe findings may be a surrogate marker of CD8+ infiltrates and HLA-ABC overexpression in NSM muscle biopsies.

E-PS-13-028

In-vivo fluorescein-assisted confocal laser endomicroscopy is a promising intraoperative tool in patients with glioblastoma: results from a prospective study

F. Nozzoli*, G. Muscas, E. Nucci, F. Ugolini, D. Massi, A. Della Puppa
*Section of Anatomic Pathology, Department of Health Sciences, University of Florence, Italy

Background & objectives: Confocal laser endomicroscopy (CLE) allows intraoperative real-time high-resolution cellular visualization and recently emerged as an interesting tool in neurosurgery and intraoperative neuropathology. We prospectively tested the accuracy of a new designed miniatured CLE in giving intraoperative assessment during glioblastoma resection.
Methods: We enrolled 18 patients with newly suspected diagnosis of glioblastoma who underwent fluorescein-guided surgery. Biopsies from both solid tumour and sodium-fluorescent margins were harvested. They were firstly intraoperatively in-vivo analysed by CLE, and subsequently processed for frozen section. A blind comparison was conducted between CLE and histological findings to test the CLE accuracy to provide the diagnosis and margins assessment.
Results: Eleven patients were female (61.1%) and the mean age at diagnosis was 62 (range 54 – 73). Blindly comparing CLE images and correspondent frozen sections slides, we obtained concordance at tumour central core in 16/18 (88.8%) and at margins in 15/18 (80.3%). Comparing CLE and permanent formalin-fixed and paraffin-embedded (FFPE) sections, concordance resulted equal at central core (88.8%) and lower at tumour margins (72.2%). Concordance between frozen sections and FFPE was 94.4% at tumour central core and 88.8% at tumour margins. Pre-operative clinical and radiological suspect of glioblastoma IDH-wildtype was then confirmed on permanent histological examination and molecular analysis in 18/18 (100%) cases.
Conclusion: While frozen section analysis still remains the gold-standard for intraoperative diagnosis, it is a time-consuming procedure. The diagnostic consistency rate we found between CLE and frozen sections suggests the implementation of CLE as a complementary tool for intraoperative diagnosis and margins assessment of in-vivo tissue specimens during glioblastoma surgery. Main limitations include the relative low number of patients enrolled and the fact that histological sections cut-plane and CLE images scan-plane may not be exactly complementary, inherently limiting the comparative analysis.

E-PS-13-029

Sebaceous adenoma arising in intraventricular ruptured dermoid cyst: report of a rare case

B.G. Özamrak*, S. Ekmekci, Y. Pekcevik, H.B. Benek
*Izmir Provincial Health Directorate, Izmir City Hospital, Department of Pathology, İzmir, Turkey

Background & objectives: Intracranial dermoid cysts (DC) are cystic, slowly growing lesions consisting of mature squamous epithelium, cutaneous adnexal features. Rarely, tumours originating from ectodermal elements may arise within them. We present a rare case of sebaceuous lesion arising within intraventricular dermoid cyst.
Methods: A 43 year-old-male presenting with sudden speech impairment was admitted to hospital. Computed tomography showed a 48x44x40 mm, T1 & T2 hyperintense cystic heterogenous lesion, located in left frontotemporal region with low ADC value. The lesion was reported consistent with ruptured DC.
Results: Upon histological examination, cystic area lined with keratinized squamous epithelium was observed. A solid area of 10 mm showed lobular proliferation of sebaceous elements with well circumscribed nodular growth. The proliferation consisted of centrally located sebaceous cells which contain intracytoplasmic lipid vacuoles and basaloid cells at the periphery of the lobules. Histopathological features were found consistent with sebaceous adenoma (SA) arising in DC.
Conclusion: Epidermal and dermoid cysts are relatively common among benign cystic lesions, even in intracranial localizations. Depending on their size and location, these congenital lesions can be asymptomatic detected incidentally during screening or can lead to aseptic meningitis, may rupture, exert pressure in surrounding tissues and cause symptoms such as headache, convulsions, ischemia. Since DCs harbor adnexal elements, adnexal tumours may occur seldomly. SA is known to show malignant transformation, a close follow up may be needed in these cases.

E-PS-13-030

An extremely rare case of bone metastases in a patient with grade 4 IDH-mutant astrocytoma

A. Pestana Lopes*, R. Lyrio, M. Mafra
*Hospital da Luz Lisboa, Portugal

Background & objectives: Isocitrate dehydrogenase (IDH)-mutant astrocytomas generally have a better prognosis than their wild-type counterpart. Extracranial metastases are exceedingly rare. We, hereby, present a case of bone metastases in a patient with grade 4 IDH-Mutant Astrocytoma.
Methods: A 46-year-old man was diagnosed with a right parietal space-occupying lesion showing expansive growth, which was excised. Histopathology revealed an astrocytoma IDH and TP53 mutant. He started radiation therapy and adjuvant temozolomide. Post 4 cycles of chemotherapy, he presented with severe back pain. MRI showed vertebral body lesions and a 23mm paravertebral mass (L2-L3), which prompted pathological confirmation by biopsy.
Results: A CT-guided biopsy of a bone lesion revealed marrow infiltrating neoplastic cells arranged in sheets, with eosinophilic cytoplasm, excentric nuclei, with associated necrosis and macrophages. These cells were positive with glial fibrillary acidic protein (GFAP), OLIG2, IDH1 (R132H), and showed ATRX loss, mutant expression of p53 (null-type). The final diagnosis was bone metastasis from a grade 4 IDH-Mutant Astrocytoma. Soon after this diagnosis, the patient worsened clinically and eventually succumbed to the disease.
Conclusion: Extracranial metastases from gliomas are extremely rare and poorly understood. Further studies may provide better understanding about the underlying pathogenic mechanisms and contribute to the subsequent identification of clinical and histologic features that might be useful in these patients' management and follow-up.

E-PS-13-031

Estimation of microvascular density in meningioma and its correlation with WHO histological grade

I. S Nair*, A. Mathews, N. Radhakrishnan, J.K. K M
*Regional Cancer Centre, Thiruvananthapuram, India

Background & objectives: Meningiomas exhibit wide morphological spectrum reflected by the 15 subtypes.Microvascular proliferation (MVP) is used in the grading of gliomas.Though not included in the WHO criteria for meningioma grading,we have observed them in some cases especially in atypical meningiomas.

Methods: Pathology records were searched and all cases of meningioma reported in our department from 2015-2020 (5 years)were reviewed.Slides and blocks were retrieved for 50 identified cases and immunohistochemistry with CD105 and ERG were performed.Microvascular density(MVD) assessment with CD105 expression in various grades of meningioma was done.Positive staining was given an average score based on number of vessels stained in hotspots.
Results: Total cases-50;Atypical meningioma-37cases,grade 1-10cases and grade 3-3cases.Age range:5-73 years. M:F ratio-1.02:1.Common sites:frontal brain(n=13),falx cerebri(n=11) and parafalcine location(n=5). MVP was noted in following number of cases:Grade 2-18(48.64%),Grade 1-1(10%),Grade3-2(66.7%).Florid endothelial hyperplasia not amounting to MVP was identified in 6 cases of grade 2 and 5 cases of grade 1.Association of MVP with WHO grades showed p value of 0.065.MVD evaluation with CD105 showed average score of 20 in grade 1,35 in grade 2 and 30 in grade 3.However,angiomatous subtype(grade 1)showed a stronger staining pattern with average score of 100.Based on one way ANOVA,there is significant association of florid MVP with CD105 staining intensity(<0.001).Conflicting results were obtained when this was quantified through ERG.
Conclusion: In this study,we demonstrated that MVP could be correlated with higher grades of meningioma.This finding could be an interesting feature in daily practice to help evaluate risk of progression.In our study,expression of ERG gave no significant association making it a futile marker for assessment of MVD when compared to CD105.However more studies of CD105 expression correlated with survival status are needed to determine if this can benefit patient in anti-angiogenic therapies and prognostication.

E-PS-13-032
Primary intracranial sarcoma, DICER1 mutant – case report of a very rare and recently described entity
D. Sá*, G. Carrola, M. Mexia, R. Taipa, M. Pinto, A. Coelho, F.E. Costa, J.R. Vizcaíno
*Anatomic Pathology Service, Pathology Department, Unidade Local de Saúde de Santo António, Portugal

Background & objectives: The primary intracranial sarcoma, DICER1-mutant is a rare sarcoma that was first described in 2018. It occurs predominantly in children with a median age at diagnosis of 6 years, although rare cases have been described in adults (range: 2–76 years).
Methods: We report a case of a 50-year-old woman that was referred to a neurology consultation due to a 3-month history of paraesthesia and weakness on the left hand and forearm. An MRI was performed and showed a 5cm extra-axial right parietal lesion with areas of necrosis and haemorrhage. The patient was then submitted to surgical excision of the parietal tumour.
Results: We received an irregular and whitish 5cm brain excision specimen and four small white fragments. At histologic examination the neoplasia was composed of intertwining fascicles of spindle cells, some of them with nuclear atypia. There were areas of low cellularity with myxoid stroma associated with the presence of cells with rhabdoid morphology. Numerous mitotic figures were identified as well as areas of necrosis. Immunohistochemistry showed expression of Vimentin and p53 (mutant-type) in the spindle cells and of Desmin, Myogenin and MyoD1 in the cells with rhabdoid morphology. SOX10, S100, EMA, GFAP, OLIG2, CD34, STAT6, AE1/AE3 were negative. There was loss of expression of H3K27me3. NGS showed a DICER1 mutation.
Conclusion: DICER1 mutations can be either somatic or germinal as part of DICER1 syndrome. An association with neurofibromatosis type 1 has also been observed. Therefore, genetic counselling and germline testing may be warranted in these patients. The prognosis remains unknown, because only limited clinical data are available so far. In one series of 22 patients, an aggressive clinical course was suspected, but long-term follow-up data were not sufficient for reliable conclusions. Our patient died of disease 21 months after the diagnosis.

E-PS-13-033
Solid growth pattern with at least focal comedonecrosis is suggestive of the mammary origin of brain metastases: a clinico-pathologic study on a series of 30 cases
S. Salzano*, J. Farina, R. Caltabiano, L. Salvatorelli, G. Angelico, G.M. Vecchio, G. Magro, G. Broggi
*Department of Medical, Surgical Sciences and Advanced Technologies "G.F. Ingrassia", Anatomic Pathology, University of Catania, Italy

Background & objectives: This study emphasizes the diagnostic relevance of growth patterns in identifying brain metastases from breast carcinoma, selecting purely specific morphological features that could suggest the mammary origin of a metastatic lesion in the brain, even when clinical data is lacking.
Methods: We retrospectively analysed 30 brain metastasis specimens from the Pathology archive of our Department, focusing on the presence of solid growth pattern, comedonecrosis and glandular differentiation. Breast origin was immunohistochemically confirmed by the presence of mammary origin markers (GATA-3 and mammaglobin).
Results: All patients in the study were females, 27 of them with cerebral metastases and 3 with cerebellar metastases. The following immunophenotypes (when available) were found: triple negative/basal-like (8 cases), luminal A (3 cases), luminal B (1 case) and HER-2- enriched (5 cases). The following histologic features were observed: diffuse solid growth pattern without glandular differentiation (14 cases); heterogeneous solid growth pattern with glandular differentiation (9 cases); focal solid growth pattern (7 cases). Diffuse comedonecrosis was seen in only 1 case, while it was heterogeneous in 9 cases and focal in 9 cases.
Conclusion: Our findings highlighted that most cases histologically exhibited a solid growth pattern with at least focal comedonecrosis, producing an overall morphology closely reminiscent of high-grade ductal carcinoma in situ of the breast. Recognizing these histological patterns may be crucial for pathologists, especially in the absence of complete clinical histories.

E-PS-13-034
Metachrone glioblastoma in survivors of carcinoma
V. Scripcaru*, L. Eva, G.F. Dumitrescu, A. Scripcaru, A.M. Dumitrescu, A. Sava
*Department of Morpho-Functional Sciences I, Grigore T. Popa University of Medicine and Pharmacy, Iasi, Romania

Background & objectives: Glioblastoma is a high-grade astrocytic tumour with a poor prognosis. The aim of study was to identify the possible role of a prior cancer in the pathogenesis of glioblastoma as there are few articles on this issue.
Methods: We retrospectively reviewed the patients who were admitted, diagnosed and surgically treated for a cerebral glioblastoma in the Emergency Clinical Hospital "Prof. Dr. N. Oblu" in Iasi, Romania, during a period of 14 years (2010-2023). We selected the cases who had a history of prior carcinoma. Data relating to epidemiological features and pathological characteristics were analysed.
Results: There were 11 cases of glioblastomas (1,51% of all surgically treated glioblastomas) with carcinoma history treated with chemo- and/or radiotherapy. Sex ratio F:M was 1.75. The younger group (median age 48 years) had previously breast carcinomas (n=3) and intestinal adenocarcinomas (n=3) and glioblastomas were diagnosed after a median interval of 58 months. In the elderly group (median age 66.8 years) prior cancers were mostly squamous cell carcinomas (n=3) located in penis, cervix, or larynx and a glioblastoma developed after a mean time of 118 months. Histologically, patients with prior breast

and digestive carcinomas expressed the giant cell subtype of glioblastoma, but the others developed small cell glioblastomas.
Conclusion: Not every brain tumour in a patient diagnosed with a prior carcinoma is a metastasis one. In rare cases, there is the possibility of a metachronous glioblastoma. The origin histological type of carcinomas prior to glioblastoma were miscellaneous. We suggest two etiopathogenic hypotheses of glioblastoma development in these cases: a genetic one associated with a possible effect of anticancer therapy, with significance for younger patients, and another one related to environmental factors, in the case of elderly patients.

E-PS-13-035
ALK-positive histiocytosis in the spinal cord of an infant, mimicking a glial tumour
M. Senchenko*, N. Myakova, A. Drui, L. Papusha, D. Konovalov
*Dmitry Rogachev National Medical Research Center of Paediatric Haematology, Oncology and Immunology, Russia

Background & objectives: ALK-positive histiocytosis can affect the central nervous system (CNS) without extraneuronal signs of the disease. We report a case of ALK-positive histiocytosis in the spinal cord with diffuse S100 positivity leading to an incorrect diagnosis of diffuse high-grade glioma (DHGG).
Methods: Diagnosis of DHGG was established after histological examination using immunohistochemical (IHC) stains for S100, GFAP, NF, Ki-67. RNA sequencing revealed a KIF5B::ALK fusion. After a molecular genetic study, additional IHC stainings for CD163, CD14, ALK, Olig2, Cyclin D1 were performed.
Results: The 9-month old girl's MRI showed a spinal cord isolated lesion (Th5-Th12). Histological examination revealed a hypercellular tumour with mild nuclear pleomorphism and high mitotic activity. The tumour had diffuse S100 and focal GFAP expression. NF-staining showed scattered residual axons. According to these features, diagnosis of DHGG was established. After detection of KIF5B::ALK fusion additional IHC was performed revealing diffuse expression of CD163, Cyclin D1, CD14, ALK. Olig2 was negative. Considering these results the diagnosis of ALK-positive histiocytosis was established. Initially chemotherapy according to the Baby-POG protocol for high-grade gliomas was prescribed and led to the disease progression. After the diagnosis revision the therapy was switched to alectinib.
Conclusion: ALK-positive histiocytosis is a rare primary CNS neoplasm with S100 expression in some cases. Therefore, it can lead to an incorrect diagnosis of a glioma and subsequent inappropriate treatment. ALK-positive histiocytosis should be considered in cases of CNS tumour with diffuse S100 and focal GFAP expression, which probably related to the residual glia. Therefore, additional IHC staining for CD163, CD14, Olig2, Cyclin D1, ALK is recommended.

E-PS-13-036
Pleomorphic xantoastrocytoma with receptor tyrosine kinase fusions: histologic and immunophenotypic features - overview of three cases
M. Senchenko*, L. Papusha, A. Drui, D. Konovalov
*Dmitry Rogachev National Medical Research Center of Paediatric Haematology, Oncology and Immunology, Russia

Background & objectives: The most common genetic alteration of pleomorphic xantoastrocytoma (PXA) is a mutation in BRAF gene. However, there have been recent reports about paediatric PXA with receptor tyrosine kinase (RTK) fusions. We present three paediatric cases of PXA with RTK fusions.
Methods: Immunohistochemical staining for S100, GFAP, CD34, NF was performed in all cases, while staining with Olig2 only in two cases. RNA-sequencing revealed GOPC::ROS1, NOS1AP::NTRK1, SFPQ::ALK fusions. DNA methylation profiling demonstrated close proximity to a PXA (score >0.9) in all cases. There was CDKN2A/CDKN2B deletion detected in two cases.
Results: The age of the patients ranged from 1 to 24 months. Histology of all cases revealed well-circumscribed, hypercellular tumour consisted of highly pleomorphic cells in two cases. In one case, the tumour was composed of monomorphic cells with gemistocytic features. Eosinophilic granular bodies were detected in one case. Characteristic features of PXA such as Rosenthal fibers, xanthom cells, perivascular infiltrates and reticular fibrosis were absent in all cases. The tumour cells were extensively immunoreactive for S100 (n=3), Olig2 (n=2), negative for CD34 (n=3). Expression of GFAP was diffuse and weak in case with monomorphic gemistocytes, focal in cases with prominent pleomorphic features. NF staining revealed residual axons at the periphery.
Conclusion: RTK fusions in PXA extends the molecular spectrum of PXA. In our series of cases, all children were under three years old. Histologically tumours were characterized by the absence of typical features PXA: Rosenthal fibers, xanthom cells, perivascular infiltrates, reticular fibrosis, CD34-expression and eosinophilic granular bodies in two cases.

E-PS-13-037
Loss of H3K27me3 in meningiomas: a multicentre study
C. Sönmez*, A. Erşen Danyeli, Ş. Çetin, İ. Kulaç, F. Aker
*Hatay Defne State Hospital, Department of Pathology, Turkey

Background & objectives: Loss of H3K27me3 in meningiomas has been associated with recurrence and poor outcome as well as histopathological grading. In this study, we aimed to determine the correlation between conventional histopathological grading criteria and loss of H3K27me3 in meningiomas.
Methods: H&E stained sections of 36 grade 1, 74 grade 2 and 26 grade 3 meningiomas from four different centres were re-examined. Loss of H3K27me3 was evaluated. The relationship between the data of the cases (histologic grade, hypercellularity, nucleolus prominence, small cell formation, necrosis, sheeting pattern, mitotic count, Ki-67 proliferation index, presence of brain invasion) and loss of H3K27me3 was evaluated.
Results: Forty-three cases were excluded because no staining was detected in the internal control with H3K27me3 antibody. Loss of staining in tumour cells was observed in 2 of grade 1 cases (6.5%) , 10 of grade 2 cases (24.4%) and 11 of grade 3 cases (52.4%), while internal and external controls were positive with H3K27me3. Histological grade, hypercellularity, necrosis, patternless pattern, mitotic count and Ki-67 proliferation index were significantly correlated with H3K27me3 loss (p:0.001, p:0.032, p:0.001, p:0.004, $p<0.001$, $p<0.001$, $p<0.001$, $p<0.001$, $p<0.001$, respectively).
Conclusion: The correlation of loss of H3K27me3 with WHO grading seems to be strong. This finding may add to the histopathological data we have used so far in predicting recurrence or survival.

E-PS-13-038
SOX10 expression in hemangioblastomas – an immunohistochemical study of 27 cases
J. Soukup*, D. Netuka
*Military University Hospital Prague; Department of Pathology, Charles University, First Faculty of Medicine and General University Hospital in Prague; Charles University, Faculty of Medicine in Hradec Králové and University Hospital Hradec Králové, Czech Republic

Background & objectives: Hemangioblastomas are CNS neoplasms with uncertain histogenesis and variable immunoprofile. In the past, SOX10 has not been studied systematically in hemangioblastomas. Following an index case with focal SOX10 immunoreactivity, we performed a study of SOX10 in a cohort of hemangioblastomas.

Methods: In total, 27 CNS hemangioblastoma from 24 patients (18 females and 9 males) were retrieved from the files of the institution and reviewed prior to inclusion. SOX10 immunohistochemistry (EP268, 1:800) was performed on whole sections. Immunohistochemistry for Olig2 (EP112, 1:200) and neurofilaments (2F11, 1:100) was performed in SOX10-positive cases. Percentage of positive cells and colocalization of the markers were assessed.
Results: Variable number of SOX10-positive cells was observed in 14 (52%) cases, ranging from <1% to 10%. In 8 (30%) cases, SOX10+ cells were localised at the periphery of the tumour and colocalized with Olig2-positivite cells, being compatible with entrapped glial cells of adjacent brain. In 5 (19%) cases, SOX10+ cells showed elongated wavy nuclei and either obvious schwannian morphology or association with neurofilaments and lack of Olig2, these being consistent with entrapped Schwann cells of peripheral nerves. In 4 (15%) cases, including index case, SOX10 marked Olig2-negative cells with morphology of hemangioblastoma stromal cells, lacking associated neurofilaments. These comprised <1%, 1%, 2% and 10% of cells in individual tumours.
Conclusion: SOX10 positive cells in hemangioblastomas usually represent entrapped Schwann cells or glia. In rare instances, a small subset of hemangioblastoma cells with otherwise unremarkable morphology can show SOX10 immunoreactivity. This must be considered in limited tumour samples.

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E-PS-13-039
Morphology and immunohistochemistry with surrogate molecular markers diagnose most brain tumours: highlights on the balance between microscopy and genetic diagnosis of brain tumours in the clinical practice
A. Vamanu*, S. Downes, C. Troakes, R. Laxton, I. Bodi, Z. Reisz, S. Al-Sarraj
*London Neurodegenerative Diseases Brain Bank, Institute of Psychiatry, Psychology & Neuroscience, King's College London, United Kingdom

Background & objectives: Following the introduction, genetic analysis has been shown to alter the initial diagnosis in approximately 15–25% of cases. Genetic alterations, such as IDH1, ATRX, and H3K27M have significantly improved the diagnostic accuracy of the morphology and immunohistochemical (IHC) tests.
Methods: We reviewed the microscopy/IHC reports of 537 recently diagnosed CNS tumours and compared them to the genetic/integrated reports; including Next Generation Sequencing and Methylation array.
Results: The microscopy/IHC for surrogate molecular markers was sufficient to accurately diagnose 75.2% of paediatric and 89% of adult tumours. The genetic tests result in significant change in diagnosis for 5.1% of paediatric and 8.8% of adult tumours, whilst improved diagnosis is seen in 19.7% of paediatric and 2.3% of adult tumours.
Conclusion: This study provides insights into the stability of clinical brain tumour diagnoses using microscopy/IHC and highlights the improvement of neuropathologists' skills in integrating the IHC for surrogate molecular markers. The genetic tests remain an essential tool not only to support the diagnosis but to diagnose controversial and difficult cases and add important information about other genetic alterations, which may be linked to the biological behaviour of the tumours and be vital for targetable therapy.

E-PS-13-040
Next generation sequencing of 400 adult-type diffuse gliomas revealed diverse oncogenic fusions with potential therapeutic impact
A. Vamanu*, K. Eggleton, R. Ellmers, P. Hirani, C. Limbachia, L. Bhaw, R. Laxton, I. Bodi, S. Al-Sarraj, Z. Reisz
*London Neurodegenerative Diseases Brain Bank, Institute of Psychiatry, Psychology & Neuroscience, King's College London, United Kingdom

Background & objectives: A subset of adult-type diffuse gliomas harbour oncogenic gene fusions that may open new opportunities for personalised medicine. To improve patient selection, more data would be desired regarding the clinical behaviour and the associated genetic profile of the fusion-positive tumours.
Methods: A retrospective departmental study analysed the molecular profile of a large cohort of adult-type diffuse gliomas (400 cases) using targeted (DNA/RNA) next generation sequencing panel (NGS) and DNA methylation array (Illumina EPIC BeadArrays, Brain tumour classifier- MNP v12.5 R package). Cases harbouring clinically relevant gene fusions were reviewed for clinical, multi-omics and follow-up data (progression-free/overall survival) and for therapeutic management.
Results: Oncogenic gene fusions were identified in 4.0% of the adult-type gliomas with a mean age of 66.3 years (M:F=7:9). Among the 14 cases of IDH-wildtype glioblastomas, FGFR3 (7/14) and EGFR fusions (6/14) were the most frequent associated with mesenchymal and RTK2 methylation subclasses, respectively. CDKN2A/B deletion (9/14) and EGFR amplification (6/14) were common copy number changes. A single case harboured an NTRK2 fusion. Nine tumours had methylated MGMT gene promoter (9/14). IDH-mutant astrocytomas (1 high-grade/1 low-grade) harboured MET and ALK fusions. Despite adjuvant chemo-radiation, 9 cases showed early progression (within 4-8 months), one patient developed lung metastasis and 5 patients died of the disease (OS: 6 days-52 months).
Conclusion: Our findings indicate that NGS can identify diverse oncogenic fusions in IDH-wildtype glioblastomas (6.0%) and IDH-mutant astrocytomas (3.4%), but not in oligodendrogliomas. The prognosis appears to be adverse in half of the cases despite high frequency of MGMT promoter hypermethylation and aggressive adjuvant chemoradiation. In the future, randomised clinical trials would be important to investigate the efficacy and clinical utility of targeted therapies.

E-PS-13-041
Retinal vasculopathy with cerebral leukodystrophy – a case report
A. van der Biezen*, M.N. Villca Huayta, C. Vieru, F. Arías
*Hospital General Universitario Gregorio Marañón, Spain

Background & objectives: Retinal vasculopathy with cerebral leukoencephalopathy (RVCL) is a rare autosomal dominant disorder involving highly vascularized tissues including the brain, retina, liver, kidney, and other systemic microvessels due to frameshift mutations in the TREX1 gene.
Methods: We report a case of a 56-year-old male patient who had been experiencing tingling sensations in his right thigh. Over time, the patient's condition progressed to muscle weakness, atrophy, and restricted movement in the foot. MRI showed two ring-enhancing tumour-like masses affecting the superficial and deep white matter of both cerebral hemispheres, with calcifications areas. The patient underwent a biopsy.
Results: Histology revealed foci of white matter coagulative necrosis with microcalcifications, surrounded by reactive gliosis and non-foamy macrophages in the white matter. No evidence of malignancy, granulomas nor fungal or bacterial organisms were noted. Small vessels within the lesions showed focally thickened and hyalinized walls with the

presence of occasional nonspecific perivascular chronic inflammatory infiltrates without signs of vasculitis or amyloid deposits. There was relative sparing of cortical gray matter. The patient was subsequently diagnosed with pulmonary and extrapulmonary sarcoidosis, retinal vasculopathy, hypertension, subclinical hypothyroidism and presented an acute colonic perforation. Genetic studies demonstrated the presence of a heterozygous pathogenic variant in TREX1.
Conclusion: Patients diagnosed with RVCL-s often undergo brain biopsy to exclude malignancy. Pathologists must be aware of the pathological features of this condition in order to recommend genetic studies and genetic counseling. Early recognition of this entity can reduce the need for repetitive biopsies.

E-PS-13-042
Brain-tissue textiloma: a potential diagnostic pitfall
A. Yavuz*, B. Altunay, G.A. Ocak, İ.E. Gürer
*Akdeniz University Hospital, Turkey

Background & objectives: Textiloma, also known as gossypiboma, arises from retained surgical haemostatic surgical materials, causing diagnostic challenges by mimicking various conditions. In this case of an elderly patient with aphasia, highlights the clinical and pathological features of brain textiloma.
Methods: Pathological examination was performed by routine hematoxylin-eosin and immunohistochemical staining.
Results: 72-year-old patient presented with aphasia. Brain CT imaging revealed an extensive parenchymal hematoma in the left frontal and frontobasal regions, compressing the anterior horn of the left lateral ventricle, which accompanied by surrounding hypodense edema and haemorrhagic densities. Initially, the patient underwent surgery with the suspicion of intratumoural hemorrhage, due to the widespread hematoma mass observed on radiological imaging. Due to the swelling and bleeding in the first surgical site, a second operation was performed one month after the initial one. Histopathological examination of the material from the second surgery showed a foreign body consistent with hemostatic material and necrotic haemorrhagic tissue, confirming the diagnosis of textiloma.
Conclusion: A 72-year-old patient with aphasia and brain textiloma demonstrates the diagnostic complexity of this rare condition. Textiloma, often resulting from retained surgical or hemostatic materials, can mimic various postoperative complications, including tumour recurrence, abscess, and radiation necrosis. Nonspecific radiological features of this condition, necessitate a thorough review of surgical history and careful histopathological examination to confirm the diagnosis. Therefore, textiloma should be considered in the differential diagnosis of postoperative neurological symptoms.

E-PS-14E-Poster Session Other Topics

E-PS-14-001
The frequency and impact of missed histopathology reports
S. Al Harthi*, R. Al Ajmi
*OMSB, Oman

Background & objectives: We aimed to investigate the frequency of missed histopathology reports over a six-months peroid. The primary goal is to assess the consequences of missing reports on patient outcomes, the quality of healthcare services, and the impact on healthcare costs.
Methods: The study was conducted at a single centre. The 6-months timeframe encompassed all specimens processed in the laboratory during the first week of each month from January to June 2022. The estimated minimum sample size was 582, with a 95% confidence interval and a 3% margin of error. Data collection was facilitated through the data information systems at the centre.
Results: Out of 586 specimens, 475 (81%) reports were viewed, while 111 (19%) reports were missed. Five patients (4.5%) reports returned to the Emergency Department with recurring initial complaints, and their reports were again unreviewed. This includes severe inflammation requiring treatment (n=3), gastric intestinal metaplasia (n = 2), colonic low-grade dysplasia (n = 3), Barrett's oesophagus (n = 2), and symptomatic H. pylori infection (n = 2). There were also repeated colonoscopic biopsies with no result review of the last biopsy (n=3). Out of 462 patients who attended their follow-up appointment, 85% had their results reviewed while 5% were missed. Compared to 55% missed reports of patients who failed to show-up.
Conclusion: Although the study did not uncover any serious adverse effects, it highlighted critical issues such as delayed diagnosis, the importance of early detection for effective treatment, increased costs associated with repeated samples, and unnecessary histopathological examinations. Medicolegal issues can also arise; for instance, in cases of incomplete or improper surgical resection.

E-PS-14-005
Efficacy of a peer to peer histopathology education scheme to improve engagement at a UK Medical school
A. Chang, E. Bearblock*, S.J. Cadman, E. Jackson, M. Kalogeropoulou, J.K. Knight, M. Pandiaraja, C.L. Soh
*Nottingham University Hospital NHS Trust, United Kingdom

Background & objectives: Variation exists in histopathology curricula across United Kingdom medical schools. Junior doctors often report feeling underprepared for the histopathology encountered in clinical practice. To bridge this gap, we designed and implemented a peer-to-peer histopathology teaching programme at a United Kingdom Medical School.
Methods: The 11-session scheme was delivered to penultimate year students via Zoom, covering system-based histology, and contextualising this in physiology and clinico-pathology. Topics covered included (non-exhaustive: general histopathology, haematopathology, gastrointestinal pathology, neuropathology, and uropathology). As part of the teaching, a pre- and post-course questionnaire asked participants to rate their confidence/understanding on a scale of 1 (no confidence) – 5 (extremely confident).
Results: Across 11 sessions, there were 546 responses. Average response to the question 'How confident were you in this topic before training?' on the 1-5 scale was 2.75. The average response to the question 'How confident were you in this topic after training?' was 4.14. This represents a 50.5% increase in self-reported confidence (two-tail paired t-test generates a P(T<=t) of 2.2E-139). Participants also subjectively rated the 'helpfulness' of the content with an average of all responses at 4.71 (on a scale of 1-5, with 5 being extremely helpful). A significant proportion of feedback commented on the peer-to-peer nature improving their accessibility to histopathology.
Conclusion: We demonstrate the effectiveness of peer-to-peer education as a means to increase student engagement and confidence with histopathology and clinicopathology. One of the key benefits of peer-to-peer (or near-peer) education is the more profound understanding of the confidence gaps of the participants through learned experience, and this facilitates more effective tailored learning to the student body. We encourage all educational institutions to support the implementation of peer-to-peer teaching as one part of their pathology education curriculum.

E-PS-14-006
Unusual, isolated localizations of Kaposi sarcoma: a series of 6 cases
O. Belkacem*, I. El Hadhri, H. Hamchi, M. Krifa, S. Mestiri, Z. Lajmi, M. Mokni
*University Hospital Sahloul, Tunisia

Background & objectives: Kaposi's Sarcoma (KS) is frequent among HIV patients, characterized by low-grade vascular tumours mainly affecting mucocutaneous sites. Although visceral involvement is uncommon, it can occur without associated skin lesions, underscoring the diverse clinical presentation of this neoplasm in immunocompromised individuals.
Methods: This study has included all patients diagnosed with Kaposi sarcoma excluding the cutaneous-mucosal localizations between 2008 and 2020, identified through imaging features and confirmed by histopathological examination and immunohistochemical study.
Results: There were 4 male and 2 female patients aged between 29 and 50 years, with a mean age of 37 years. The medical history included kidney transplant in 2 cases with immunosuppressants, and HIV positivity in 2 cases. The tumours were located in the stomach in 3 cases, the liver in 1 case, and the tonsil in 2 cases. Histological examination revealed a proliferation of spindle cells with pale cytoplasm, elongated or ovoid nuclei, and mild nuclear atypia. These neoplastic cells surrounded vascular slits containing a few well-individualized capillaries within the extravasation of erythrocytes. Immunohistochemical study showed positivity of neoplastic cells with anti-HHV8 confirming the diagnosis of Kaposi sarcoma.
Conclusion: In summary, our study reports isolated visceral Kaposi's Sarcoma (KS) in Tunisian patients, emphasizing its unique presentation in immunocompromised individuals. These cases, lacking mucocutaneous involvement, highlight the need to consider visceral KS in such populations.

E-PS-14-007
Scurvy, still among us
I. Bernal Simón*, D.X. Ugás Burranca, A. Ordóñez Arrillaga, M. Conde Ferreirós, A. Ezkurra Altuna, Y.P. Rodriguez, A. Juaristi, N. Segués Merino, M.Y. Silva Carmona, I. Ruiz
*Donostia University Hospital (Donostia-San Sebastián), Spain

Background & objectives: Scurvy is a nutritional disorder resulting from ascorbic acid (vitamin C) deficiency. This condition is rare in developed countries but remains prevalent in certain populations, including those with substance abuse disorders, low socioeconomic status and individuals on restricted diets.
Methods: A 55-year-old woman presented to the emergency room with a complaint of dizziness, headache, anorexia and discomfort lasting four days. Additionally, she described the onset of a generalized ecchymoses, purpuric macules and subcutaneous nodules distributed on the lower extremities over the last few weeks. She had no past surgical history and did not smoke or drink alcohol.
Results: On physical examination, skin revealed erythematous-violaceous lesions, perifollicular petechiae, "corkscrew" hairs, ecchymoses and subcutaneous nodules on the lower extremities. An additional finding was complete loss of dentition. Her initial hemogram showed anemia and because of an increased suspicion of scurvy, the vitamin C levels was ordered, results of which were 0,28mg/dL (0,40-2,00). Skin biopsy showed perifollicular erythrocyte extravasation with an associated chronic inflammatory infiltrate, a characteristic "corkscrew" hair shaft within a dilated follicle with perifollicular hyperkeratosis. Lobular panniculitis with areas of fat necrosis and numerous lipophages were also seen. There was no evidence of vasculitis. After receiving vitamin C supplementation, the patient recovered quickly and her dermatological lesions significantly improved.
Conclusion: Ascorbic acid is an essential cofactor for propyl and lysyl hydroxylases necessary for collagen synthesis not stored or synthesized in the body and requires intake from fruits and vegetables. Deficiency results in incomplete hydroxylation of procollagen precursors and manifests clinically in collagen-rich tissues such as skin, gums and vessels. This case highlights the importance of maintaining a high index of suspicion for scurvy in a malnourished patient who presents with lesions in the skin and characteristic "corkscrew" hairs.

E-PS-14-008
Reduce, reuse, and recycle (3R) in pathology department: do we know how to do?
B. Calim-Gurbuz*, S.K. Dursun, G. Kolak Gözüküçük, Y. Ulu, R. Dogukan, Z. Tosuner
*Istanbul Basaksehir Cam and Sakura City Hospital, Turkey

Background & objectives: The climate crisis poses a threat to humanity, and comprehensive measures are being implemented in various fields. It has been documented that laboratories are inherently hazardous in terms of waste production, material, and energy usage.
Methods: The workflow in the Pathology Department was analysed from the initial step of materials to the final pathology report. Training meetings on reduce, reuse, and recycle (3R) were organized for all employees in the Pathology Department in February 2024. To assess the impact of these meetings, an 11-item questionnaire was administered before/after the meetings, and their responses were statistically analysed.
Results: A total of 75 employees participated in the meetings and completed the questionnaire. They were categorized into four groups: doctors (40%), macroscopic technicians (15%), technicians in other areas (30%), and secretaries (15%). Correct responses regarding the 3R process significantly increased after the meetings among all groups ($p < 0.001$). The correct disposal bins for clean gloves, disposable cups, and boxes with food residue showed the most significant changes after the meetings ($p < 0.001$). Correct responses for medical waste bins and the correct disposal locations for batteries were higher before the meetings, therefore there were no statistically significant changes after the meetings ($p>0.05$).
Conclusion: As resources in our world continue to deplete, it becomes imperative to find environmentally friendly solutions in laboratories. While the impact of pathology laboratories on patients' lives is undeniable, it is essential to ensure that our actions during this process do not harm the environment. To safeguard the planet's resources, hospitals should adhere to the principles of 3R. Employees should receive education on environmentally friendly practices, and their adherence to these practices should be regularly monitored.

E-PS-14-009
Mucosal melanomas: insights into clinicopathological and molecular profile in a series of 41 cases
A. Carrasco Lorenzo*, C. Teixido, N. Castrejon, C. Montironi, A. Saco, J. Lop, R. Albero, A.P. García, L. Alos
*Pathology Department, Biomedical Diagnsotic Centre, Hospital Clinic, University of Barcelona, Barcelona, Spain

Background & objectives: Mucosal melanomas are infrequent tumours that originate from mucosal surfaces, accounting for less than 1% of all melanomas. We aimed to present our experience with these tumours, specifically documenting their clinicopathological characteristics and mutational profile.
Methods: This retrospective study involved reviewing the pathology files of Hospital Clinic, (UB), to identify mucosal melanomas originating in the head and neck region, vulvovaginal area and digestive tract between 2016 and 2023. Clinicopathological characteristics were examined. Molecular analysis was conducted in 34 cases, with 24 of them undergoing NGS (Oncomine Assay Thermo-Fisher) and BRAF investigation by RT-PCR in 10 cases.
Results: Forty-one mucosal melanomas were collected: 21 (54%) from the head and neck region (17 sinonasal and 5 of the oral mucosa); 17 (41.5%) from the vulvovaginal area; and 2 (4.5%) from the digestive tract. The patients were 29 females (70.7%) and 12 males (29.3%), with

a median age of 68 years. Most melanomas were diagnosed in stage IV (73%) and 19.5% of the patients died before 12 months from the diagnosis. The molecular profile showed NRAS as the prevalent driver gene (20.7%), followed by KIT and PIK3CA (6.9%), and BRAF (5.9%).
Conclusion: Mucosal melanomas often present in patients above the seventh decade of life. They are highly aggressive tumours, frequently diagnosed at an advanced stage and showing a very poor outcome. NRAS is the most common driver gene involved across all sites.

E-PS-14-011
Assessment of safety measures in pathology laboratories and evaluation of infectious, tumourous, and physical risks: the first survey in Morocco reviewing current practices
S. Chaib*, J. Kharmoum, M. Eljiar, i. eliahiai, K. Morabit, O. Faraji, Z. Ayoubi, G. Erradi, M. Chraïbi
*Laboratory CHU Tangier, Morocco

Background & objectives: Occupational hazards, infectious contaminations, carcinogenic risks pose significant concerns in pathology labs. Safety protocols came to manage these risks. This study assesses safety practices among Moroccan pathologists, aligns them with international standards, and raises awareness of infectious and tumourous risks.
Methods: We conducted the first national anonymous assessment of safety measures in pathology labs and knowledge evaluation regarding cancerogenic and infectious risks in Morocco. 112 Moroccan pathologists, including professors, residents, and specialists aged 26 to 70, participated. They received an anonymous questionnaire in March 2024. Data included demographics, protective equipment use, accidents, and risk perceptions. Consent was obtained from all participants.
Results: 88.4% lacked training in safety and quality measures, indicating significant training gap. Personal protective equipment (PPE) use was inconsistent with only 32.1% using it consistently, despite 100% glove use. Sharp instrument injuries were reported by 90.2%, mainly during macroscopic work. Among electric saw users, 71.2% lacked safety programs, resulting in 7.8% injuries. Chemical (75.9%) and biological fluid (50%) exposure were common. Airborne formaldehyde caused eye irritation (97.3%) and headaches (60.7%), primarily due to inadequate PPE. While 81.3% were aware of formaldehyde's carcinogenic risks, knowledge gaps existed. 76.8% were unaware of tuberculosis risks. Only 9.8% conducted regular biological monitoring for infectious hazards. The survey reveals equipment deficiencies and demands safety tools.
Conclusion: Morocco still lags in safety measures, and pathologists lack crucial information that could impact them. Our survey shows pathologists are keen to understand their risks better. It's important to fill training gaps, raise awareness, and provide proper protective gear for pathology labs' safety. Strict standards are needed, with early training. Training programs and practical national guides will be the first steps as a solution. The ILAC's ISO15189 standard for medical labs sets a good example, ensuring labs run safely.

E-PS-14-012
Clinical-pathological correlations and immunohistochemical analysis of 13 primary Merkel cell carcinoma cases
C. Costras*, M.I. Craescu, P.L. Chiriac, S.M. Sabo, T. Tebeica
*Colentina Clinical Hospital, Romania

Background & objectives: This study presents a comprehensive retrospective analysis focusing on clinical-pathological correlations and immunohistochemical profiles in a series of 13 Merkel Cell Carcinoma (MCC) cases.
Methods: MCC is a rare aggressive neuroendocrine malignancy with increasing incidence rates and significant mortality. The study included a cohort of patients diagnosed with MCC over a decade (2014 – 2024) with clinicopathological data collected and correlated with immunohistochemical staining results.
Results: Patients had a median age of 70. 7 were males (54%) and 6 were females (46%). Site predilection were as following: face (3 cases), legs (3), arms (3) buttoks (2), thigh (1). Majority of lesions were dermal based (7), with subcutaneous invasion in 5 cases, with predominantly nodular architecture. Areas of necrosis correlated with larger tumours (>2cm). Angiolymphatic invasion identified in significant number of cases (7); one case had gastric and one had lymph node metastasis. Positive staining for CK20, synaptophysin, and CK7 negativity confirmed MCC and distinguished it from other diagnoses. Two of seven cases were p63 positive and were associated with high ki67 index or high mitotic count.
Conclusion: Through correlating clinicopathological features with immunohistochemical profiles, this study provides valuable insights into the diagnostic and prognostic implications of MCC. Additionally, it highlights the importance of incorporating IHC analysis into the routine pathological evaluation of MCC cases for accurate diagnosis, risk stratification, and guiding therapeutic decisions. This retrospective series contributes to the growing body of evidence aimed at optimizing the management and outcomes of patients with Merkel Cell Carcinoma.

E-PS-14-013
Revisiting dajani scoring system for assessing male infertility: a new standard for testis biopsies?
G. Courtoy*, G. Tagmouti, L. Demoster, S. Khajjou, C. Degailler, H. Locy, R. Forsyth, W. Waelput
*Vrije Universiteit Brussel (VUB), Experimental Pathology (EXPA); Universitair Ziekenhuis Brussel (UZ Brussel), Department of Pathology, Belgium

Background & objectives: The recent increase in male infertility consultations emphasizes the need for improved diagnostics. Histopathological grading, like the Johnsen score, is pivotal yet labor-intensive. Our study evaluates the Dajani system's effectiveness, reproducibility, and efficiency via histochemistry and immunohistochemistry.
Methods: Fifty fine needle testis biopsies obtained from UZ-Brussel Fertility clinic underwent staining for hematoxylin-eosin (HE), Ki-67, or H3K27me3, then digitized. Inter-observer variability was evaluated for 5 investigators on whole slide images (WSIs) using PathoTrainer. Intra-observer assessment included a 7-day wash-out and randomization. Consensus scores were determined after deblinding. Classification time per WSI was monitored.
Results: The effectiveness of the Dajani system was demonstrated by the high agreement among investigators on both HE and immunostaining, yet superior with the Ki-67 dataset (consensus score >80%). Ki-67 staining exhibited significantly higher reproducibility compared to HE ($p<0.05$) in both intra-observer and inter-observer analyses. Subgroup analysis highlighted Ki-67's superior ability to better identify A2 and C classes, with Ki-67 enabling faster classification than HE ($p<0.05$).
Conclusion: These findings support the use of the Dajani system for assessing male reproductive health, especially using Ki-67 staining to enhance accuracy and efficiency. Protocol standardization for staining and interpretation, cut-off definition, leveraging WSI, and the development of artificial intelligence for augmented digital image analysis can further reduce variability, improve diagnostics, and facilitate personalized medicine.

E-PS-14-014
Cutaneous piloleiomyomas with fumarate hydratase deficiency: a retrospective study
M.T. Dawid De Vera*, C. Ramírez Sánchez, E. Gallego Domínguez, I. Hierro Martín
*Hospital Universitario Virgen de la Victoria, Spain

Background & objectives: Cutaneous piloleiomyomas (CL) are benign smooth muscle proliferations, sporadic or linked to hereditary syndromes like cutaneous leiomyomas with fumarate hydratase deficiency (CL-FH). The morphology and immunohistochemical FH loss can aid in patient management and the detection of germline mutations.
Methods: A search for skin-localized myomas diagnosed from 2004 to 2024 was conducted. Cutaneous angioleiomyomas were excluded. Histological characterization was performed and punch biopsies were taken for tissue arrays. Array sections were evaluated and FH immunohistochemistry was performed and evaluated on selected cases. Association between clinical and histopathological features of CL and FH deficiency was evaluated using non-parametric tests on SPSS.
Results: Thirty-three CL were examined. Eighteen were men and 15 were women, with a mean age of 52,3 years. CL exhibited different intensities in the FH staining and four samples (12,1%) revealed FH deficiency by immunohistochemistry. Three patients were men, and the mean age was 46,5 years (32-59 y). The woman included did not present uterine leiomyomas and none of the patients had a history of renal tumour. All patients were symptomatic (p=0,01) and presented multiple lesions (p=0,001) preferentially in the head and neck area (50%). Histologically, all cases presented eosinophilic cytoplasmic inclusions (p=0,013). No significant differences were found in the remaining clinical and histopathological variables included in this study.
Conclusion: Cutaneous leiomyomas with fumarate hydratase deficiency (CL-FH) are linked to uterine leiomyomas and, in 10-15% of cases, with renal cancer in the so-called hereditary leiomyomatosis and renal cell carcinoma syndrome (HLRCC). HLRCC is due to a heterozygous germline mutation in the FH gene which encodes an enzyme involved in the Krebs cycle. FH immunohistochemistry might be performed in symptomatic patients with multiple CL and eosinophilic cytoplasmic globules. Complete loss of FH staining could guide the clinical management of these patients.

E-PS-14-015
Intrathoracic primary malignant mesencymal tumours: a single centre study
A. Demirci*, M. Toker, M.A. Inan, N. Akyurek, G. Esendagli
*Turkey

Background & objectives: Thoracic mesenchymal tumours are rare. They constitute approximately 5% of mediastinal tumours benign and malignant together. This study aims to reveal the incidence, demographic distribution, and histopathological characteristics of primary malignant thoracic mesenchymal tumours.
Methods: Cases registered in our clinic was revised retrospectively. Thoracic primary malignant mesenchymal tumours between January 2019 and March 2024 were analysed.
Results: In 2037 thoracic surgery patients a total of 20 tumours were obtained. There were 8 solitary fibrous tumour, 3 inflammatory myofibroblastic tumour, 2 Ewing sarcoma, and 1 of each liposarcoma, leiomyosarcoma, angiosarcoma, intimal sarcoma, synovial sarcoma, peripheral neuroblastic tumour, primary pulmonary myxoid sarcoma with EWSR1-CREB1 fusion. 11 of the cases are female and 9 are male. The average age is 50 (ranged from 11 to 75).
Conclusion: Since thoracic primary mesenchymal tumours are rare, more studies/case reports are needed to increase the data of the literature.

E-PS-14-017
Updating macroscopic examination protocols and introduction of scientist histodissection – a quality improvement project
L. McKenna, A. Freegrove*, S. Al Mandhari
*Ireland

Background & objectives: Macroscopic examination is an essential step in the pathological examination of a specimen. Scientist histodissection is an increasingly important allowing for division of workload and scientist specialisation. Standardised block-taking has been shown to decrease workload and sample quality.
Methods: An audit was undertaken to assess the baseline number blocks taken for common specimens. The current macroscopic manual was reviewed against the latest ICCR and RCPath datasets to ensure all relevant details were captured. The protocols and dictation templates were updated and this was introduced prior to commencement of a specialist scientist in histodissection.
Results: At baseline, there was a huge variation in number of blocks taken. The new protocol highlights the standardised number of blocks required and prints the correct number of cassettes. The updated dictation templates are in line with the latest ICCR and RCPath datasets. Commencement of the specialist scientist in histodissection allows for starting of training of other medical scientists and encourages CPD certification. With the division of workload, the trainee doctors are able to spend more time on microscopic assessment. Teaching sessions on the new protocol are to be undertaken. Interesting case discussions with pathology and scientific staff are set to be introduced.
Conclusion: The macroscopic examination is essential. Introduction of scientist histodissection is essential to allow for scientist specialisation. Standardisation allows for uniformity of sampling and dictation. A re-audit will be undertaken after 3 months to assess whether there is a change in quality of block taking and workload.

E-PS-14-018
Audit on addendum reports with focus on report coding
L. Gallego*, F. MacSweeney
*University Hospital Waterford, Ireland

Background & objectives: Addendums reports following an original are sometimes necessary in Histopathology. In Ireland, there are targets recommended by a National Quality Improvement Body. We aim to verify if our department meets this target and to study the correct coding of addendums.
Methods: From a total of 26686 cases in one year, we extracted all cases coded as amended, corrected and supplementary. We calculated the percentage of these reports and compared it to the national recommended target. Subsequently, we implemented the definitions and the categorisation of discrepancies in amended/corrected reports and audited 20% of the supplementary in order to evaluate the coding.
Results: Pre review data showed that the percentage of supplementary reports (new information) was 5.53% and the combined amended/corrected (change on diagnosis/typing error) was 0.37%, both meeting the national targets of 10% and 1% respectively. During the review of coding, we noted that 50% of the amended reports were miscoded, and fit better the category of corrected. On the other hand, 23.6% were miscoded as corrected when they should have been coded as amended. Lastly, only 3.8% of the audited supplementary reports were miscoded, requiring different coding like MDT agreement/disagreement or Intradepartmental Consult. Overall, the error rate was 9%, but this did not make a major difference on the final percentages.
Conclusion: Monitoring the taxonomy and rates of addendum reports aids to maintain a high quality practice. It is also important to understand the coding system in order to track this data. In our department, national targets were met even after a review of coding. However, we noted a tendency to code amended reports as corrected reports. Even though the error rate on coding was not big, continuous training on this subject are required to follow the guidelines.

E-PS-14-019
PRAME in melanocytic lesions and its correlation with TILs
L. Gallego*, F. MacSweeney
*University Hospital Waterford, Ireland

Background & objectives: PRAME is a novel antibody against preferentially expressed antigen of melanoma and it has been discussed as a promising target for personalised treatment with T-cell receptor-redirecting agents. We aim to estimate a correlation between TILs and PRAME positivity.
Methods: We performed a retrospective analysis on the cases where PRAME was used in 2023, excluding all non-melanoma cases. We divided a cohort of 20 cases on brisk and non-brisk, and we correlated this information with PRAME's result in order to express a correlation coefficient. Finally, we used other stains to identify TILs in non-brisk cases and detect further correlation.
Results: We found 20 invasive melanoma cases where PRAME was used. Of these cases, 10 cases (50%) were reported as brisk. On the other hand, 10 cases (50%) were reported as non-brisk melanomas. Of the brisk cases, 90% of the cases were PRAME positive (strong and diffuse nuclear staining). Of the non-brisk cases, 70% of the cases were PRAME negative (none or focal/weak staining of a few cells). After staining the non-brisk cases that were PRAME positive with CD3 and CD8 in order to visualise the presence of T cells within the tumour, we noted a scattered or focal to null infiltration of these lymphocytes.
Conclusion: PRAME has been introduced to the melanoma panel for selected/difficult cases. When it comes to its relation with brisk infiltrating of T cells, we calculated a correlation coefficient of 0.61 (moderate correlation). One Brisk case was PRAME negative and the Non-Brisk cases that were PRAME positive did not show a big T-cell infiltrate with other stains. This indicates that PRAME positivity and brisk infiltration have no clear correlation. Bigger samples could aid to assess a connection.

E-PS-14-021
Extragonadal germ cell tumours: 24 years cases review
L. Hato Salmón*, V. Macarrón, M.I. Esteban-Rodríguez, R.M. Regojo Zapata
*La Paz University Hospital, Spain

Background & objectives: Germ cell tumours (GCT) are rare neoplasms that arise primarily in the gonads and, more rarely, in other locations through which primordial germ cells migrated during embryogenesis. Our objective is to evaluate the clinicopathological characteristics of extragonadal primary GCTs.
Methods: We conducted a retrospective review of biopsies diagnosed as GCT at our centre since 2000, aiming to identify cases where the tumours are located outside the gonads. From these, we extracted clinicopathological variables including age, gender, histological type and location. Cases of gonadal germ cell tumours and metastases originating from gonadal sources were excluded from this analysis.
Results: Among the 92 cases analysed, the majority were observed in females (51/92) and the average age was 13.84 years (70.65% under 16 years old). The most common extragonadal histological types were mature cystic teratoma (50%) and immature teratoma (15.21%). The sacro-coccygeal region (34.78%) emerged as the most frequent location, primarily associated with mature cystic teratoma, followed by the central nervous system (21.73%), predominantly linked with germinoma. Other diagnosed histologies included germinoma (13.04%), yolk sac tumour (11.95%), mixed GCT (7.60%), embryonal carcinoma (1.08%), and choriocarcinoma (1.08%).
Conclusion: In our study, sacrococcygeal region emerged as the predominant location for extragonadal GCT, diverging from the commonly cited mediastinum in literature, probably due to the important inclusion of paediatric population in the study. Following sacrococcygeal region, the most prevalent sites were the central nervous system, mediastinum and retroperitoneum. These tumours predominantly manifest during childhood, with a slightly elevated occurrence in females. Mature cystic teratoma stands out as the most frequently identified histological type, succeeded by immature teratoma.

E-PS-14-022
Inhalation of lead nanoparticles induces cytoskeletal changes in the brain corresponding to neurodegenerative diseases
A. Jedlickova*, D. Kristekova, P. Coufalik, L. Vrlikova, L. Alexa, D. Luskova, K. Krumal, V. Jakesova, Z. Vecera, A. Hampl, P. Mikuska, J. Dumkova, M. Buchtova
*Masaryk University, Brno, Czech Republic

Background & objectives: Lead is known for its ability to cross the blood-brain barrier, accumulate in the brain, and induce neurotoxicity. We focus on the impact of lead nanoparticles, which may manifest a unique effect on neural tissue in comparison to ionic form.
Methods: Mice were exposed to lead nanoparticles (PbO or Pb(NO3)2) in whole-body inhalation chambers mimicking real-life exposure. Brain and olfactory epithelium were evaluated by histological methods (including transmission electron microscopy), immunohistochemistry, and molecular approaches (qPCR, SDS-PAGE Western Blot). The direct effect of PbNPs on neural tissue was determined in vitro using trigeminal ganglia cell cultures.
Results: PbNPs are transported to the brain by blood as well as through the olfactory pathway, which is accompanied by serious damage to olfactory epithelium disabling olfaction. Two types of PbNPs with different solubilities uncovered the distinct effect of the nanoparticle and ion form of lead on neural tissue. The clearance ability of the brain to remove PbNPs was low and demonstrated the necessity of a long clearance period in order to restore pathological features induced by lead exposure. The disruption of the actin cytoskeleton in the hippocampus and isocortex was associated with alteration of PI3K/Akt/mTOR signaling including expression and phosphorylation of Tau in exposed animals or trigeminal ganglia cell cultures.
Conclusion: The penetration of PbNPs through the blood-brain barrier and the olfactory epithelium causes pathological changes corresponding to neurodegenerative disorders through cytoskeleton disturbances on several levels. Targeting of cytoskeletal components may therefore enable the development of directed treatment preventing neurodegenerative features of lead-exposed organisms.

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E-PS-14-023
Cutaneous Immunoglobulin A (IgA) associated lymphocytic vasculopathy: a diagnostic dilemma resolved on immunofluorescence
A.A. Khan*, A.K. Yadav
*Vardhman Mahavir Medical College, India

Background & objectives: Cutaneous IgA associated lymphocytic vasculopathy is a novel clinical and histopathological entity resembling Schamberg's disease and is characterized by palpable purpuric rashes involving the lower limbs. Among small vessel vascular injury syndromes IgA mediated lymphocytic vasculopathy appeared as distinct subtype.
Methods: We describe a case of a 24-year-old male presenting with multiple discreet non blanchable reddish brown papules and macules on the lower half of both the legs. Systemic examination was unremarkable. Punch biopsy was done for definite diagnosis. DIF

was performed on the lesional skin by the overlay of flourorescein-conjugated antibodies upon sections cut from frozen skin.
Results: Histopathological examination of the specimen revealed focal areas of spongiotic vesicles containing lymphocytes in the epidermis and perivascular lymphomononuclear infiltrate with prominent erythrocyte extravasation and endothelial cell proliferation in the superficial dermis. On lesional direct immunofluorescence(DIF), granular IgA deposits were noted in the intraepidermal spongiotic vesicles and perivascular areas of the dermis. On the basis of clinical picture, histopathology and DIF findings, the case was diagnosed as IgA associated lymphocytic vasculopathy. Similar histopathological findings may be seen in Schamberg's disease. DIF, however, is typically negative.
Conclusion: IgA associated lymphocytic vasculopathy closely mimics pigmented purpuric dermatosis (PPD) and its diagnosis requires correlation of clinic-pathological findings. The histological demonstration of lymphocytic vasculitis does not necessarily exclude the presence of immune complexes and, therefore, DIF should be performed to detect rarer variants of lymphocytic vasculopathy, as exemplified in our case.

E-PS-14-024
Inter-assay comparison of two PD-L1 IHC 22C3 pharmDx Assays for Dako Autostainer Link 48 (SK006) and Omnis (GE006) in different cancer types
H.L. Kristoffersen*, R. Røge, S. Nielsen
*NordiQC, Denmark

Background & objectives: PD-L1 IHC status is required to stratify patients for immunotherapy. We examined the analytical concordance between two 22C3 assays SK006 and GE006 in NSCLCs, TNBCs, HNSCCs and urothelial carcinomas (UC). At present GE006 is only validated by vendor for NSCLCs.
Methods: IHC for PD-L1 was performed on serial sections on seven TMAs comprising 38 NSCLCs, 101 UCs, 57 TNBCs and 107 HNSCCs according to vendor recommended protocol settings with the two 22C3 assays; SK006 and GE006. PD-L1 expression was scored using the relevant scoring method (TPS or CPS) with the respective cut-off for the different cancer subtypes included.
Results: In total, 284 tumours were scored. Twenty were excluded due to missing tumour cells. Overall, an analytical concordance of 98,6% (280/284) was obtained. For NSCLCs using TPS with cut-off at 1% and 50% and UCs using CPS≥10 completely identical results were obtained. The 22C3 GE006 assay induced a slightly increased sensitivity (not statistically significant) in TNBCs and HNSCCs as 1/56 and 3/101 were PD-L1 positive defined by CPS≥10 and CPS≥1, respectively, using GE006 compared to SK006. 5/101 HNSCCs showed a TPS≥50 for both PD-L1 IHC assays. No tumours were evaluated as negative using GE006 and being positive when using SK006.
Conclusion: In this study, the two companion diagnostic assays provided highly concordant levels of PD-L1 expression in different cancer subtypes, using the present range of clinically relevant cut-off levels. The results indicate that the 22C3 PD-L1 assay GE006 for Omnis is interchangeable for the 22C3 assay SK006 for Autostainer Link 48 and thus GE006 being applicable to be used for many cancer subtypes for PD-L1 IHC status.

E-PS-14-025
A rare case of primary localized cutaneous nodular amyloidosis with extensive osseous metaplasia
F. Kubba*, L. Ian
*Ealing Hospital, London North West University Healthcare NHS Trust, United Kingdom

Background & objectives: Primary localized cutaneous amyloidosis is characterised by extracellular deposition of amyloid protein (AL type or AA type) in previously normal skin without internal organ involvement. There are three clinical subtypes; macular, lichenoid, and nodular amyloidosis.
Methods: A 56-year-old Asian male presented with a 6-month history of swelling and pustules on the chin which had not responded to topical antibiotics, steroids, or oral antibiotics. On examination there was a 4x3cm indurated plaque with a nodular component and an apple-jelly appearance. The rest of the cutaneous and physical examination was unremarkable. No associated systemic illness was reported.
Results: Microscopically, the punch biopsy from the lesion showed mild hyperkeratosis with amorphous pink staining, PAS-positive deposited material in the dermis with extensive osseous metaplasia. Focal plasmacytic aggregates were present in the deep dermis. Congo red histochemical stain showed apple-green birefringence consistent with nodular cutaneous amyloidosis. Systemic amyloidosis was excluded following review at the local tertiary amyloidosis centre. A diagnosis of primary localised cutaneous nodular amyloidosis (PLCNA) was made. The lesion was treated with intralesional triamcinolone 10mg/ml on two occasions 6-months apart without significant improvement. Surgical excision was declined by the patient. At 6-year follow-up there are stable appearances of the lesion and no evidence of systemic involvement.
Conclusion: PLCNA is the rarest subtype of cutaneous amyloidosis and most commonly reported on the distal limbs or head and neck. The mean age of presentation is 55 years with no gender predominance. Although cutaneous amyloidoma can form calcifications, ossification is extremely unusual with only two previous cases described. An estimated lifetime risk of development of systemic amyloidosis of between 7% and 50% of cases suggests long-term follow-up assessments are required.

E-PS-14-026
Papular eczema mimicking papular mucinosis in a young patient, a diagnostic pitfall
F. Kubba*, L. Ian, M. Ratynska
*Ealing Hospital, London North West University Healthcare NHS Trust, United Kingdom

Background & objectives: A 22-year-old Asian male presented to clinic with a chronic localised slightly itchy papules on the shins and forearms. There was no significant past medical history including atopic dermatitis or asthma in childhood. There was no family history of note.
Methods: On clinical examination there were small skin-coloured papules measuring less than 4mm present diffusely over the shins, distal thighs, and forearms without secondary postinflammatory changes.
A diagnostic punch biopsy of the skin was performed for clinicopathologic correlation in view of the atypical features. The clinical diagnosis was more in favour of a localised papular mucinosis, based on the information supplied.
Results: Microscopically sections showed mild hyperkeratosis, hypergranulosis and mild acanthosis. Increase superficial dermal capillaries and sparse dermal lymphocytes were noted with pale blue material between collagen fibres. Alcian blue stain was positive thus supporting papular mucinosis.
At clinical follow-up the patient had diffusely dry skin and areas of excoriation on the shins and arms with itching on the limbs and back. Features were suggestive of papular eczema with lichenification.
Blood tests were normal (Full blood count, renal, liver, HIV and hepatitis screen, ANA negative, ENA negative, complement normal). However, IgE was significantly raised at 1116 IU/ml. Clinical and biochemical features were consistent with endogenous eczema (papular eczema variant).
Conclusion: We have reported a 22-year-old male patient presenting with slightly itchy papule on the shins and forearms. The diagnostic punch biopsy suggested the presence on dermal mucin deposition

favouring the diagnosis of papular mucinosis. However the clinical course and raised IgE levels shifted the balance towards papular eczema. Although the mucin deposition is regarded as a genuine finding, it is best considered as a nonspecific secondary postinflammatory change to the atopic dermatitis. We regard this as a diagnostic pitfall.

E-PS-14-027

Morphologic diagnostic significance of microanatomical melanoma metastasis location in sentinel lymph node

G. Belevičiūtė, P. Skučaitė, J. Makštienė, M. Kupryte*, L. Poškienė
*Lithuanian university of health sciences, Lithuania

Background & objectives: Histopathologic status of sentinel lymph node is a powerful prognostic factor for primary cutaneous melanoma, contributing towards planning treatment. Study aim is to determine if microanatomical location of lymphonodal metastasis can be a relevant diagnostic tool defining metastatic melanoma status.
Methods: 151 cases with melanoma metastasis in sentinel lymph node were selected in retrospective study, evaluating morphologic microanatomical metastasis location (sinus, parenchymal, extracapsular) significance in context to patient's age, gender, morphologic melanoma type, Breslow thickness, and pT stage of melanoma TNM classification. Statistical analysis of Mann-Whitney U and $\chi 2$ tests was applied ($p<0.05$).
Results: Predominant morphologic types of melanoma (Breslow thickness median=4.05 mm, interquartile range=4.09 mm) for 53.6% (n=81) males and 46.4% (n=70) females were nodular (35.8%, n=54) and unspecified (33.1%, n=50) with frequent pT4b stage (45.7%, n=69). Lymphonodal parenchyma was the most common microanatomical localization (61.6%, n=93), following sinus (57%, n=86) and extracapsular (12.6%, n=19) microanatomical sites. Patients with lymphonodal sinus metastasis were younger compared to metastasis-negative cases (median=61 years, interquartile range=29 years vs median=71 years, interquartile range=20 years; $p<0.05$), extracapsular metastasis was more common for males ($p<0.05$) and less likely to be detected in nodular and unspecified melanomas ($p<0.05$). No significant tendencies were detected in context of Breslow thickness and pT stage.
Conclusion: Study results demonstrated significant tendencies of sinus and extracapsular melanoma metastasis of sentinel lymph nodes in context of melanoma patient's age, gender, and melanoma type. Detected microanatomical tendencies in metastatic lymphonodal melanoma may suggest a potentially novel direction for further scientific research in melanoma metastasis morphology and disease prognosis, considering new guidelines for treatment strategies in advanced melanoma cases.

E-PS-14-028

Malakoplakia manifesting as a pelvic mass: a case report

Z. Lajmi*, S. Yacoub, S. Mestiri, M. Mokni
*University Hospital Sahloul, Tunisia

Background & objectives: Malakoplakia is a rare granulomatous inflammatory disease that usually affects the genitourinary tract and clinically mimics malignant tumours. It is defined histologically by Michaelis–Gutmann bodies and it is believed to be associated with defective macrophage function.
Methods: We present a case of a 61-year-old diabetic woman initially presented with symptoms of acute pyelonephritis and renal failure. Abdominal computerized tomography showed a right iliac fossa solid mass with heterogeneous enhancement measuring 8.5cm. The mass invaded the appendicular tip and extended to the right ureter, psoas muscle and to external iliac arteries. Appendicectomy and mass biopsy were performed.
Results: On gross examination the appendix surface was lined by multiple yellowish nodules that extended to the mesoappendix. Microscopic examination of biopsy specimen and appendix showed confluent sheets of histiocytes with eosinophilic granular cytoplasm and basophilic round bodies that stained with Periodic Acid-Schiff (PAS), Grocott-Gomoriand and Von-Kossa calcium, consistent with Michaelis-Gutmann bodies.
Conclusion: Malakoplakia is rare chronic inflammatory disease that most commonly affects immunocompromised adult women due to incomplete degradation of gram negative bacteria by macrophages. Microscopic hallmarks are Michaelis-Gutmann bodies. Special stains as PAS and Von-Kossa calcium are easy and mandatory tools to confirm diagnosis of malakoplakia and rule out other severe granulomatous diseases including tuberculosis. Therefore, awareness of pathologic criteria of malakoplakia is crucial to avoid misdiagnosis and give patients the opportunity to receive timely and adequate treatment.

E-PS-14-029

A unique presentation of lupus tumidus showing improvement with sun exposure

N. Lao*, A. Wang
*Canada

Background & objectives: Lupus erythematosus tumidus is an autoimmune disease commonly manifesting as rashes to the upper trunk and lateral face. Classically, lupus tumidus is associated with smoking and ultraviolet (UV) light exposure.
Methods: A 64-year-old male with history of metastatic prostate cancer presented to dermatology clinic with a 20-year history of rashes affecting his upper trunk. The rash appeared as erythematous papules with some coalescing in a psoriasiform pattern. The patient could not remember an inciting event, but over the years noted the rash worsened in the winter and improved in the sun.
Results: He described a 30 pack-year history of smoking. His medications included apalutamide and Lupron. He had underwent several punch biopsies in the past with no definitive diagnosis. A repeat biopsy was performed. The biopsy showed evidence of superficial and deep perivascular and periadnexal inflammation without atypia. There was evidence of increased dermal mucin by Alcian blue stain and plasmacytoid dendritic cells. Overall, the results of the biopsy favoured a diagnosis of lupus tumidus. The patient was prescribed betamethasone dipropionate 0.05% and his rash cleared completely.
Conclusion: This case represents a unique presentation of lupus tumidus with improvement following sun exposure. UV exposure is thought to be a key environmental trigger in the development of lupus tumidus. The proposed mechanisms primarily implicate UVB in abnormal cytokine release, nuclear damage, and defective removal of apoptotic cells. Despite this, small pilot studies have shown success using UVA-1 therapy in treating chronic cutaneous lupus compared to placebo. This case expands on the current knowledge and known presentations of lupus tumidus.

E-PS-14-030

Extensive immunophenotyping of circulating tumour cells for diagnostic monitoring in gastrointestinal cancer in correlation with conventional histological classification in gastric and colorectal cancer

P. Loehr*, J. Waidhauser, P. Grochowski, N. Reitsam, B. Grosser, F. Sommer, A. Rank, B. Märkl
*Haematology and Oncology, Medical Faculty, University of Augsburg, Germany

Background & objectives: Recently we identified SARIFA as a histopathological biomarker in colorectal and gastric cancers, which is linked to poor prognosis and intricately associated with fatty acid metabolism. This study aims to elucidate the underlying pathophysiological mechanisms by immunophenotyping circulating tumour cells.
Methods: Using CellSearch in 19 patients with colorectal or gastric cancer undergoing surgical treatment, we employed flow cytometry to

analyse peripheral venous blood samples and freshly resected surgical specimens. We specifically investigated the expression of SARIFA-associated fatty acid transport proteins (CD36 and FABP4) and checkpoint inhibitor ligands (PD-L1 and PD-L2). These results were correlated with multiplex immunohistochemical staining.
Results: No significant differences were observed in EpCAM-positive CTC counts between peripheral venous blood samples and colorectal surgical specimens in patients with colorectal cancer. In contrast, a significant reduction in EpCAM-positive CTCs was noted in patients with gastric cancer when comparing these sample types. Additionally, there was a notable decrease in CTCs positive for CD36, FABP4, PD-L1, and PD-L2 in the surgical specimens from gastric cancer patients. Correlating the results with histopathological findings, CD36- and FABP4-positive CTCs were significantly increased in venous blood samples taken from SARIFA-positive cases.
Conclusion: These findings underscore the potential of CTC flow cytometry as a novel diagnostic modality for investigating tumour biology and monitoring disease progression in patients receiving surgical treatment. Especially the assessment of blood from fresh surgical specimens offers access to the compartment of mesenterial blood avoiding additional interventions. It can be used as an adjunct to the conventional histopathological workup in GI cancers.

E-PS-14-031
Two new cases of neutrophilic sebaceous adenitis: an extremely rare entity
M. Matanie*, L. Rames, P. Vuattoux, Z. Christelle, N. Ortonne
*Henri-Mondor University Hospital, APHP, France

Background & objectives: Neutrophilic sebaceous adenitis is an exceedingly rare disease with only 10 cases reported in the literature between 1993 and 2023. It involves more frequently men than women. Herein, we describe another two new cases.
Methods: A 74-year-old man presented with pruritic, papulopustular lesions scattered on the face, pubis, and penis. Blood tests showed moderately elevated neutrophil levels. A 27-year-old woman presented with pruritic erythematous infiltrated lesions on the face, back, chest, upper limbs, and abdomen, associated with a subcentimeter submandibular adenopathy. No bacteriological agents, and neither a medication history nor sun exposure was identified.
Results: Cutaneous punch biopsies were performed, and histological examination revealed, in both cases, a normal epidermis, a dermal inflammatory infiltrate composed of lymphocytes, histiocytes, and neutrophils with perisebaceous distribution, infiltrating sebaceous glands with scattered necrotic sebocytes in the sebaceous lobules. The inflammation was entirely localized on sebaceous glands, without involving the hair follicle. A diagnosis of neutrophilic sebaceous adenitis was established. In both cases, treatment consisting of topical steroids resulted in regression of the lesions during hospitalization.
Conclusion: NSA is a rare disorder of unknown cause that presents with recurrent circinate plaques on the face characterized histologically by neutrophilic inflammation of the sebaceous glands accompanied by necrotic sebocytes. This is only the second case reported in women. The pathogenes is still unknown. The role of photoexposure, autoimmunity and of Demodex mites was discussed. Different treatments have been reported with variable results. Further studies are required to determine the cause of this rare desease.

E-PS-14-032
Two incidental cases of well-differentiated papillary mesothelial tumours
O.F. Mülkem*, N.S. Şeker, E. Dündar
*Eskisehir Osmangazi University, Turkey

Background & objectives: Well-differentiated papillary mesothelioma which was an unusual mesothelial neoplasia affecting the peritoneum has recently been renamed well-differentiated papillary mesothelial tumour (WDPMT) by the World Health Organization. This change in terminology creates confusion. The prognosis for WDPMT is still unclear.
Methods: Two cases of well-differentiated papillary mesothelioma detected during surgical intervention in patients admitted to our hospital in 2024 for different reasons are presented here. Tumoural malignant implants were suspected in both cases. Similar sections and immunohistochemical studies were performed in both cases.
Results: The first case was a 67-year-old male with diffuse malignant gastrointestinal stromal tumour involvement. She underwent radical resection for excisional treatment. A neoplastic lesion adjacent to the omentum was observed during surgery. Our second patient, a 79-year-old male patient, was taken to laparotomy for ileus. A lesion suspicious for implantation is seen in the pelvic peritoneum. Both cases showed stromal papillary proliferations. The papillae were lined with single-row cuboidal to columnar epithelium. EMA applied to both cases was focally positive, calretinin, and WT-1 were diffusely positive. No nuclear loss was observed with BAP-1. P53 showed patchy staining. Desmin was negative.
Conclusion: WDPMT needs to be differentiated from mesothelioma and mesothelioma in situ. Although the cells in WDPMT are benign, borderline cases can be encountered. The literature shows that multiple immunohistochemical studies and fluorescent in situ hybridization are necessary for differentiation. The mesothelial nature of the lesion is known. Reactive processes or genetic pathways may be involved in the etiology. There is a need for more etiologic and genetic data in the literature.

E-PS-14-033
Rosai-Dorfman disease: a report of 5 cases and review of literature
L. Njim*, M.M. Hamzaoui, A. Ben Mabrouk, S. Mabrouk, S. Ben Hammouda, A. Zakhama, A. Bellalah
*Fattouma Bourguiba University Hospital, Monastir, Tunisia

Background & objectives: Rosai-Dorfman Disease (RDD), also known as sinus histiocytosis with massive lymphadenopathy, is a rare form of non-Langerhans cell histiocytosis. It was incorporated as a histiocytic neoplasm in the fifth edition of the World Health Organization classification of hematopoietic tumours.
Methods: We conducted a retrospective analysis of the medical records of 5 RDD patients diagnosed between January 2018 and December 2023 in the Department of pathology in Fattouma Bourguiba Hospital of Monastir. We report the clinicopathological features of this entity with a review of literature.
Results: In our serie, The mean age was 41 years, with a male predilection. Among the 5 cases, 4 were purely extranodal and one was both nodal and extranodal : one case in the oral cavity, 2 cases in bones (maxilla and metacarpal bones), and 2 cases in the cutaneous and subcutaneous layers (2 cases). Biopsy was done in all cases. Histologically, extranodal RDD exhibited varying degrees of stromal fibrosis, with polygonal histiocytes containing well-preserved lymphocytes and plasma cells. Nodal RDD was characterized by dilated sinuses infiltrated with histiocytes, often displaying emperipolesis images. In immunohistochemistry, these histiocytes expressed S100 protein and CD68. CD1a was negative.
Conclusion: RDD is one of 3 major types of histiocytosis, along with Erdheim-Chester disease and Langerhans cell histiocytosis.Pathologic diagnosis of extranodal RDD may be difficult and immunohistochemistry is frequently required for definitive diagnosis.The variety of pathological aspects and the spectrum of different clinical forms were deeply investigated. Despite recent advancements in the dissection of pathogenetic mechanisms of RDD, with the identification of gene mutations in the MAP kinase pathway, several biological and clinical aspects of this disease remains to be elucidated.

E-PS-14-034

Novel use of simulation in histopathology training – the histopathology bootcamp

R. O'Carroll*, R. Farrell, F. Kelly, D. Byrne, S. Phelan, L. Aalto
*Division of Anatomic Pathology, Galway University Hospital, Ireland

Background & objectives: Simulation is widely used in medical specialty training and has improved training outcomes. The use of simulation in histopathology training has not been previously reported. Our objective was to develop a simulation based induction programme for early stage trainees.
Methods: Six interactive stations were developed. 18 trainees participated, in groups of 6:-
1. Simulated skin dissection, using porcine specimens.
2&3. Interactive sessions delivered by medical scientists and pathologists, explaining laboratory processing, immunohistochemistry, molecular pathology methods.
4. Ergonomic use of a microscope and approach to H&E evaluation.
5. Interactive discussion on Immunohistochemistry interpretation.
6. Simulated post-mortem external examination, using a mannequin
Results: Formal feedback was obtained from all participants and was universally positive. Participants suggested repeated training cycles occurring earlier in the training year to give incoming trainees a stronger foundation entering the specialty. Trainees suggested a greater time allocation to dissection simulations and lab workflow stations, and the addition of more autopsy and molecular pathology teaching. Feedback from faculty was also positive; - trainers enjoyed delivering the stations and felt the format was beneficial.
A limitation of this format was that not all participants were at the same stage of training, with some finding the format too basic.
An additional benefit was interaction and opportunities for networking among new trainees.
Conclusion: Simulation is a key avenue to expand the knowledge base and procedural confidence of medical trainees but has not been used in histopathology. This Bootcamp was devised as a pilot programme for early stage trainees. We now aim to develop this into a recurring National induction day for new entrant trainees, which will serve to provide a broad grounding in the work of the laboratory. Use of simulation for more complex dissection for advanced trainees will also be explored.

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E-PS-14-035

Cutaneous metastases of solid tumours – a single institution experience with small dermatological biopsies

I. Petrovic*, K. Kundovic, D. Petrovic, M. Bosić, J. Stojković Filipović, D. Škiljević, M. Mijuskovic, B. Lekić, S. Minić, M. Gajic Veljic, V. Reljić, D. Zivanovic, J. Perić, M. Petrovic, E. Manojlović Gačić
*Faculty of Medicine, University of Belgrade, Serbia, Institute for Oncology and Radiology of Serbia, Belgrade, Serbia

Background & objectives: Cutaneous metastases (CM) are a rare and their diagnosis can be challenging if they are initial manifestation of neoplastic disease. The aim of our study was to describe their clinicopathological features and challenges which can be encountered in diagnostic process.
Methods: We screened the histopathology records of small dermatological biopsies diagnosed at the Institute of Pathology Faculty of Medicine in Belgrade in 8-year period (2016 – 2023). Patients with clinical suspicion of CM and patients with histopathological diagnosis of CM were included in the study. Haematological tumours were excluded.Demographic characteristics, clinical presentation, and discordance between referral and final diagnosis were analysed.
Results: CM were identified in 29/44 patients and 37/56 biopsies included in the study (66% each). They were common in women (59%) and older patients (>60 years old) (65%), and usually presented on chest (57%) and as a plaque (44%) or nodule (26%). CM was the first presentation of neoplastic disease in 12 patients (27%). In 11 patients with history of neoplastic disease (42%), CM was not identified; instead, other primary skin tumours, reactions to antineoplastic treatment, and inflammatory changes including acantholytic dermatoses were noted. Breast cancer was the most prevalent primary malignancy to metastasize to the skin (49%), mostly hormone receptor negative with HER2 3+ expression (6/11 tested samples).
Conclusion: Our study confirmed rare prevalence of cutaneous metastases of solid tumours in dermatopathological practice and showed common occurrence in patients with breast cancer. Cutaneous metastasis can be a first sign of neoplastic disease in almost third of such patients. Patients with previous history of malignant tumours should be carefully evaluated as both primary cutaneous tumours and inflammatory dermatoses need to be considered in differential diagnosis.

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E-PS-14-036

Pilomatrixcarcinoma: when histology meets immunohistochemistry to perform a diagnosis

E. Ponce Casas*, F. Felipo Berlanga, S. García-Fuertes, R. Vilorio, M. Garcia Garcia, C. Cabañuz Rocatallada, L. Requena Caballero
*Hospital Clínico Universitario Lozano Blesa, Spain

Background & objectives: Pilomatrixcarcinoma is a rare and locally aggressive malignant skin tumour that arises from the hair follicle matrix or, more rarely, from malignant transformation of pilomatrixoma. It presents as a solitary nodule, primarily in the head and neck region.
Methods: We present the case of a 72-year-old man who consulted dermatology for a 0.9 cm papular lesion in the left temporal area. Following its excision, the specimen was referred for study.
Results: Microscopically, the lesion was predominantly dermal, with lobulated borders, well-demarcated by basalioid cells with hyperchromatic nuclei and prominent nucleoli, with clear cells and focal ghost cells, along with frequent mitotic figures; these features were suggestive of malignant adnexal tumour with trichilemmal or matrical differentiation. Immunohistochemical profiling showed diffuse positivity for CK8/18, CK20, Ber-Ep4, and E-cadherin, focal positivity for CK5/6, CD56, and EMA, and negativity for CK7, chromogranin, synaptophysin, enolase, SOX-10, CEA, and androgen receptors. The neoplastic cells were also diffusely positive for beta-catenin, contrasting with negativity in ghost cells. Adipophilin and FXIIIa were negative, ruling out a sebaceous origin. Thus, integrating these findings led to a definitive diagnosis of pilomatrixcarcinoma.
Conclusion: Pilomatrixcarcinoma is a locally aggressive tumour of the hair follicle, whose metastatic potential is not clear, but distant metastases and mortality have been described. It requires a detailed histological evaluation to differentiate it from other neoplasms originating from cutaneous appendages or from basal cell carcinoma with follicular differentiation. Features of malignancy with presence of clear and ghost cells, in addition to a beta-catenin and CK 5/6 expression, and negativity for sebaceous markers, helps guide the pathologist to a certain diagnosis.

E-PS-14-038

Regarding 2 cases: breast implant-associated anaplastic large cell lymphoma

M.A. Riera Bello*, L.A. Luizaga Velasco, J. Lopez Díaz, A. Calderon Romero, C. Ferrer Cassado, C. Gonzales Minguez, X. Tarroch Sarasa
*Hospital Universitari Mutua Terrasa, Spain

Background & objectives: Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) is a rare T-cell lymphoma. Patients with textured breast implants show a higher risk. Histologically, it is similar to other CD30 positive T lymphomas, but it has a different clinically course.
Methods: All cases of BIA-ALCL diagnosed in our Hospital between 2021-2023 were retrospectively studied; epidemiological (location, age, gender), histological, immunohistochemical and radiological review.
Results: 2 cases were found; 1 left breast and 1 bilateral; ages 52 and 61 years old.
Cytohistological studies showed a population of large atypical lymphoid cells, some of the "horseshoe" type on a proteinaceous background and connective tissue with fibrin.
Immunohistochemistry: positivity for CD30 (diffuse-intense), CD8 and granzyma; negativity for ALK-1, CD20, PAX5, CD3, CD4, CD2, CD7, CD5, EMA, CD56, perforin, CD45 and EBER (in situ hybridization).
Molecular: 1 with monoclonal TCR Gamma and TCR Beta; 1 cytometry case suggestive of T lymphoma.
Conclusion: BIA-ALCL are rare and must be reported. The diagnosis should be made in patients with textured breast implants and in the case of lymphomas that do not express T lymphoid markers. The diagnosis is based on positivity for CD30; its expression alone is insufficient and must be clinically correlated. Surgical resection should be considered for all cases. In the last 10 years, 79 cases have been confirmed in Spain, with two of those cases diagnosed and treated in our centre.

E-PS-14-039
Impact of prolonged ischemia and fixation time on tonsil specimens stained with PD-L1 IHC 22C3 pharmDx
C. Roach*, K. Kersch, J. Musser, S. Tabuena-Frolli, S. Hund, K. Kulangara
*Agilent Technologies, USA

Background & objectives: PD-L1 IHC 22C3 pharmDx is a qualitative immunohistochemical (IHC) assay for PD-L1 expression in FFPE specimens routinely processed for diagnostic evaluation. A pre-analytical variable study has been performed to assess the effects of ischemia and fixation time on PD-L1 expression.
Methods: Fresh tonsil tissues were procured, prepared and then subjected to ischemic times of 0.5 - 72 hours. Specimens were then fixed in 10% NBF for 6 - 72 hours. Nineteen benign tonsil specimens were prepared with various conditions and were stained by IHC using PD-L1 IHC 22C3 pharmDx.
Results: Stained slides were evaluated and assessed for any changes in PD-L1 expression and overall tissue quality by comparing specimens prepared with various ischemic and fixation times. The data demonstrated average IHC intensity of PD-L1 expression with minimal differences of ≤ 0.5 intensity grade between sections processed with fixation times 6-72 hours and ischemia time 0.5-72 hours. However, while the PD-L1 expression was preserved even with long ischemic times of 72 hours, the tissue was morphologically degraded which was most prominent starting at 24 hrs.
Conclusion: Pre-analytical effects in IHC can be minimized with standardization of specimen handling leading to enhanced specimen quality and antigen preservation. FFPE tissues prepared with various fixation times ranging from 6-72 hours demonstrated negligible variability in intensity between conditions. FFPE tonsil tissues prepared with ischemia time of 24 hours or more demonstrated equivalent PD-L1 expression; however, degraded tissue quality and poor cellular morphology was observed.

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E-PS-14-040
Cost-effectiveness for companion BRCA testing and adjuvant olaparib treatment in patients with BRCA mutated high-risk HER2-negative early breast cancer
E. Sheppard*, W. Ma, Y. Punekar, G. Sagoo, S. Nikolova
*Astrazeneca, United Kingdom

Background & objectives: As healthcare treatment evolves towards precision medicine, innovative methods to assess the value of integrating companion diagnostics(CDx) in clinical practice, adequate reimbursement levels are becoming essential. Cost-effectiveness analysis is an established tool used to inform the reimbursement of health technologies.
Methods: A decision-tree model was developed to estimate the incremental cost effectiveness of companion BRCA testing and olaparib use versus no testing and standard of care for patients with BRCA mutated high-risk HER2-negative early breast cancer from a United Kingdom NHS/PSS perspective.
Results: BRCA testing combined with treatment with adjuvant olaparib was associated with an ICER of £49,327 per QALY gained and an ICER of £86,349 per QALY gained for TNBC and HER2-/HR+ patients, respectively, compared to no testing and treatment with SoC. This difference in ICER is due to significantly improved outcomes for TNBC patients who were treated with targeted therapy. For both patient subgroups with early breast cancer, testing and olaparib improved patient outcomes and, despite its relatively high cost, the test and treat strategy was deemed to represent an acceptable use of resources.
Conclusion: The advancement of high-throughput sequencing technologies, coupled with the rise of targeted treatments in recent years, has facilitated a shift from conventional medical practices to individualised oncology therapeutic approaches. Our analysis presented the value in combining genetic sequencing and targeted therapy for breast cancer patients carrying BRCA mutations, and also provided the prototype of a testing model that can be utilised to promote precision medicine for better patient outcomes.

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E-PS-14-041
Natural and accidental deaths depicted on postmortem computed tomography: a case series
N. Solomon*, J. Elifritz, N. Adolphi, H. Sanchez, B. Gosangi, J. Kroll, B. Daly, D. Gascho, M. Thali, S. Thorn, M. Revzin, A. Sinusas
*Department of Radiology, Yale School of Medicine, USA

Background & objectives: Postmortem (PM) imaging has emerged as a useful tool in death investigations, providing more accurate data on the circumstances and conditions leading to death compared to clinical diagnosis alone, and improving many aspects of the process of PM evaluation.
Methods: This presentation will focus on PM computed tomography (CT) findings in cases from both hospital and forensic settings that were imaging as part of death investigation. Select PM magnetic resonance imaging (MRI) cases will also be included. Case history and other relevant information will be provided.
Results: This presentation will focus on natural and accidental causes of death, featuring a series of cases demonstrating imaging findings confirming or strongly indicative of the cause, including medical causes like pneumonia and cerebral infarct, traumatic causes like acute aortic injury, and accidental cases like drowning. The presentation will also discuss the various benefits of including PM CT and other PM imaging techniques in death investigation, including the conservation of time and resources, protection of morgue personnel, and preservation of data.

Conclusion: While PM imaging can serve a wide variety of purposes in both hospital and forensic settings, one of the most obvious is to help determine cause and manner of death, and many centre have adopted whole-body PM CT to triage decedents for either external examination or traditional autopsy. The popularity of this method is only anticipated to continue to grow, blurring the line separating the specialties of pathology and radiology.

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E-PS-14-042

Chromosome 12p amplification and p53 abnormalities appear to be rare events in spermatocytic tumours (ST) with conventional morphology

A. Strakova Peterikova*, D. Trpakova, P. Steiner, P. Martinek, M. Michal, K. Michalova
*Bioptical Laboratory, Ltd,Pilsen, Czech Republic

Background & objectives: Most ST are benign with conventional morphology, yet some exhibit anaplastic features/undergo sarcomatoid transformation, leading to aggressive behaviour. Recent studies have identified anaplastic STs with aggressive clinical course, along with one aggressive ST with conventional morphology.
Methods: Given the molecular factors contributing to aggressiveness were identified, this study included a cohort of mostly conventional ST with the aim to investigate the potential presence of hallmarks of aggressiveness. As molecular background potentially contributing to aggressive behaviour was unveiled (TP53 mutation/12p amplification-a hallmark of seminoma), we performed FISH for analysis of 12p abnormalities, and IHC for p53, OCT3/4, SSX.
Results: Eighteen cases of conventional STs and one case of anaplastic ST were identified. The median age of the patients was 59 yrs. The size ranged from 0.7 to 18 cm. Follow-up was available for 5 patients with conventional morphology, with median 82 months. All patients are alive and well. Immunohistochemically, 17/19 cases were positive with SSX, the remaining cases were focally positive and negative, respectively. Sixteen cases showed normal p53 expression, 3 cases showed aberrant p53 expression (focal overexpression in 2 cases, complete negativity in 1). All cases (19/19) were negative for OCT3/4. FISH analysis did not reveal gain 12p in any of the cases.
Conclusion: The occurrence of aggressive features, such as 12p amplification and p53 abnormalities, appears to be infrequent in STs with conventional histology. Our findings suggest that routine evaluation of ST for the presence of 12p and p53 alterations is not warranted in conventional STs; such assessments should be limited to tumours displaying histopathologic features associated with aggressive behaviour (e.g. anaplastic or sarcomatoid).

E-PS-14-043

Changes in biochemical parameters and expression of the Hif-1a gene in rat dermal fibroblast culture cells under hypoxic exposure

E. Ponomarenko, M. Diatroptova, V. Mkhitarov, N. Zolotova, N. Tikhonova*, K. Artemyeva, O. Makarova
*Petrovsky National Research Center of Surgery, Russia

Background & objectives: Cultivation of fibroblasts in vitro allows dynamic assessment of functional changes in cells during different periods of hypoxic exposure. The purpose was to evaluate functional changes in dermal fibroblasts in culture under hypoxic conditions using biochemical and molecular biological methods
Methods: Fibroblast culture was obtained from rat skin after grinding and exposure to collagenase. Changes in cells were assessed under normoxia (CO2 incubator conditions) and hypoxic exposure (95% N2, 5% CO2) for 1 and 3 hours. Level of Hif-1a mRNA expression in fibroblasts was determined by PCR. ATP content was determined in cells using high-performance liquid chromatography.
Results: With hypoxia for 1 hour, glucose in cells decreased from 0.21(0.14;0.41) to 0.07(0.01;0.15) mmol/l (p=0.14), LDH from 39(14;60) to 9(6;12) units/l(p=0.01), AsAT from 15.6(8.0;34.5) to 1.8(0;3.8) units/l(p=0.02). After 1 hour of hypoxia, ATP in cells also decreased from 7.7(6.7;8.2) to 4.7(4.4;4.8) μmol/l (p=0.02). After 3 hours of hypoxia, there is tendency to restore the indicators. After 3 hours of hypoxia, glucose increased to 0.56(0.06;0.66) mmol/l (p=0.08) and LDH to 17(9;30) units/l (p=0. 37), AsAT up to 3.8(1.2;19.2) units/l (p=0.62), ATP up to 7.7(6.0;8.3) μmol/l (p=0 ,39). Level of Hif-1a during 1 hour hypoxia did not change, after 3 hours hypoxia decreased to 0.009(0.008; 0.013), p=0.34 compared to control.
Conclusion: According to the results of the study, all metabolic reactions slow down within a period of up to 1 hour. During the period of hypoxic exposure from 1 to 3 hours, there is a partial restoration of biochemical parameters, which indicates the adaptation mechanisms of cells under hypoxic conditions during this period.

E-PS-14-044

Interaction of endogenous adipose tissue with injured uterus as an indicator of uterine wound healing

N. Tikhonova*, V. Aleksankina, A. Milovanov, T. Fokina, E. Kuznetsova, N. Nizyaeva, L. Mikhaleva
*Petrovsky National Research Center of Surgery, Russian Federation

Background & objectives: The role of endogenous adipose tissue in the restoration of the uterine wall after damage is not well researched, although known about the positive effect of cell fraction from adipose tissue on the repair of the damaged uterine wall.
Methods: Histological examination with Mallory staining and FABP4, CD68, CD206 and CD204 immunohistochemical staining of the uterine wound healing on the 7th (n=5), 30th (n=5) and 60th (n=6) days after full surgical incision of the rat uterine wall.
Results: On 7th day at injured site revealed the absence of serous sheath. In fatty tissue fusion with the uterine wall, there was a significant amount of corona-like structures that disappeared by 30th day. Healing area in half of animals remained covered with adipose tissue on 30th day. Between uterine wall and adipocytes there was a strip of connective tissue. There was no fat attached to the damage area at 60th day. By 30th day, the number of cells of CD68+, CD206+, CD163+ in attachment adipose region has decreased significantly. Difference between 30th and 60th days for these markers in fat tissue attached to damage area and outside is not detected
Conclusion: Experimental research suggests that by 60th day after surgery (which corresponds to 12th sexual cycle following a full-thickness surgical incision), the uterine wall should be devoid of adipocytes and fusion with fat tissue. Adipose clusters in the uterine scar indicate that cell interaction is disrupted.

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E-PS-14-045

Review of specimen labelling in a tertiary referral centre (TFC)

L. Timon*, R. O'Connor
*Department of Histopathology, St. James's Hospital, Dublin, Ireland

Background & objectives: Approximately 1000 cases are sent annually from an affiliated hospital to a TFC. A proposal to standardise labelling was implemented in January 2024. We aimed to conduct a retrospective review to investigate whether the proposed change has been implemented successfully.
Methods: The optimal format for case labelling was proposed as surname, first-name, DOB, MRN. Patient data was collected for cases referred between January and March in 2023 and 2024. This data was analysed by comparing patient details with the labelled referral form on the in-house laboratory system. For every label type reviewed, a number was assigned based on format identified.
Results: Data from 211 patients in 2023 and 194 in 2024 were collected. Overall, approximately 35 different label formats were identified between both years. In 2023, 23 of 35 formats were observed with 70.1% of cases received labelled as 'forename, surname' with multiple variations in additional information provided. Following standardisation attempt, 2024 data showed improvement with only 18.6% cases labelled as 'forename, surname'. However, 19 different formats were still evident showing a wide range in the order of information provided including name, date-of-birth, medical-registration number, phone number and address.
Conclusion: Improvements in patient labelling is evident following implementation of a more standardised process in 2024. However, formatting still remains a problem with 35 label types provided within the 6-month time frame. Therefore, issues with patient and specimen identification may still remain. A standardised process for printing labels would likely be of benefit in minimising errors in patient identification and preventing adverse events occurring. Increased awareness and efforts to improve standardisation are of importance in ultimately improving patient care and safety.

E-PS-14-046
Early activation of neutrophils in an early lupus model of systemic lupus
S. Carrasco, B. L. Liphaus, T. Vasconcelos Peixoto, T. Martins Lima, S. Catanozi, L. Gomes Rodrigues, A. Dos Santos Filho, W. Paganelli Rosolia Teodoro, A.P. Pereira Velosa*, D. Levy, F. Garcia Soriano, C. Goldenstein-Schainberg
*Division of Rheumatology, Faculdade de Medicina da Universidade de São Paulo, Brazil

Background & objectives: Neutrophils death, mainly NETosis can be a source of exposure of autoantigens for the development of Lupus. We analysed whether the administration of Pristane produces NETosis in quantity and early enough to be considered the primary event triggering Lupus.
Methods: Female wild-type Balb/c mice 8 to 10-week-old received an intraperitoneal injection of Pristane 0,5ml (n=6; Pristane mice) or saline (n=6; control). Blood (B), peritoneal lavage (PL), bone marrow (BM) and spleen (SP) were collected to evaluate neutrophil activation, low-density granulocytes (LDGs) and neutrophil extracellular traps (NETs) formation after 5 days of stimulus.
Results: Within 5 days, Pristane mice acutely presented a significant increase in the number of circulating activated neutrophils (Ly6G+CD11b+; $p<0.001$), (LDGs - CD15+CD14low, $p<0.001$) and NETs formation (Sytox+; $p<0.001$) by both neutrophils and LDGs compared to the group control and also in the blood in the 12 days group prior to the stimulus (T-12 days) ($p<0.001$). The same result was observed where the injury primarily occurred (PL), and in the sites of immune cell production (BM) and of immune cell response (SP).
Conclusion: We demonstrated that intraperitoneal infection of pristane induced important changes in neutrophils, especially a large amount of NETosis. This response of the innate system to Pristane, in the first 5 days after the injection, is what it may triggers the acquired immune alteration. Which leads to the production of autoantibodies typical of lupus disease.

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E-PS-15E-Poster Session Paediatric and Perinatal Pathology

E-PS-15-001
Placental involvement in multiple sulfatase deficiency
C. Antoniacomi*, G. Fiandrino, S. Cesari, A. Arossa, F. Sirchia, F. Inzani
*Department of Molecular Medicine, University of Pavia, Italy

Background & objectives: Metabolic storage disorders are inborn errors of metabolism characterized by the accumulation of substrates in different tissues, depending on the specific enzyme defect. The placenta is frequently involved and accumulation in syncytiotrophoblast and/or mesenchymal cells may constitute an early indicator.
Methods: This report focuses on the placental histology from a 22-week of gestation (wog) foetus first presenting at 16 wog with right-sided hydrothorax that spontaneously subsided, followed by worsening ascites, mild hepatosplenomegaly, without ultrasound signs of foetal anemia. Karyotype and array comparative genomic hybridization were negative. Based on the histological findings at foetal autopsy, next generation sequencing (NGS) was initiated.
Results: Placental examination revealed foamy deposits confined to the stromal cells of the chorionic villi, without affecting the syncytiotrophoblast. Similar accumulations were observed in the cytoplasm of hepatocytes. These morphological observations suggested an inborn error of metabolism. NGS identified compound heterozygous mutations in the SUMF1 gene, indicative of Multiple Sulfatase Deficiency (MSD), a rare autosomal recessive lysosomal/microsomal storage disease resulting in the accumulation of sulfated glycosaminoglycans, sphingolipids and steroid sulfates.
Conclusion: The stromal cell-limited accumulation pattern in the chorionic villi in a case of MSD contributes to our understanding of the variegated manifestations of lysosomal storage disorders and further highlights the value of histopathological examination of the placenta in cases of non-immune non-anemic hydrops fetalis.

E-PS-15-002
Exploring the diversity of placental heterotypic tissue: insights from two case reports
J. Azevedo*, A. Varelas, J. Pacheco, A. Costa Braga
*Department of Pathology, Portuguese Oncology Institute of Porto (IPO-Porto), Portugal

Background & objectives: Placental heterotopic tissue is a rare and incidental finding with unknown development mechanism and impact. The placental heterotopias described in the literature include adrenocortical, hepatic and adipose tissue. No case of placental peripheral nervous heterotopia has been described to date.
Methods: We report two cases of heterotopic tissues found incidentally in placental parenchyma. Case 1: 29-year-old primigravida with 37 weeks of gestation was referred for caesarian section of a dichorionic diamniotic pregnancy, with no complications. Case 2: 39-year-old pregnant woman with a preterm delivery at 24 weeks of gestation, whose infant died 28 days after birth from sepsis.
Results: In case 1 a well-circumscribed intravillositary fascicular structure morphologically compatible with a peripheral nerve was identified within a stem villi. Intermixed Schwann cells displayed large, round, hyperchromatic nuclei with strong and diffuse expression for pS100. The diagnosis of placental peripheral nerve heterotopia was proposed. In case 2, a well-circumscribed nodular lesion located within a chorionic stem villi composed of cohesive and monotonous cells organized

in trabeculae was found. These cells exhibited abundant eosinophilic cytoplasm with apical reinforcement. Hematopoietic foci were present. Immunohistochemical study showed: granular cytoplasmic staining for HepPar-1; nuclear and cytoplasmic weak expression for Arginase-1; strong canalicular expression for Glypican-3. The diagnosis of placental heterotopic liver tissue was performed.
Conclusion: Placental heterotypic tissue presents diagnostic challenges. The rarity of this finding could be explained by the sparse sampling in daily practise. To the best of our knowledge, we present the first case of placental peripheral nerve heterotopia. The exact mechanism and impact associated with each heterotopia remains unexplored, therefore multicentre studies are needed to better characterize and understand this entity.

E-PS-15-003
Case report: ileo-ileal intussusception caused by ileal angiomyolipoma in 13-year-old female
G. Bal*, E. Kul, C. Tanik, F. Kabukcuoglu
*University of Health Sciences Türkiye, Sisli Hamidiye Etfal Training and Research Hospital, Turkey

Background & objectives: Angiomyolipoma (AML) is a benign mesenchymal tumour, primarily found in the kidney, characterized by abnormal blood vessels, smooth muscle, and adipose tissue. Extrarenal AMLs are rare but have been reported in various locations the colon, spermatic cord, duodenum and ileum.
Methods: Formalin-fixed biopsy samples were embedded in paraffin, and the sections were stained with hematoxylin and eosin, along with various immunohistochemical (IHC) stains. Additionally, a literature search was conducted to compare findings with similar cases reported in histopathological studies.
Results: A 13-year-old female patient presented with acute abdominal pain and signs of intestinal obstruction, leading to the surgical removal of an ileal segment. The resected ileal segment contained a 5x5x3 cm bilobed, polypoid mass with a uniformly fatty appearance on the cut surface. Histological analysis revealed mature adipose tissue, thick-walled blood vessels, and spindle-shaped smooth muscle cells without nuclear atypia or active mitosis. Immunohistochemical staining was positive for vimentin, SMA, desmin, CD31, CD34, and D2-40, but negative for HMB-45, Melan-A, and CD117, confirming the diagnosis of an ileal angiomyolipoma.
Conclusion: Angiomyolipoma of the ileum is an exceedingly rare entity, particularly challenging to diagnose preoperatively due to its nonspecific symptoms and the rarity of extrarenal AMLs. This case underscores the importance of considering AML in the differential diagnosis of ileal intussusception, especially in patients presenting with nonspecific abdominal symptoms. The findings from this case contribute to the limited literature on ileal AML and emphasize the need for awareness among clinicians and pathologists to improve diagnostic accuracy and patient outcomes.

E-PS-15-004
Correlation of the umbilical cord coiling pattern and foetal outcome: a single-centre observational analitical study
D.P. Burlacu*, A. Burlacu, E. Ladanyi, B. Szabo, P.A. Calburean, T. Mezei
*Scju Mures, Romania

Background & objectives: The umbilical cord (UC) anatomically embodies the feto-placental bridge with major role in foetal development due to the vascular structures embedded in Wharthon's jelly. This study aimed to determine any associations between UC coiling pattern and medical disorders of pregnancy.
Methods: An observational analitical study was conducted at the Clinical Emergency Hospital of Targu-Mures, Romania between January 2023-December 2023. Consecutive singleton placentas with attached UC sent to Pathology Department for various feto-maternal conditions were considered for appropriate measurements. The coiling number and direction (sinistral or dextral) of the umbilical cord were assessed per first 10 centimetres measured at the placental end.
Results: Of 187 cases this study included, 57.21% (97) had sinistral and 42.79% (90) had dextral UC coiling. The minimum and maximum maternal age group was 12 to 44 years old. Sinistral UC coiling was associated with an increased risk of spontaneous abortion and stillbirth (25.77%, p=0.028). Sinistral coiling was also associated with extreme prematurity (p=0.013), smaller birth weight (p=0.040) and lower placental weight (p=0.029). A lower 1 minute (p=0.045) and 5 minutes Apgar Score (p=0.017) were associated with sinistral coiling. No relevant risk of premature rupture of membranes (PROM) was observed (p=0.324). No significant association of sinistral coiling and metabolic or blood-related maternal diseases was observed (p=0.385 and p=0.725).
Conclusion: Recently reported data outlines that approximately 25% of all pregnancies have a dextral UC coiling direction. Compared to literature, our data revealed an almost double percentage of pregnancies with a dextral coiling. In our selected group, certain pathologies were more associated with sinistral coiling, as compared to dextral. These included an increased risk of stillbirth or prematurity and lower birth weight. Larger studies are required to determine the clinical applicability of these data in case of detecting a pathologic pregnancy.

E-PS-15-005
Paediatric small round blue cell tumours: immunohistochemical approach on small biopsy
G. Cacciola*, G.G.M. Attanasio, S. Poidomani, L. Salvatorelli, G. Angelico, G. Magro
*Department of Medical and Surgical Sciences and Advanced Technologies, G.F. Ingrassia, University of Catania, Catania, Italy

Background & objectives: Small round blue cell tumours (SRBCT) are rare malignant showing morphological and immunohistochemical overlapping features. The aim of the present study is to investigate the utility of WT1 and cyclin D1 immunohistochemistry in the diagnosis of SRBCTs on small biopsies.
Methods: Bioptic tumour samples were retrospectively collected and included in the study: i) 44 neuroblastomas (NB); ii) 34 rhabdomyosarcomas (RMS) (16 embryonal RMS, 14 alveolar RMS, 3 spindle cell/sclerosing RMS); iii) 11 lymphoblastic lymphomas (LLs); iv) 14 Ewing Sarcomas (EWS;) 3 Wilms' tumour. Immunohistochemical analyses were performed with the following antibodies: Cyclin D1, WT1, Desmin, SMA, myogenin, CD99, TdT, NB86, CD56.
Results: All RMSs expressed at least two myogenic markers, no staining for CD99, NB84 and TdT was detected. All EWSs expressed CD99, none of the cases was positive for myogenic markers, NB84, CD56 and TdT. All NBs exhibited immunostaining for NB84 and CD56, no staining was observed for the myogenic markers, CD99 and TdT. All LLs were positive for TdT and other specific lineage markers. All Wilms' tumours showed cytoplasm/nuclear expression of WT1. All RMSs showed diffuse cytoplasmic staining for WT1, while the other SRBCTs were negative. All EWSs and NBs displayed a nuclear expression of cyclin D1 while no immunoreactivity for cyclin D1 was observed in the other SRBCTs.
Conclusion: Cytoplasmic expression of WT1 has diagnostic utility for the diagnosis of RMS on small biopsies. Cyclin D1 can be a useful marker to be used along with CD99 and NB84 to confirm the diagnosis of EWS or NB on small biopsies, respectively. Accordingly, WT1 and cyclin D1 could be included in the immunohistochemical panel of paediatric SRBCTs.

E-PS-15-006

Epidemiological characteristics and anatomopathological aspects of paediatric autopsies in a specific region

J. Carneiro Melo*, Á. Macêdo Freire, A.C. Carvalho Ferraz, V. Régia Oliveira Almeida, A.T. Galdino Saraiva, J. Oliveira Fernandes, S. Samuel Feitosa Machado, C. Gleidiston Lima da Silva
*University of Fortaleza, Brazil

Background & objectives: Autopsy is an important tool for diagnostic elucidation, epidemiology and medical education. The objective is to describe the clinicopathological characteristics of 15 paediatric autopsy cases.
Methods: Retrospective study of paediatric autopsies performed in 2023 at the Death Verification Service of Southern Ceará, Northeast Brazil. Data from clinical history, autopsy findings and post-mortem diagnosis were analysed. Fifteen paediatric autopsy cases were included in this study, 6 patients were female and 9 were male.
Results: Twelve cases were classified as infants (0-6 months: 8 cases, 7-24 months: 4 cases), and 3 were children (aged 4, 7, and 9 years). Sepsis was identified as the primary cause of death in 10 cases, with 7 due to community-acquired pneumonia (CAP), 1 bacterial meningoencephalitis, 1 gastroenteritis, and arbovirus infection. Acute respiratory failure was the terminal cause in 3 cases, resulting from CAP (2) and meconium aspiration syndrome (1). Hypovolemic shock was identified as the terminal cause in one case due to splenic sequestration crisis and another infectious gastroenteritis.
Conclusion: Over 85% of the described deaths are due to complications of infection, primarily from the respiratory tract. The majority involve preventable causes of death when diagnosed and treated promptly. Autopsy studies expose common causes of death in the paediatric population and highlight relevant issues related to medical care and socioeconomic conditions that go along the health-disease process of Brazilian children.

E-PS-15-007

Histopathological characterization of Eosinophilic oesophagitis in children at a private laboratory in Northeast Brazil: 2012-2023

J. Carneiro Melo*, D. Nunes Oliveira, H. Baltasar Ribeiro Nogueira, H. Neves Feitosa Filho, A. de Carvalho Assunção, E. Correia Eulálio, J. Pedro Veras Torres, E. Sampaio de Lima, G. Ferreira Morgantteti, G. Alencar Medeiros, G. Azevedo Silveira
*University of Fortaleza, Brazil

Background & objectives: Eosinophilic oesophagitis (EoE) is a chronic immune-mediated inflammatory disease of the oesophagus. Brazil reported 2.48 cases per 100,000 children in 2014. Responses to treatment vary, highlighting the need for epidemiological research. Study examines histopathological aspects of paediatric EoE.
Methods: A retrospective cross-sectional study assessed histopathological records of children with EoE, as per Convention on the Rights of the Child (CRC), aged under 18, in a private lab in Northeast (NE) Brazil from 2012-2023. Criteria: ≥15 eosinophils/HPF40, eosinophils in epithelium, basal hyperplasia, microabscesses, degranulation, sloughing, lamina propria fibrosis. Data analysed using SPSS, chi-square test applied for correlations.
Results: Total of 212 compatible reports with paediatric EoE. Mean age 9.4 years, prevalence of 67.45% (143) male patients, an odds ratio (OR) of 2.050; 95% CI: 1.529 - 2.749; p <0.001. All showed eosinophil infiltration and ≥ 15 eosinophils HPF40. Eosinophil degranulation 59.43% (126) OR: 11.914; 95% CI: 8.914 - 15.926; p <0.001; intercellular edema 82.07% (174) OR: 4.491; 95% CI: 3.146 - 6.412; p <0.001; basal hyperplasia 48.11% (102) OR: 1.609; 95% CI: 1.215 - 2.112; p <0.001; eosinophilic microabscesses 35.84% (76) OR: 12.238; 95% CI: 8.921 - 16.788.
Conclusion: The study reveals histopathological findings of eosinophilic oesophagitis in Northeast Brazil. Highlights high prevalence among male children and typical histopathological findings. The importance of doctors providing complete clinical data when requesting biopsy is emphasized, as in addition to defining the diagnosis, endoscopy with biopsy is also important for the objective assessment of therapeutic response.

E-PS-15-008

Intracardiac yolk sac tumour in a 2-year-old child: histopathological and immunohistochemical insights - a rare case report

P.L. Chiriac*, A. Vasile, R. Tanasă
*Colentina Clinical Hospital, Romania

Background & objectives: Intracardiac yolk sac tumours (YSTs), primarily cardiac neoplasms, present unique challenges in paediatric oncology. Unlike gonadal YSTs, their intracardiac localization is exceptionally rare, with scant medical documentation. This case report details a 2-year-old's YST, likely the sixth reported case globally.
Methods: Initially, a CT scan was performed, primarily suggesting the diagnosis of myxoma. However, subsequent histopathological examination became necessary due to inconclusive findings and the absence of evidence of other tumours on CT or echocardiography. A comprehensive histopathological examination, including hematoxylin and eosin staining and immunohistochemical analyses were performed.
Results: Histopathological assessment revealed a malignant proliferation of round, oval, and elongated cells with marked cyto-nuclear atypia and increased mitotic activity. Zonal clarifications and vacuolization were notable features within the tumour tissue. Immunohistochemical staining demonstrated intense and diffuse positivity for AE1/AE3 and SALL4, alongside variable expression of Glipican 3. Notably, OCT3/4 and ERG showed negativity in tumour cells. These findings supported the diagnosis of a yolk sac intracardiac tumour, likely representing the sixth reported case globally.
Conclusion: This case emphasizes the exceptional rarity of yolk sac intracardiac tumours in paediatric patients, likely representing the sixth documented case globally. It underscores the necessity of contemplating uncommon diagnoses, such as yolk sac tumours, despite initial imaging favouring more prevalent entities like myxoma, particularly in the absence of evidence of other neoplasms on CT or echocardiography. Thorough histopathological and immunohistochemical analyses are indispensable for accurate diagnosis and individualized therapeutic interventions in such infrequent cardiac neoplasms.

E-PS-15-009

Pure high-grade foetal adenocarcinoma of the lung of a 17-years-old girl: case report

P.L. Chiriac*, R. Tanasă, F. Vasilescu, A. Enculescu, A. Vasile
*Colentina Clinical Hospital, Romania

Background & objectives: This case report describes a rare instance of pure high-grade foetal adenocarcinoma of the lung (HG-FLAC) in a 17-year-old girl, typically seen in elderly male heavy smokers, staged at pT3N0.
Methods: A 17-years-old female presented with acute respiratory failure and hemoptysis in June 2022. After a chest X-ray was revealed an abnormal shadow in the right basal lung field. A chest computed tomography (CT) scan showed a 4,5/7,4/8 cm pulmonary lesion in the right cardio-phrenic angle, with cranial expansion in the mediastinum, initially suspicious of neuroblastoma or inflammatory myofibroblastic tumour.
Results: A needle biopsy of the mass was performed; it reveals non small cell carcinoma, with histopathological aspects of adenocarcinoma. A right lower lobectomy and mediastinal lymph node dissection were performed.

Grossly, the specimen showed a well-established boundary as a greyish lesion with bleeding areas. The histopathological examination showed a solid proliferation of columnar atypical cells with clear/eosinophilic cytoplasm and complex glandular structures, morphological resemblance to foetal lung, and significant tumour necrosis. Conventional lung adenocarcinoma, another histological component or morulae were not found. The imunohistochemical analysis showed positivity for CK7, beta-catenin positivity in cell membrane. TTF-1, chromogranin, AFP, p63, vimentin, glypican, SALL4 were negative. The final histopathological diagnosis was HG-FLAC pT3N0.
Conclusion: We report a very rare case of pure H-FLAC of a young female. This histology has been considered to predict an extremely poor prognosis.

E-PS-15-010
Congenital infantile fibrosarcoma with ETV6::NTRK3 fusion of the oropharynx: a case report
Y. Chun*
*Korea University Guro Hospital, Republic of Korea

Background & objectives: Infantile fibrosarcoma is a malignant fibroblastic tumour that occurs predominantly in infancy, characterized by the ETV6::NTRK3 fusion. It typically presents as a highly vascular mass, often resembling vascular tumours, and shows local aggressiveness with rare metastasis.
Methods: We present a case of congenital infantile fibrosarcoma with ETV6::NTRK3 fusion of the oropharynx. A premature male, born at 30 weeks and 5 days due to placental abruption, experienced massive bleeding from a protruding oral mass and died 3 hours later. Prenatal ultrasound and MRI revealed a 7x5 cm solid oropharyngeal mass, suspected as an epignathus.
Results: Biopsy showed a hypervascular, solid tumour with features resembling a vascular tumour. Microscopic examination revealed a primitive ovoid/round cell or spindle cell tumour with haemangiopericytoma-like vessels and aggregates of undifferentiated small round cells. Immunohistochemical staining was positive for vimentin, CD99, FLI-1, and glypican. Differential diagnoses included vascular tumours such as Kaposiform hemangioendothelioma and epignathus. However, next generation sequencing confirmed ETV6::NTRK3 fusion, establishing the diagnosis of infantile fibrosarcoma.
Conclusion: This case underscores the diagnostic challenge of congenital infantile fibrosarcoma, often misdiagnosed as other entities such as vascular tumours due to hypervascularity or epignathus due to location. Molecular characterization, particularly identifying ETV6::NTRK3 fusion, is essential for accurate diagnosis. The advent of targeted tyrosine kinase inhibitor therapies may change the management of infantile fibrosarcoma, emphasizing the necessity for precise diagnosis in this rare paediatric malignancy.

E-PS-15-011
Difficult diagnosis in an aggressive non-Hodgkin lymphoma with atypical evolution
T. Ciolan*, A. Loghin-Ostafi, C.F. Șerban, D. Mihăilă, E. Cojocaru, C. Acatrinei, D. Zamosteanu
*"Grigore T. Popa" University of Medicine and Pharmacy, Romania

Background & objectives: Sporadic Burkitt lymphoma (BL) represents a highly aggressive non-Hodgkin B cell lymphoma in children, commonly described in head, neck and abdominal region. We present a challenging BL case with unusual site and discrepancies between histological and imaging response to treatment.
Methods: A 16-year-old female patient previously diagnosed with dwarfism, congenital heart defects and NYHA II heart failure was admitted to the Intensive Care Unit in critical status due to cardiac tamponade. After pericardiocentesis, CT angiography revealed an expansive mass in the anterior mediastinum, requiring a biopsy for diagnosis. A small tissue fragment was harvested and processed for histopathological and immunohistochemistry exams.
Results: Microscopic exam showed a tumour proliferation of medium, monomorphic, hyperchromic cells with nuclear granular chromatin and inconspicuous nucleoli, tumour necrosis, positive for CD20, PAX5, CD10, BCL2 and negative for CD3, TdT, CD34, CD99, CD23. The extremely small biopsy did not allow broader immunohistochemistry and molecular panels. Based on histology, immunohistochemistry and clinical characteristics, presumptive diagnosis was BL. After eight months of targeted treatment, the patient's clinicobiological profile indicated remission, despite the absence of imaging regression signs. Thus, another biopsy was performed, indicating extensive tumour necrosis with multiple calcifications; one specimen showed peripherally broad collagen fascicles with adipocytes, strands of foamy macrophages and reactive lymphoid infiltrate; no tumour cells were identified.
Conclusion: This case report is valuable considering the inconsistencies between the favourable histological response after treatment and the unchanged imaging tumour size, explained by the complete tumour cell destruction, without necrotic tissue resorption. We also highlight the uncommon site of development – in anterior mediastinum, female gender (usually seen in men) and cardiac tamponade that led to the tumour detection. Nonetheless, we underline the difficulty of histopathological diagnosis, given the limited biopsy material in a patient with cardiac comorbidities and dwarfism.

E-PS-15-012
High grade round cell sarcomas with BCOR alterations - case report
L. Ćuković*, L. Simić, J. Stefanović, G. Nikolic
*Serbia

Background & objectives: Round cell sarcomas with BCOR alterations represent a unique subgroup of soft tissue sarcomas which shares morphology with the Ewing sarcoma family as well as other malignant round blue cell tumours, thus making them difficult to diagnose.
Methods: Here we present nine year old boy presented with the one-sided axilar soft tissue mass. Surgery was performed and tumour was 100 mm in maximal diameter. On gross section, tumour was well circumscribed, gray-cream colored, soft, homogeneous and partially cystic mass with necrotic foci and hemorrhage.
Results: On histology, tumour was composed of connective-vascular and muscular tissue diffusely infiltrated by small cells, ranging from round to spindle-shaped, within a collagenized/hyalinized stroma. Cystic formations were present. There foci of necrosis and hemorrhage were seen. Surgical margins were without tumour. Immunohistochemical findings revealed positivity for vimentin diffusely, CD99 diffusely, SATB2 diffusely, ERG focally, TLE diffusely, INSM1 diffusely, EMA focally, Bcl-2 diffusely, and negatively for LCA, CD3, CD31, CD34, CKAE1, desmin, NKX2.2, and WT1. Ki-67 is positive in 60% of tumour cells. Molecular analysis for SS18 gene showed no rearrangement, while the rearrangement of the BCOR gene was detected. The diagnosis of the high grade BCOR rearranged sarcoma was made.
Conclusion: Round cell sarcomas with BCOR alterations constitute a distinct, genetically defined category of soft tissue sarcomas with specific clinical and histopathological features. Recognition of these features and confirmation of BCOR genetic alterations are essential for accurate diagnosis and tailored treatment planning. Ongoing research into the molecular pathways influenced by BCOR alterations will be crucial for developing more effective targeted therapies, potentially improving outcomes for affected patients.

E-PS-15-013
Congenital oesophageal stenosis - a report of two cases
M. Đuknić*, J. Jevtić, M. Jovanović, S. Glumac, S. Sinđić Antunović, M. Lukač, D. Vujović, N. Ristić, R. Jankovic
*University of Belgrade, Faculty of Medicine, Institute of Pathology, Serbia

Background & objectives: The incidence of congenital oesophageal stenosis (CES) in general population is approximately 1 in 25000 to 50000 live births. CES can be presented as isolated malformation or associated with malformations of other parts of gastrointestinal tract or other systems.
Methods: There are three main types of CES: fibromuscular stenosis (FMS), ectopic tracheobronchial remnants in the oesophageal wall (TBR) and a membranous webbing or oesophageal membrane (EM). We report the clinical and histopathological features of two cases with different types of CES.
Results: Patients were 1-year-old female with TBR and 8-year-old male with FMS. The main symptoms in female infant were dysphagia, vomiting and malnutrition, while 8-year-old boy had symptoms related to severe gastro-oesophageal reflux disease. Both patients underwent partial oesophagectomy. Grossly, thickening of the oesophageal wall and narrowing of the lumen with slight proximal dilatation were seen. Microscopically in case with TBR, there were seromucous glands in tunica submucosa, muscularis and adventitia, as well as tubular structures with ciliated pseudostratified columnar epithelium. In tunica muscularis, focally, parts of mature hyaline cartilage were found. In FMS case, abundant collagen fibers and disorganized smooth muscle cells were found in submucosa.
Conclusion: When diagnosing CES, it is important to be aware of its associations with other malformations. Symptoms related with CES, especially FMS, could be very mild within first years of life with delayed diagnosis. There is no enough evidence of relationship between treatment options (surgery or dilatation) and type of CES, mainly because the histopathological analysis is not always available.

E-PS-15-014
A giant congenital cervical teratoma: a case report of a non-well-known entity
G. Escuer-Albero*, M. De Uribe Viloria, I. Sánchez Ramírez, R.M. Regojo Zapata, J.J. Pozo Kreilinger
*La Paz University Hospital, Spain

Background & objectives: Cervical teratoma is a rare congenital extragonadal germ cell tumour. The degree of maturity of its components and its relationship with malignant behaviour are unclear. Our case presented is an antenatal mass with nodal involvement.
Methods: In this case, extensive sampling was carried out to ensure the correct representativeness of the specimens. Immunohistochemical techniques were used to define the different components. The patient's electronic medical record and cases described in the literature were reviewed for the case report.
Results: We received a polilobulated mass measuring 7.5 x 6 x 5 cm with a spongy consistency and some cystic components. Histologically it was composed of a mixture of differentiated elements, an important component of immature neuroglia and a minimal foci of yolk sac tumour (YST) of 1x1 mm. That foci of YST grew predominantly in a reticular/microcystic pattern and stained with alpha-fetoprotein (AFP), glypican 3 and CK AE1/AE3 immunohistochemical techniques. Based on these findings, the patient was diagnosed with grade 3 immature SCT (both Norris and Gonzalez-Crussi grading systems). The two lymph nodes were completely occupied by a predominant mature neuroglial component.
Conclusion: Teratomas contain tissue from all three germ cell layers with a mixture of immature tissue. The degree of immature elements does not have a well-established grading system - although there are two proposals - and has not been related to prognosis: complete resection is considered curative. However, in a few cases in the literature nodal involvement of both mature, as in our case, and immature components has been identified, independent of the presence of foci of YST.

E-PS-15-015
A case report of giant oesophagogastric tumour in a paediatric patient, emphasizing the importance of clinicopathological and genetic testing for accurate diagnosis
S. Gamba Torrez*, S. Rubio Mediavilla, T. Zudaire Fuertes, A. Hogeboom Gimeno, H. Hernández Vargas, R.C. Narvaiza Martinez, J.J. Sola Gallego
*San Pedro Hospital, Spain

Background & objectives: X-linked Alport's syndrome–diffuse leiomyomatosis (AS–DL) is a very rare variant of Alport's syndrome characterized by hematuric nephropathy, ocular lesions, sensorineural deafness, and leiomyomas of the gastrointestinal, respiratory, and female reproductive tracts associated with mutations in the COL4A5 gene.
Methods: A 15-year-old female with recurrent gross hematuria since the age of 7, proteinuria (<500mg/24hrs), and experiencing chest pain, dyspnea, and dysphagia. Renal biopsy and genetic testing in another hospital (2017) were inconclusive. UroCT ruled out urinary and renal malformations. Thoracic CT revealed a mass originating from the oesophageal wall and cardia extending 20 cm to 47 cm from the incisors.
Results: Ecoendoscopy-guided biopsy revealed a smooth muscle tumour suggestive of leiomyoma. Total esophagectomy was performed. Macroscopically, there was a circumferential and continuous thickening of the oesophageal and proximal stomach wall, up to 3 cm thick at the oesophagogastric junction. Histologically, the muscular layer displayed a diffuse or multiple expansile and confluent nodular pattern of spindle cells arranged in interlacing and disorganized fascicles without atypia or mitosis. Immunohistochemistry showed positivity for smooth muscle actin and desmin, and negativity for DOG-1, CD-117, and CD-34. Germinal molecular study confirmed a heterozygous deletion in Xq22.3, involving exon 1 of COL4A5 and exons 1 and 2 of COL4A6, consistent with X-linked Alport's syndrome–diffuse leiomyomatosis (AS–DL).
Conclusion: Oesophageal leiomyomatosis is an exceedingly rare condition. May occur sporadically or be associated with congenital factors, such as genital and tracheobronchial smooth muscle proliferation. However, 60-70% of cases are linked to Alport's syndrome (AS). It is important to consider AS diagnosis in patients exhibiting similar clinical presentations. In this specific instance, a repeated directed genetic study played a pivotal role in both diagnosis and treatment, underscoring the significance of employing a multidisciplinary approach to ensure precise diagnosis and effective treatment.

E-PS-15-016
Chronic chorioamnionitis with plasma cell predominance resulting in premature membrane rupture and foetal demise in 2nd trimester of gestation: first case reported
C. Gouta*, D. Krasias, N. Athanasiadis, N. Tsiaras, E. Viktoratou, I. Tsakiridis, S. Angelidou
*Department of Histopathology, Hippokration General Hospital of Thesaloniki, Greece

Background & objectives: Chronic chorioamnionitis is characterised by the infiltration of foetal membranes by mononuclear cells, predominantly CD3-positive T cells. Plasma cells are rarely found, and their presence is mostly related to viral infection.
Methods: A 34-year-old pregnant woman, G2P1L1, with no relevant medical history, was referred to our hospital due to premature rupture of membranes and anhydramnios detected during level 2 ultrasound at 21 weeks of gestation. During the 4th day after admission, absence of foetal cardiac activity was observed, therefore, labour induction was performed resulting in the delivery of a stillborn female foetus.

Results: Microscopic examination of the placenta revealed dense infiltration of foetal membranes and chorionic plate by plasma cells and less commonly by lymphocytes. Focal necrosis and a few subchorionic neutrophils were occasionally observed. There were no signs of chronic lymphoplasmacytic deciduitis, chronic intervillositis or chronic villitis/villitis of unknown etiology. Consequently, the diagnosis of chronic chorioamnionitis with plasma cell predominance was established.
Conclusion: The presence of plasma cells has been commonly reported as a hallmark of many immunological and infectious placental pathological occurrences. Specifically, chronic infectious villitis with plasma cells has been strongly related to CMV, HSV and EBV infection. However, there is scarce information about the role of plasma cells in chronic chorioamnionitis with no case of plasma cell predominance having been reported before. Our case report contributes to the literature presenting a first-seen pathological expression of a quite infrequent entity.

E-PS-15-017
Heterotopic foetal liver tissue in the placental parenchyma: a case report of a rare entity
C. Gouta*, D. Krasias, N. Savvidou, C. Yphanti, P. Ipsilantis, A. Kougioumtzidou, S. Angelidou
*Department of Histopathology, Hippokration General Hospital of Thesaloniki, Greece

Background & objectives: Heterotopic hepatic tissue has been infrequently described in extraembryonal structures, with only 15 cases reported so far. Furthermore, the occurrence of ectopic adrenocortical tissue has been recently questioned with the suggestion that ectopic liver has been continuously misinterpreted as such.
Methods: We report the case of a 29-year-old pregnant woman, G2P1L1, with no previous medical history who presented at the emergency department due to premature labour onset at 34 weeks of a twin gestation. Cesarian section was performed, and two viable female infants were delivered weighing 2190 gr (foetus A) and 2030 gr (foetus B) respectively.
Results: Gross examination showed a fused, discoid-shaped placenta, on the chorionic plate of whom a thick dichorionic diamniotic diaphragm and two eccentric umbilical cords on each side were observed. Microscopic examination revealed findings of mild maternal inflammatory response stage 1, namely acute chorionitis grade 1, limited to the side of the disc that corresponded to foetus A. On the opposite side, an incidental small (dmax 0,96 mm) focus of ectopic liver tissue was discerned into the placenta parenchyma. The lesion was well-circumscribed, composed of polygonal cells with clear cytoplasm and a rich vascular network and was surrounded by a fibrous capsule. Immunohistochemical examination for SF1, glypican 3 and HepPar-1 was performed.
Conclusion: Liver tissue choristomata have been occasionally reported in abdominal locations but rarely in the umbilical cord or the placenta parenchyma. Until now, only 15 cases of intraplacental ectopic liver have been described, most of which emerged as incidental findings in premature placentas. Differential diagnosis includes chorangioma, monodermal teratoma, trophoblastic disease and ectopic adrenocortical tissue, the existence of the latter being strongly questioned by a recent study. Our case report contributes to the literature discussing the controversies around this rare entity.

E-PS-15-018
Widespread axonal dystrophy precedes atrophy and white matter spongiform change in adenylosuccinate lyase deficiency
O. Greenberg*, Y. Fisher, K. Chong, S. Shinar, P. Krishnan, P. Shannon
*Mount Sinai Hospital - Pathology Department, Toronto, Canada

Background & objectives: Adenylosuccinate lyase deficiency (ADSL) is a clinically well characterized autosomal recessive disorder of purine metabolism with prominent central nervous system (CNS) effects. Its foetal pathology is not described. We characterize the early neuropathology of severe ADSL deficiency.
Methods: Two affected sibling foetal autopsies are described. Antenatal ultrasound and MRI demonstrated microcephaly with delayed sulcation, periventricular cysts and enlarged extra-axial spaces: the pregnancies were interrupted at 29 and 26 weeks respectively followed by systematic post mortem and whole exome sequencing performed on parents and both sibs.
Results: The brains of both fetuses were similar, with microcephaly and delayed gross maturation. There was hippocampal and dentatoolivary dysplasia, as well as mild loss of bulk in the long tracts. Histology demonstrated numerous and widely distributed dystrophic axons at all levels of CNS organization, but particularly in the grey matter of the spinal cord, brainstem, thalamus, basal ganglia and the future molecular layer of the cerebral cortex. Small defects in the Purkinje cell layer were noted. Both sibs were compound heterozygotes for known pathogenic variants of the ADSL gene (paternal c.1277 G>A and maternal c.340 T>C).
Conclusion: Severe ADSL deficiency presents with foetal hypokinesia, and rapidly fatal neonatal encephalopathy. The available imaging and pathological literature demonstrates widespread white matter rarefaction and neuronal loss. This is the first report of the foetal pathology that we are aware of. Axonal pathology precedes white matter spongiosis and early neuronal defects are relatively subtle.

E-PS-15-019
Retrospective clinicopathological study of paediatric renal malignant tumours diagnosed in a tertiary hospital over the past 5 years
M. Guerrero Gómez*, S. Hakim Alonso, I. Marquina Ibáñez, J. Alfaro Torres, B. Roche Latasa, L. Ollero Domenche, J. Medrano Ruiz, J.L. Delgado Fernández, J. Martínez Castillón, L. Leon, N. Marínez Arnau
*Hospital Universitario Miguel Servet, Spain

Background & objectives: Paediatric renal malignant tumours are rare entities. Studying their different types, histopathological characteristics and their typical clinical presentations could be interesting for the pathologist's daily practice in order to diagnose them accurately.
Methods: A retrospective review was done using Dedalus and Hospital databases, searching for all paediatric renal malignant neoplasms, with their corresponding coding, including patients diagnosed over the past 5 years at our hospital with ages ranging from 0 to 14. With the intent of typifying these entities, histopathological, epidemiological and clinical patients' data were collected.
Results: Fifteen cases of paediatric renal malignant neoplasms were found: 2 rhabdoid tumours (13,3%), 3 clear cell sarcomas (20%) and 10 Wilms tumours (66,7%), affecting 8 males and 7 females, ranging from 5 months to 9 years old at diagnosis. All of them were unifocal except one Wilms tumour. Four neoplasms were metastatic at diagnosis. They measured between 2 and 15 cm. Margins were positive in both cases of rhabdoid tumour as well as in 2 Wilms tumours. Immunohistochemistry developed as expected in each presumptive diagnosis. All of them were treated according to the UMBRELLA PROTOCOL SIOP-RTSG 2016. All patients are still alive, except those with rhabdoid tumour.
Conclusion: Renal paediatric malignant tumours are a rare type of cancer that can show a variety of histologic types. Despite the limited number of cases, our series show clinical, pathological and epidemiological characteristics similar to those described in the literature: Wilms tumours were the most frequent subtype in our series and account for 66,7%. Clear cell sarcomas and rhabdoid tumours were exceedingly rare neoplasms (3 and 2 cases respectively in our series). Rhabdoid tumours were the more aggressive neoplasms.

E-PS-15-020

The aiagnostic value of calretinin immunohistochemistry in rectal biopsy specimens with incomplete structure in the diagnosis of Hirschsprung's disease: an institutional experience

E. Horvath*, E. Lockli, Z. Derzsi
*George Emil Palade University of Medicine, Pharmacy, Science and Technology of Targu Mures, Department of Pathology, Romania

Background & objectives: The diagnosis of Hirschsprung's disease is based on histopathological evaluation of hematoxylin and eosin-stained sections. The aim of this study is to evaluate the additional diagnostic value of calretinin immunohistochemistry in rectal biopsy specimens with incomplete submucosa.
Methods: We analysed 48 cases of Hirschsprung's disease diagnosed in our pathology department between 2016 and 2023. Descriptive statistics of diagnostic variables in the group of biopsy specimens (n=32) and bowel resection specimens (n=16) were performed. The pattern of calretinin expression in biopsies and bowel resection specimens was analysed and compared between specimens with complete and incomplete submucosa.
Results: The age of the patients ranged from 2 days to 13 years. Thirteen of the cases had a suboptimal amount of submucosa and in ten (10/13) of these cases dysplastic ganglion cells were seen on H&E examination. Hypertrophied nerve trunks were seen in all specimens (mean 28.2 ± 2.5 μm). In the 10 cases mentioned above, calretinin IHC showed no evidence of immunostained cells, only mast cells were stained. In two biopsies with suboptimal submucosa on calretinin IHC, nerve fibres were seen in the lamina propria and muscularis mucosae, even in the absence of ganglion cells. In bowel resection specimens, calretinin staining characterised the aganglionic-ganglionic transition segment well.
Conclusion: Calretinin immunohistochemistry can assist the pathologist in diagnosing cases of ganglion cell paucity, dysplastic ganglion cells and specimens with incomplete submucosa. Interpretation of the staining is aided by the presence of submucosal mast cells, which serve as a positive control for calretinin immunohistochemistry. The absence of ganglion cells associated with hypertrophied nerve trunks and calretinin-positive nerve fibrils in the lamina propria, muscularis mucosae and superficial submucosa should be interpreted with some caution. In these cases rebiopsy is the optimal solution.

E-PS-15-021

Diagnostic difficulties in a case of Hepatoblastoma with carcinoma features

E. Izycka-Swieszewska*, M. Chodyna, H. Garnier, E. Wojciechowska, M. Murawski, J. Stefanowicz, P. Czauderna
*Medical University of Gdansk Dpt. of Pathology & Neuropathology, Poland

Background & objectives: Hepatoblastoma with carcinoma features (HBC) including biphasic HCN NOS, equivocal HCN NOS, and HB FPAs, shows HB- HCC combination histologically and genetically, being unstable neoplasms with higher mutation and CNA burdens than HB) (Sumazin et al., J Hepatol 2022)
Methods: A case report of 2- year- old boy with a problematic extremely rare liver tumour with high serum AFP levels, finally diagnosed as a hepatoblastoma with carcinoma features (HBC). Morphological and immunohistochemical study.
Results: Tumour biopsy poor and scanty, diagnosis in the primary centre of epithelial hepatoblastoma, foetal variant; B-catenin in part nuclear. Consultation – dgn confirmed, no material for IHC. Chemotherapy introduced, then radical tumour resection: Hepatoblastoma mixed epithelial type: embryonal, macrotrabecular HCC- like, pleomorphic, 50% necrosis. IHC: B-catenin membranous patchy; SALL4 focally; GPC3, GS, and HepPar + patchy. Chemotherapy continued, rapid multifocal relapse within the liver and lungs, biopsy and resection: the tumour compatible with HCC. The molecular studies and reconsultation performed in USA, UCSF- prof. D. Lopez- Terrada laboratory: pathogenic mutations in ARID1A (p.S709fs), CTNBB1 (p.K335T), and NRAS (p.G13R). Microsatellite stable but relatively high tumour mutational burden of 6.2 mutations/ megabase.
Conclusion: The patient's histology and molecular findings were compatible with a rare hepatocellular neoplasm NOS with combined/ overlapping histological features of hepatoblastoma and hepatocellular carcinoma = Hepatoblastoma with carcinoma features. HBC constitutes a new category. The case was problematic because of small primary biopsy material, the post chemotherapy changes involved diverse histological patterns with aggressive histology, clonal evolution, and finally HCC component predominance. In paediatric liver tumours diagnostics, a direct patho- clinical cooperation, proper immmunophenotyping, and molecular testing are pivotal.

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E-PS-15-022

Rare and unusual youngest case of aggressive plasma cell neoplasm in a 12-year-old boy

S. Jakkulwar*, V. Agarwal, S. Gujral, N. Oza
*Histopia Lab, India

Background & objectives: Plasmablastic lymphoma (PBL) is an aggressive high grade non-Hodgkin lymphoma, occurs predominantly in adult patients with concomitantly afflicted with HIV infection. In contrast to several reports and studies of PBL in adult patients, PBL is very rare in paediatric patients.
Methods: We report a case of 12-year-old boy with painful lesion over right clavicle. Needle biopsy was performed. Morphology and immunophenotyping confirmed the diagnosis of aggressive plasma cell lymphoma - Plasmablastic lymphoma was offered.
Results: An 12-year-old male presented right clavicular lesion. PET CT revealed hypermetabolic enhancing soft tissue mass lesion involving lateral half of right clavicle, osteolytic lesion involving manubrium sternum, iliac bone. An incisional biopsy was performed and histology reveal malignant round cell tumour arranged in dyscohesive sheets. Individual tumour cells show round nuclei, coarse chromatin, inconspicuous nucleoli and scant cytoplasm. Tumour cells show focal clear cell change. Mitotic figures seen. Spotty foci of necrosis is seen. By immunohistochemistry, the tumour cells show diffuse strong positivity for CD30, EMA, CD138, MUM1, MIC2, CD43, CD79a. Kappa light chain restriction is noted. MIB1 labelling index is approximately 90%
Conclusion: Plasmablastic lymphoma is an aggressive malignancy with particularly poor outcome in the setting of concomitant HIV infection. High index of suspicion is necessary. The combination of cognizance of this rare tumour in the paediatric population coupled with antiretroviral therapy (which precedes the diagnosis of lymphoma) and prompt initiation of aggressive multimodality treatment may, in future, facilitate improved outcome in paediatric patients with Plasmablastic lymphoma.

E-PS-15-023

Citrullinemia: a rare case of an autosomal recessive hereditary disease

K. Kosov*, E. Guryanova, N. Zhuravleva, V. Diomidova, A. Pavlov, N. Uhterova
*I.N.Ulianov Chuvash State Universit, Russia

Background & objectives: Citrullinemia is a rare autosomal recessive hereditary disease characterized by a violation of the urea cycle. Occurs with defects in the ASS1 or SLC25A genes.

Methods: We report a case of a 20-day-old foetus with citrullinemia and demonstrate a multi-stage approach to making a pathoanatomical diagnosis, which included an autopsy stage with an assessment of organometric and morphometric parameters, microscopic and biochemical examinations of organs.
Results: Pathologically, the child revealed: Type 1 Citrullinemia, acute neonatal form, microscopically - "accumulation cells" in the stroma of the thymus, spleen, liver, in the lumen of the alveoli; hepatosplenomegaly (liver-290.6 g, spleen-24.2 g); subtotal vacuole and fatty degeneration, necrobiosis of hepatocytes, cytolysis syndrome: hyperammonemia (biochemical blood test - ammonia: 129 mmol/l).
Complication: Acute endogenously toxic hepatic encephalopathy: macro- and macroscopically — total leukomalacia; during biochemical examination of the liver and brain, ammonia was detected using qualitative reactions. Edema and swelling of the brain, with the insertion of the tonsils of the cerebellum into the large occipital foramen: microscopically - destructive edema in the brain stem, leukomalacia of the spinal cord.
Conclusion: The stigmas of dysembriogenesis: a sharp brachycephalic head shape (head index — 1.18 (nome 0.75-0.799), enlarged earlobes, snub nose, short neck, C-shape of the gallbladder, scalloped edge of the spleen. Dyschrony of thyroid gland development according to the retardant type. Secondary immunodeficiency: premature atrophy of the thymus, delimphotization of the spleen, lymph nodes of the mesentery and perigastric region. The main danger of acute hyperammonemia is critical intoxication of the body, which ends in a comatose state and death.

E-PS-15-024
KRAS mutation in a metanephric stromal tumour with a large cellular component in an infant
S. Mangray*, N. Patel, N. Shillingford, E. Uzun, L.J. Wang, C. Jackson, E. Yakirevich
*Nationwide Children's Hospital, USA

Background & objectives: The majority of metanephric tumours (MTs) harbour BRAF V600E mutation, but a rare case of metanephric adenoma (MA) with a KRAS mutation was previously reported. Herein, we report the first case of metanephric stromal tumour (MST) harbouring a KRAS mutation.
Methods: The clinical presentation, pathologic findings, and molecular work-up of an MST are reviewed as part of a retrospective interrogation for BRAF V600E mutation by RT-PCR and Sanger sequencing in a series of paediatric MTs (age range 4 months-16 years). Five MAs, one MST, and one metanephric adenofibroma (MAF) were studied.
Results: BRAF V600E mutation was present in 3 of 5 MAs and the MAF, but was absent in the MST. The MST occurred in a 4-month-old boy who presented with haematuria. Nephrectomy revealed an unencapsulated 4.3 cm mass confined to the kidney. Histologically, fibrous (40%) and cellular (60%) components were present. The fibrous component was moderately cellular with cuffing ("onion-skinning") around entrapped tubules, and focal angiodysplasia was noted. Packed round and spindle cells with up to 35 mitoses/10 HPFs formed the cellular component.
FISH studies performed on the MST (cellular component) were negative for ETV6, EWSR1, and SS18 rearrangements. However, next-generation sequencing (NGS) of tumour revealed a KRAS mutation (c.180_182delinsACG,p.Q61R).
Conclusion: The intermixed fibrous and cellular components in this MST are akin to that in a mixed classic and cellular congenital mesoblastic nephroma, and the large cellular component directed comprehensive molecular work-up. We recommend testing for upstream KRAS mutation in the RAS-RAF-MAPK pathway or NGS in challenging MTs when BRAF V600E mutation is absent since tumour relapse and related death have been reported, albeit rarely, in MTs, and there may be a role for actionable therapy, based on the molecular signature.

E-PS-15-025
A rare case of a medulloblastoma diagnosed in a foetal autopsy
J. Gama*, C. Courelas, J.P. Maldonado, J. Amaral, A.C. Lai, C. Cerdeira, R. Pina
*Unidade Local de Saúde de Coimbra, Portugal

Background & objectives: Medulloblastomas are the second most common central nervous system (CNS) malignancy in childhood, representing 20% of CNS neoplasms in this age group. Patients with 21-trisomy have a lower chance of developing solid neoplasms.
Methods: We present a case report of a 15-week old foetus, with a 21-trisomy detected by MLPA. In the ultrasonography, the absence of nose bones and nuchal translucency was detected, and the parents opted for medical termination of pregnancy.
Detailed gross examination and histological examination were carried out. Genetic testing of the foetus and the parents was done.
Results: During the autopsy the absence of nose bones was confirmed. A cervical cystic hygroma, clinodactyly of the 5th finger of the left hand, and single hand crease was described. In the brainstem and periventricular area a tumour was found, which the histopathological examination showed to be a medulloblastoma. The parents were tested and a balanced Robertsonian translocation 45,XX,t(14;21)(q10;q10) was found in the mother.
Conclusion: We describe a case of a medulloblastoma in a 15-week old foetus with 21-trisomy. Medulloblastomas are a rare finding in foetuses and even rarer in the setting of 21-trisomy. This case shows the importance of performing a rigorous autopsy to identify associated lesions that would be missed in the prenatal setting.

E-PS-15-026
Immature platelet fraction - flow cytometry biomarker used to express the inflammatory response and oxidative stress in Romanian preterm newborns
E. Matei*, I. Franciuc, M. Aşchie, A. Mitroi, A. Chisoi, I. Poinăreanu, N. Dobrin, A.G. Stoica, T.V. Surdu, M. Manea, C. Ştefanov, G. Cozaru
*Cedmog, Ovidius University, Constanta, Romania

Background & objectives: Aggregation involves platelet-to-platelet adhesion, which is necessary for hemostasis after the initial adhesion of platelets to the injury site. Our study presented that the immature platelet fraction (%) in preterm and full-term newborns represents a promising clinical biomarker in neonates.
Methods: Immature platelet fraction (%) was analysed by flow cytometry technique with platelet membranes glycoproteins (GPIIIa-CD61) and thiazole orange dual stain in prematurity-related morbidities such as respiratory distress syndrome (RDS), intraventricular bleeding (IVH), and anemia of prematurity (AoP) preterm newborn cases reported to healthy full-term newborns.
Results: The immature platelet fraction presented significantly decreased values in preterm newborns reported to healthy full-term newborns (11.83 ± 5.70 vs. 15.78 ± 4.85, $p<0.05$). Preterm newborns presented significantly lower values of immature platelets fraction in RDS+ reported to RDS− (11.51 ± 4.30 vs. 18.75 ± 9.32, $p<0.05$). IPF was significantly lower for AoP+ neonatal cases than AoP− neonatal cases (AoP+:10.65 ± 2.79 vs. AoP−:16.76 ± 7.77, $p \leq 0.05$). Preterm newborns presented significant positive correlations between IPF and clinicopathological characteristics (RDS+: $r = 0.398$, $p <0.05$; IVH+: $r = 0.376$, $p<0.05$; AoP+: $r= 0.390$, $p<0.05$).
Conclusion: IPF % is a valuable flow cytometric method to measure the young and immature platelet fraction in peripheral blood samples,

representing a biomarker for thrombopoiesis and neonatal clinical outcomes pathology.

E-PS-15-027

PD-L1 expression in peripheral neuroblastic tumours: the first evidence of a possible therapeutic target

M. Mazzucchelli*, G. Angelico, L. Salvatorelli, G. Broggi, G. La Cava, J. Farina, G. Tinnirello, L. Memeo, G. Magro
*Department of Medical, Surgical Sciences and Advanced Technologies "G.F. Ingrassia", Anatomic Pathology, University of Catania, Italy

Background & objectives: Neuroblastoma is the most common among peripheral neuroblastic tumours and it represents the third most common childhood neoplasm. In the present study, we evaluated the PD-L1 expression by immunohistochemistry in peripheral neuroblastic tumours as a new possible therapeutic target.
Methods: We retrospectively collected 17 patients with peripheral neuroblastic tumours (15 poorly differentiated neuroblastomas, 1 differentiating neuroblastoma, 1 nodular ganglioneuroblastoma). Formalin-fixed-paraffin-embedded tumour samples were tested with PD-L1 SP263 assay. The tumour proportion score (TPS) was assessed, and the combined positive score (CPS) was calculated as well. A semiquantitative assessment for the extent of diffuse/fibrillary PD-L1 was also conducted.
Results: PD-L1 positivity was found in 7 cases (41%). Three cases showed PD-L1 membranous and cytoplasmic positivity both in tumour cells (2 with intermediate expression, 1 with only focal staining) and immune cells; the remaining 4 cases showed PD-L1 staining restricted to the immune cells. PD-L1 expression in the immune cells was diffuse (60%) in one case, intermediate (10-40%) in 5 cases and focal (2%) in the remaining case.
Although in this study only membranous PD-L1 staining was considered positive, other staining patterns were observed (e.g., PD-L1–positive fibrillary staining in the well differentiated, Schwannian stroma component in 4 neuroblastomas, and membranous staining restricted to the ganglion cells in one case).
Conclusion: Neuroblastoma is not generally a highly immunogenic tumour. However, in the present study, we have found a good percentage of these tumours with PD-L1 expression; this expression appears to be higher in better differentiated tumours, e.g. differentiating neuroblastoma and nodular ganglioneuroblastoma. This finding may represent a new potential therapeutic target for these tumours. However, due to the rarity of these paediatric neoplasms, more studies on larger series are needed.

E-PS-15-028

A mass that grows with the baby: a case of fibrous hamartoma of infancy

L.D. Micoogullari*, R.E. Cecen, D. Kizmazoglu, O. Ulusoy, F.C. Sarioglu, H. Guleryuz Ucar, S. Aktas
*Izmir Katip Celebi University Ataturk Training and Research Hospital, Medical Pathology, Turkey

Background & objectives: Fibrous hamartoma of infancy (FHI) is a benign rare neoplasm affecting infants. FHI is characterized by triphasic morphology consisting of fibroblastic fascicles, nodules of primitive cells and mature adipose tissue. In this case, we report FHI in a 9-months-old girl.
Methods: A lumbosacral mass specimen, measuring in total of 7x4x3 cm, on cut surface with a tan-yellow color consisting of haemorrhagic, fibrotic and lipomatous areas was sampled. Paraffin-embedded tissue sections of this specimen were evaluated for the histopathological characteristics. Demographic, clinical and imaging data were collected.
Results: A 9-months-old girl admitted to the hospital with complaint of a congenital lumbosacral mass which was initially thought to be multiple Mongolian blue spots. Mother described the mass as it had been growing as the baby grew, but the growth rate has increased in the last few months. Her examination showed a moveable, painless mass with bluish color at the lumbosacral region. Magnetic resonance imaging revealed a subcutaneous mass with 5,5 cm in greatest width showing contrast enhancement. Histopathological examination revealed a characteristic organoid triphasic morphology with bland fibroblastic fascicles, mature adipose tissue and primitive looking oval-to-stellate shape cell nodules with myxoid stroma. Diagnosis of FHI was made.
Conclusion: FHI is a rare benign soft tissue neoplasm affecting mostly infants under 2 years of age. Rapidly growing nature and difficulties in making diagnosis may lead to misdiagnosis of this entity. While excision is curative, it is known that local recurrences could be encountered. Also, recent studies have shown that FHI cases often harbor EGFR exon 20 insertion/duplication mutations. Therefore, FHI should be considered in the differential diagnosis of a rapidly growing soft tissue mass in an infant.

E-PS-15-029

Paediatric melanoma: about two observations

W. Ouahioune*, N. Moulai, M. Guermi
*Faculty Of Medecine of Blida, Algeria

Background & objectives: Paediatric melanoma is rare. It represents for 3% of all paediatric cancers. Our objective is to report two observations of post pubertal paediatric melanomas.
Methods: Our observations concern two adolescents: Young girl of 14 years of clear phototype, followed for treatment of a pigmented lesion of the knee which appeared 04 years ago. A 17-year-old boy followed for axillary metastasis of melanoma of unknown primary. No personal or family history of nevus or melanoma was found in our two patients.
Results: We have examined:
- in the 14-year-old girl: a skin lesion measuring 34x20x12 mm, polypoid, ulcerated, infiltrating the hypodermis, poorly pigmented, strongly expressing HMB45, Melan A and Sox10. Ki67 was above 80%. Testing for the BRAFV600E mutation by RT-PCR came back negative. We retained the diagnosis of nodular post-pubertal melanoma.
- in 17-year-old boy: a lymph node massively infiltrated by a proliferation of poorly pigmented epithelioid cells, strongly expressing HMB45 and Melan A with mutation of BRAF V600E gene by RT-PCR. All clinical, endoscopic and radiological explorations did not find the primary melanoma.We retained the diagnosis of metastasis melanoma with unkown origin.
Conclusion: The particularity of our two observations lies in the development of melanoma in adolescents without a pre-existing naevus (dysplastic naevus, congenital naevus, Spitz naevus). Also, we found ourselves with an even rarer and more serious form of lymph node metastasis with no known primary melanoma in a 17-year-old adolescent.

The rarity of paediatric melanoma requires caution before confirming this diagnosis.

E-PS-15-030

Congenital intracranial adamantinomatous craniopharyngioma: a case report with histopathological and molecular characterization

E.M. Pena Burgos*, P.J. Armijos González, M. Arias Duart, C. Martínez Payo, C. Bravo Arribas, R.M. Regojo Zapata
*Hospital General Universitario Gregorio Marañón, Spain

Background & objectives: Congenital intracranial tumours are exceedingly rare neoplasms that only account for 1% of brain tumours in childhood. To our knowledge, only thirty congenital intracranial

craniopharyngiomas have been published in literature, with only one of them presenting histopathological and molecular characterization.
Methods: We present the case of a 39-year-old woman with a single pregnancy conceived spontaneously. A foetal intracranial mass located in the sphenoid bone base was detected in the 20 weeks' ultrasonography. It was a 44x25 mm heterogeneously hyperechogenic ill-defined mass that was growing towards both hemispheres. Given the poor prognosis, legal pregnancy interruption was decided, and autopsy study was performed.
Results: A 20-week-old male foetus that weighted 528g was received at the Pathology Department. External examination showed no relevant findings except for increased head circumference. Internal evaluation revealed an intracranial yellowish mass in the suprasellar region. It was histopathologically composed by squamous epithelium with peripheral nuclear palisading, stellate reticulum, wet keratin and calcification deposits. The epithelial cells showed immunoreactivity for high- and low- to intermediate molecular weight cytokeratins. A complete absence of all pituitary hormones and neuroendocrine markers was seen. A p.T41A (c.121A>G) mutation in exon 3 of the CTNNB1 gene was detected. No BRAF p.V600E mutations were demonstrated. No extracranial findings were present.
Conclusion: Adamantinomatous craniopharyngiomas should be included in the differential diagnosis of sellar and suprasellar congenital intracranial tumours despite its very low frequency. The only previous published case with molecular characterization did not detect neither CTNNB1 nor BRAF mutations. Our case harbors a CTNNB1 mutation, similar than in post-natal diagnosed craniopharyngioma cases. A correct characterization of this tumours is essential to improve the management and prognosis of the patients.

E-PS-15-031
Massive subchorionic thrombohematoma (Breus' mole): case series with gross and histopathological description of this exceedingly rare entity
E.M. Pena Burgos*, L. Hato Salmón, R.M. Regojo Zapata
*Hospital General Universitario Gregorio Marañón, Spain

Background & objectives: Massive subchorionic thrombohematoma is an extremely infrequent placental condition that consist in a maternal subchorionic bleeding associated to intrauterine growth restriction, intrauterine foetal death, preeclampsia, and placental insufficiency. To our knowledge, less than forty cases have been reported in literature.
Methods: We present 14 new cases [14/4869 placentas (0.002%)] diagnosed from 2016 to 2023. The average maternal age was 32.6 years. Maternal cardiopathies were present in 35% of the cases and preeclampsia in one case. The average gestational delivery weeks were 35.1. Intrauterine growth restriction was present in 50% of the cases. No foetal deaths were registered in our series.
Results: Placentomegaly (> p90) was seen in two cases and placental hypoplasia in two cases (< p10). In all cases, foetal side presented yellowish areas with increased consistence that affected from 20 to 100% of the surface, with a depth between 1 and 2.3 cm. Gross serous cyst formations were observed in two cases. No retroplacental hematoma were registered. Circumvallate/circummarginate membranous insertion was seen in three cases and marginal/velamentous insertion in five cases. Intraparenchymal hematoma was detected in a case. Maternal vascular malperfusion pattern (accelerated villous maturation/villous distal hypoplasia) was observed in ten cases. Delayed villous maturation was observed in one case. Chorangiosis was only observed in the twin pregnancy.
Conclusion: Breus' mole should be thought in the differential diagnosis of intrauterine foetal growth, especially in cases of maternal cardiopathy. The presence of yellowish areas (with a depth > 1cm) ± cystic cavities on foetal surface are key to diagnosis. Abnormal membranous or umbilical cord insertion, and maternal vascular malperfusion pattern have been found in our series. Prenatal diagnosis and a close ultrasonographic follow-up of Breus' mole is recommended, considering the end of the pregnancy in cases of severe placental insufficiency.

E-PS-15-032
CD 56 positive clear cell sarcoma of the kidney - case report
J. Stefanović*, G. Nikolic
*Serbia

Background & objectives: Clear cell sarcoma of the kidney (CCSK) is a rare paediatric renal tumour, accounting for a small percentage of all paediatric renal malignancies. It is characterized by its aggressive behaviour and potential for late recurrence and metastasis.
Methods: We report the case of a two-year old boy who presented with renal mass who received four cycle of chemotherapy according to Umbrella protocol. Total nephrectomy was performed under suspicion of Wilms tumour.
Results: Macroscopically, in the lower pole of the kidney, lobulated mass measuring 120x95x90 mm was revealed. The tumour exhibits a variegated appearance with areas of pale yellowish coloration. On histology, the tumour was composed predominantly of uniform, small, round cells with clear cytoplasm. The cells are arranged in nests or cords, separated by a delicate network of fibrovascular septa. Immunohistochemical analysis showed diffuse positivity on CD56, Cyclin D1, bcl-6, p53 and vimentin. Tumour was negative for CD57, CKAE1/AE3, EMA, Pax-8, Desmin, WT-1, and Synaphtophysin. Proliferative index Ki-67 was 50%. Fish analysis showed absence of rearranged BCOR and YWHAE gene in the tumour. The diagnosis of clear cell sarcoma was made.
Conclusion: CCSK is a rare but significant paediatric renal tumour with unique diagnostic and therapeutic challenges. Our case showed CD56 diffuse positivity, which is according to our knowledge very rare, which bring us to the question about further biological behaviour of the tumour and prognosis. Further research and case documentation are essential to enhance our understanding and management of CCSK.

E-PS-15-033
Comprehensive assessment of changes in neuronal structures in the heart in miscarriages at 15-21 weeks of gestation
O. Sudareva*, E. Ignatieva, S. Lezhenina, A. Polkovnikov, N. Zhuravleva, E. Guryanova
*I.N.Ulianov Chuvash StateUniversity, Russia

Background & objectives: We analysed the dynamics of macro- and pathomorphological parameters in the neuronal structures of the heart and conductive cardiomyocytes of foetuses 15-22 weeks of gestation under the influence of various intrauterine factors.
Methods: The autopsy protocols of miscarriages at 15-22 weeks of gestation were studied. The following was carried out: a study of the foetal heart (weight and size of the organ with weighing of its chambers, ventricular index); staining of heart microslides stained with hematoxylin-eosin, van Gieson and Bielschowsky-Gross; immunohistochemistry with NSE, S-100, synaptophysin; statistical and correlation analyses of the results obtained.
Results: The main lethal factors were malformation, intrauterine infection and foetal hypoxia. Of these, in 50% of cases intrauterine growth retardation was observed. Cardiac macrometry was hemodynamically significant and directly depended on the gestational age of the foetus. In all cases, in the epicardium and in the thickness of the myocardium along the vessels, positively stained S-100 and NSE neuroblasts and neurocytes in the nerve ganglia were noted; Expression was pronounced during intrauterine hypoxia in 68.8% of cases. In all groups, the expression of synaptophysin was positive; only at 15-18 weeks

of gestation its level was extremely low and correlated with signs of sclerosis and hypogangliosis in the intracardiac nerve ganglia.
Conclusion: The age-related dynamics of pathohistological indicators of the neuronal support of the heart in miscarriages at a gestation period 15 - 22 weeks are directly dependent on the gestational age and are not specific to the nature of the influence of antenatal factors. Intrauterine hypoxia as a damaging factor causes ischemic-degenerative changes in the intracardiac autonomic ganglia, which may be reflected in the occurrence of disturbances in the contractile and conductive functions of the heart muscle in the postnatal period.

E-PS-15-034
Sectional case of a combination of coronary artery malformation and non-compact myocardium of the left ventricle in an infant (a 7-month-old child: sudden coronary death)
O. Sudareva*, S. Lezhenina, E. Ignatieva, A. Grigorieva, E. Guryanova
*I.N.Ulianov Chuvash StateUniversity, Russian Federation

Background & objectives: We present a rare sectional case of macro- and microscopic examination of a removed heart in a 7-month-old child with a combination of non-compact myocardium of the left ventricle and malformation of the coronary vessels.
Methods: At autopsy, the sizes of vessels and outlet openings, foetal communications, heart mass with separate weighing of its chambers, and ventricular index were assessed. Histological sections of the heart were stained with hematoxylin and eosin, according to van Gieson, an immunohistochemical method with staining for neuronal markers. Determination of troponin I in cadaveric blood.
Results: At autopsy: the heart weight was 51 g, eccentric hypertrophy and myogenic dilatation of the right heart's parts. Contrasting heart's vessels revealed dilation of the mouth of the left coronary artery with the formation of a coronary-left atrial fistula, an aneurysm of the initial section of the anterior interventricular branch of the left coronary artery with parietal thrombosis and repeated myocardial microinfarctions in the anteroseptal region of the left ventricle. Blood troponin I 1,000ng/ml. Histologically: hypogangliosis; the compact layer of the left ventricle is thinned, with dystrophy and necrosis of cardiomyocytes, an abundance of thin-walled blood vessels; in the spongy myocardium's layer there is subendocardial sclerosis and lipomatosis.
Conclusion: The combined heart's pathology caused disturbances in the conductivity and rhythm of heart contractions in the patient during his lifetime. IHC heart's examination showed a decrease in the expression of S-100, NSE and synaptophysin, which confirmed hypoganglionosis and sclerosis. Vascular malformation and preserved spongy layer of the myocardium are combined with a tendency to thrombus formation due to the "inferior" wall of malformed arteries, hence microinfarctions in the left ventricle of the heart. Accordingly, death occurred from cardiogenic shock.

E-PS-15-035
Systemic assessment of pathomorphological changes in the lungs in premature infants at a gestation period of 21-28 weeks
O. Sudareva*, E. Ignatieva, S. Lezhenina, E. Guryanova, P. Grigorieva
*I.N.Ulianov Chuvash StateUniversity, Russia

Background & objectives: Postnatal development of the lungs in premature newborns plays a large role in the formation of bronchopulmonary dysplasia and chronic interstitial lung diseases. We analysed the dynamics of pathomorphological changes in the lungs in newborns at 21-28 weeks of gestation.
Methods: A retrospective analysis of autopsies of 34 live-born premature babies was carried out using a unified histological method with assessment of the stage of lung development, alveolar count, thickness and cellular composition of interalvelar septa, and the effectiveness of the air-hematic barrier. Lung sections were stained with hematoxylin and eosin as standard, additionally with the Pas reaction and van Gieson.
Results: Histological examination of the lungs revealed the following microscopic changes: hypoplasia of the terminal parts of the acini in 75% of cases, caused by sclerosis and edema of the surrounding tissue, degeneration and necrosis of epithelial cells; inadequately functioning aerohematic barrier even against the background of artificial ventilation of the lungs and endotracheal administration of Kurosurf (at 22-24 weeks it functioned 5%, at 24-26 weeks and 26-28 weeks by 10 and 15% respectively); the proliferative activity of the epithelium of the alveolar ducts depended on the gestational age (the shorter the gestational age, the less pronounced it is) and was directly related to the development of areas of sclerosis around.
Conclusion: The development of pathomorphological changes in the bronchopulmonary system in live-born preterm infants at a gestation period of 21-28 weeks is associated with age and the presence of comorbid pathology, which undoubtedly affects the formation of pulmonary parenchyma and mesenchyme in the postnatal period ($p < 0.01$). A strong direct correlation (CI=98%) was revealed between the development of pneumosclerosis around the acini stem cell niches and the maturation of the lung parenchyma, which contributes to the formation of chronic lung pathology.

E-PS-15-036
Paediatric mediastinal NUT carcinoma: a diagnostic challenge on a small biopsy
A. Syrnioti*, V. Antari, A. Tragiannidis, E. Hatzipantelis, T. Koletsa
*Department of Pathology, School of Medicine, Aristotle University of Thessaloniki, Greece

Background & objectives: NUT carcinoma is a recently described malignancy characterized by NUT gene rearrangements that most commonly affects midline structures of the upper aerodigestive tract or the mediastinum and displays a dismal clinical outcome.
Methods: We describe a case of NUT carcinoma, in a 13-year-old male with persistent chest pain, dyspnea, and fever. Imaging revealed an 11-cm mediastinal mass, causing midline structure displacement, left pulmonary artery branch encasement, left upper lobe bronchial obstruction, pleural and pericardial effusion. Serum alpha-fetoprotein (aFP) levels were mildly elevated. Hematoxylin-eosin and immunohistochemical stained sections from a mass biopsy were examined.
Results: Microscopic examination revealed an undifferentiated malignant neoplasm, infiltrating the pulmonary parenchyma, characterized by small to medium-sized cells, with scant, clear cytoplasm and round or irregular hyperchromatic nuclei. Tumour cells were arranged in solid groups or diffuse sheets, among abundant neutrophils. On immunohistochemical evaluation, neoplastic cells were positive for AE1/AE3, CK8/18, p63, synaptophysin, CD99, CD117, and PAX8. Few cells exhibited chromogranin, CK19, SALL4, and aFP immunoreactivity. The Ki67 proliferative index was 80%. Despite the absence of abrupt keratinization, NUT carcinoma was suspected and confirmed with the immunostain for NUT protein. Moreover, BRD4-NUTM1 fusion gene was demonstrated on exome sequencing. Subsequently, the patient received chemotherapy and died 3 months after the diagnosis.
Conclusion: NUT carcinoma is a highly aggressive, and underrecognized malignancy, that poses significant diagnostic and therapeutic challenges. In our case, the young age, the mediastinal tumour location, and the elevated serum aFP levels, combined with the focal SALL4 and aFP immunohistochemical expression, in a small biopsy specimen, were pitfalls that could have led to confusion with a germ cell tumour. NUT immunohistochemistry or molecular testing along with a high level of suspicion are essential for a definitive diagnosis.

E-PS-15-037

Chronic and passive pneumopathy in a 4-month-old boy with hypertrophic cardiomyopathy

E. Tomé de Sousa, L. Vasconcelos Cavalcante*, A.W. Barreto Rodrigues, P. Ye Wenyan, G. Gotardo Aguiar Gurgel, R. Soares Macedo, J. Aguiar de Arruda Coelho, J. Carneiro Melo
*University of Fortaleza, Brazil

Background & objectives: Hypertrophic cardiomyopathy, a rare genetic condition most commonly observed in adults, was initially described in 1907. This study aims to share the autopsy of a 4-month-old boy.
Methods: Autopsy case report through analysis of medical data, macroscopic and microscopic examinations, and observation of histological slides with pathological findings, the patient was diagnosed with hypertrophic cardiomyopathy. Patent ductus arteriosus was detected, unrelated to pulmonary hypertension, and PCA was detected as a sequelae of syphilis, different from what is common in the literature.
Results: Lungs with chronic pneumopathy, chronic and passive signs of congestion, thickening of the interalveolar septa caused by moderate mononuclear inflammatory infiltrate and proliferation of myofibroblasts in the interstitium. Heart showing cardiomyocyte hypertrophy and extensive areas of subendomyocardial fibrosis in addition to recent ischemic cardiomyocyte necrosis. The liver exhibited vascular congestion resulting in sinusoidal enlargement along with diffuse steatosis. Furthermore, hypercellularity was observed in the splenic white pulp, characterized by frequent lymphoid follicles and prominent germinal centres. Kidney indicating intense congestion and tubular necrosis acquitted. Edema, congestion and moderate lymphocytic infiltrate related to mild cerebral edema.
Conclusion: Hypertrophic cardiomyopathy is a rare hereditary disease in children, but studies show that it has a poor prognosis, often leading to the patient's death. This fact highlights the importance of carrying out neonatal screening tests, such as pulse oximetry, which can detect congenital heart disease, allowing the patient to undergo early treatment, avoiding negative outcomes.

E-PS-16E-Poster Session Soft Tissue and Bone Pathology

E-PS-16-001

Hibernomas express alpha methylacyl CoA racemasa

B. Aguiar Losada*, M. Conde Ferreirós, M.Á. Resano Abarzuza, S. Abdulkader Sande, M. Vieytes Molares, A. López Cousillas, A. Moreno Barcos, I. Ruiz Díaz, A. Ordoñez Arrillaga, D.X. Ugás Burranca, J.A. Ortiz Rey
*Spain

Background & objectives: Hibernoma is a lipoma subtype that contains prominent brown adipocytes which resemble normal brown fat, admixed with white adipose tissue. This tumour represents 2% of lipomas. Brown adipocytes could be misinterpreted as other cells such as histiocytes or even lipoblasts.
Methods: We have gathered 16 hibernomas from 2015 until 2024 diagnosed in two Spanish hospitals. Formalin-fixed paraffin-embedded sections were immunostained with an antibody against AMACR (Alpha methylacyl CoA racemase) (clone 13H4) with a multimer based method (Optiview, Ventana). Intensity and extension of staining were evaluated. 17 sections of normal brown fat were also stained.
Results: The histological sections of hibernomas showed they were composed by large number of pale and eosinophilic brown fat cells with multivacuolated, eosinophilic granular cytoplasm and a small central nucleus admixed with variable amount of univacuolated white cells. Immunohistochemistry for AMACR revealed that 15 of the 16 hibernomas were intensely and diffusely positive, with a cytoplasmatic granular staining patterning brown cells. One of the cases was negative. Normal brown fat samples were also positive.
Conclusion: The result of our study suggests that AMACR is expressed in normal brown fat and in most of the hibernomas. White adipose tissue is negative for this marker. AMACR could be useful for the diagnosis of hibernomas differentiating them from their mimics. The expression of AMACR could be related to the metabolic characteristics of brown fat cells.

E-PS-16-002

Soft tissue Rosai-Dorfman disease: a case report

A.Y.S.H. Al Saadi*
*Oman Medical speciality Board, Oman

Background & objectives: Rosai–Dorfman disease (RDD) is a rare proliferative histiocytic disorder of unknown aetiology. It typically affects the lymph nodes but it can occur in extra nodal sites including the head and neck, skin, CNS and soft tissue.
Methods: This case report describes a soft tissue RDD in a 16 years old male who presented with clinical features indicative of pilonidal sinus with abscess collection. Subsequent histopathological examination, however, revealed RDD.
Results: Extra nodal RDD comprise 43% of all cases. Histologically, RDD classically characterised by the presence of mixed inflammatory infiltrate of s100 positive histocytes, plasma cells and lymphocytes. Emperipolesis, which is presence of intact phagocytized lymphocytes, is considered the hallmark of this disease. However, these classical features are seen less often in soft tissue RDD where there is abundant collagen deposition and fibrosis which can give storiform appearance and inconspicuous emperipolesis.
Conclusion: RDD is a rare benign inflammatory process that should be considered in the differential diagnosis of a soft tissue tumour. Histologically they have more subtle features compared to its lymph node counterpart. Thus, RDD in this site can be confused with other pathologies such as sarcomas, inflammatory pseudotumours and other fibrohistocytic lesions which make it challenging for the physicians to reach the correct diagnosis

E-PS-16-003

Erdheim-Chester disease - case report and literature review

A. Al-Sulaimani*
*Oman Medical speciality board, Oman

Background & objectives: Erdheim-Chester disease (ECD) is a rare, multisystemic non-Langerhans cell histiocytosis which can exhibit a wide range of clinical presentations. We present a rare case of Erdheim-Chester disease with multisystemic involvement.
Methods: A 46-year-old female presented with arrythmia was found to have a right atrial mass on Magnetic Resonance Imaging (MRI), further investigations revealed several bone and muscle lesions. A biopsy was obtained from the left distal vastus muscle, and subsequent histopathological examination confirmed the diagnosis of ECD. Genetic testing detected a BRAF mutation. The patient was then commenced on targeted therapy.
Results: Erdheim-Chester disease is a rare form of histiocytic neoplasm with multi-organ involvement, it is characterized by the accumulation of bland, lipid-laden histiocytes along with fibrosis and mixed inflammatory cells. A slight male predominance is observed, and it is most commonly diagnosed during the sixth decade of life. ECD can affect any organ, with symmetrical involvement of the long bones being the most commonly reported. Due to the unpredictable nature of the disease, patients can be symptom-free or can present with site-specific symptoms. Diagnosis of ECD requires a multidisciplinary approach, as it can be difficult to identify. Accurate diagnosis

is crucial since most cases show much better outcomes with targeted therapies.
Conclusion: The diagnosis of Erdheim-Chester disease is challenging and requires a high index of clinical suspicion and careful consideration, this case report aims to describe the clinical, radiological, molecular and histopathological findings of multiple-organ involvement of ECD. The prognosis of ECD is organ-dependent, however, recent advancement in targeted therapies with kinase inhibitors have improved outcome and survival.

E-PS-16-004
Intraosseous haemangioma: series of cases diagnosed in the pathology department of the Basurto University Hospital, Bilbao, Spain
R.I. Alvarado Cuenca*, L. Aguirrezabal Marcotegui, I. Fernandez de la Prieta, J.C. López Duque, A. Ugalde Olano, I. Cearra Guezuraga, C. Jiménez Zapater, A. Azueta Etxebarria
*Pathology Department- Basurto University Hospital, Spain

Background & objectives: Intraosseous haemangioma(IH) is a rare, benign, slow-growing tumour of the bone. IH are rare conditions comprising 0.5 to 1% of all intraosseous tumours. Vertebral bodies are most common site. The objective of this study is to describe our case series.
Methods: This study is descriptive, retrospective and diagnosed in the last ten years (2013-2023) in our institution. We checked our database and selected every intraosseus hemangiomas. which resulted in a total of 7 cases. The clinical history, localization and histology was reviewed.
Results: According to the cases studied, 67% of the cases were in the skull, followed by facial area 29% and very rare location in bone flat representing one case, 14%. Histologically the variant cavernous was predominantly most frequently with 86%. The 71% of the cases were female, with a mean age of 51 years and a predominance of right laterality in 57%. The most frequent clinical presentation was asymptomatic (71%) followed by mild chronic pain. All lesion were excised with no recurrence reported.
Conclusion: The literature report most frequency in the vertebral bodies. In this study, reported mostly in the craniofacial skeleton and the very rare location like flat bone in one case. Vascular tumours of bone can be diagnostically challenging especially in rare locations such as our in the cubital bone.

E-PS-16-005
A spectrum of mesenchymal tumours with unusual locations arising in blood vessels: single centre case report series
T. Angelovska*, M. Kochoska, V. Risteski, V. Veslievska, S. Antovic, N. Jankulovski, S. Dohcev, B. Nikolovska, M. Bogdanovska-Todorovska, R. Jovanovic, S. Kostadinova-Kunovska
*Institute of Pathology, Faculty of Medicine, University Ss. Cyril and Methodius, Skopje, Republic of North Macedonia

Background & objectives: The occurrence of certain tumours in atypical sites can be confusing for clinicians and is diagnostic challenge for pathologists, thus it is important to report such cases. We present three cases of mesenchymal tumours with vascular origin in unexpected locations.
Methods: We retrieved cases from our database, diagnosed by standard histochemical and immunohistochemical methods. We present two cases of vascular neoplasms, gallbladder hemangioma and vulvar angiosarcoma, each of them reported in only around 10 cases in literature hitherto. The third case, a vascular leiomyosarcoma, which mostly arises in the inferior vena cava, with around 70 cases of renal vein leiomyosarcoma reported.
Results: Case 1 - Gallbladder hemangioma: 44-year-old male with a sub-serous, plaque-like vascular proliferation in the gallbladder. Microscopy showed anastomosing, cavernous blood vessels lined with benign endothelium, and less frequent thrombosed venules. Case 2 - Vulvar epithelioid angiosarcoma: Flashy appearing, necrotic, and haemorrhagic tumour in a 44-year-old female, covered by ulcerated, livid skin. Solid sheets of highly pleomorphic epithelioid and polygonal cells (EMA, ERG, CD34, CD31, Podoplanin positive signal) were present, with focal vessel formation. Case 3 – Renal vein leiomyosarcoma: 46-year-old woman, presented with a whorled whitish-gray mass in the renal vein wall, microscopically composed of spindled cells, positive for Smooth-muscle-actin, Desmin and Caldesmon, with focal necrosis and adventitial infiltration.
Conclusion: While gallbladder hemangioma can mimic malignancy and poses a risk of rupture and hemorrhage, renal vein leiomyosarcoma and vulvar angiosarcoma are highly aggressive tumours with poor prognosis, thus precise diagnostics and prompt treatment are of utmost importance. These case reports show rare neoplasms in unexpected locations and present a diagnostic challenge for clinicians, as well as pathologists. Essentially the pathologist should always be ready to expect the unexpected.

E-PS-16-006
A rare vascular tumour mimicking epithelioid malignancies, pseudomyogenic hemangioendothelioma: a case report
R.R. Askin*, B. Bilgic, G. Uverengil, H. Ozger
*Istanbul Faculty of Medicine, Turkey

Background & objectives: Pseudomyogenic hemangioendothelioma(PHE) is a rare vascular tumour primarily affecting young adults. Histologically, PHE exhibits spindled or epithelioid cells with eosinophilic cytoplasm and vesicular nuclei. Diagnosing this tumour can be challenging due to its rarity and morphological similarities with other tumours.
Methods: Here we present a case of PHE in an 11-year-old male, featuring multiple intramedullary lesions in the metaphysis of the left distal femur and proximal tibia, alongside additional lesions consistent with nonossifying fibroma. Following diagnosis via Tru-Cut biopsy, excision was conducted, and the sample forwarded for histopathological evaluation.
Results: In the biopsy, large epithelioid cells with an eosinophilic cytoplasm and prominent atypical nuclei were observed. Extensive immunohistochemical analysis revealed strong positivity for ERG, occasional positivity for keratin, and weak positive staining for smooth muscle actin. While CAMPTA1 was negative, TFE3 showed focal positivity. Based on both the immunohistochemical findings and morphological features, the diagnosis of PHE was established.
Conclusion: In the differential diagnosis, epithelioid morphology of the lesion may prompt consideration of epithelioid sarcoma, rhabdomyosarcoma and epithelioid osteosarcoma. Therefore, due to its rarity, PHE may not be considered, potentially leading to misdiagnosis. Immunohistochemical methods can offer valuable assistance in such cases.

E-PS-16-007
Epithelioid hemangioendothelioma of the abdominal wall: report of a rare entity
O. Belhadj*, S. Makni, S. Graja, C. Chaari, M. Miled, N. Gouiaa, T. Sellami Boudawara, C. Kammoun
*Department of Pathology, Habib Bourguiba University Hospital, Sfax, Tunisia

Background & objectives: Epithelioid hemangioendothelioma (EHE) is an intermediate malignant vascular tumour. It was first described in 1982 by Weiss and Enzinger. EHE tend to affect males with a median age of 36 years old. It occurs especially in the liver and lung.

Methods: Herein, we describe the case of a 62-year-old man previously diagnosed with diffuse large B-cell lymphoma in remission for 2 years who presented with subcutaneous nodules on the abdominal wall that had been progressing for two months.
Results: The clinical examination reveals firm and painless nodules. A surgical excision was performed. Histological examination showed a dermal proliferation of epithelioid cells arranged in sheets or cords with myxo-hyaline background. The tumour cells had an eosinophilic cytoplasm with moderate cytologic atypia and rare mitoses. Occasional intracytoplasmic vacuolization was identified. An immunohistochemical study was performed to help make the diagnosis. Tumour cells were strongly and diffusely positive for cluster of differentiation 34 (CD34) and CD31. The diagnosis of EHE was retained. A thoraco-abdominal scan and magnetic resonance imaging were performed, with no abnormalities. The patient is followed now for 12 months with no apparent recurrence.
Conclusion: Cutaneous EHE is exceptional. The immunohistochemical study is used to confirm the diagnosis and rule out other tumours such as epithelioid angiosarcoma, melanoma or undifferentiated carcinoma. Molecular studies can be useful in showing fusion genes, such as WWTR1-CAMTA1 or YAP1-TFE3. Treatment is mainly surgical. EHE is characterized by aggressive clinical outcomes; therefore, a close follow-up is necessary to prevent tumour recurrence and metastasis. The originality of this case lies in its rarity and the unusual location.

E-PS-16-008
A report of an exceptional case of rhabdomyosarcoma of the tongue harbouring THBS1::ALK fusion and literature review
E. Bellan*, C. Vieru, C. Borga, L. Favero, M. Sbaraglia, A.P. Dei Tos
*Department of Integrated Diagnostics, University Hospital of Padua, Padua, Italy

Background & objectives: Rhabdomyosarcomas (RMS) in the adult population are ultra-rare high-grade sarcomas. The WHO classification defines distinct subtypes based on morphology, molecular, and clinico-pathologic features. Herein, we describe a case of RMS with inflammatory myofibroblastic tumour-like morphology and harbouring a *THBS1::ALK* fusion.
Methods: We present the clinical, radiological, histopathological, immunophenotypic, and molecular findings (obtained using the Archer FusionPlex Sarcoma Panel v2) of a case of RMS unclassifiable according to current WHO criteria and associated with a novel *ALK* gene rearrangement. Following this index case, we herein review the available literature.
Results: A 76 year-old female presented with an exophytic 3 cm tongue mass treated with partial glossectomy. Histologically, the lesion was characterized by a proliferation of epithelioid and spindle cells organized in a fascicular growth pattern, set in a myxoid stroma associated with a lymphoplasmacytic infiltrate. Morphologically, the neoplastic cells displayed nuclear atypia and abundant eosinophilic cytoplasm. Mitotic activity was high, perineural infiltration and multiple lymph node metastases were observed. The tumour showed immunopositivity for desmin, myogenin, MyoD1, SMA, ALK D5F3 and focally S100. RNA-based molecular studies identified a *THBS1::ALK* fusion transcript.
Conclusion: Rhabdomyosarcomas are a heterogenous group of malignant neoplasms rarely occurring in adults. Immunohistochemical ALK-positivity has been described in RMS, however underlying *ALK* rearrangements are rare events. This is the first case harboring *THBS1::ALK* fusion, which was previously described in inflammatory myofibroblastic tumours. Albeit showing different clinical behaviour, myogenic marker positivity is exclusive of rhabdomyogenic differentiation aiding in the differential diagnosis between these two entities. Our case highlights the increasing complexity of morphologic classification of RMS.

E-PS-16-009
Recurrent leiomyosarcoma of the inferior vena cava: histological insights and clinical implications
W. Ben Makhlouf*, A. Zehani, A. Ayari, A. Khadhar, I. Chelly, H. Azouz, K. Bellil, S. Haouet
*Pathology department, Salah Azaeiz Institute, Tunesia

Background & objectives: Leiomyosarcoma originating from the inferior vena cava (IVC) is a rare malignant tumour arising from the smooth muscle cells of the vascular wall. This pathology often presents asymptomatically or with non specific symptoms, leading to late diagnosis and poor prognosis
Methods: This study presents a case of recurrent leiomyosarcoma of the inferior vena cava, describing its histological features alongside a review of relevant literature.
Results: A 63-year-old woman presented with abdominal pain. CT scan revealed mass within the IVC. surgical resection was performed. histopathological examination revealed a sarcomatous proliferation consisting of elongated bundles of intersecting smooth muscle cells. The spindle-shaped cells exhibited poorly defined eosinophilic cytoplasm, elongated hyperchromatic nuclei with conspicuous atypia, and numerous mitoses (estimated at 13 mitoses/10 high-power-fields). Additionally, the tumour exhibited extensive necrosis (50% of tumour volume). Immunohistochemical analysis showed diffuse and intense staining for smooth-muscle-actin and desmin. The diagnosis of leiomyosarcoma of the IVC was made. Follow-up revealed tumour recurrence after 5 years, necessitating the resection of the IVC and its collateral branches for treatment.
Conclusion: Leiomyosarcomas originating from vascular structures are rare, with the IVC being the predominant site. Recurrence and metastases are common, occurring in 30% to 50% of cases respectively, and prognosis remains poor, with a median survival of less than 25 months. Early detection and aggressive management strategies are crucial in improving outcomes for patients with this challenging malignancy.

E-PS-16-011
The contribution of BCOR antibody to differential diagnosis in round cell sarcomas in the light of the 2020 WHO new classification and re-assessment with histopathological parameters
H. Bilgi*, C. Comunoglu
*Prof. Dr. Cemil Tascioglu City Hospital, Turkey

Background & objectives: In the new WHO classification there are 4 groups under the title undifferentiated round cell sarcomas of bone and soft tissues. Ewing's sarcoma (ES), sarcomas with BCOR rearrangement (BRS), sarcomas with CIC rearrangement (CRS) and EWSR1-non-ETS fusion round cell sarcomas.
Methods: Between the years 2016-2022 in the Department of Medical Pathology of Prof. Dr. Cemil Taşcıoğlu City Hospital, 59 cases diagnosed with Ewing sarcoma, PNET, undifferentiated round cell sarcoma, round cell malignant mesenchymal tumour, were examined histopathologically. The results of the patients whose EWSR1 rearrangement, BCOR rearrangement by FISH method, BCOR and CIC:DUX4 gene alteration by next generation sequencing were recorded.
Results: In our study, cases were reclassified immunohistochemically NKX2.2, CD99, FLI-1, Ki-67, BCOR studies and using combination of histopathological findings. All cases were divided into 3 groups based on the combination of histopathological and immunohistochemical findings: ES group, BCOR group and unclassifiable group. There were 49 cases (83.07%) in the ES group, 6 cases (10.16%) in the BCOR group, and 4 cases (6.77%) in the unclassified group. Among these groups, there were 19 cases of Ewing Sarcomas, 3 cases of BCOR and 1 case of CIC::DUX4 whose specific molecular changes were detected by molecular studies.

Conclusion: Molecular methods are the gold standard for appropriately classifying round cell sarcomas. Although immunohistochemical examination has limited contribution to classification, it is very useful in selecting patients to be referred for molecular testing. In our study, the sensitivity and specificity of NKX2.2 in the diagnosis of ES was found to be high, especially when used together with CD99 and FLI-1. For BRSs, the sensitivity and specificity of the BCOR immunostaining in spindle cell tumours with myxoid stroma are quite high.

E-PS-16-012

Symplastic/pseudoanaplastic Giant cell tumour: an uncommon variant of Giant cell tumour of bone

L. Bouzidi*, S. Graja, M. Zghal, S. Makni, C. Chaari, M. Triki, N. Gouiaa, T. Sellami Boudawara, M. Bouhamed
*Department of Pathology, Habib Bourguiba University Hospital, Sfax, Tunisia

Background & objectives: Giant cell tumour of bone (GCTB) is considered as a benign but locally aggressive tumour. It often occurs in long bones. Symplastic/pseudoanaplastic GCTB is an uncommon variant of conventional GCTB. The diagnosis of this entity could be challenging.
Methods: A 19-year-old Women was presented to the department of orthopedic surgery with gradually increasing pain in the left humerus.
Results: On clinical examination, there was a diffuse swelling of the left humerus, with limited range of movements. Conventional radiography revealed a well delimited lytic lesion. Curettage of the lesion was performed. The histological examination revealed a highly cellular lesion composed of pleomorphic mononuclear cells admixed with osteoclast-like giant cells without atypia. Mitoses were numerous (25M/HMF). Foci of necrosis were identified without osteogenesis. Immunohistochemical study was performed to help make the diagnosis. Mononuclear cells were positive for G34W and SATB2. The diagnosis of symplastic/pseudoanaplastic GCTB was retained. Adjuvant treatment with denosumab was indicated.
Conclusion: Symplastic/pseudoanaplastic GCTB is exceptional. It shows similarities with giant cell-rich osteosarcoma and sarcomatous transformation of GCTB making the diagnosis challenging. The use of immunohistochemical study and molecular analysis is helpful. In fact, mutation in H3F3A (G34W) is specific of GCTB and have been described in approximately 92 % of GCTB. Conventional treatment of GCTB is curettage or en bloc resection. Recent studies report the role of Denosumab (monoclonal antibody) which restrain the osteoclastic activity and can produce 90% tumour osteonecrosis.

E-PS-16-013

Cutaneous mesenchymal neoplasm with ALK gene rearrangement in children: study of two cases and review of the literature

F. Cappello*, L. Santoro, E. Bellan, C. Borga, L. Favero, M. Sbaraglia, A.P. Dei Tos
*Italy

Background & objectives: Recently, a series of mesenchymal cutaneous neoplasms with ALK gene rearrangements has been described to arise in adults. However, their diagnosis is challenging and behaviour is poorly understood. In addition, in the paediatric population, these entities are not well recognized.
Methods: Two cases of cutaneous mesenchymal neoplasm with ALK fusions occurring in paediatric patients were retrieved from the archives of our institution. Clinical information for both cases was obtained. Immunohistochemistry for ALK and for different melanocytic, neural, epithelial, smooth muscular, vascular and histiocytic markers was performed. Tumour samples were also analysed by targeted RNA-sequencing approach to confirm ALK gene rearrangements.
Results: The first case was a polypoid cutaneous lesion in the upper back of a 10-year-old boy. The second case was a cutaneous nodule in the right pectoral region of a 2-year-old boy. They were both well-circumscribed neoplasms consisting of a cellular proliferation of spindled and epithelioid cells arranged in bundles and fascicles. Both lesions were characterized by a rich network of thin-walled vessels. These lesions were diffusely positive for ALK, and were negative for pancytokeratin, S100 protein, CD34, SMA, desmin and CD68. The second case was positive for EMA. Molecular analysis revealed CLIP2::ALK and DCTN1::ALK fusion, respectively. Both patients show no evidence of disease more than 3 years after diagnosis.
Conclusion: We presented two unusual cases of cutaneous mesenchymal neoplasms with ALK rearrangements occurring in children. The two fusion genes were previously described in soft tissue inflammatory myofibroblastic tumour, epithelioid fibrous histiocytoma and non-neural granular cell tumour of the skin. However, the morphologic features we reported did not fulfill the criteria of aforementioned entities, supporting the idea that these cases may represent a new entity. To better understand this group of lesions it is necessary to collect more cases.

E-PS-16-014

Immunoglobulin G4-related disease presented as a retroperitoneal mass: report of a rare entity and review of the literature

S. Charfi*, S. Makni, S. Graja, O. Boudaouara, M. Miled, T. Sellami Boudawara, M. Mellouli
*Department of Pathology, Habib Bourguiba University Hospital, Sfax, Tunisia

Background & objectives: Immunoglobulin G4-related disease (IgG4-RD) is considered a non-malignant fibroinflammatory disease characterized by the presence of a dense lymphoplasmacytic infiltration, rich in IgG4-positive plasma cells. It can occur in many organs; however, autoimmune pancreatitis is the common manifestation.
Methods: A 70-year-old man presented to the Urology Department with lower back pain. The patient had a history of myeloma treated with autologous hematopoietic stem cell transplantation in 2017, actually in remission. A computed tomography (CT) scan performed demonstrated a retro-peritoneal cystic mass encasing the ureter. Surgical excision of the cystic mass was performed.
Results: On gross examination, the cystic mass measured 5.8x5 cm, and dissection showed a gelatinous and haemorrhagic content. Histologically, the cyst wall showed a storiform fibrosis associated with lymphocytic and plasmocytic infiltrate. Obliterative endophlebitis and rare eosinophils were identified. Immunohistochemistry revealed positive cytoplasmic staining for IgG4 with approximately 34 cells/high power field in the hot spot area. Based on these findings, the diagnosis of IgG4-RD was retained. The postoperative period was uneventful without recurrence in 9 months of the follow-up period.
Conclusion: IgG4-RD is a rare fibro-inflammatory disease that affects many organs such as the pancreas, biliary tract, lymph nodes and retroperitoneum. It is characterized by elevated serum IgG4 concentrations. Pathogenesis of IgG4-RD still underrecognized. The diagnosis is based on the association of clinical, serological, and pathological criteria including lymphoplasmacytic infiltrate, storiform fibrosis, obliterative endophlebitis, and mild to moderate eosinophilia. Prompt recognition of this disease allows for early diagnosis and treatment. Therapy is based on glucocorticoids and immunosuppressive.

E-PS-16-015

Primary splenic angiosarcoma

V. Chonov*, G. Trenova, D. Bozhkova
*Bulgaria

Background & objectives: Primary splenic angiosarcoma is one of the rarest malignancies and accounts for 2.6% of all soft tissue angiosarcomas. We present the case of a 19-year-old woman with a splenic tumour and complaints of pains in the upper left abdomen.
Methods: Imaging studies - CT of the chest, abdomen and small pelvis - do not show any other pathological abnormalities, except for the presence of spenomegaly with a hypodense formation in the upper pole of the spleen . After splenectomy, macroscopically, a spleen was found with a poorly demarcated dark red-brown tumour formation measuring 10/9.5/6 cm with multiple necrotic fields.
Results: The histological finding showed areas of necrosis and areas of drained spindle cells with marked cellular and nuclear polymorphism and pathological mitoses arranged in nests or forming slit-like vascular spaces. From the performed immunohistochemical study, it was established that the tumour cells express CD34 and Factor VIII and are negative for CKAE1/AE3, and the proliferative index is a lot high – Ki 67 -80%. On the basis of the histological appearance of the tumour and the immunohistochemical profile, primary splenic angiosarcoma is accepted for diagnosis.
Conclusion: Primary splenic angiosarcoma is rapidly proliferative neoplasia with a high rate of metastasis, despite its insidious, often asymptomatic presentation. The diagnosis is challenging and is made only after splenectomy. Treatment involves surgical removal of the spleen followed by chemotherapy. Ideally, it should be performed before splenic rupture, with a direct impact on survival.

E-PS-16-016
A rare case of follicular thyroid carcinoma metastasis to the sacral region: a case report with literature review
A. Dahmane*, F. Gargouri, K. Tlili, N. Mansouri, C. Louati, I. Msakni
*Tunisia

Background & objectives: Follicular thyroid carcinoma (FTC) is the second most common form of thyroid cancer after papillary thyroid carcinoma. Distant metastases most commonly occur in the bones and lungs, with metastases to the sacral region being extremely rare.
Methods: In this case report, we describe an extremely rare case of occult follicular thyroid carcinoma that was diagnosed as hematogenous metastasis to the sacral region and treated at our institution.
Results: The 77-year-old female patient, who underwent thyroidectomy 52 years ago and parathyroidectomy 8 years ago, presented with bilateral, predominantly right-sided lumbosclerotic pain. Simultaneously, she reported increasing heaviness in the right lower extremity, intermittent urinary incontinence, and constipation. Physical examination revealed a palpable, solid mass 3 cm in length that was non-mobile and located at S1, with no signs of inflammation. Magnetic resonance imaging of the spine revealed secondary tissue lesions, specifically a bilateral iliac-lumbosacral lesion centered in S1 with central canal invasion. Biopsy of the sacral mass revealed a differentiated adenocarcinoma with vesicular architecture. Immunohistochemical analysis also revealed the presence of metastases of a follicular thyroid neoplasm.
Conclusion: Bone metastases from FTC after thyroidectomy are rare and often indicate advanced disease. FTC metastases in the sacrum and spine, which present as single foci with neurological symptoms, are rarely documented. Tailored treatment plans that take into account individual patient factors and disease specifics are crucial for reducing the risk of recurrence. A multidisciplinary approach involving oncologists, endocrinologists and surgeons may be required for comprehensive treatment of such cases.

E-PS-16-017
Osteosarcoma of the jaw in a teenager – report of a case
B. Dantas Martins*, R. Cabrera
*Instituto Português de Oncologia de Lisboa Francisco Gentil, Portugal

Background & objectives: Osteosarcoma of the jaw is rare and occurs in patients 10–20 years older than those with tumours arising in other sites. We describe a case developing in a young adult, that was treated with multimodal therapy.
Methods: A previously healthy 18-year-old female presented with swelling and pain in the mandible, two weeks after a tooth extraction. Imaging studies revealed a rapidly growing 7 cm destructive bone lesion. Core biopsy showed a chondroblastic conventional osteosarcoma. Segmental mandibulectomy was performed after 3 cycles of doxorubicin and cisplatin chemotherapy.
Results: On gross examination, a 7 cm bony intraosseous mass was observed. Histologically, a partial response was obtained. Chemotherapy-related changes included a framework of acellular tumour osteoid, necrosis and approximately 20% of viable tumour cells. Chondroblastic areas were sparse. Surgical margins were free of disease. Seven months after the onset of symptoms, the patient is recovering well, with no evidence of disease.
Conclusion: Complete surgical excision is the treatment of choice, and the role of neoadjuvant chemotherapy is controversial. In this case, however, it may have aided to obtain clear surgical margins. Neoadjuvant chemotherapy may help local control, decrease the rate of distant metastases, and improve disease-specific survival.

E-PS-16-018
Inguinal lymphadenopathy - a frequent manifestation of a rare primary mesenchymal tumour
S. Despotovic*, L. Simić, M. Mihajlović, S. Rajkovic, G. Đuričić, J. Sopta
*Faculty of Medicine, University of Belgrade, Serbia

Background & objectives: Intranodal palisaded myofibroblastoma (IPM) is a very rare benign mesenchymal tumour of the (most commonly, inguinal) lymph nodes. The definite cells of origin are still unknown, but intranodal smooth muscle cells or myofibroblasts are the most suitable candidates.
Methods: We report a series of three patients, two female, 64 and 56 years old, one male patient, 59 years old, all presented with a painless mass in the inguinal region. Blood examination was within normal range and ultrasound and MRI imaging described calcified/necrotic enlarged lymph node, with suggestion for excision and pathohistological analysis.
Results: On the microscopic examination all three tumours appeared as relatively monotonous proliferation of spindle cells forming short fascicles, with focal nuclear palisading and amianthoid fibers (highlighted with Masson trichrome and elastic stain). All three tumours had regions of hyalinized and myxocollagenous matrix and extravasated red blood cells. The tumour cells were positive for alphaSMA, HHF-35 and cyclin-D1 [MOU2]and negative for desmin, S100, CK AE1/AE3, EMA, GFAP, NF and CD34. Ki67 showed range of nuclear positivity in tumour cells, from 3% to 10% in our cases.
Conclusion: IPM is rare, but important to recognize, benign tumour of lymph node, and should be considered in the differential diagnosis of localized (dominantly inguinal) lymphadenopathy. Smooth muscle cells/myofibroblastic origin, Cyclin-D1 positivity and predilection for inguinal lymph nodes, make this tumour interesting from the pathogenetic point of view and reporting and investigating new cases might shed light on still unresolve features of this entity.

E-PS-16-019
Challenging presentations of synovial sarcomas: shedding light on the uncommon
A.P. Diazgranados Daza*, T. Silva, I. Colmenero, G. Tapia, J.F. Chabla Jaramillo, M. Sesé, J. Hernandez-Losa, S. Ramon y Cajal Agüeras, C. Romagosa
*Vall d'Hebron University Hospital, Barcelona, Spain

Background & objectives: Synovial sarcoma (SS) is an aggressive mesenchymal neoplasm and its conventional diagnostic involves the well-known histological patterns (monophasic/biphasic/poorly-differentiated), with cytokeratin expression and SS18 rearrangement evidence. We present three cases of atypical SSs due to unusual morphology, immunophenotype and molecular features.
Methods: A review of three cases of unusual forms of SSs was performed. Haematoxylin and Eosin-stained slides, immunohistochemically stained slides for CK (AE1/AE3), EMA, SS18-SSX1/2, SS18 break-apart FISH probe, and NGS Archer Fusion Plex Sarcoma v2 were analysed in all cases.
Results: The median age of the patients was 29.3 years old. Tumour location was mainly in the deep soft tissue of the lower extremities and upper trunk. Histologically, the first case showed an epithelioid/small cell proliferation arranged in a pseudo vascular/alveolar pattern; the second and third cases presented a spindle monophasic arrangement with high-grade to poorly differentiated features. All cases showed positive expression for CK (AE1/AE3) and EMA, two cases showed positivity for SS18-SSX1/2 except case 2. Cases 1 and 2 presented SS18 FISH translocation, while case 3 was negative. All cases showed the SS18-SSX2 fusion gene after NGS analysis.
Conclusion: Our cases on atypical presentations of SS shows unusual morphological, immunophenotype, and molecular features. We consider it relevant to include SS as a differential diagnosis when faced with pseudo-vascular/alveolar patterns. Even in cases with more typical morphology of SS, there is a possibility of finding negative results in either IHC or FISH techniques due to cryptic or complex rearrangement. We highlight the importance of identifying these uncommon presentations that may lead us to a misdiagnosis in atypical forms of SS.

E-PS-16-020
Extrapulmonary inflammatory myofibroblastic tumour: a case series
R. Doghri*, S. Elfekih, A. Khemir, H. Arbi, I. Sassi, N. Baccar, N. Boujelbene, L. Charfi, G. Sahraoui, K. Mrad
*Pathology Department, Salah Azaiez Institute, Tunisia

Background & objectives: Inflammatory myofibroblastic tumour (IMT) is a rare condition mainly reported in the lungs. Its occurrence in other anatomic locations is extremely rare. This study aimed to investigate the clinical and pathological characteristics of extra-pulmonary IMT.
Methods: It was a retrospective study collecting cases of extra-pulmonary IMT by searching the pathology department database. All pathological and clinical data were reviewed.
Results: Twelve cases were collected over a 19-year period. Six patients (50%) were male and 6 were female (50%). Mean age was 22,3 years. The main locations where IMT has developed were as follows:abdominal in 5 cases, orbital in 3 cases, urinarybladder in one case, coccyx in one case, subcutaneous in one case and thenar eminence in one case. They demonstrated common microscopic features: fascicles of spindle cells along with an inflammatory infiltrate without atypia nor mitosis. Tumour cells were either desmin or smooth muscle actin positive in all cases. Anaplastic lymphoma kinase was tested in 7 cases with a positivity in only one case.
Conclusion: Extrapulmonary IMT is uncommon, typically diagnosed through exclusion during histopathological examination. Thus, confirmation of the diagnosis and assessment of ALK expression status often requires performing immunohistochemistry to assess ALK expression status alongside other markers.

E-PS-16-021
Understanding histological organ involvement in retroperitoneal sarcomas: implications for recurrence risk
L. Dore*, L.M. Cenzi, Ö. Mintemur, L. Samà, V. D'amato, F. Sicoli, P.G. Colombo, A. Bonometti, A. Bertuzzi, P. Navarria, F. Cananzi, S. Renne
*Department of Biomedical Sciences, Humanitas University, Milan, Italy; Department of Pathology, IRCCS Humanitas Research Hospital, Milan, Italy

Background & objectives: Retroperitoneal sarcomas are rare and aggressive tumours, often recurring locally despite extensive surgery. Understanding the factors contributing to this aggressiveness is essential for improving patient outcomes. We aimed to identify prognostic factors for local recurrence in retroperitoneal sarcomas.
Methods: We analysed data from a prospectively maintained database, including 191 patients with surgery for primary sarcom: 85 cases of dedifferentiated liposarcoma, 59 well-differentiated liposarcoma, and 47 leiomyosarcoma. Clinical, surgical, neoadjuvant therapies, and histological data were recorded, with a focus on the extent of histological organ involvement (HOI).
Results: Median age was 63 years(range: 22-90); 99/191(51.83%) were male. Median tumour size was 19 cm(range: 3.5-60); the most resected organ was kidney (68.59%). 68 (36.76%) were grade 1, 63 (34.05%) as grade 2 and 54 (29.19%) as grade 3. Preoperative therapy was performed in 55 (29.80%), with radiotherapy in 15 (7.85%), chemotherapy in 25 (13.09%) and combined chemo-radiotherapy in 15 (7.85%). HOI was classified into four degrees (absent, perivisceral, initial, advanced). the majority of tumours had an advanced HOI; those with initial/advanced involvement were larger; most of the neoadjuvated cases had more frequently advanced HOI than those who didn't receive it. We finally built a tool to predict local recurrence.
Conclusion: Histological organ involvement (HOI) may serve as a prognostic indicator for local recurrence in retroperitoneal sarcomas. Our multidisciplinary approach identified key factors influencing recurrence risk, paving the way for personalized management strategies. Despite the challenges posed by these rare and aggressive tumours, our study offers insights to optimize patient care.

E-PS-16-022
Pleomorphic hyalinizing angiectatic tumour of the foot - case report
L. Dragostin*, A. Coman, M. Cioplea, L. Sticlaru, S. Zurac
*Department of Pathology, Colentina University Hospital, Bucharest, Romania

Background & objectives: Pleomorphic hyalinizing angiectatic tumour (PHAT) is a very rare tumour of the soft tissue of unknown origin, non-metastasizing but locally invasive with a high risk of recurrence.
Methods: We present the case of a 62 year old male with a clinical palpable painless mass located on the dorsal site of the left foot. Upon physical examination, the mass presented as a soft lesion and due to the infiltrative nature in the surrounding tissue, the tumour couldn't be completely excised, therefore fragments were sent in for histopathological examination.
Results: Gross examination revealed three tissue fragments resembling adipose tissue with minimal congestion. Cut section showed homogenous adipose tissue-like appearance with focal white-grayish zones. Microscopic examination revealed a proliferation of spindle cells with moderate nuclear pleomorphism, occasional nuclear pseudoinclusions and intracytoplasmic haemosiderin deposits, arranged in fascicles or sheets, entrapping bundles of ectatic small/medium sized blood vessels, with thin walls surrounded by a thick rim of amorphous eosinophilic material. Immunohistochemical studies were performed in support of the diagnosis, the tumour showing CD34 positivity and S100, AE1/AE3, SMA and desmin negativity, with an extremely low Ki-67 index (1%).
Conclusion: The tumour shares several features with schwannomas and hemosiderotic fibrolipomatous tumours, which were considered for differential diagnosis. Due to the rare nature of this entity, with only around 100 cases reported in medical literature, it is still an important pathology to be taken into consideration.

E-PS-16-023

An unusual case of kaposiform hemangioendothelioma incidentally discovered within florid lymphangioma-like changes: a case report

S.K. Dursun*, F.M. Doğukan
*Basaksehir Cam ve Sakura City Hospital, Department of Pathology, Turkey

Background & objectives: Kaposiform hemangioendothelioma (KHE) is a rare, locally aggressive vascular tumour that presents at an early age. It is clinically associated with Kasabach-Merritt syndrome (KMS). We present an unusual case of KHE incidentally discovered within a background of florid lymphangioma-like changes.
Methods: A 2-year-old male presented with persistent abdominal distention for 6 months. Imaging revealed a multiseptated, multiloculated cystic mass filling the abdomen and followed by a subsequent resection.
Results: A multicystic mass measuring 28x17.5x3 cm composed of cysts with clear fluid was seen on gross examination. On microscopic examination, there were numerous cystic spaces which were bordered by a single layer of endothelial cells and a lymphocytic infiltrate. Small nodules of spindled cells were present between the dilated lymphatic spaces. Immunohistochemical staining was positive for D2-40 and CD31 in both spindle cell clusters and lymphatic endothelium and for CD34 and SMA in spindle cell areas. The Ki-67 proliferation index was 10-15%. No staining for Glut-1 and HHV8 was observed. The diagnosis was confirmed to be "microscopic KHE foci in a background of florid lymphangioma-like changes".
Conclusion: Kaposiform hemangioendothelioma is a rare and locally aggressive vascular tumour primarily affecting children. Approximately half of KHE cases can lead to KMS, and around two-thirds exhibit associated lymphatic abnormalities. The coexistence of KHE and lymphatic abnormalities remains poorly understood, with various hypotheses proposed. Documentation of KHE cases amidst extensive lymphangioma-like changes, an area with limited literature, is crucial for determining the primary pathogenic event and understanding the causal relationship between these entities.

E-PS-16-024

Giant cell fibroblastoma: a diagnostic challenge

N. Ellouze*, M. Njima, A. Ben Mabrouk, S. Mabrouk, A. Bellalah, L. Njim
*Tunisia

Background & objectives: Giant cell fibroblastoma (GCF) is a rare mesenchymal tumour of intermediate malignancy occurring mainly in children. It belongs to the dermatofibrosarcoma spectrum. Herein, we report a case of this entity in order to avoid misdiagnosis and discuss the differential diagnosis.
Methods: We report a case of GCF in a 5-year-old infant who was presented with a painless presacral mass with no other associated signs. Doppler ultrasound revealed a subcutaneous mass with heterogenous echostructure. The mass was doppler vascularised. On MRI exam, the diagnosis suspected was a desmoid tumour or a fibrosarcomatous tumour. Then, the patient underwent total excision of the mass.
Results: The grossing examination showed a polypoid nodule measuring 2cm. Histopathology revealed a dermal tumour proliferation formed by fibroblastic cells. The tumour cells are arranged in short bundles, taking on a storiform appearance. These cells are monomorphic spindle-shaped with eosinophilic cytoplasm sometimes charged with melanin pigment. The nuclei are oval with slight atypia and no mitosis. These fibroblastic cells are associated with floret-like multinucleated giant cells which were often surrounding pseudovascular spaces. The tumour infiltrated the hypodermis, with the persistence of a few adipocyte lobules embedded in this proliferation. At the Immunohistochemical study, the cells were positive for the anti-CD34 and negative for the anti-ALK.
Conclusion: GCF is a rare tumour with an intermediate risk of malignancy. It poses diagnostic challenges to the pathologist because it may be confused with malignant mesenchymal tumours with different prognosis such as the infantile fibrosarcoma and the inflammatory myofibroblastic tumour. Thus, a genetic study is sometimes carried out to eliminate differential diagnoses. The treatment of GCF is surgical and the prognosis is favourable. Local recurrence occurs in 50% of cases. No metastases have been reported to date.

E-PS-16-025

Plexiform fibrohistiocytic tumour: a rare case report

N. Ellouze*, S. Mabrouk, A. Ben Mabrouk, S. Ben Hammouda, D. Beltaifa, M. Njima, A. Zakhama
*Tunisia

Background & objectives: Plexiform Fibrohistiocytic Tumour (PFT) is a very rare soft tissue tumour, with a low malignancy potential, that usually affects children and young adults. Its main site of occurrence is the extremities. Herein, we report a case of this tumour.
Methods: A 46-year-old woman without any particular medical history, presented to the orthopaedic surgery department with a painless swelling of the leg with no other associated signs. On clinical examination swelling was mobile and firm in consistency, measuring 4 cm. MRI was consistent with an aggressive tumour. Consequently, the patient underwent total excision of the mass.
Results: On gross examination, the cut surface showed a whitish, poorly circumscribed tumour measuring 4 x 3 cm. On microscopic examination, the tumour was composed of bundles of fibroblastic spindle cells. These bundles are arranged in a plexiform pattern, forming nodules around the periphery. These nodules are separated by extensive hyaline fibrosis. Tumour cells present slight atypia without mitosis. They are mixed with histiocytic cells and a moderate lymphocytic and plasmocytic infiltrate. The tumour infiltrates adipose tissue, striated muscle, and extended to the surgical margins. By immunohistochemistry, spindle cells were positive for SMA, and histiocytic cells were positive for CD68.
Conclusion: PFT exhibit a low grade malignant behaviour, that can be easily misdiagnosed as benign tumour. It may present differential diagnosis with many other tumours both on clinical and histological grounds. They include plexiform neurofibroma, plexiform schwannoma, cellular neurothekeoma, fibrous hamartoma of infancy, deep benign fibrous histiocytoma, benign and malignant soft tissue giant cell tumour, and myofibromatosis. Immunohistochemical study is useful for ruling these differential diagnoses. Treatment mainly relies on local excision with recurrence in 20-30% cases. Distant metastasis is exceptional.

E-PS-16-026

Titanium debris in acetabular cup failures after total hip arthroplasty: histopathological perspectives

S.K. Fokter*, Ž. Ledinek, E. Punzón-Quijorna, I. Novak, A. Moličnik
*University Medical Centre Maribor, Slovenia

Background & objectives: Approximately 1 million total hip arthroplasties (THA) are conducted annually worldwide, primarily employing titanium alloys. This study presents two cases of THA with significant Ti-alloy debris release.
Methods: Two active males (36 and 45 years old) underwent primary THA. Seventeen years (case 1) and 19 months (case 2) post-surgery, revisions were performed due to varying mechanisms of acetabular cup failure.
Results: During revision of the case 1, protrusion of the alumina ceramic head through the Ti-alloy acetabular cup was found. Trace element analysis indicated extremely elevated levels of serum Ti (1237.6 μg/L; norm <6.0 μg/L). In the case 2, the ceramic acetabular

liner was found fractured and the serum Ti level was 223.3 µg/L. Histological analysis of tissue samples of both patients showed wear-induced synovitis with multinucleated foreign-body giant cells. Accumulation of metal wear particles was confirmed by micro Particle Induced X-ray Emission (micro-PIXE).
Conclusion: These cases underscore THA failure complexities due to substantial Ti-alloy debris release. Vigilant monitoring is warranted for potential long-term effects, despite rare adverse events reported with Ti-implants.

E-PS-16-027
Endogenous ochronosis: a case report of an unusual disease
N. Franco*, S. García-Fuertes, C. Cabañuz, D. González-Suárez, J. Ros-Giménez, N. Sanz-Pérez
*Hospital Ernest Lluch, Spain

Background & objectives: Endogenous ochronosis is a rare autosomal recessive disease caused by a deficiency of the enzyme homogentisic acid oxidase. Its low incidence and lack of clinical suspicion explain why most patients already have joint symptoms at diagnosis, mostly irreversible.
Methods: A 68-year-old man, with history of bilateral patellar pathology, is evaluated in our centre with signs of edema, joint effusion, cruciate ligament sprain and fracture of posterior horn of the external meniscus with total destruction of cartilage. Knee arthroscopy was performed with consequent referral of the obtained biopsies to our service.
Results: A left knee patella biopsy was received, as well as fragments of synovium and meniscus. Grossly, thew all showed a generalized dark brown coloration. The synovium and meniscus histological study revealed the presence of islets of pigmented cartilage around which there was a sinovial papillary proliferation with chronic inflammation and gigantocellular foreign body type reaction. Likewise, the bone biopsy demonstrated an extensive brownish pigment deposit, all of which was compatible with a diagnosis of ochronosis.
Conclusion: Ochronosis is an unusual entity with difficult diagnosis due to the absence of clinical suspicion. At joint level, it can cause early arthropathy, known as ochronotic arthropathy, very disabling, with knee joint as the most commonly affected one. Determination of homogentisic acid in urine analysis is pathognomonic of the disease. However, the non-specificity of symptoms in a context of low clinical suspicion, places histological study as a prior tool for confirmatory diagnosis.

E-PS-16-028
Exploring the uncommon: a case of a malignant peripheral nerve sheath tumour infiltrating the adrenal gland
A. Georgiou*, A. Therapontos, P. Vlachou, D. Efthymiou, S. Avgousti, G. Kyriakopoulos
*Department of Pathology, Evaggelismos General Hospital, Athens Greece

Background & objectives: Malignant Peripheral Nerve Sheath Tumours (MPNSTs) are rare, often originating from peripheral nerves. Typically found in the trunk or extremities, adrenal gland localization is uncommon. We present a case of a MPNST infiltrating the adrenal gland in a 32-year-old patient.
Methods: For consultative evaluation we received FFPE tissue blocks from a surgically removed adrenal gland with an infiltrating tumour. Initially we requested hematoxylin/eosin slides and immunohistochemical staining to determine mesenchymal, epithelial or neuroendocrine differentiation and proliferation rate estimation of the Ki-67 index. Further investigations aimed to assess histone H3K27 methylation status and SMARC protein expression. FISH was utilized for supplementary analysis.
Results: The neoplastic tumour predominantly consisted of medium-sized, spindle-shaped cells displaying some epithelioid features, characterized by dark nuclei with fine granular chromatin and amphiphilic cytoplasm. Cells tended to grow uniformly in dense bundles, with visible staghorn vessels and small areas of necrosis. Mitotic index was estimated at approximately 32 mitoses/2mm², consistent with an increased Ki-67 ≈75%. Immunohistochemical investigation revealed no specific cellular differentiation (negative for CK7, CK8,18, Desmin, Myogenin, SOX-10 and S-100 among others.). Notably, complete loss of H3K27me3 status was indicated. FISH analysis was negative for mdm2 gene amplification as well as for translocations of SS18 and EWSR1 genes translocation.
Conclusion: The morphological, immunohistochemical and molecular findings suggested the diagnosis of MPNST. Adrenal localization of MPNST is exceedingly rare, with only a few reported cases worldwide, most usually associated with pheochromocytoma and ganglioneuroma, or in the context of neurofibromatosis 1 (NF-1). The rarity of such cases underscores the importance of reporting them to enhance awareness among clinicians and pathologists, facilitating timely diagnosis and management.

E-PS-16-029
Angiomatoid fibrous histiocytoma in the hand: a rare clinical presentation and diagnostic challenge
J. Ichikawa*, T. Kawasaki, H. Imada, S. Kanno, M. Wako, T. Fujimaki, S. Ochiai, H. Haro
*University of Yamanashi, Japan

Background & objectives: Angiomatoid fibrous histiocytoma (AFH), a rare soft tissue neoplasm, rarely involves the hand. Diagnosis can be difficult, even with histopathology, because specific immunohistochemistry (IHC) markers are lacking. We present a diagnostically challenging case of AFH in a rare location.
Methods: A 59-year-old woman presented with a mass between her right middle and ring fingers. Magnetic resonance imaging revealed, respectively, low- and high-intensity signals on T1- and T2-weighted images with homogeneous enhancement. An open biopsy suggested nodular fasciitis or an inflammatory myofibroblastic tumour. Therefore, we recommended surgery several times but she refused. After 6 years, she accepted surgical treatment.
Results: A marginal resection was performed. Histopathologically, the tumour was surrounded by foci of lymphoplasmacytic cuffs and a hyalinized collagen fibrous pseudocapsule, whereas pseudoangiomatous spaces were not identified. Heterogeneous spindle mesenchymal cells showing nuclear atypia in the background of edematous or collagenous fibrous stroma, but lacking mitotic activity, proliferated alongside large pleomorphic cells intermingled with some storiform to irregular multinodular forms. IHC indicated that the tumour was weakly positive for CD99, focally and slightly positive for EMA, and negative for ALK, CD68, AE1/AE3, CD34, desmin, and SMA. FISH showed a positive EWSR1 split signal. The final diagnosis was AFH. There was no recurrence at the 1-year follow-up.
Conclusion: To our knowledge, there are only 7 reported cases of AFH involving the hand or fingers. AFH has a wide morphological spectrum from myxoid to fibrous components. Lack of specific immunophenotypic markers can lead to misdiagnosis, as in our case. Advantages of FISH for detecting EWSR1-CREB1, EWSR1-ATF1, and FUS-ATF1 have recently been reported. Recurrence rates range from 10–20%, metastasis less than 5%, and mortality below 1%. Careful follow-up is essential, especially for marginal resection cases such as ours.

E-PS-16-030

Chondroblastoma with secondary aneurysmal bone cyst: rare capitate involvement and diagnostic pitfalls with magnetic resonance imaging

J. Ichikawa*, T. Kawasaki, M. Wako, N. Taniguchi, S. Ochiai, H. Haro
*University of Yamanashi, Japan

Background & objectives: Chondroblastoma typically arises in long bone epiphyses. Chondroblastoma sometimes occurs with secondary aneurysmal bone cyst (ABC) formation, leading to difficulty in differential diagnosis. We report a challenging case of chondroblastoma, with a rare location, and describe diagnostic pitfalls of MRI.
Methods: A 33-year-old man, with right-wrist pain and swelling for 3 years, showed radiolucency within the capitate but no calcification on radiography and computed tomography. MRI revealed a homogeneous signal with low intensity on T1- and high intensity on T2-weighed images without fluid levels. There was weak peripheral enhancement on gadolinium-enhanced T1. Difficulty in differential diagnosis by imaging necessitated incisional biopsy.
Results: Incisional biopsy suggested benign cystic tumours. Tumour resection was followed by bone grafting. Histopathologically, the tumour revealed mononuclear tumour cells (chondroblasts) in a solid growth pattern, with polygonal, somewhat eosinophilic cytoplasm and round to ovoid, indented, or lobulated nuclei and evenly distributed chromatin. Cartilaginous matrix showed ossification and there was also focal calcification. Tumour cells were accompanied by randomly distributed osteoclast-like multinucleated giant cells. Haemorrhagic findings included hemosiderin pigmentation and cystic formation. Immunohistochemically, H3.3 p.Lys36Met (K36M) showed diffuse nuclear expression on tumour cells, with positivity for S-100, cytokeratin AE1/AE3 and/or DOG1. The final diagnosis was chondroblastoma with secondary ABC change. The patient remains free of recurrence two years postoperatively.
Conclusion: There have been only 2 reported cases of chondroblastoma involving the capitate. This is the first report of chondroblastoma with secondary ABC involving the capitate. These changes in chondroblastoma often make differential diagnosis between cystic tumours, including ABC and giant cell tumour, difficult suggesting histopathological findings to be essential. The usefulness of H3K36M on immunohistochemistry was recently reported. The reported recurrence rates range from 10-32% and some cases have developed metastasis. Careful follow-up is essential.

E-PS-16-031

Primary synovial sarcoma of the bone - characteristics and the development of a diagnostic tool

J. Ichikawa*, T. Kawasaki, H. Imada, S. Kanno, N. Taniguchi, T. Ashizawa, S. Ochiai, H. Haro
*University of Yamanashi, Japan

Background & objectives: Synovial sarcoma (SS) is a spindle cell sarcoma with variable epithelial differentiation, defined by the SS18::SSX1/2/4 fusion gene, frequently occurring in deep soft tissue of the extremities. This is the first report of primary SS originating from the metacarpal bone.
Methods: A 47-year-old man had right third metacarpal bone pain and swelling. Radiography and computed tomography (CT) revealed third metacarpal disappearance with reticular calcification and no periosteal reaction. Magnetic resonance imaging (MRI) revealed signal iso-intensity on T1-, moderately high heterogeneous signal intensity on T2- and weak heterogeneous enhancement on gadolinium-enhanced T1-weighted images. Difficulty in differential diagnosis by imaging necessitated incisional biopsy.
Results: Incisional biopsy suggested SS of the bone. We amputated the middle finger and reconstructed the interdigital space with osteotomy of the capitate. Histopathologically, the tumour revealed a biphasic pattern with epithelial and spindle cell components and remaining bone surrounding tumours. Immunohistochemistry (IHC) indicated positivity for SS18:SSX, SSX, cytokeratin AE1/AE3, EMA, CAM5.2, vimentin, bcl-2, and CD99/MIC-2 and negativity for desmin and CD34. Fluorescence in situ hybridization (FISH) showed a positive SS18 split signal. The final diagnosis was SS of bone. Adjuvant chemotherapy was administered. The patient remains free of recurrence two years postoperatively.
Conclusion: The age, sex predominance, and histological type characteristics were similar between SS in bone and the extremities. Confirmation of the fusion gene using FISH is crucial for precise diagnosis of SS. However, decalcification can produce a weak fluorescence signal in FISH. The development of SS18::SSX and SSX antibodies in IHC was recently reported. The positivity and specificity for these antibodies were so high that they compensated for the limitations of FISH.

E-PS-16-032

Synovial chondromatosis: rare metacarpophalangeal joint involvement and diagnostic challenges with magnetic resonance imaging

J. Ichikawa*, T. Kawasaki, H. Imada, K. Onohara, S. Kanno, M. Wako, N. Taniguchi, S. Ochiai, H. Haro
*University of Yamanashi, Japan

Background & objectives: Synovial chondromatosis (SC) involving the hands is rare. Characteristic computed tomography (CT) and magnetic resonance imaging (MRI) findings are diagnostically useful. We report a challenging case of SC with a rare location and the diagnostic pitfalls of MRI.
Methods: A 44-year-old man had discomfort in the metacarpophalangeal (MP) joint, right little finger, for eight years. Plain radiography and CT showed no MP joint calcification. MRI revealed a low-intensity signal on T1-weighted images and a low-intensity signal with focal high signals on STIR. Based on clinical and imaging findings, we suspected a tenosynovial giant cell tumour (TSGCT) and planned surgery.
Results: Surgery was performed using both a dorsal and a palmar approach. We easily identified the capsule. The joint capsule was opened and the presence of white loose bodies was confirmed. Macroscopically, the tumour was hard and white in color. The histopathological findings showed that the tumour consisted of multilobulated hyaline cartilage with enlarged nuclei and binucleated cells. Approximately 70% of the tumour consisted of hyaline cartilage with proteoglycans, whereas the remaining 30% consisted of fibrous tissue, as demonstrated by Elastica Van Gieson staining. Therefore, the final diagnosis was SC with fibrosis. The patient remained recurrence-free one year postoperatively.
Conclusion: To date, only nine cases of SC involving MP joints have been reported. Calcification was observed on CT in 70–95% of cases and the most frequent pattern, about 75%, on MRI was high intensity on STIR. Absence of these characteristic findings resulted in preoperative misdiagnosis. In general, low intensity on STIR indicates calcification but can also represent fibrosis in SC. In our case, diagnosing SC by MRI was limited, highlighting the importance of histopathological findings for accurately diagnosing SC.

E-PS-16-033

Sarcoma with BCOR genetic alterations: a clinicopathological study of six cases

O. Jaber*, M. Sughayer, W. Naser, I. Sultan, H. Halalsheh, S. Abdel Al, A. Shehadeh, O. Albtoush, Y. Saleh, S. Yaser
*Department of Pathology and Laboratory Medicine, King Hussein Cancer Center, Jordan

Background & objectives: Sarcoma with BCOR genetic alterations includes sarcoma with BCOR gene fusion and sarcoma with BCOR

internal tandem duplication (BCOR-ITD). Herein, we report the clinical and pathological characteristics of six cases, marking the first study from the Middle East.
Methods: Pathology files were searched for "sarcoma with BCOR" from 2012 to 2023. Six cases were found. Four were referred to our centre diagnosed as synovial (n=3) and Ewing (n=1) sarcomas. Pathological and molecular features (available for 4 patients) were studied. The patients were treated with Ewing sarcoma protocol. Follow up (11 months to 11 years) was available for 5 patients.
Results: Cases included 4 males and 2 females, of 1-22 year old (median 13.5), 4 in soft tissue and 2 in bone. Tumours ranged from 2.4 to 18.2 cm (mean 12.3 cm) and showed monomorphic round to short spindled cells in a variably myxoid background with rich capillary network. One case had hemangiopericytoma-like vessels. Mitoses ranged from 0 to 20/10 HPFs (mean 5.8). Necrosis was present in two cases, of which one had higher nuclear grade. Positive IHC included BCOR (n=5), CD99 (n=5), SATB2(N=5), TLE-1(n=5) and PanTRK (n=1). Two cases had BCOR::CCNB3 fusion and 2 had BCOR-ITD. Following therapy, none had recurrences and one showed complete pathological response to neoadjuvant chemotherapy.
Conclusion: At our centre, sarcoma with BCOR genetic alterations are rare. Similar to reported literature, predominance in males and younger age was noted. They can involve bone or soft tissue. They show a monomorphic round to spindled cell morphology in a rich capillary background and are diffusely positive for BCOR. Rarely, PanTRK immunostain is positive. They are often misdiagnosed and need expertise and advanced diagnostic tools. Those sarcomas, likely, have more favourable prognosis compared to clinical outcomes reported for Ewing sarcoma.

E-PS-16-034
Mesenteric cystic lymphangioma: case report
H. Kandemir*
*Health Sciences University Izmir, Turkey

Background & objectives: Mesenteric cystic lymphangiomas (ML) are congenital malformations.ML most commonly originates from the small intestine. Clinically, they can present with acute or chronic abdominal pain. Cystic lymphangiomas consist of lymphatic spaces of varying sizes containing collagen, smooth muscle fibers and lymphoid cell aggregates
Methods: A Case Presentation with Rare Localization for Contribution to the Literature
Results: A 34-year-old female patient presented with complaints of abdominal pain. A cystic lesion measuring 12x6 cm was observed on computed tomography. Biochemical examination revealed normal liver and kidney function tests, as well as normal electrolyte levels. The mass was excised, and during dissection, the cyst ruptured. Upon examination, the material was found to be fragmented, measuring 11x6x2 cm, surrounded by adipose tissue, and containing numerous cystic spaces. Sections revealed a tumour composed of numerous cystic spaces separated by septa containing single-layered flat cells, edema, adipose tissue, and focal lymphocytic aggregates. Immunohistochemical analysis showed that the cells covering the cysts were positive for CD31 and D2-40. The case was diagnosed as Mesenteric cystic lymphangioma
Conclusion: Mesenteric cystic lymphangiomas (ML)are congenital malformations.ML most commonly originates from the small intestine and is rare in adulthood. Clinically, they are often asymptomatic but can present with acute or chronic abdominal pain, abdominal swelling, or palpable masses. Cystic lymphangiomas consist of lymphatic spaces of varying sizes containing collagen, smooth muscle fibers, and lymphoid cell aggregates, unrelated to the adjacent normal lymphatic system. Radiological imaging can be useful in distinguishing between malignant and benign lesions, while the definitive diagnosis is made through pathological examination.

E-PS-16-035
Keratin-positive giant cell-rich tumour of soft tissue - a case report
S. Kaymaz*, G.H. Cavus, A. Namal, A.M.Ö. Men, N. Çomunoğlu, Ş. Batur
*Istanbul University-Cerrahpasa Medicine School Department of Pathology, Turkey

Background & objectives: Giant cell tumour of soft tissue is a rare neoplasm. It is composed of mononuclear cells and osteoclast-like multinucleated giant cells. A mesenchymal tumour resembling this tumour morphologically but showing keratin positivity was recently reported as some case reports.
Methods: A 34 year old woman presented with chest pain. After the initial physical examination a chest X-ray and a subsequent chest CT was performed. CT showed a 48x43x40 mm mediastinal mass that expands and destructs the 2nd costa. The patient was admitted to surgery and the mass was excised.
Results: In the macroscopical examination a 7x4,5x4 cm tumoural mass was seen. It appeared to have a lobulated architecture and irregular margins. The microscopical examination showed a mesenchymal tumour that is composed of mononuclear cells with round to oval nuclei, foamy macrophages and osteoclast-like giant cells in a richly vascularised stroma. Large areas of cholesterol clefts inside the tumour were also seen. In the immunohistochemical examination; the mesothelial markers like Calretinin, D240, WT1, BerEP4 were negative. The markers for mesenchymal tumours like Desmin, SMA, CD34 were also negative. The mononuclear cells showed cytoplasmic positivity with CK7 and OSCAR CK. We demonstrated HMGA2::NCOR2 fusion with NGS.
Conclusion: A giant cell-rich mesenchymal neoplasm with morphological features that resembles giant-cell tumour of soft tissue but distinctively shows female predominance, keratin expression was recently reported as case reports and series in the literature.These tumours harbor HMGA2::NCOR2 fusion, which we demonstrated in our case with NGS.There are fewer than 30 cases of these tumours reported in the literature so far. Due to the rarity and diagnostic difficulty of these tumours, we present our case hoping it will contribute to the literature.

E-PS-16-036
Bone and soft tissue sarcomas: experience from the pathological anatomy laboratory, Mohammed VI University Hospital, Tangier, Morocco
J. Kharmoum*, M. Eljiar, I. Eliahiai, S. Chaib, K. Morabit, O. Faraji, Z. Ayoubi, G. Erradi, S. Alaoui Rachidi, M. Shimi, M. Chraïbi
*Pathology Department, Mohammed VI University Hospital, Tangier and Faculty of Medicine and Pharmacy, University Abdelmalek Essaâdi, Tetouan, Morocco

Background & objectives: Soft tissue and bone sarcomas are rare malignant tumours encompassing highly heterogeneous histological subtypes, posing diagnostic challenges. This is a descriptive and analytical study aiming to specify the epidemiological and histopathological characteristics of these sarcomas.
Methods: This prospective study was conducted from the laboratory's inception (July 2020) until January 2024. It includes cases of bone and soft tissue sarcomas collected at the pathological anatomy department of Mohammed VI University Hospital in Tangier.
Results: 35 patients were included in our study, with ages ranging from 7 to 84 years. 62.9% were male. Biopsy specimens accounted for 74.3% of samples, while 25.7% were surgical specimens. We analysed 54.3% of bone sarcomas and 45.7% of soft tissue sarcomas. Histological diagnosis revealed osteosarcoma as the most common bone sarcoma (63.2%), while liposarcoma was the most frequent soft tissue sarcoma (18.8%), followed by rhabdomyosarcoma (12.5%). The radiological

correlation was necessary in 52.6% of bone sarcomas. Discussion of cases with an external pathologist was conducted in 42.9% of cases.
Conclusion: Our study aims to thoroughly analyse the epidemiological characteristics of sarcomas in the northern region of Morocco. The main challenge faced is the availability of molecular biology techniques, which are crucial for accurate diagnosis and optimal therapeutic management. This underscores the need to establish a network for sarcoma review in Morocco with molecular biology facilities to ensure optimal patient care.

E-PS-16-037
CD34-positive spindle cell tumour with FGFR1::TACC1 fusion: entity of uncertain behaviour
M.A. Krupinska*, R. López Henríquez, J.S. Marrero Afonso, C.N. Hernández León
*Hospital Universitario de Canarias, Spain

Background & objectives: The fusion gene FGFR1::TACC1 has been previously identified in primary central nervous system neoplasms and soft tissue tumours like GIST or uterine sarcoma. Some of these tumours exhibited an aggressive course.
Methods: A 59-year-old female presented with a progressively growing, painless mass of the left forearm. MRI scan revealed the presence of a sarcomatous growth affecting the extensor carpi radialis brevis muscle, suggestive of liposarcoma.
Results: The surgical specimen contained a tumour measuring 3.5x3.5x2.5 cm. Microscopic examination showed a composition of mildly atypical spindle cells arranged in loose short fascicles, intermingled with inflammatory cells and extravasated erythrocytes. Mitotic activity was low (<10 mitoses/2mm2), and no necrosis was found. The tumour borders were infiltrative, containing some residual entrapped atrophic muscle fibers. The neoplastic proliferation was strongly and diffusely immunoreactive for CD34. Focal staining for Calponin and SMA was observed. Desmin, Beta-catenin, S100, EMA, CD10, STAT6, NTRK, ROS1, and ALK stains were negative. FISH analysis indicated the absence of MDM2 amplification and no rearrangement of COL1A1 or SS18(SYT). Molecular study using Archer FusionPlexSarcomaV2 panel detected FGFR1::TACC1 fusion.
Conclusion: In this particular case, the immunohistochemical and molecular results support a diagnosis of a fibroblastic/myofibroblastic tumour of uncertain behaviour. Notably, there have been no reported cases in the literature of a soft tissue tumour harboring FGFR1::TACC1 fusion as a primary occurrence in this anatomical location. The patient remains in good health without any evidence of disease recurrence at the 5-month follow-up post-surgical intervention.

E-PS-16-038
Malignant granular cell tumour of the thigh: an extremely rare entity with highly aggressive behaviour
M.A. Krupinska*, R. López Henríquez, J.S. Marrero Afonso, C.N. Hernández León
*Hospital Universitario de Canarias, Spain

Background & objectives: Granular cell tumour shows neuroectodermal differentiation and consists of epithelioid/polygonal cells with abundant finely granular eosinophilic cytoplasm resulting from massive accumulation of lysosomes. Although most of these tumours have indolent course, about 2% present malignant behaviour.
Methods: A 46-year-old male presented with a rapidly growing mass of the right proximal thigh causing paresthesia. MRI scan revealed the presence of a sarcomatous growth affecting muscles of the anterior compartment and associated with local lymphadenopathy.
Results: The surgical specimen contained an unencapsulated solid tumour measuring 11x6x4.5 cm. Microscopically, it was composed of polygonal and occasionally spindle cells with granular eosinophilic cytoplasm, forming nests or fascicles, and immersed in a sclerotic stroma. The cells showed irregular, vesicular nuclei with prominent nucleoli, anisonucleosis and hyperchromatism. Mitotic figures were conspicuous, counting up to 6 mitoses per 2 mm2, but no necrosis was found. The tumour was positive for SOX10, S100 (patchy), Inhibin A, PASD, Calretinin and NSE. SMA, STAT6, HMB45, CK(AE1/AE3), ERG and MUC4 were not expressed. Lymphovascular invasion and regional lymph node metastases were identified.
Conclusion: Malignant granular cell tumour is an extremely rare aggressive sarcoma with a high rate of metastases and poor prognosis. Increased cellularity, prominent spindling, high N:C ratio, vesicular nuclei with prominent nucleoli, marked pleomorphism, increased mitotic activity (>2 mitoses/2mm2) and geographical necrosis are associated with aggressive behaviour.

E-PS-16-039
Primary cutaneous extraskeletal osteosarcoma of the thigh: a case report
M.A. Krupinska*, R. López Henríquez, J.S. Marrero Afonso, C.N. Hernández León
*Hospital Universitario de Canarias, Spain

Background & objectives: Extraskeletal osteosarcoma is a high grade neoplasm characterized by the production of malignant osteoid in otherwise unclassified soft tissue sarcoma with no connection to the skeletal system. Rarely, it presents as a cutaneous tumour.
Methods: A 75-year-old female presented with a rapidly growing mass in the femoral triangle region of the left thigh. The patient linked it to a recent trauma. MRI study identified the presence of a sarcomatous growth affecting the dermis and subcutaneous tissue.
Results: Grossly, the surgical specimen revealed a dermo-hypodermic solid well-circumscribed ulcerated tumour measuring 6x5,5x4,5 cm. Microscopically, it was highly cellular with large areas of hemorrhage and necrosis as well as foci of lymphovascular invasion. Pleomorphic spindle cells with marked atypia were intimately associated with osteoid. The mitotic activity was extremely high, exceeding 50 mitotic figures per 2mm2. Intratumoural thin-walled staghorn-like dilated blood vessels were imparting a hemangiopericytoma-like pattern. The tumour cells were strongly and diffusely immunoreactive for SATB2. Weak staining for CD10 and focal expression of SMA were present. Desmin, caldesmon, CD34, CD31, CK(AE1/AE3), S100, HMB45, MUC4, and TFE3 stains were negative.
Conclusion: Extraskeletal osteosarcoma is an aggressive tumour associated with short survival. Distant metastasis, old age (> 60 years), large tumour size (> 10 cm), and positive margin status are associated with poor prognosis. Our patient developed pulmonary metastases and died 5 months after the diagnosis.

E-PS-16-040
Intranodal palisaded myofibroblastoma – a rare cause of lymphadenopathy
O. Kuczkiewicz-Siemion*, J. Tuziak, A. Szumera-Ciećkiewicz
*Department of Pathology, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland

Background & objectives: Benign mesenchymal tumours are unusual cause of lymphadenopathy. Intranodal palisaded myofibroblastoma [IPM] is an extremely rare entity characteristically located in the inguinal region, presenting myofibroblastic cell origin. The

pathogenesis remains unclear, but it may be associated with gain-of-function CTNNB1 mutations.
Methods: We present a 57-year-old female who was admitted to our Institute for histopathological consultation. She complained of a left inguinal region lesion/ lymphadenopathy (diameter 2 cm), which has enlarged for 2 months. The surgical excision of the tumour was performed.
Results: Fragments of a spindle cell lesion with medium cellularity, low-grade cytological atypia, and mitotic activity up to 2/1,734 mm² were found. No tumour necrosis was detected. The tumour stroma was collagenous, slightly edematous, with thin-walled blood vessels and haemorrhages; there were numerous deposits with the appearance of amianthoid fibers. Reactive lymph node tissue was visible on the periphery. Immunohistochemical profile of the lesion showed: SMA(+), Caldesmon(-), Desmin(-), CD31(-), B-catenin(-), CyclinD1(-), CD34(-), ERG(-), MUC4(-), S100(-), SOX10(-), CKAE1/AE3(-), EMA(-), CD45(-), HHV8(-), Rb(+/-) heterogeneous reaction, reduced in some cells, PGR(-), Ki67(+) low (1-3%).
Conclusion: The entire microscopic image, together with the immunohistochemical evaluation, supports the diagnosis of intranodal palisaded myofibroblastoma; it is a very rare lesion (approximately 100 published cases), mostly benign, with a small percentage of cases possibly subject to local recurrence or malignant progression. It is essential to recognize the typical morphology of IPM in differential diagnosis of localized lymphadenopathy, especially of the inguinal region.

E-PS-16-041
Myxoinflammatory fibroblastic sarcoma with VGLL3 amplification – case series study
O. Kuczkiewicz-Siemion*, K. Olszewska, M. Grabowska-Kierył, A. Wojnowska, M. Wągrodzki, D. Pierzchała, P. Wołoszyn, A. Wojewódzka, A. Szumera-Ciećkiewicz
*Department of Pathology, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland

Background & objectives: Myxoinflammatory fibroblastic sarcoma (MIFS) is a rare, low-grade soft tissue tumour that mainly arises in the extremities of young to middle-aged adults. Histologically, it has a characteristic appearance and lacks a distinctive immunophenotype.
Methods: We present 4 cases of MIFS that were diagnosed in our Institute; all cases underwent microscopical, classical immunohistochemical [SMA, Desmin, Caldesmon, MyoD1. Myogenin, S100, SOX10, H3K27me3, MDM2, CD34, STAT6, CKAE1/AE3, INI1, MUC4, CD10, FXIII, BCL2] and molecular assessment of VGLL3 gene status by FISH technique.
Results: In the study, 3 females [mean age 63 years old] and 1 male [39 years old] were included; all lesions were located in the lower extremities with a mean diameter of 57mm. Histologically, MIFS showed solid and myxoid areas, low mitotic activity, mixed inflammatory infiltrates, and the presence of typical virocyte-like (Reed–Sternberg-like) or lipoblast-like cells. No specific and reproducible immunophenotype was seen, but all cases had VGLL3 amplification.
Conclusion: According to the literature review, VGLL3 amplification was described in various soft tissue neoplasms, and it seems to be present in nearly half of all reported MIFS cases. The presence of VGLL3 amplification is helpful in differential diagnosis, but it should always correspond with the clinical context and immunohistochemical pattern. The appropriate classification is beneficial for further large-scale studies under that rare entity.

E-PS-16-042
NTRK-rearranged spindle cell neoplasms – report of two cases with divergent morphology
O. Kuczkiewicz-Siemion*, K. Seliga, A. Tysarowski, M. Wągrodzki, P. Wołoszyn, D. Pierzchała, A. Wojewódzka, A. Szumera-Ciećkiewicz
*Department of Pathology, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland

Background & objectives: NTRK-rearranged spindle cell neoplasms (NTRK-RSCNs) are a group of molecularly defined rare soft tissue tumours, which has been recently classified as provisional (acc. to WHO Classification of Tumours, Soft Tissue and Bone Tumours, 5th. Edition).
Methods: We present 2 cases of NTRK-RSCNs diagnosed in our Institute. The cases underwent microscopical, immunohistochemical [S100, SOX10, H3K27me3, SMA, Desmin, Caldesmon, CD34, STAT6, CKAE1/AE3, SS18-SSX(E9X9V), STAT6, PRAME, MelanA, anti-pan-TRK] and molecular assessment by Targeted Next Generation Sequencing using FusionPlex Sarcoma v2 panel (ArcherDx).
Results: In the study, two females aged 29 and 34 were included. The locations of the lesions were the lumbar area and forearm, with a mean diameter 11cm. In the gross examination, the lesions presented as firm, beige-brown, glossy, and subfascial tumours. Histologically, NTRK-RSCNs showed haphazardly arranged monomorphic spindle cell phenotype with stromal hyalinization. The first case presented with high-grade cytological atypia, mitotic activity to 12/10HPF, and the presence of tumour necrosis, while the second showed low-grade morphology without significant mitotic activity and necrosis. In both cases, NTRK1 gene fusions were detected with the following fusion partners: LMNA-NTRK1 and TPR-NTRK1, respectively.
Conclusion: Identifying patients with NTRK gene fusions is crucial, as they could benefit from targeted therapy using TRK inhibitors. This requires a detailed description of emerging entities like NTRK-RSCNs because testing for NTRK rearrangement is not routinely performed. In two cases, we report a spectrum of histological grades, including a high-grade phenotype.

E-PS-16-043
Primary intraneural PEComa with ASPSCR1-TFE3 fusion
A.B. Larque Daza*, L. Rojo, M. Rodrigo, L. Sisuashvili, T. Silva, J. Hernandez, C. Romagosa
*Pathology Department, Biomedical Diagnostic Center (CDB), Hospital Clinic, Barcelona, Spain

Background & objectives: The ASPSCR1-TFE3 fusion gene had only been reported in alveolar soft part sarcoma (ASPS) and some carcinomas. However, it has also been described in PEComas, recently. We report on the first case of primary intraneural PEComa with ASPSCR1-TFE3 fusion.
Methods: 49-year-old woman with costal/abdominal pain, was detected a 2 centimeter intercostal nodule protruding into the pleura without any bone involvement. Past medical history shows significant bilateral breast carcinoma (seven years ago). Currently, there's no evidence of recurrence or metastatic disease. Surgical exeresis with a clinical suspicion of peripheral nerve sheath tumour probably schwannoma was performed.
Results: Histologically, we observe a neoplasia covered by a fibrous-looking capsule with some nerve fibers embedded in the capsule. The tumour cells have an epithelioid morphology with large cytoplasm arranged in a solid/alveolar pattern, in relation to a fine vascular network. Inmunohistochemistry shows diffuse and intense positivity for TFE3 and SOX10 and focal positivity for HMB45. SMA staining highlights scattered fibrous tracts. S100 was negative but highlights nerve fibers at the periphery. PAX-8 and synaptophysin were negative. The ASPSCR1-TFE3 fusion gene was confirmed by sequencing study. The pathological diagnosis was mesenchymal neoplasia with TFE3 rearrangement. Follow up reports the patient is alive without recurrences or other suspicious soft tissue lesions.
Conclusion: This unique case reports a primary intraneural TFE3-rearranged PEComa with ASPSCR1-TFE3 fusion, which contributes to

expand the spectrum of TFE3 fusion genes of these types of tumours. Although ASPSCR1-TFE3 fusion had been associated with ASPS, recent studies have reported cases of PEComa with this fusion. Based on the literature evidence and findings in our case, which include positivity for melanocytic markers, we consider this tumour a PEComa and to our knowledge, intraneural PEComas have not been described.

E-PS-16-044

Coupled inhibition of transcription and translation as potential therapeutic approach for dedifferentiated liposarcoma

V. Lee*, S.M. Leong, D. Wang
*Department of Pathology / National University Singapore, Singapore

Background & objectives: Dedifferentiated liposarcoma (DDLPS), known for its limited treatment options, presents a pressing clinical challenge. Our study investigates the combined inhibition of transcription and translational activities as promising therapeutic strategies to address this unmet medical need.
Methods: We treated in vitro models with A1874 (transcription inhibitor targeting BRD4) and SBI-0640756 (translation inhibitor targeting eIF4G1) individually or in combination, to examine their impacts on cellular processes. RNA-seq and Ribo-seq analyses provided insights into molecular pathways. Findings were validated in patient-derived HSC40 and immortalized LPS141 and LP6 cell lines. Therapeutic efficacy will be assessed using a murine xenograft model.
Results: Utilizing MTT assay, our study demonstrated significant proliferation inhibition in our cell lines upon treatment with either A1874 or SBI-0640756. Notably, combining both compounds exhibited enhanced efficacy, suggesting synergistic potential. RNA sequencing and Ribo-seq analyses unveiled distinct transcriptional and translational modulation by combination therapy, particularly affecting crucial signaling pathways like NF-KB and p53. These findings highlight the potential of combination therapy as an advantageous treatment approach for DDLPS.
Conclusion: The study illustrates the notable therapeutic efficacy of A1874 and SBI-0640756, both individually and in combination, against DDLPS. Notably, the combined treatment showcases superior effectiveness, indicating synergistic interactions. This synergy is likely attributed to the modulation of critical oncogenic pathways, resulting in enhanced tumour growth suppression compared to monotherapy. These results advocate for continued clinical exploration of A1874 and SBI-0640756 combination therapy as a promising treatment avenue for DDLPS.

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E-PS-16-045

The role of FZD10 in synovial sarcoma

V. Lee*, A. Sim, D. Virshup
*Department of Pathology / National University Singapore, Singapore

Background & objectives: Progress in synovial sarcoma (SS) therapy has been limited. In SS, SS18-SSX upregulates Wnt signaling. We aim to survey if our local SS cohort shows upregulation of FZD10 and determine how FZD10 acts as a driver for sarcomagenesis.
Methods: We recruited 23 patients for evaluation of FZD10 expression and nuclear localization of β-catenin from tissue microarray samples. We further used CRISPR/Cas9 to generate null knockout (KO) of FZD10 in SS cell lines SYO-1 and HS-SY-II. After Western blotting confirmed gene KO, soft agar colony formation assay was performed to determine the effect of loss of FZD10 on cell clonogenicity.
Results: Immunohistochemical staining revealed approximately 60% of patient cohort show high FZD10 expression. Furthermore, most samples did not show nuclear β-catenin staining, indicating that Wnt signaling is not active in these samples. We also noted that elevated expression of FZD10 did not correlate with nuclear localization of β-catenin, suggesting that FZD10 serves a β-catenin independent function. Confirming the biological importance of FZD10 in sarcomagenesis, two independent FZD10KO clones from SYO-1 and HS-SY-II SS lines showed statistically significant decreased colony formation in 3D culture as compared to cells that received non-targeting guides (NTC) ($p < 0.05$, two-tailed t test).
Conclusion: Our results suggest that FZD10 does not propagate signalling through the β-catenin pathway but has a separate role in Wnt signalling. The SS models developed here are potential tools to study a hitherto unrevealed function of FZD10, and may provide insight into how targeting FZD10 (or its downstream partners) can be used for the stratification of SS patients for more focused treatment strategies.

E-PS-16-046

Rhabdomyossarcoma versus "Triton" tumour – a case report

N. Lopes*, F. Cunha, F. Santos
*IPO Lisboa Francisco Gentil, Portugal

Background & objectives: In the paediatric population, spindle cell rhabdomyosarcoma (SCRMS) is an aggressive neoplasm frequently encountered in the paratesticular region. Malignant peripheral nerve sheath tumours (MPNST) with complete rhabdomyoblastic differentiation closely mimic SCRMS and distinguishing these two entities may have therapeutic implications.
Methods: We describe the case of a paratesticular tumour morphologically consistent with a SCRMS, but showing complete loss of H3K27me3.
Results: A previously healthy 14-year-old boy presented with a right paratesticular mass. Scrotal ultrasound described a highly vascularized, 6,5 cm paratesticular mass, locally confined. Orchidectomy revealed a highly cellular, fasciculated, spindle cell sarcoma with nuclear atypia and elevated mitotic rate. Scant rhabdomyoblasts were identified. Immunohistochemistry showed strong and diffuse desmin expression, associated with myogenin and myoD1 positivity. S100 protein was negative. Diagnosis of SCRMS was considered, but complete loss of H3K27me3 was identified. Fluorescence in situ hybridization revealed CDKN2A gene homozygous deletion and SUZ12 gene rearrangement. A MPNST with complete rhabdomyoblastic differentiation was diagnosed. No clinical evidence of neurofibromatosis type 1 (NF1) was found.
Conclusion: Differential diagnosis between MPNST with complete heterologous rhabdomyoblastic differentiation, also known as "Triton" tumour, and SCRMS can be challenging. Recently, H3K27me3 loss has been described as a useful marker for MPNST. Without performing H3K27me3 in an otherwise typical SCRMS, "Triton" tumour may not be considered. Regarding the association between MPNST and NF1 and possible different future therapeutic approaches, these entities should be thoroughly distinguished. Correlative genetic finding, as in our case, may also support to the final diagnosis.

E-PS-16-047

Fibrous dysplasia of the maxilla and mandible - our 5-year institutional experience in light of literature review

A. Lazim, S. Amer, Y. Belogrivtseva, K. Khouri, R. Kuklani, D. M Proca*
*Temple University, USA

Background & objectives: Fibrous dysplasia (FD) is a benign intraosseous lesion. It is a developmental condition which mimics a tumour on radiological studies. FD is a sporadic condition caused by the inability to produce mature bone due to a genetic mutation in GNAS1.

Methods: FD in the jaw is a rare skeletal disorder characterized by the abnormal development of fibrous tissue, leading to the replacement of normal bone with weakened and expansile fibrous tissue. Common symptoms include facial deformity, pain, and functional issues. Diagnosis often involves imaging studies and is confirmed through biopsy. Treatment varies based on the severity of symptoms.
Results: We report of six FD in the mandible and maxilla diagnosed in our facility between 2015 - 2020 with mean age 44 years (range, 12-72 years). The maxilla was affected in most cases (n=4). Male: female ratio was 2:1. Some of the lesions showed ground-glass opacity on imaging. Microscopic examination revealed foci of relatively dense fibrous tissue containing irregularly shaped trabeculae of woven and lamellar bone. Some trabeculae were associated with newly forming, spontaneous bone derived from the surrounding fibrous tissue. Each case demonstrated blending of fibrous and osseous tissue, with resultant secondary bony metaplasia, producing immature, haphazard, and weakly calcified woven bone.
Conclusion: The clinical, radiographic, and the morphological appearance of FD exhibit a substantial overlap with other fibro-osseous lesions, including malignant neoplasms, such as low grade osteosarcoma. FD involves the maxilla almost two times more often than the mandible. It frequently appears in the posterior region of the jaw bone and is usually unilateral. The importance of this study is to differentiate FD from other fibro-osseous lesions of the mandible and maxilla.

E-PS-16-048
Sporadic malignant melanotic nerve sheath tumour: rare clinical case
D. Murzaeva*, R. Talybov, V. Mochalov, A. Bunyat, D. Sitovskaya, Y. Zabrodskaya
*Almazov National Medical Research, Tyumen State Medical University, Russia

Background & objectives: Malignant melanotic nerve sheath tumour is rare tumour which is characterized by aggressive clinical course. In CNS WHO 2021 classification has been changed its position from benign to malignant tumours, however, there are not guidelines for such patients.
Methods: Herein, we described a case report of Sporadic malignant melanotic nerve sheath tumour without clinical or morphological features of anaplasia. A Computed tomography was performed. Patient underwent surgical treatment with subsequent histological and immunohistochemical examination.
Results: We present a rare case of MMNST in a 36-year-old woman with a paravertebral 37x31x50 mm tumour of Th4-Th6 vertebrae. There was not mitosis, necrosis, invasive growth. The proliferative activity was low, also presence of capsule, cystic component, growth from nerve - these features help distinguish from melanoma. Immunohistochemical studies in tumour cells showed expression of S100, MelanA, melanoma cocktail, CD56, PGP9.5, NF1, NF2; no expression of GFAP, multiCK, CD45. Ki-67/MIB1 proliferative activity index up to 3-7% (estimated at pigment-free areas). No relapses or metastases during three years of observation.
Conclusion: The clinical case of a rare nerve tumour underscores the key importance of morphological research in determining the degree of anaplasia of nerve tumours. The diagnosis of malignant melanotic nerve sheath tumour must combine a multimodal approach, and a complete excision of the tumour must be performed, followed by a long follow-up. Further study of molecular genetic anomalies in this pathology is needed to develop targeted therapy.

E-PS-16-049
Tumour immune microenvironment in recurrent schwannomas
D. Murzaeva*, A. Bunyat, N. Matiashina, A. Bunyat, J. Belikova, A. Simonov, D. Matveeva, A. Musikhina, Y. Zabrodskaya, A. Sufianov
*Almazov National Medical Research, Tyumen State Medical University, Russian Federation

Background & objectives: Relapse rates of schwannomas occur in 2-40% of cases depending on the extent of surgical treatment. There remains insufficient research on the tumour microenvironment of schwannomas, particularly regarding the role of macrophages in tumours with an unfavourable clinical course.
Methods: We analysed a cohort of 513 patients who underwent total microsurgical resection of schwannoma. Patients were divided into two groups: with tumour recurrence and without recurrence. H&E and IHC slides stained for CD163, CD68, CD3, CD8, CD20, MMP2, MMP3 from 24 patients were evaluated. IBM SPSS Statistics v.26 program and non-parametric statistical methods were used.
Results: In our study the immunohistochemical expression level of CD163 for non-recurrence tumours was 55% (Q1-Q3: 30-70%) whereas it was 50% (Q1-Q3: 37,5-80%) for recurrence. The CD68 positive cell percent was 50% (Q1-Q3: 35-70%) and 60% (Q1-Q3: 40-70%), p=0,266. The CD20 positive cell percent pattern was 1% (Q1-Q3: 1-1%) and 0% (Q1-Q3: 0-1%), p=0,045. The CD3 positive cell percent was 5,5% (Q1-Q3: 2,0-7,0%) and 10,0% (Q1-Q3: 5,0-17,5%), p=0,045. The CD8 positive cell percent was 53,5% (Q1-Q3: 1-6%) and 4% (Q1-Q3: 2-5, p=0,799. The MMP2 (metalloproteinase 2) percent was 62,5% (Q1-Q3: 37,5%-70,0%) and 35% (Q1-Q3: 22,5-42,5%), p=0,039. The MMP3 (metalloproteinase 3) percent was 45,0% (Q1-Q3: 30,0-62,5%) and 15,0% (Q1-Q3: 10,0-42,5%), p=0,028.
Conclusion: Recurrent schwannomas have a higher percentage of MMP2, MMP3, of CD163+ and CD68+ macrophages, CD20+ B-lymphocytes and lower levels of CD3+ T-lymphocytes. Thus, ICH expression of tumour immune microenvironment cells may serve as a promising predictor of tumour recurrence.

E-PS-16-050
A rare sarcoma with YAP1::KMT2A::YAP1 fusion arising from the abdominal wall
M.H. Nam*, Y. Kao
*Department of Pathology, Wan Fang Hospital, Taipei Medical University, Taipei, Taiwan

Background & objectives: Sarcomas with YAP1::KMT2A::YAP1 fusion are a group of very rare and recently described tumours. Initial reports note that they have sclerosing epithelioid fibrosarcoma (SEF)-like and/ or low-grade fibromyxoid sarcoma (LGFMS)-like morphology, but are negative for MUC4 immunostain.
Methods: We report a 72-year-old woman presenting with a painful right lower abdominal subcutaneous tumour. The morphologic features, immunohistochemical profile, and molecular finding are described.
Results: An excisional biopsy of the tumour revealed a focally infiltrative tumour in the dermis and subcutis, with zonal variation in cellularity. The tumour cells ranged from spindle, ovoid, to epithelioid, with nuclei containing fine chromatin and occasionally visible nucleoli. The stroma was predominantly densely fibrotic. The hypocellular areas were deceptively bland. Some scattered atypical cells and mitotic activity up to 5 mitoses/mm2 were noted in the cellular areas. Immunohistochemically, the tumour cells were positive for ERG (moderate), SMA (focal), CD34 (few), and negative for desmin, MUC4, beta-catenin (membranous staining only), and CK(AE1/AE3). The presence of YAP1::KMT2A and KMT2A::YAP1 fusion transcripts were detected by RT-PCR, compatible with a complex YAP1::KMT2A::YAP1 fusion.
Conclusion: YAP1::KMT2A::YAP1 fusion sarcomas can be composed mainly of deceptively bland cells at times, without SEF-like and/or LGFMS-like morphology. Zonal variation and focally high mitotic counts are hints that lead to the diagnosis for this case. Of the cases with KMT2A::YAP1 fusion reported, the age ranged from 9- to 91-year-old (median: 42-year-old), with various primary sites. Local

recurrences and distant metastases are also described. Awareness of this entity is crucial in preventing misdiagnosis and providing adequate management.

E-PS-16-051

Subungual glomus tumour: a case report of a relatively rare soft tissue neoplasm

A. Neamţu*, A. Sabău, D.M. Chiorean, O.S. Cotoi
*Victor Babes University of Medicine and Pharmacy, Romania

Background & objectives: Glomus tumours represent relatively rare mesenchymal neoplasms comprising cells akin to the smooth muscle fibers of the Sucquet-Hoyer canal of the glomus body, constituting less than 1.6% of soft tissue tumours. They are predominantly located in the digital extremities.
Methods: A 49-year-old male was admitted by the Surgery Department for paroxysmal pain, cold sensitivity, and point tenderness in the distal extremity of finger IV-left hand. Based on the intraoperative appearance, the presumptive diagnosis was foreign body granuloma in the subungual region, followed by surgical excision. The specimen was further assessed in the Pathology Department, undergoing histopathological and immunohistochemical analysis.
Results: Grossly, the tumour was irregular-shaped, dimensions of 11x4x3 mm, presenting smooth glossy surface, yellowish-white color, and elastic consistency. Microscopically, the proliferation was peripherally partially delimited by a fine fibrous capsule and constituted by small tumour cells, arranged in nests, with well-defined cell borders (highlighted in PAS-H staining), centred by round, uniform, monomorphic nuclei, and with abundant eosinophilic cytoplasm. Nests of tumour cells were separated by a stroma with areas of hyalinization and blood vessels of various calibers, dilated, with numerous capillaries, some with a thickened wall, occasionally with erythrocytes in the lumen. Immunohistochemically, both SMA and CD34 showed a positive reaction characteristic to a glomus tumour of the glomangioma type.
Conclusion: As glomus tumours are relatively rare, continued clinical awareness is necessary to enhance diagnostic accuracy among pathologists, employing both the characteristic histopathologic appearance and the immunohistochemical features. These tumours, despite being characterized by their occurrence in the subungual region, can be found in various other localizations throughout the body.

E-PS-16-052

Molecular diagnostics of undifferentiated sarcomas - institutional experience

K.O. Orte*, J. Tuominen, J. Lasota, M. Miettinen, M. Kallajoki
*Department of Pathology, University of Turku and Turku University Hospital, Turku, Finland

Background & objectives: Gene fusions are important driver mutations in sarcomas. RNA sequencing has enabled the recognition of previously undescribed fusion genes. We combined RNA sequencing and methylome classification to traditional methods to re-classify a group of undifferentiated high-grade sarcomas.
Methods: 16 WHO grade 2-3 sarcomas (8 spindle cell or pleomorphic undifferentiated sarcoma, US, 1 leiomyosarcoma, LS, and 7 undifferentiated small round cell tumours, USRCT, years 2010-2020) collected from the archives of Turku University Hospital (TYKS, Turku, Finland) were re-evaluated to correspond the latest WHO classification. Targeted broad-spectrum RNA sequencing and methylome classification were used to define a morpho-molecular diagnosis.
Results: 12 of the 16 samples (7 US, 1 LS and 4 URSCT) had fusion transcripts. Only 2 of them were previously described. EWSR1::BEND2, previously described in astroblastomas, was detected in a bladder USRCT (Methylome: undifferentiated sarcoma). YWHAE::NUTM2B reclassified a uterine tumour as a high-grade endometrial stromal sarcoma (Methylome: undifferentiated sarcoma). However, fusion transcript was not found in CIC-rearranged USRCT. Genes, known to be rearranged in different tumours (e.g. MDM2, MET, HMGA2), were associated with previously undescribed fusion transcripts in the US group. Methylome classification grouped 3 of 9 US tumours into specialized tumour groups, LS was recognized and 1 of the 5 USRCTs classified as an epitheloid sarcoma.
Conclusion: Broad spectrum RNA sequencing may help in diagnosing rare undifferentiated sarcomas but some rearrangements may be difficult to detect on RNA level due to technical limitations. It is not rare that previously undescribed fusion trancripts are found, and their clinical significance is unclear. They can, however, sometimes justify molecularly guided off-label treatment. Methylation classifier is a useful aid for morphological diagnostics but may group tumours falsely and should be interpreted against the background of morphology and immunohistochemical findings.

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E-PS-16-053

Clinico-pathological spectrum of lipomatous tumours: a 10 years single-centre experience

A.I. Patrichi*, S. Gurzu
*Pathology Department, UMFST Targu Mures, Romania

Background & objectives: Lipomatous tumours, ranging from benign lipomas to high-grade liposarcomas, make up a large part of soft-tissue tumours. Their varied nature presents challenges in diagnosis and treatment, highlighting the need for a deeper understanding of their biological behaviour.
Methods: This study assesses clinicopathological aspects of 430 benign and malignant lipomatous tumours diagnosed at the Department of Pathology, Clinical County Emergency Hospital of Targu Mures, Romania focusing on demographics, incidence, histological subtype, and their relation to clinical diagnoses. It includes a comprehensive evaluation of general clinico-pathological parameters, classifying each case according to the latest WHO guidelines for soft tissue tumours.
Results: Between 2013 and 2023, we diagnosed 384 lipomas, 11 atypical lipomatous tumours/well-differentiated liposarcomas (ALT/WDLS), and 35 liposarcomas. We observed a female predisposition for lipomas (64%) and liposarcomas (67%), but a male predominance for ALT/WDLS (65%). Lipomas were mostly diagnosed in the 5th and 6th decades (51%), while ALT/WDLS and liposarcomas were more common in the 6th and 7th decades (44% and 52%, respectively). Lipomas frequently affected the trunk (40%) and head and neck (33%), with fewer in extremities (27%). For liposarcomas, the trunk, especially the retroperitoneum (90%), was predominant, while ALT/WDLS was most common in extremities (50%). No head and neck cases were found in liposarcomas, contrasting with ALT/WDLS distribution.
Conclusion: Lipomatous tumours represent a group with marked heterogeneity particularly in terms of location. Moreover, in addition to the pronounced clinico-pathological heterogeneity, the existence of a borderline category (ALT/WDLS) makes it more difficult to predict the evolutive potential and prognosis.

E-PS-16-054

Malignant chondroblastoma of the rib with cutaneous metastases and molecular characterization in a 57-years old patient: case report of this exceptional presentation

E.M. Pena Burgos*, J.J. Pozo Kreilinger, F. Alijo Serrano, M. Cuervo Dehesa, L. Lombardía, C. Agra Pujol
*Hospital General Universitario Gregorio Marañón, Spain

Background & objectives: Chondroblastomas represents less than 1% of bone tumours and most commonly arises in the epiphyseal region of long bones in adolescents and young adults. They are currently classified as a benign neoplasm and "benign" lung metastases have been reported.
Methods: We present the case of a 57-year-old previous healthy man that noticed a rapid growing mass in his left chest. Radiological images revealed a 10cm large ill-defined mass with an osseous epicentre in the sixth anterior costal rib. It was completely removed with free margins. Seven years later he presented two superficial movable lesions in the scalp that were removed.
Results: The costal mass was histologically composed by fused nests of discohesive polygonal cells with grooved nuclei and scattered osteoclast-like giant cells embedded in an eosinophilic chondroid matrix. It presented a permeative growth pattern with entrapped pre-existing bone trabeculae. No clearly "chicken-wire" calcification was detected. Moderate atypia and necrotic foci were present. No abundant mitotic figures were observed. No soft tissue extension was observed. Cutaneous metastases demonstrated the same histopathological findings. Both metastases and the primary tumour showed diffuse immunoreactivity for H3K36M. The molecular study of the H3F3B gene demonstrated the same mutation in the original mass and in both cutaneous metastases [p.K37M (c.110A>T) of the exon 2].
Conclusion: The main histopathological differential diagnosis should be made with chondroblastoma-like osteosarcoma, that usually present more striking cytologic atypia, an infiltrative growth pattern and distant metastases but neither H3K36M immunoreactivity nor H3F3B gene mutations have been reported. Malignant chondroblastomas are more frequent in unusual locations such as rib, or scapula, and in older adults. Only two previous reported cases of malignant chondroblastomas presented scalp metastases.

E-PS-16-055
Thoracic epithelioid hemangioendothelioma: an example of the utility of molecular diagnosis in limited specimens
E. Ponce Casas*, C. Cabañuz Rocatallada, S. García-Fuertes, R. Vilorio, E. Mejia, M. Garcia Garcia, G. Rios, F. Felipo Berlanga
*Hospital Clínico Universitario Lozano Blesa, Spain

Background & objectives: Epithelioid hemangioendothelioma (EHE) is a rare malignant vascular tumour, with an incidence of less than one in a million. It most commonly involves somatic soft tissue, lung and liver. Molecular identification of WWTR1-CAMTA1 or YAP1-TFE3 gene fusions aids in diagnosis.
Methods: We present the case of a 44-year-old woman, in whom a 22 mm mediastinal mass contacting the superior vena cava was detected. She underwent endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) and two conventional smears and a cell block was obtained.
Results: Microscopically, we identified a cellular proliferation arranged in nests and cords, on a myxohyaline stroma. These cells exhibited eosinophilic cytoplasm with some vacuoles, round and oval nuclei with vesicular chromatin, and occasional prominent nucleoli. Some osteoclast-type giant cells were appreciated; no mitotic figures or necrosis were observed. Immunohistochemically, the cells were positive for CD31 and ERG, while negative for CKAE1/AE3, S100, and AML. The proliferation index measured by Ki67 was 5%. With histopathological suspicion of EHE, a next-generation sequencing (NGS) study was performed, detecting the WWTR1-CAMTA1 fusion transcript.
Conclusion: Diagnosis of soft tissue tumours in small samples is a challenge because the histologic features may not be represented. EHE represents a small fraction of vascular sarcomas. The differential diagnosis includes vascular tumours such as intimal sarcoma, angiosarcoma, epithelioid hemangioma, and additionally, carcinomas metastases. This case exemplifies the relevance of molecular identification, such as WWTR1-CAMTA1 gene fusions, which plays a fundamental role in this case.

E-PS-16-056
NKX2.2 expression in Ewing sarcoma: differences in sensitivity between pre-treatment biopsy and surgical specimen - a case series
A. Prat*, M.A. Di Muro, S.F. Acosta, T. Vazquez, S. Bagué Rosell, R. Orellana, C. Fumagalli
*Hospital of Santa Creu and Sant Pau, Spain

Background & objectives: Diagnosis of Ewing sarcoma (ES) often requires immunohistochemical and molecular techniques. Recently, NKX2.2 staining has been reported as a useful marker for ES (sensitivity 80-93%). This study aimed to evaluate NKX2.2 immunoexpression in ES (both initial biopsies and resection specimens).
Methods: 14 consecutive cases of ES diagnosed between 2015-2023 were selected. Pre-treatment biopsy and resection specimens with residual tumour were available for review in each case. Clinical and pathological data were collected. NKX2.2 was evaluated in both samples considering the extent (percentage of positive cells 0:<5%; 1+:5-25%; 2+:25-50%; 3+:50-75% and 4+:75-100%), and intensity (weak, moderate or strong) of the staining.
Results: The study included 6 females and 8 males (median age: 26years-old). Tumour location: extremities (7), axial (6), and visceral (1). Decalcification with formic acid was done in 6 resection specimens. All cases showed some NKX2.2 staining. 11/14 (78%) of initial biopsies showed positivity in more than 25% of cells. Sensitivity was lower in resection-specimens since 71% of cases showed some expression but only 50% expressed NKX2.2 in more than 25% of cells. NKX2.2 loss of expression was found in 4/14 (28%) of surgical specimens, regardless of whether they were decalcified or not. NKX2.2 was negative in haemorrhagic and apoptotic/necrotic areas, both in initial biopsies and resection-specimens.
Conclusion: This study proved that NKX2.2 is a useful marker for ES, although with lower sensitivity in resection specimens possibly related to tissue handling with decalcification. Other factors (pre-analytic handling, length of formalin exposure, additional therapies…) should be considered since low expression was also detected in non-decalcified cases. Pathologists should be aware that there may be only focal/patchy staining in initial biopsies. Also, a negative staining is possible due to haemorrhage, apoptosis and necrosis.

E-PS-16-057
Massive localized perineal lymphedema: case report of a challenging entity
G. Radu*, O.S. Cotoi, E.A. Szasz
*Mureș County Clinical Hospital, Romania

Background & objectives: Massive Localized Lymphedema (MLL) is a rare benign soft tissue entity that typically arises in obese patients. It is usually referred to as pseudosarcoma. Its intricate pathophysiology involves both lymphatic flow obstruction and localized ischemia with wound-like regeneration processes.
Methods: A fifty-eight-year-old obese male (BMI=32.87) with a history of metabolic syndrome was admitted to hospital for two polypoid perineal masses measuring 20x17x8 cm and 12x10x5 cm respectively, that developed over an eight-years period. The overlying skin exhibited induration with a "peau d'orange" appearance. After surgical excision, specimens were further processed in the department of Pathology of Mureș County Clinical Hospital.
Results: On gross examination, both masses revealed an heterogenous aspect with sharply thickened skin and tan edematous subcutaneous tissue alternating with brown gelatinous areas. At microscopy, the two lesions disclose similar aspects, consisting of a subcutaneous growth covered by an acanthotic epidermis with mild hyperkeratosis. The underlying proliferation was composed of 4 main components: ectatic lymphatic capillaries, thick fibrotic septa, mature adipocytes and an edematous hypocellular stroma with "floret-like" multinucleated cells.

In our case, we ruled out the possibility of a malignant condition due to the slowly growing pattern, decreased mitotic activity, and lack of atypical structures. Based on morphology, a diagnosis of MLL was established.
Conclusion: With obesity being a global health concern, understanding MLL has become crucial. Generally, MLL is a benign, reactive condition but in rare cases it can also progress to angiosarcoma, phenomenon known as Stewart-Treves syndrome. Challenges arise from its clinical and histological resemblance to liposarcoma, underlining the potential for MLL to be misdiagnosed. With few cases being described in the literature, there is a constant need for research in this field as well as introduction of rigorous histopathological diagnostic criteria.

E-PS-16-058
CIC-rearranged sarcoma: a seven-case study
M. Reis*, G. Teixeira, M. Yamashita, M. Cruz, A. Silva, S. Sargentini, L. Marques, R. Manuel Reis
*Barretos Cancer Hospital, Brazil

Background & objectives: CIC-rearranged sarcoma is a rare and aggressive small round cell sarcoma. It is more common in young adult patients and involves deep soft tissues. Patients are treated with Ewing sarcoma's protocol, but the prognosis is worse, making specific therapies necessary.
Methods: We selected seven patients diagnosed with CIC-rearranged sarcoma in a cancer hospital between 2020 and 2023. All cases had formalin-fixed paraffin-embedded (FFPE) material and an immunohistochemistry study available for pathological review, and all cases were confirmed by fluorescence in situ hybridization (FISH). Clinical data were retrieved from an electronic medical record system.
Results: Six cases involved primarily soft tissues; one involved the parotid. All cases presented as a malignant small round cell tumour with a high mitotic index and necrosis; one exhibited myxoid stroma. Immunohistochemistry: WT-1 nuclear staining in all but one dot-like staining case; CD99 weak membranous staining in all but one cytoplasmic case; Desmin negative in all cases; Myogenin and NKX2.2 negative in six cases; ERG and FLI-1 staining in three and four cases, respectively; TLE-1 at least weak staining in five cases. All patients had lung metastasis at diagnosis, and five patients developed lymph node metastasis. Five patients died, with the most prolonged survival being one year and five months.
Conclusion: The immunohistochemical profile is similar to that described in the literature, whose positivity of WT-1 and CD99 corroborates the diagnostic. Negative desmin, myogenin, and NKX2.2 help to differentiate from desmoplastic small round cell tumour, rhabdomyosarcoma, and Ewing sarcoma. The aggressive behaviour with metastases and the low rate of therapeutic response to regimens classically proposed for Ewing sarcoma reinforce the uniqueness of this entity and the need for an accurate diagnosis, which will allow better stratification and development of specific therapies.

E-PS-16-059
Malignant chondroblastoma
M. Reis*, L. Melo, M. Cruz, D. Losada, S. Sargentini, M. Yamashita, L. Feltrin
*Barretos Cancer Hospital, Brazil

Background & objectives: Malignant chondroblastoma is a recently described entity that shares the H3F3B(K36M) point mutation with its benign counterpart and is a differential diagnosis for chondroblastoma-like osteosarcoma.
Methods: A case of an eleven-year-old boy with a painful mass in his right knee for two years. Radiographically, an aggressive bone tumour at the distal femur and proximal tibia and fibula with cortical destruction and extension to soft tissues. Chest exam showed multiple bilateral pulmonary masses compatible with metastasis. Biopsy was not able to document malignancy, and amputation was recommended.
Results: A macroscopic exam revealed a 20.0-centimeter multinodular withe mass occupying all the knee. Histopathology closely resembled conventional chondroblastoma but with infiltrative borders, some cytologic atypia, and four mitoses per 10 HPF. It did not exhibit bone production by cytologically malignant cells. Immunohistochemistry showed S100, SOX9, and anti-histone H3K36M staining. Next-generation sequencing was performed, and an H3F3B K36M mutation was detected (p.Lys36Met). The patient received chemotherapy treatment and underwent surgical resection of lung lesions, which resembled the bone tumour.
Conclusion: The absence of bone production by cytologically malignant cells associated with diffuse nuclear expression of anti-histone H3K36M and detection of H3F3B K36M mutation are consistent with the diagnosis of malignant chondroblastoma over chondroblastoma-like osteosarcoma. We hope that as soon as this entity is studied and described, the better the patient assistance and recovery will be.

E-PS-16-060
Synovial sarcoms presenting atypical FISH positive pattern with loss of green signal. Molecular characteristics of 2 new cases and systematic review of the literature
J. Ryś*, A. Kruczak, A. Adamczyk, K. Mularz, M. Rozmus-Piętoń, K. Majchrzyk, A. Harazin-Lechowska
*Department of Tumour Pathology, Maria Sklodowska-Curie National Research Institute of Oncology, Krakow Branch, Poland

Background & objectives: Synovial sarcoma accounts up to 10% of STSs. Most tumours harbour translocation t(X;18); SS18-SSX fusion gene. In FISH break-apart assay the positive criterion is unpaired red and green signals. The atypical FISH means a missing a green or red signal.
Methods: FFPE and HE stained tumour sections were reviewed by two pathologists. All immunohistochemical staining were made automatically using DAKO Omnis autostainer. Vysis LSI SS18 Dual Color Break Apart Probe (Abbott Molecular) was used for hybridization to 18q11.2. Three investigators evaluated the FISH slides independently. Both tumours were analysed using Archer FusionPlex Sarcoma V2 assay and Illumina MiniSeq sequencer
Results: During the time period from 2011 to 2024 in the Department of Tumour Pathology 60 synovial sarcoma cases were analysed using FISH for SS18 gene rearrangement. Among them there were two (3.3%) FISH-positive cases showing loss of a green signals. Both these tumours were classified as monophasic fibrous sybtype of synovial sarcoma characterized by positive IHC reaction to EMA, S100 protein, and SS18-SSX chimeric protein. By using the SS18 break-apart probe for FISH detection we observed complete loss of a green signal with 1 red signal and 1 fused yellow signal (1F + 1R). NGS analysis revealed in one case a SS18-SSX1 fusion, and the SS18-SSX2 in another.
Conclusion: Atypical SS18-break apart FISH pattern with loss of green signal should be interpreted as a peculiar unbalanced rearrangement of the SS18 gene and subsequent SS18-SSX fusion (IHC or/and NGS) test should be recommended in such cases.

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E-PS-16-061
Low-grade fibromyxoid sarcoma: unusual morphological findings
X. Sanjuán*, M. Pané Foix, S. Villatoro, M. Varela, N. Vicente, M. Guerrero, R. Bosch
*Departament d´Anatomia Patològica. Hospital Universitari de Bellvitge. Idibell, Spain

Background & objectives: Low-grade fibromyxoid sarcoma (LGFMS) is an uncommon type of low-grade fibroblastic sarcoma. Apart from the usual morphology, < 10% of cases may have focal pleomorphism or nuclear atypia, hypercellularity, epithelioid or round cell features, and heterotopic ossification.
Methods: We reviewed the cases of LGFMS diagnosed in our centre between the years 2009 and 2024, most confirmed by MUC4 immunohistochemistry or FUS rearrangement. We did a descriptive study of the variables sex, age, location and tumour size. We reviewed the histological slides of all cases in search of unusual morphological findings.
Results: We obtained 12 cases of LGFMS. The male/female ratio was 6/6. The average age was 47.9 years (22 - 75). The most frequent location was extremities (6), followed by trunk (5), and 1 case of visceral location. Tumour size varied between 3 and 16 cm (mean 6.9 cm). In terms of morphology, 11 tumours showed alternating fibromyxoid areas typical of LGFMS, while 1 showed a hyalinizing fusocellular tumour with giant rosettes. In addition, we detected other morphological findings such as cystification (5 cases), multinucleated cells (1 case), ischemic type necrosis (2 cases) and an hemangiopericytoid vascular pattern (2 cases).
Conclusion: We would like to highlight a series of morphological findings that can rarely occur in LGFMS and, that detected in a core needle biopsy (CNA), could make us wrongly rule out this diagnosis, such as:
1. Cystification
2. multinucleated cells
3. Ischemic necrosis

4. Hemangiopericytoid vascular pattern

E-PS-16-062
PRRX1-rearranged mesenchymal tumour: a case report of an emerging and likely underrecognized entity
I. Savic*, A. Brent, C.V. Angeles, D. Rottmann, E. Abdulfatah, J. McHugh, S. Schechter, N. Brown, K. Perry
*Institute of Pathology, Faculty of Medicine, University of Belgrade, Belgrade, Serbia

Background & objectives: PRRX1-rearranged fibroblastic tumour is a recently described entity that is morphologically characterized by a well-circumscribed spindle cell proliferation in the background of myxoid and collagenous stroma. The tumours behave in an indolent manner and typically exhibit PRRX1::NCOA1 or PRRX1::NCOA2 fusion.
Methods: We reviewed the case of a 44 year old male who presented with a subcutaneous mass in the right flank. The mass had been present for at least two years. The patient underwent resection and all Hematoxylin and Eosin (H&E) and immunohistochemical (IHC) stained slides were reviewed.
Results: The sections of the 5.3 cm mass showed a lobulated proliferation of spindled to ovoid cells. The background stroma consisted of varying amounts of "ropey" collagenous to myxoid stroma. Staghorn like vessels with perivascular hyalinization were also present. Significantly increased mitoses or necrosis was not identified. IHC was performed and the cells were negative for CD34, MUC4, STAT6, EMA, SOX10 and desmin. Next generation sequencing identiifed a PRRX1::NCOA1 fusion. In the two months following the resection, the patient has been free of recurrence.
Conclusion: PRRX1-rearranged mesenchymal tumours are a recently described tumour that historically overlap with other hyalinizing spindle cell neoplasms such as solitary fibrous tumour or low-grade fibromyxoid sarcoma. Although these tumours are still being characterized, they seem to have a more indolent behaviour than these diagnostic alternatives.

E-PS-16-064
Collagen V-oral immunotherapy attenuated synovitis, repair and protect articular cartilage in mBSA/CFA-induced arthritis
L. Keren Ramos da Silveira*, S. Catanozi, M.A. Amador Pereira, A. Dos Santos Filho, S. de Morais Fernezlian, A. Flores Yanke, Z.A. Jesus Queiroz, V. Elias Contini, T. de Matos Lobo, S. Carrasco, C. Machado Baldavira, R. Fuller, V.L. Capelozzi, A.P. Pereira Velosa, W. Paganelli Rosolia Teodoro
*Division of Rheumatology, Faculdade de Medicina da Universidade de São Paulo, Brazil

Background & objectives: Chronic joint inflammatory processes may expose hidden antigens, such as collagen V (ColV), leading to autoimmunity. Our aim was to evaluate the cellular response, inflammatory process, and osteochondral damage after oral immunotherapy with ColV in arthritis model.
Methods: Arthritis was induced by intra-articular injection of mBSA/CFA into the right knee in male Lewis rats (IA, n=20). After 14 days a group was treated with ColV (IA-Col V, n=10) and the animals were submitted to euthanasia on the thirtieth day. The articular tissues were evaluated by immunostaining and splenocytes were stimulates with ColV in vitro to evaluate IL10 expression.
Results: We found decrease in synovitis in the IA-Col V group compared to the IA group ($p<0.0001$). We observed increased of FoxP3+ and IL-10+cells, as intense double immunostaining for IL-10+ and FoxP3+ cells in the IA-Col V compared to IA ($p=0.0001$). In vitro, we found increased IL-10 expression by ColV-stimulated spleen lymphocytes in the IA-Col V compared to IA ($p=0.007$). IA-Col V showed increased Col I ($p=0.03$) and decrease ColV ($p=0.0001$) synovial expression. In the cartilage, the IA-Col V group showed less spatial disarray and cellular clusters and less subchondral trabecular loss compared to the IA group. Cartilage thickness was preserved in the IA-Col V compared to IA ($p<0.038$).
Conclusion: Oral treatment with ColV attenuated the inflammatory process and promoted synovial repair and cartilage preservation in experimental arthritis, opening up a perspective for the use of this strategy in arthritis treatment.

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E-PS-16-065
Neoplastic stromal cells with activated PDGFRβ signalling as a potential new therapy target in giant cell tumour of bone
I. Staniczkova Zambo*, D. Zoufaly, M. Hermanova, J. Neradil, S. Paukovcekova, M. Mahdal, L. Pazourek, P. Mudry
*1st Department of Pathology, St. Anne´s University Hospital and Faculty of Medicine of Masaryk University and International Clinical Research Center, St. Anne´s University Hospital in Brno, Czech Republic

Background & objectives: Denosumab treatment in advanced giant cell tumour of bone (GCTB) inhibits giant cells without reducing the risk of recurrence. Recently, denosumab also induces PDGFRβ activation in neoplastic stromal cells. The combination of denosumab and PDGFRβ-inhibitor is promising in GCTB treatment.
Methods: Three patients (20 years old female, 19 years old male and 17 years old male) with locally advanced GCTB (distal ulna, distal radius and hallux, respectively) received 3-months denosumab with the addition of sunitinib for one month followed by surgery. The presence of both giant cells and stromal cells was evaluated, the latter using histone H3G34W immunohistochemical detection.
Results: In all cases, intial biopsy showed typical GCTB morphology, histone H3G34W expression confirmed the presence of neoplastic

stromal cells. After combined neoadjuvant therapy, complete depletion of giant cells was identified in all cases. The non-ossified portion of lesions resembled a scar tissue both macroscopically and histologically. No stromal cells were detectable in male patients, whereas the female patient had 90% loss of neoplastic cells. In the follow-up period 15-43 months, none of the patients relapsed.
Conclusion: Treatment of GCTB with denosumab in combination with sunitinib could become an effective precision therapy of locally advanced tumours and GCTBs with unfavourable localization, especially in axial skeleton.

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E-PS-16-066
Histopathology assessment of joint components reveals a similar pattern in focal chondral lesions and osteoarthrosis
D. Ubrig Munhoz, C. Machado Baldavira, A.P. Pereira Velosa, V.D. Rodrigues de Souza, J. Alves Almeida, P. Nogueira Giglio, M. Kawamura Demange, V.L. Capelozzi, W. Paganelli Rosolia Teodoro*, R. Gomes Gobbi
*Division of Rheumatology, Faculdade de Medicina da Universidade de São Paulo, Brazil

Background & objectives: We hypothesize that osteoarthrosis (OA) and focal chondral lesions (FCL) are part of the same spectrum of disease. In the present work, we investigated the lesional morphological findings of articular cartilage yield on histology and histochemistry.
Methods: A comparative study was carried out between patients with knee OA and knee FCL regarding the evaluation of osteochondral biopsies. A total of 24 patients were selected to compose the cohort being 10 with knee OA, 10 with knee FCL and 4 with control. Biopsies of macroscopically normal trochlear cartilage outside the loading area were used as a control.
Results: In the analysis of subchondral bone, using the OARSI histopathological score, we evaluate the OA and FCL and compared to the control group. High mean of OARSIs score presented statistical significance when compared OA and FCL to control group ($P<0.01$, to both). To evaluate cartilage thickness, we observed statistical power between OA (centre and peripheral) low means compared to the control ($P=0.01$, $P=0.003$, respectively). When we evaluated the loss of proteoglycan, a difference with statistical power was observed between the OA (centre and peripheral) and FCL centre comparing the control ($P=0.009$, $P=0.004$, $P=0.04$, respectively). A similar mean was observed between chondral regions.

Conclusion: In the current study, our results demonstrated that although arthrosis and focal chondral lesion are different clinical diseases the histopathological criterial are similar suggesting that both represents same spectrum of diseases.

E-PS-16-067
Differential diagnosis of telangiectatic osteosarcoma: correlation between radiological and pathological findings
M. Veras Lista*, M.I. Ttito Condori, A. Val-Carreres Castellote, S. Simonyan Hovhannisyan, C.A. Batista Batista, A.B. Enguita Valls
*Hospital 12 de Octubre, Spain

Background & objectives: Telangiectatic osteosarcoma (TOS) is a rare entity that poses a diagnostic challenge concerning aneurysmal bone cysts (ABC), for they share similar radiographic and pathological findings. We aim to characterize its main features and differential diagnosis through a complex case.
Methods: A 5-year-old male without previous medical history develops hip pain over a three-months-period. A magnetic resonance (MR) reveals a heterogeneous, infiltrative mass in the right iliac region with cystic areas, seen as hypodense areas by CT-scan. Histological and molecular findings are reviewed and, after a literature research, the differential diagnosis based on tumour location, epidemiology, radiology and histology is discussed.
Results: Core-needle biopsy (CNB) reveals a pleomorphic cell population and osteoclasts intermixed with osteoid on a necrotic background. There are multiple vascular structures, though no clear cysts are observed. MDM2 amplification by FISH and next-generation sequencing are negative. Upon correlation with radiological findings, the sign-off diagnosis is an osteoblastic tumour, suggesting in the first place a TOS and including an ABC in the differential.
Systemic treatment and an hemipelvectomy are performed. Macroscopic examination of the surgical specimen reveals an infiltrating tumour composed of solid areas and multiloculated, haemorrhagic cysts, which histologically correspond to dilated blood vessels and are intermixed with pleomorphic, osteoid-producing cells. Diagnosis of telangiectatic osteosarcoma is confirmed.
Conclusion: CNB of bone pathology are challenging, for they may not be representative of the whole tumour and a higher-grade area or an important element of the lesion may not be included. Thus, diagnosis relies heavily on clinical and radiological correlation, and requires the work of a multidisciplinary team. Upon a bone biopsy of a lesion with radiological evidence of a cystic component and lytic behaviour, TOS should be ruled out, even if cystic structures are not histologically evident.

E-PS-16-068
Intraosseous spindle cell rhabdomyosarcoma with FET (EWSR1)-TFCP2 and LOC101929418-ALK fusions: a case report and literature review
C. Vieru*, M.L. Abascal Camacho, M.N. Villca Huayta, A.J. Van Der Biezen, C. Agra Pujol, F. Arías, V. Parra Blanco, F. Alijo Serrano
*Hospital General Universitario Gregorio Marañón, Spain

Background & objectives: Intraosseous spindle cell rhabdomyosarcoma (RMS) is a subtype of spindle cell/sclerosing rhabdomyosarcomas defined by TFCP2 or NCOA2 rearrangements. It is a rare entity with less than 50 cases reported to date in the literature.
Methods: We are reporting the only case of intraosseous RMS diagnosed in our hospital. It was evaluated through microscopic examination, immunohistochemistry, fluorescence in-situ hybridization and gene sequencing. A literature review was conducted to explore related cases. We describe clinical, radiological, histopathological, immunophenotypic and molecular features.
Results: A 20-year-old male with a 2-year history of refractory dental infections presented with a 1.5 months history of rapidly growing right mandibular angle lesion. Imaging revealed a 63x33 mm lytic tumour that microscopically showed a mitotically active malignant mesenchymal proliferation with spindle, epithelioid and scattered rhabdoid morphology, marked atypia and nuclear pleomorphism. Immunohistochemistry showed positivity for MyoD1 and CKAE1/AE3 and negativity for desmin and myogenin. RNA-based NGS (Archer FusionPlex Sarcoma Panel) revealed EWSR1-TFCP2 and LOC101929418-ALK gene fusions. After unsuccessful chemotherapy, Alectinib (ALK inhibitor) combined with radiotherapy was initiated. Despite initial stability, pulmonary metastases appeared and the patient died 15 months after diagnosis.
Conclusion: Intraosseous spindle cell rhabdomyosarcoma (RMS) with TFCP2 rearrangement is a highly aggressive tumour with an early onset, fast progression and poor response to standard therapies. Our case, one of the few cases described with two gene fusions, contributes to understanding its molecular profile. Further clinical studies are required to explore the efficacy of targeted therapy for ALK and for the development of new effective treatment approaches. Early and accurate diagnosis remains crucial for prognosis and effective therapeutic management.

E-PS-16-069
Intranodal palisaded myofibroblastoma - rare cause of limfadenopathy - case report
A. Wasążnik-Jędras*, M. Kołos
*Poland

Background & objectives: The aim is to present a case report of intranodal palisaded myofibroblastoma (IPM), which is a rare cause of lymphadenopathy. Benign mesenchymal neoplasm shows a predilection for inguinal nodes, mainly in middle-aged male patients. Surgical removal is curative.
Methods: Formalin fixed and parafin-embedded sections were treated with H&E and immunohistochemical stains (SMA, CyclinD1, Beta-Catenin, CKAE1/AE3, CD117, DOG-1, Caldesmon, Desmin, S100, Melan-A, HMB-45, CD31, CD34, ERG, CD23, TdT, Ki-67).
Results: A 70-year-old male patient with left-sided inguinal lymphadenopathy after radical prostatectomy and removal of left groin leiomyoma. A lymph node measuring 4x3x2.5cm was excised. Microscopically centrally located nodal lesion consisting of monomorphic spindle cells without atypia accompanied by extracellular deposits of collagen fibers and haemorrhages. No foci of necrosis or mitotic figures were found. Differential diagnosis included: schwannoma, leiomyoma, Kaposi's sarcoma, lymphangioleiomyomatosis, follicular dendritic cell sarcoma, as well as metastases of cancer, melanoma and GIST. Tumour cells expressed SMA, CyclinD1 and Beta-Catenin; Ki-67 was 1%. On this basis IPM was diagnosed. The previously removed left groin tumour was re-evaluated - IPM was also diagnosed.
Conclusion: The characteristic microscopic image of IPM is usually sufficient to establish the diagnosis. In the presented case only re-evaluation allowed for the correct diagnosis of both removed groin tumours. Based on this, it can be concluded that this is a case of bifocal or recurrent IPM. Therefore, it should be remembered that in some cases, only a combination of appropriate examination of the material, clinical data and the necessary immunohistochemical staining is the key for appropriate diagnosis

E-PS-16-070
Leiomyosarcoma of the inferior vena cava: a case report
M. Zghal*, M. Triki, S. Fendri, S. Makni, C. Kammoun, T. Boudawara, L. Bouzidi
*Department of Pathology, Habib Bourguiba University Hospital, Sfax, Tunisia

Background & objectives: Leiomyosarcoma (LMS) of the inferior vena cava (IVC) is a rare malignant tumour, originating from the smooth muscle cells of the media and accounting for 2% of all LMS. We aimed to analyse the clinico-pathological features of this rare entity.
Methods: A 70-year-old woman, presented vague and paroxysmal abdominal pain. Physical examination revealed a large and fixed abdominal mass. Computed tomography (CT) showed a right lobulated retroperitoneal mass measuring 25x17x11 cm. The tumour caused a mass effect on the duodenum, the pancreas, the right kidney and the renal vein. A gastrointestinal stromal tumour was suggested and a CT-guided biopsy was performed.
Results: Histological examination revealed cellular proliferation of intersecting fascicles of spindle cells with eosinophilic cytoplasm, pronounced nuclear pleomorphism and a mitotic rate of 21/10 high power fields. Immunohistochemical study was positive for SMA and H-caldesmone and negative for CD34, MDM2, Dog1 and S-100. Findings were consistent with LMS. Tumour resection was performed in bloc with right kidney and segment of IVC. The tumour was well circumscribed infiltrating the perirenal fat and IVC wall, with grey-white cut surface associated with hemorrhage and necrosis. Histological analysis confirmed biopsy findings. The tumour emerged from the IVC media, which supported the diagnosis of IVC LMS. The tumour was of grade 2 FNCLCC. Margins were positive.
Conclusion: LMS of IVC is an exceedingly rare and aggressive tumour, representing 0.7% of all retroperitoneal tumour. IVC is the most affected vessel among vascular LMS. It is mostly seen in women, and the diagnosis is often delayed because of the lack of symptoms. Although CT is a sensitive tool in establishing the diagnosis, tumour with large extraluminal component require differentiation from hepatic, renal, digestive tumours or other retroperitoneal structures. Pathological examination remains the only tool to set the final diagnosis.

E-PS-17E-Poster Session Digital and Computational Pathology

E-PS-17-001
The pathology portal – an online educational platform
E. Abu*, J. Martin
*United Kingdom

Background & objectives: Digital pathology can provide broad and convenient learning opportunities. The portal's objective is to develop a user-friendly online learning platform with interactive functionality, equitable access to quality-assured learning resources, and specialist content for trainees and practitioners across all pathology specialties.
Methods: Discovery trainee and trainer interviews framed the development. Prototype, alpha and beta releases expanded the NHS Learning Hub platform. Clinical case format, whole slide imaging viewing (WSI), single-best-answer and multiple-choice questions with feedback were developed, plus simple content upload. 'Match game' question format, annotation-based questions for WSI, and image carousel function followed. Editorial teams have developed and quality-assured the content.
Results: The platform launched in August 2022 with histopathology, cytology, neuropathology and cytology material. Other specialty content includes genomics, endoscopy videos for gastrointestinal curricula, and frozen sections. All other specialty areas are currently developing. The portal has provided good collections of teaching materials designed to support broad adaptive learning and development through graded curricula in pathology specialties. It has also provided continuing professional developments for established practitioners in different stages of their careers. The portfolio includes over 5100 resources, including cases, interactive modules, books, image library collections and EQA slides. There have been over 100,000 launches of resources. Feedback is excellent (90% 5 star), and content and usage continues to grow.
Conclusion: The Pathology Portal is an online educational platform developed by The Royal College of Pathologist and the technology-enhanced learning team at National Health Service (NHS) England in collaboration with the Institute of Biomedical Science and other professional bodies. It is a rapidly expanding, convenient, freely accessible, online interactive learning platform to support pathology learning, supporting United Kingdom and international pathology students, trainees and practitioners in all pathology specialties.

E-PS-17-002
AdaSlide: adaptive compression framework for digital pathology slides
S. Ahn*, J. Lee, S.H. Lee
*Department of Pathology, Korea University Anam Hospital, Korea University College of Medicine, Republic of Korea

Background & objectives: Digital pathology images require large amounts of storage space, naturally leading to cost issues. Here, we propose a compressing modality for whole slide images that adaptively employs the compression ratio based on information across regions of slides.
Methods: AdaSlide, an Adaptive compression framework for digital pathology Slides, consists of a compression decision agent (CDA) and a foundational image enhancer (FIE). The CDA utilizes reinforcement

learning to evaluate each patch's necessity and degree of compression, ensuring minimal information loss and maintaining diagnostic integrity. The FIE, trained on diverse cancer types and magnifications, ensures high-quality image restoration post-compression.
Results: We assembled the PanCancer dataset from 30 TCGA projects, comprising 1.8 million patches extracted from 930 WSIs. Using this dataset, we trained two key modules: the FID and the CDA. The FID enhanced compressed images through encoding and decoding steps, while the CDA autonomously determined the compression level based on the image's information content. We evaluated AdaSlide's performance across various downstream tasks, including patch-level classification, segmentation, and slide-level classification. The results indicated minimal degradation in prediction performance when comparing pre- and post-AdaSlide outputs, demonstrating the effectiveness of AdaSlide in maintaining prediction accuracy while reducing image size.
Conclusion: This framework paves the way for more efficient storage and transmission of digital pathology data without compromising diagnostic utility.

E-PS-17-003
CutMix-augmented subtype classification in gastric spindle cell tumour
S. Ahn*, S.H. Lee
*Department of Pathology, Korea University Anam Hospital, Korea University College of Medicine, Republic of Korea

Background & objectives: The tumour subtypes are crucial for the decision of treatment strategy in clinical practice. For deep learning-based approaches, there are challenges with an imbalanced distribution across subtypes. Here, we propose a simple and effective augmentation strategy to mitigate this.
Methods: In this study, we retrospectively reviewed and collected the whole slide images of gastric spindle cell tumours from three hospitals: gastrointestinal stromal tumour (n = 502), leiomyoma (n = 145), and schwannoma (n = 35). We performed CutMix augmentation on classes with lower ratios, creating additional patches. Further, Uniform Manifold Approximation and Projection feature visualization was applied.
Results: Through the augmentation strategy, the trained model achieved a betterIt is expected that our pipeline would offer significant support in clinical environments for the categorization of different subtypes of gastric cancer F1-score from 0.977 to 0.989 for GIST, from 0.720 to 0.744 for leiomyoma, and from 0.763 to 0.791 for schwannoma.
Conclusion: Our study confirmed the effectiveness of the deep learning approach in challenging tasks involving a subtype classification of gastric spindle cell tumours and validated the efficacy of a simple augmentation strategy.

E-PS-17-004
Comparative impact of specialized educational content versus regular postings on user engagement in pathology on X (formerly Twitter)
B.K. Aktas*, Y. Chornekyy, O. Yilmaz

*Turkey
Background & objectives: X, formerly known as Twitter, is known for its educational and promotional benefits in Pathology. This prospective study aims to compare the engagement statistics of an account that exclusively shares educational content with an account that posts typical daily updates.
Methods: This study employs a controlled before-and-after design to assess the impact of posting engaging pathology cases on X engagement. For one month, the intervention account, @ychornenkyy, shared four gastrointestinal or liver pathology board-style multiple-choice questions weekly. The control account, @BKA_MD, maintained regular activity with typical pathology and non-pathology content. Engagement statistics were collected 48 hours after every post and analysed.
Results: Prior to the study, both the intervention and control accounts had similar follower counts, activity patterns, and baseline statistics. The primary outcome revealed an increase in follower counts of 117 for the intervention account and 95 for the control. For secondary outcomes, the intervention account achieved significantly higher visibility with an average of 2748 impressions, versus 1460 for the control. Despite this, the control account received more likes (22 vs. 18) and profile visits (70 vs. 18). The intervention account led in retweets (4) and detail expands (56), compared to the control (0 and 14). Engagement was also greater in the intervention group, with 228 versus 126 for the control.
Conclusion: This study on X (formerly Twitter) demonstrates that specialized educational content significantly enhances user engagement compared to regular postings. The intervention account, which focused on pathology-related multiple-choice questions, showed greater visibility and interaction, evidenced by higher impressions and retweets. Conversely, the control account maintained strong direct interactions through likes and profile visits. Both strategies attracted new followers, indicating that tailored content can effectively engage and expand a niche audience, thus enhancing visibility and influence within specific professional fields.

E-PS-17-005
PathoBox: facilitating dataset creation for pathology algorithm development
V. Almeida*, R. Jesus, Y. Castilla, L. Veloso, A. Silva, M. Reis Silva, I. Rodrigues, L. Bastião, L. Carvalho, V. Sousa
*Institute of Anatomical and Molecular Pathology, Faculty of Medicine of the University of Coimbra, Portugal

Background & objectives: The integration of AI tools into pathology diagnostics has advanced significantly, encompassing tasks such as object recognition, and whole-slide image segmentation. PathoBox will allow for the creation of datasets conducive to developing new algorithms for clinical pathology practice.
Methods: PathoBox is a collaborative digital pathology platform, accessible through a common web browser, that encompasses storage and visualization of digital slides. Images from different scanners can be uploaded to the platform and annotated by algorithms. The resulting data can be curated by pathologists through advanced annotation tools, to create labeled datasets used to create new algorithms.
Results: PathoBox was successfully used to upload 57 slides of lung tissue that were automatically annotated by a lung tumour foci algorithm. Clinical validation involving three pathologists and digitized slides from four scanning systems demonstrates promising results. Preliminary findings indicate high-precision segmentation across different histopathological subtypes of adenocarcinomas, correlating well with validation data. The AI tool significantly reduces biopsy analysis time, potentially facilitating seamless integration into clinical practice. In addition to automated detection, our service incorporates a continuous improvement approach using Active Learning techniques. This method allows model results to be iteratively refined by expert pathologists. This continuous feedback contributes to the expansion and refinement of the database used for training.
Conclusion: Our aim is to develop a robust digital pathology platform with a focus on integrating and developing analysis algorithms, whose output can be validated by pathologists. Image datasets from different scanners and pathologies can be uploaded and annotated by the algorithms. An AI-based algorithm for detecting and segmenting lung tumour foci was successfully developed and integrated into the platform. The algorithm's output is compatible with commonly used open-source software, fostering collaboration and further research in the field of pathology AI.

E-PS-17-006

Prospective deployment of artificial intelligence pathology platform to three United Kingdom hospitals for real-time use in patient pathways

J. Andreasson*, H. Montgomery, S. Johnston, M. Broadmore, C. O'Brien, K. White, S. Florio, A. Kansara4, J. Oxley, D. Snead, M. Dolton, M. Horton, C. Verrill
*Paige, Inc., United Kingdom

Background & objectives: Artificial intelligence (AI) technologies in digital pathology are often assessed offline or as a standalone modality, rather than in live clinical pathways. This is due to, among many factors, the technical performance requirements for real-time delivery of AI outputs.
Methods: Real-time deployment of clinical AI software that helps pathologists in diagnosing prostate cancer core needle biopsy specimens was required to deliver a multicentre health economics study program. First, technical requirements for image and data transfer were determined for three separate hospitals. Then, a test environment was created and validated prior to end user acceptance testing, followed by live use.
Results: Three United Kingdom hospitals had different existing digital pathology infrastructure, and unique clinical deployment requirements. To deliver the two-year study, three distinct solutions were architected adhering to local hospital and pathology department requirements. The final solutions were: (1) direct laboratory information management system (LIMS) integration; (2) specimen tracking system integration with local image file export to dedicated server; and (3) image management system (IMS) daily export with direct cloud upload and scheduled scripted ingestion. Once the solutions were approved, delivered and validated, all sites accessed the AI software platform to use on their consecutive core needle cases for prospective case review as part of the study protocol.
Conclusion: A primary barrier to evaluating AI systems in a prospective environment, rather than on a retrospective cohort outside of patient pathways, is the complexity of integrating the AI systems into existing health information systems, which requires sourcing image files, and associating the corresponding metadata. The three deployments required close multidisciplinary discussion at each site including biomedical scientists, information technology (IT) teams, pathologists, and the industry partner. Secure cloud computing allows timely delivery of AI results for real-time clinical use.

Funding: The study is funded by the NHSx Artificial Intelligence in Health and Care Award: Driving system-wide improvements with real-world economics evidence and subspecialist-led adoption guidelines for full workflow implementation of AI with Paige Prostate cancer detection, grading and quantification tool in histopathology departments (AI_AWARD02269). The views expressed in this publication are those of the authors and not necessarily those of the NHS, NHSx or the Department of Health and Social Care.

E-PS-17-007

Detecting abnormal p53 immunohistochemical expression patterns in patients with Barrett's oesophagus using artificial intelligence

M. Botros*, L. Verheijen, O.J. De Boer, E.J. Bekkers, C.I. Sánchez, S. Meijer
*Amsterdam UMC, The Netherlands

Background & objectives: Identifying Barrett's oesophagus (BE) patients at risk of oesophageal adenocarcinoma progression is challenging, but p53 expression holds promise as a predictive biomarker. We aimed to develop an AI system for detecting abnormal p53 immunohistochemical (IHC) expression, aiding early progression detection.
Methods: A training dataset was constructed of 1472 biopsy images extracted from p53 IHC stained slides at 10x magnification (1 µm/pixel). A ResNet-18 pre-trained on ImageNet was then fine-tuned with biopsy images resized to a 1024x1024 resolution. The network's output layer consisted of two nodes: one to indicate the presence of over-expression and one for an absent expression pattern.
Results: The system was evaluated on a test set of 60 biopsy images with an equal spread in classes: 15 images showing normal p53 IHC expression, 15 abnormal over-expression, 15 abnormal absent expression and 15 double clones (images containing both absent and over-expression regions). Combining abnormal classes (over-expression, absent-expression and double clones), the system achieved an accuracy of 97% (sensitivity: 0.96, specificity: 1, false positive rate: 0, false negative rate: 0.04). Using Gradient-weighted Class Activation Mapping (Grad-CAM), we demonstrate the network's precision in identifying abnormal expression regions within the biopsy samples.
Conclusion: In conclusion, our study underscores AI's potential to aid in detecting abnormal p53 IHC expression, providing a cost-effective avenue for integrating p53 IHC analysis into routine clinical practice and enhancing prediction tools for BE progression. However, further research is needed to evaluate the AI system's clinical utility through comparison with pathologist interpretation.

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E-PS-17-008

Deep learning for giant cells arteritis diagnosis on temporal artery biopsy

R. Bourgade*, M. Elhannani, D. Loussouarn, A. Guédon, R. Péteri, C. Allix-Beguec, M. Berthier, O. Espitia, C. Roncato, C. Toquet
*University Hospital of Nantes, France

Background & objectives: Giant Cell Arteritis (GCA) is a vasculitis that can lead to severe complications. Its diagnosis is made through the analysis of a temporal artery biopsy, which can be time-consuming. Here, we explore the potential of deep learning in diagnosing GCA.
Methods: We included 366 patients for training and 58 patients for an external validation. The whole-slide images (WSI) were tessellated into tissue patches. Leveraging CTransPath representation, these patches were then embedded into low dimensional space and subsequently aggregated utilizing an Attention-Based Multiple Instance Learning (AB-MIL) mechanism. Attention heatmaps were finally generated to elucidate the underlying mechanisms of the model's predictions.
Results: Our classifier trained over >1.2M tiles, achieved a mean AUC of 0.993, a mean balanced accuracy of 0.977 and a mean F1-score of 0.976 through 4-fold cross-validation. Once the optimal combination of hyperparameters was established, we retrained a singular model on the whole training set and subsequently evaluated it on the testing set. This model achieved an AUC of 0.969, a BAC of 0.952 and a F-1 score of 0.965. According to the ABMIL mechanism, the model appears to be particularly sensitive to the presence of inflammatory infiltrate and seems to focus its attention predominantly on the media layer.
Conclusion: This methodology enables us to achieve state-of-the-art performance in GCA diagnosis. It also reveals that the model, in alignment with recent consensus, is mainly sensitive to inflammatory infiltrate, predominantly focusing its attention on the media. Even if this study needs to be validated on a larger cohort, these findings highlight the potential of deep learning to assist the pathologist in the GCA prescreening. Future research should focus on clinical outcome prediction and exploring its applicability in other vascular diseases diagnosis.

E-PS-17-010

Registration-based 3D light sheet and 2D histology image fusion tool for pathological specimen

M. Brettmacher*, P. Nolte, D. Pinkert-Leetsch, F. Bremmer, J. Mißbach-Güntner, C. Rußmann
*HAWK Goettingen, Germany

Background & objectives: The analysis of pathological changes using stained histological sections is the standard in clinical routine but is limited to two dimensions. We address this shortcoming by merging 3D light-sheet and histological imaging using our novel software.
Methods: Four different testicular tumour specimen were initially embedded in paraffin and punched to generate tissue cylinders of 5mm diameter. Each cylinder was deparaffinized, cleared, and scanned using light sheet fluorescence microscopy. Afterward, the blocks were subsequently re-embedded in paraffin, sectioned, and stained. Using our novel software tool LitSHi, we identified corresponding 2D histological sections in the 3D in silico volume.
Results: After the imaging of the 2D section under a microscope, the resulting image is preprocessed using thresholding and a morphological image filtering pipeline. The circular cut section, resulting from the punch biopsy, is detected using a Hough-circle transformation and subsequently segmented from the background. Using a template-matching approach corresponding slides in the histology and light-sheet imaging data are determined and serve as seed points for the registration process. Elastic registration based on B-Splines is used to refine the overlay of both modalities. After the successful fusion, the cut section is precisely placed into the 3D volume thus allowing for the generation of a virtual histological volume.
Conclusion: Accurately merging 2D histological sections into a 3D light-sheet volume is a difficult and time-consuming process. Ignoring this task restricts the examination of pathological tissue changes to a confined area within the specimen. With our software tool LitSHi this process is automated thus allowing medical professionals the swift fusion of both modalities. This places the histological data into a 3D context, which can be used to identify higher-level features with increased specificity.

E-PS-17-011

The use of structured reporting and SNOMED CT to render high-quality usable and computable pathology cancer reports for oncology patient care, public health, and translational research

S. Campbell*, J. Srigley, K. Sheahan, B. Rous, P. Seegers, G. Birdsong
*University of Nebraska Med Center, USA

Background & objectives: The benefits of structured pathology cancer reporting in quality and patient outcomes are well-documented. Extending these benefits on an international scale for use in patient care, public health surveillance, and translational research requires the use of computable medical terminology standards.
Methods: In 2020, SNOMED International commissioned the Cancer Synoptic Reporting Working Group (CSRWG) to develop the necessary SNOMED CT concepts for structured pathology cancer reporting data elements. The CSRWG used the structured pathology reporting data sets produced by the International Collaboration on Cancer Reporting (ICCR) and the College of American Pathologists (CAP) as the primary reference sources.
Results: As of 2024, over 1000 SNOMED CT concepts were developed or edited to represent the core (required) data elements for all adult and paediatric solid organ pathology cancer pathology data sets published by the ICCR and CAP. SNOMED CT concepts for binding to ICCR data sets (or national society correlates) are available for use within the SNOMED CT International release. Implementation guidance documentation was also created as part of this effort and is available in the SNOMED International knowledge repository. Both the ICCR and the CAP are currently in the process of developing data set release materials that include SNOMED CT terminology bindings for distribution including electronic data exchange methods.
Conclusion: The SNOMED International effort to develop a standardized, computable medical terminology for use in conjunction with ICCR and CAP pathology cancer data sets provides the substrate to make pathology cancer data electronically interoperable on the international level. SNOMED CT concepts used accommodate international variations in pathology practice while maintaining the consistent meaning of pathology information. These encoded data enable consistent, reliable aggregation and analysis of pathology data for use in public health surveillance, clinical care, and research efforts.

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E-PS-17-012

Real-world performance of computer-assisted diagnosis in urine cytology

A. Caputo*, C. Ciaparone, E. Maffei, P. Verze, P. Zeppa
*University Hospital of Salerno, Italy

Background & objectives: The increasing workloads and a global shortage of pathologists are posing demands on pathology services. Computer-assisted diagnosis (CAD) has shown promise in mitigating these problems. The aim of this study was to quantify real-world benefits of CAD in urine cytology.
Methods: We compared the diagnostic performance of three cytopathologists in diagnosing 90 urine cytology ThinPrep slides, both with and without the assistance of a CAD tool developed in-house (Fig. 1).
Results: In 70/90 cases (77.8%) pathologists were faster when using CAD. The average time per slide went down from 90.3 to 59.6 seconds (–34%) (Fig. 2). Aided diagnoses were better in 15/90 (16.7%) cases, worse in 5/90 (5.5%) cases, and equivalent in the remaining 70 (77.8%) cases.
Conclusion: CAD speeds up time-consuming tasks and enhances diagnostic accuracy, improving care of patients with urotelial carcinoma. CAD can be a solution to the increasing demands on pathology services, in this case for urine cytology specimens.

E-PS-17-013

Interpretation of cytomorphological features in thyroid fine needle aspiration biopsies using artificial intelligence

M.Y. Çelik*, Y. Albayrak, N. Yılmaz, İ.E. Gürer
*Akdeniz University Hospital, Turkey

Background & objectives: The evaluation of thyroid FNA involves numerous criteria and it can be challenging in terms of time and workload. This study aims to retrospectively select, photograph, label smears and educate an algorithm that differentiate malign and benign diagnosis.
Methods: Subsequently, with the help of a convolutional neural network model, a model is intended to learn and classify the diagnostic concepts of 'benign' and 'malignant'. Our study includes 50 benign and 50 malignant conventional smears. After photographing, 721 images as 'benign' and 710 images as 'malignant' were obtained. Annotation, image augmentation, dataset creation, model training and statistical analysis were performed.
Results: According to the results, the sensitivity rate for the benign diagnosis is 95.9%, the specificity rate is 95.6%, and the F1 score is 0.958. For the malignant diagnosis, the sensitivity rate is 95.6%, the specificity rate is 95.9%, and the F1 score is 0.957. The precision value calculated for both diagnosis groups is determined as 0.958. The Receiver Operating Characteristics (ROC) curve was plotted and area

under the curve was calculated. When measured separately for benign and malignant diagnostic classes, it was found to be 0.99 for both. Our study has demonstrated that a successful model with high sensitivity, specificity, F1 score and area under curve statistics can be trained.
Conclusion: The standardization of diagnostic categories, augmentation of input data through various steps, adjustment of model layer numbers and processes, and optimization of the training iterations led to the creation of a model with high statistical success. In the age of technology, the integration of artificial intelligence applications into our daily routines, especially in the field of medicine, will become one of the most essential aids for physicians in the diagnosis and management of various health issues.

E-PS-17-014
Hardware annotation devices in computational pathology: a comparative analysis
G.E. Corredor Alonso*, T. Falck, M. Testori, I. Bisha, Z. Kokaragac, C. Cotoi, S. Haneder
*AstraZeneca Computational Pathology GmbH, Germany

Background & objectives: Manual annotations of histological features are a cornerstone for computational pathology. This study aims to identify whether and how the annotation device, the visual impression or the time of day could affect the quality of annotations.
Methods: One pathologist annotated different areas on 15 regions of interests (ROI) on haematoxylin-eosin (H&E) samples from lung, breast, colon, and prostate cancers, using three different hardware devices (GraphPad Wacom One, Mouse Logi MX Anywhere 3 + computer and XP Deco Pro MW Pen Tablet). For each ROI annotation time were recorded and pairwise comparisons for all annotations computed and analysed.
Results: Analysis of the annotations with the three devices was performed by comparing areas, outlines, duration, and moment of the day using several statistical scores, among which: Dice score of the overlapping areas for the different annotated classes, mean average surface distance (MASD) for annotated outlines and F1 score for agreement of annotated instances. Results shown that while there is variation in the analysed metrics, especially for smaller tissue regions, none of the differences is statistically significant for the analysed cohort. This applies to the difference of the outlines, areas and the time required for annotations between devices, also the moment of the day does not seem to affect the results.
Conclusion: Usage of three different hardware devices for class annotation on H&E tissue slides does not show significant differences on the annotated areas. In case these results can be validated on a larger dataset, we can conclude that for experienced individual annotators the studied variables do not influence the quality of the generated annotations in a significant manner.

E-PS-17-015
Bridging between pathologist's assessment and automated optical density measurements identifies the influence of the overall slide staining intensity on visual scoring
C.G. Cotoi*, L. Meinecke, C.C. Sachs, M. Rebelatto, P.L. Martin, H. Hessel, A. Shumilov, S. Batelli, H. Allaei, M. Gustavson, S. Christ, S. Haneder
*AstraZeneca Computational Pathology GmbH, Germany

Background & objectives: Biomarker expression is routinely assessed by pathologists through immunohistochemistry (IHC). Computational pathology provides more robust assessment of biomarker expression in tumour cells. Our objective was to bridge between visual and computational approaches in order to assess areas of reader variability.
Methods: We analysed 34 whole slide images (WSI) tumour samples spanning 10 indications and seven IHC markers. In total, 414 regions of interest (ROIs) were visually scored (membrane staining intensity 0-3+) by 5 pathologists. A supervised deep-learning-based image analysis algorithm was also used to segment the same ROIs to objectively quantify staining intensity on both a sample and individual cell level.
Results: Analysis of staining intensity measured by optical density (OD) and visual scoring demonstrated that specific cellular OD thresholds could be derived through machine learning classification to match the visual scoring categories ($0<12$, $1+\geq12$, $2+\geq38$, $3+\geq76$) independently of indication and marker. However, cellular OD values showed intra-category variance (e.g., broad range of cellular ODs within IHC-3+ category) as well as inter-category overlap (e.g., cellular OD values for IHC-2+ sometimes greater than that for IHC-3+). Furthermore, we demonstrate that visual scoring on individual ROIs is influenced by overall staining intensity of the WSI where an ROI tends to be scored higher when the sample has a higher median OD.
Conclusion: OD thresholds that approximate IHC staining categories can be derived, allowing bridging visual and computational methods. This study provides evidence that ROI-focused IHC scoring is influenced by the overall WSI staining intensity of the tumour cells, and that this may introduce variability in the visual interpretation, quantitatively indicating how context of surrounding areas can influence pathologist scoring of specific regions. Digital quantification can provide a solution to scoring variability through objective, precise, and robust assessment of a tissue biomarker expression.

E-PS-17-016
Bridging the gap: extending artificial intelligence benefits to microscope-based pathology for prostate cancer diagnosis
J. Zhang, C. Petrucco, S. Dalrymple*
*Franklin.ai, Australia

Background & objectives: The integration of artificial intelligence (AI) in pathology possesses great potential, however widespread adoption remains limited due in part to limited digital pathology infrastructure. Here we utilised an AI model integrated within a microscope-based system in prostate cancer histopathology.
Methods: We analysed a dataset comprising 440 images of prostate needle core biopsy (NCB) specimens capturing 26 clinical findings. Using a previously trained and validated model, we evaluated separately both whole slide images (WSI) scanned, and camera integrated microscope acquired image data of the same slide. We explored both quantitative (standard performance metrics) and qualitative (visualisation) analyses to assess comparative performance.
Results: Our preliminary results demonstrate the feasibility of our approach in integrating AI technologies to microscope-based pathology. Microscope acquired images assessed by our model demonstrated strong classification precision for Acinar Gleason pattern 3, 4 and 5 along with other focal histological markers including intraductal carcinoma (Precision > 0.7 for all). These results were comparative or better than the same scanned WSIs assessed by our model highlighting that despite variations in image acquisition modalities, the AI model exhibited robust performance across both WSI and microscope image datasets.
Conclusion: We have shown that our model was robust in classification of focal markers of prostate cancer by incorporating AI techniques into traditional microscopy diagnostic methods. Importantly, we find we can add similar diagnostic and reporting value across Gleason grades (3-5) and prognostic factors such as perineural invasion, which form the basis of most prostate cancer reporting. There is potential for laboratories to use traditional microscopy combined with our model which could lower the barrier to AI adoption.

E-PS-17-017
Grayscale with colorization can offer improved compression and resolution of digital pathology images
L. Dalton*
*Dalton Pathology Research, USA

Background & objectives: Pathologists (especially the older and wiser) learned from grayscale images in textbooks and the literature. When color became an option it was often not seen to be worth the added cost in publication. In digital pathology color remains a cost.
Methods: Training images were converted to YCbCr format. CbCr underwent JPEG2000 compression at cratio=1000 while grayscale was not compressed. The extreme color compression narrowed and optimized what red or blue intensities best matched with each of 0-255 grayscale intensities. The resultant look-up table provided a colorization template. The "digital H&E stain" was applied to grayscale TCGA samples from 23 cancer types.
Results: The quality of colorized grayscale images (CGI) was judged by a pathologist having three decades experience. Assessed, was no loss iin ability to diagnose and evaluate cancers. The variation in staining between CGI and original color images was within the range typically seen in H&E stains from different laboratories. By use of CGI, images can be transmitted and/or archived in grayscale. With JPEG2000, grayscale occupies 2/3rds less memory than full color. The colorization template is only 640 bytes. After compression of full color images to equal the size of grayscale alone, resolution was lost. The color component does not compensate for lowering the grayscale component below grayscale alone.
Conclusion: Grayscale provides the diagnostic information in digital images. Sacrificing grayscale resolution to accommodate color is not sensible. Differential compression of Y (luminance) versus CbCr (chrominance) supports this claim. Minimal compression of grayscale can deteriorate quality, while color tolerates extreme compression. The human eye is more sensitive to luminance than chrominance, more-so than realized. Computer scientists are likely unaware and might misguide direction of study. CGI and extensive color compression show potential to markedly reduce the size of the pathology cloud.

E-PS-17-018
Fully automated AI solution may improve pathologists' standardization of HER2 scoring in breast cancer
L. Di Tommaso*, S. Uccella, B. Fernandes, R. Akpinar, T. Laohawetwanit, G. Mallel, R. Ziv, M. Grinwald, M. Vecsler
*Humanitas University, Italy

Background & objectives: This study aimed to evaluate whether an artificial intelligence (AI) solution used as decision support may improve pathologists' standardization of HER2 scoring in invasive breast carcinoma (BC)
Methods: Two-arm reader study evaluated HER2 scoring performance of two pathologists, each reviewing 85 HER2 (4B5) digital slides (WSI) of BC with or without the support of AI, which detects the invasive tumour area, classifies tumour cells based on their staining pattern and derives slide-level HER2 score. Both arms were compared to ground truth (GT) determined by two breast subspecialists
Results: Pathologists scoring HER2 digitally without AI had an accuracy of 69.3% (kappa 0.591) for all HER2 scores; 93.4% (kappa 0.824) for HER2-low (0 vs. 1+/2+/3+); and 78.3% (kappa 0.582) for 0/1+ vs. 2+/3+. The inter-observer agreement was 64.2% [95% CI: 52.8%,74.6%] for all HER2 scores; 88.9% [95% CI: 80.0%,94.8%] for HER2-low (0 vs. 1+/2+/3+), and 80.2% [95% CI: 69.9%,88.3%] for 0/1+ vs. 2+/3+.
The AI solution demonstrated an overall accuracy of 87.3% (kappa 0.828); 91.5% (kappa 0.807) for HER2-low (0 vs. 1+/2+/3+) and 95.8% (kappa 0.914) for 0/1+ vs. 2+/3+ cutoff
Conclusion: This study reports an independent validation of a fully automated AI solution for HER2 scoring in BC. Our results show high accuracy for the AI, suggesting that AI can improve reproducibility and standardization of HER2 scoring in BC and additional validation studies are ongoing

Funding: Research funding by Ibex Medical Analytics

E-PS-17-019
Streamlining MSI testing with AI analysis of H&E histology slides of colorectal cancer biopsies
R. Dubois*, J. Klein, O. Tchita, D. Jacobs, L. Guillou, C. Wiscart, A. Fouillet, K. Von Loga
*Owkin France, France

Background & objectives: Microsatellite Instability (MSI) is a key biomarker in colorectal cancer (CRC) with important therapeutic implications. In this study, we validate MSI1 as well as an improved algorithm (MSI2) on two external cohorts of biopsies.
Methods: Several multicentric cohorts of H&E slides of CRC were used to train the models: TCGA (859 slides from TCGA-COAD) and MPATH (1200 slides from French pathology laboratories). MSI1 was trained on TCGA and MSI2 was trained on TCGA and MPATH. For external validation, two independent cohorts of biopsies were used: USBx (99 patients) and FRBx (698 patients).
Results: MSI1 and MSI2 were validated on USBx and FRBx, using area under the ROC curve (AUC), sensitivity and specificity metrics to assess the models' performances. MSI1 reached an AUC/sensitivity/specificity of 0.87/0.94/0.62 (respectively 0.84/0.94/0.43) on USBx (respectively FRBx). MSI2 outperformed MSI1 with an AUC/sensitivity/specificity of 0.94/0.94/0.81 (respectively 0.91/0.94/0.66) on USBx (respectively FRBx). With the results of the NICHE-2 trial suggesting that neoadjuvant immunotherapy may become the standard of care for MSI CRC patients, such tools appear crucial for an improved workflow of MSI testing on biopsy specimens.
Conclusion: We show that MSI1, while trained solely on resection specimens, is able to rule out more than 40% of non-MSI biopsies with high sensitivity. MSI2, an enhanced version of the algorithm including more training samples yields substantial improvement, ruling out more than 66% of MSS biopsies with high sensitivity. This study paves the way for the use of AI-based MSI pre-screening in clinical routine on CRC biopsy specimens.

E-PS-17-020
MYCN status integrated classification of neuroblastomas by pathological image analysis using segmentation deep learning algorithms
S. Ekmekci*, E. Ipek, M.S. Apaydın, E. Ozer
*Izmir Provincial Health Directorate, Izmir City Hospital, Department of Pathology, İzmir, Turkey

Background & objectives: With the rapid development of image scanning techniques and visualization software, whole slide imaging is becoming a routine diagnostic method. In pathology imaging methods, it is important and challenging to automate image analysis efficiently and accurately.
Methods: Recently, deep learning algorithms show great promise in pathology image analysis such as tumour site identification, metastasis detection and patient prognosis. Many machine learning algorithms work by automatically segmenting pathology images. Among these algorithms, segmentation deep learning algorithms stand out due to their accuracy, computational efficiency and generalizability.
Results: Optical microscopy of pathology slides captures the histological details of tissues in high resolution. With the rapid advancement of technology, whole slide imaging is starting to become part of the routine procedure for clinical diagnosis of many diseases. The emergence of digital pathology offers new opportunities to develop algorithms and software tools that can assist pathologists in clinical diagnosis and researchers in studying disease mechanisms. In this study, in neuroblastoma cases, after digital scanning of H&E stained sections, deep learning methods were used to identify disease risk groups in 16 pathology

images and its effect on predicting MYCN genomic alteration has been investigated.
Conclusion: MYCN positive/negative data set created from patches and low risk MYCN Negative/Medium Risk MYCN Negative/High Risk MYCN data set, achieved accuracy scores of 96% and 99%, respectively, in the trained models. This study is promising in terms of its demonstration of the ability of classification of neuroblastomas in histological images by deep learning, accurately and rapidly, as well as predicting the molecular alterations in these tumours.

E-PS-17-021
Digital pathology adoption: a developing country perspective
E. Eloff*, R. Schoeman
*Ampath Laboratories, South Africa

Background & objectives: Digital pathology has improved patient safety and diagnostic efficiency globally. However, no research exists on South African histopathologists' perceptions and attitudes regarding digital pathology adoption. Understanding these factors is crucial for realising the benefits of this technology in South Africa.
Methods: Primary quantitative data was collected via a questionnaire based on the Unified Theory of Acceptance and Use of Technology (UTAUT) model and distributed to all South African histopathologists. Specific constructs evaluated were the histopathologists' performance expectancy, effort expectancy, social influence, perceived risk and facilitating conditions influencing behavioural intent to adopt digital pathology. Correlation and regression analysis techniques were used.
Results: The study comprised 23% of registered histopathologists in South Africa. Most participants use digital pathology for external quality assurance and training. Over 60% of surveyed histopathologists plan to use digital pathology in the next 12 – 24 months. Positive correlations were found between performance expectancy, effort expectancy, social influence, and facilitating conditions with behavioural intent. Increasing age and years of experience reinforced the relationship between performance expectancy and behavioural intent. A strong negative correlation was found between perceived risk and behavioural intent, negatively moderated by increasing age and years of experience. Overall, 89% of surveyed histopathologists believe that digital pathology will be helpful for their future needs.
Conclusion: Appropriate managerial strategies can help South African histology laboratories leverage the benefits of digital pathology. Managers should emphasise the expected benefits of digital pathology for histopathologists and patients during discussions on digital pathology. Appropriate training of all histopathologists on the diagnostic accuracy of digital pathology can mitigate the perceived risk of digital pathology. By adopting digital pathology, the accuracy of diagnoses can be enhanced, and healthcare outcomes improved for the benefit of both patients and healthcare professionals.

E-PS-17-022
Artificial intelligence-powered subtyping of thymic epithelial tumours from hematoxylin and eosin whole slide images
A.S. Esteve Domínguez*, F. Akram, S. Peeters, D. De Ruysscher, J. von der Thusen
*Department of Pathology and Clinical Bioinformatics, Erasmus Medical Center, The Netherlands

Background & objectives: Thymic Epithelial Tumours (TET) are rare cancers that present challenges in accurately identifying subtypes, resulting in discrepancies and influencing treatment decisions. This study develops AI models for TET histopathological subtyping to enhance diagnostic accuracy and guide treatment choices.
Methods: 49 TET patients were diagnosed by 8 pathologists with 100% consensus: 31 (A/B3/TC) and 18 (B1/B2). Another 18 had 75-99% consensus: 6 (A/B3/TC) and 12 (B1/B2). H&E WSIs were annotated with QuPath, and 512x512-pixel patches were extracted at 20X. A binary CNN classifier was trained on the 100% consensus dataset using stratified k-fold cross-validation (K=3) and tested on both datasets.
Results: The 100% consensus dataset was split first into training-validation and test sets. The model was trained using stratified k-fold cross-validation. Initial results showed promising mean AUC values of 0.92 ± 0.04 and 0.943 ± 0.037 on validation and test sets, respectively, at the patch level. Patient-level AUC was 1 and 0.89 ± 0.036 on validation and test sets, indicating effective subtype characterization. Balanced accuracy at the patch level was 0.933 ± 0.015 and 0.93 ± 0.042 on validation and test sets, respectively. At the patient level, they were 1 and 0.877 ± 0.043. On the 70-99% consensus dataset, patient-level AUC and balanced accuracy were 0.723 ± 0.046 and 0.713 ± 0.020, respectively. GradCAM activation maps revealed lymphocytes correlate with B1/B2 and epithelial cells with A/B3/TC.
Conclusion: Our models effectively distinguish between A/B3/TC and B1/B2 classes, crucial for guiding tailored treatments; for instance, B3 patients in stage IIA may benefit from postoperative radiotherapy, unlike B2 patients. High generalizability was evident in k-fold outcomes on the 100% consensus set, though performance dipped on the 70-99% consensus set, mirroring challenges faced by pathologists. These findings drive our next phase toward achieving precise diagnoses, enhancing diagnostic accuracy, and devising personalized treatment approaches for TET patients.

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E-PS-17-023
A novel bioinformatic solution for SISH-HER2 evaluation
D. Guerrero*, M. López Ferrer-Bonsoms, I. Amat, A.A. Pasco, A.S. De Oliveira, M. Aznárez, C. López-Molina, A. Córdoba
*Department of Pathology, Spain

Background & objectives: Use of algorithms in Pathology is widespread and new applications constantly emerge. We are trying to find one to facilitate the assessment of Her 2 silver-enhanced in situ hybridization thanks to collaboration with Data Science Department (Public University of Navarra).
Methods: Fifty images were taken of a case of breast cancer. These images were used to construct an algorithm based on Deep Learning tools. Its structure consisted of the synthesis of two neural networks and a circumference detection algorithm for the delimitation of the nuclei.
Results: Different results have been reached from each part of the process. Regarding the implemented neural networks, used for the detection of each signal, an accuracy of 99% has been achieved. Final results can be obtained in less than one minute once the system has been fully trained. In the case of the circumference detection algorithm, the process has been more tedious. Combining the results obtained previously and the previous knowledge about the size of the nuclei, it was possible to delimit the nuclei of the images, thus obtaining the number of signals per cell in a very precise way and with an average of half a minute per image.
Conclusion: These preliminary results support the possibility of using automation systems for the assessment of SISH-HER2 as a very accurate, powerful, time-saving tool. This is a flexible solution, open to possible changes or improvements that will allow the pathologist to have innovative and complementary systems at their disposal for their daily work.

More and more types of tumours are candidates for treatment with anti-HER2 drugs and, therefore, the use of these procedures will help to reduce the workload.

E-PS-17-024

H&E-Net: a foundation model for computational pathology based on large-scale pretraining of a clinical pathology image dataset

Q. He*, J. Wu, Y. Liu, Y. Zhang, Z. Gao, J. Li, Q. Sun, S. Zeng, Y. He, Z. Wang
*Tsinghua University, China

Background & objectives: Efficient computational pathology demands pathology-specific foundation model tailored to the heterogeneity in whole slide images (WSIs). Pathology images from clinical settings represent a rich tapestry of abnormalities. However, there is a dearth of researches on foundation models using clinical-grade data.
Methods: This study introduces H&E-Net, a foundation model for computational pathology. We construct an exclusive clinical dataset comprising over 60,000 H&E-stained WSIs encompassing more than 10 tissue types from Xijing Hospital, China. This dataset contains over 10 million patches. Our approach employs ViT-Base as backbone, utilizes DINO for self-supervised pretraining, and leverages Segmenter and Faster R-CNN for fine-tuning on downstream tasks.
Results: H&E-Net underwent comprehensive evaluation. Feature distribution and maps visualization revealed that, under zero-shot conditions, H&E-Net achieved region clustering and structure identification more efficiently compared to both ImageNet-pretrained and non-pretrained models. H&E-Net was excuted fine-tuned across a spectrum of tasks, ranging from simple patch-level tissue classification to challenging endeavors such as Region-of-Interest-level breast tumour subtyping, segmentation of 22 categories of breast tissue regions, and the detection of inflammatory cell foci in liver biopsies. Experiments demonstrated that H&E-Net can achieve AUC score to 99.997% on simple tasks. Furthermore, the eficacy of H&E-Net is particularly pronounced in challenging tasks, with improvements reaching as high as 18% compared to both ImageNet-pretrained and non-pretrained models.
Conclusion: Overall, pretrained on clinical-grade pathology image datasets, H&E-Net demonstrates significant capability in recognizing pathological characteristics, thereby enhancing model performance across diverse fine-tuning tasks. In clinical-grade environments, H&E-Net holds promise for broader application in pathology image analysis and pathology-assisted diagnostic tasks, including WSI-level analysis based on multiple instance learning, rare and complex disease diagnosis, ultimately enhancing computational pathology performance. In the future, there is potential for H&E-Net to extend its utility through large-scale pretraining of organ- or disease-specific dedicated foundation models.

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E-PS-17-025

Novel dynamic Z stacks based volumetric scanning for PAP smears paves the way for mainstream adoption of digital cytopathology

J. Jain*, R. Gupta, L.K. Puvvada, S. Unnithan, S. Thapa, P. Perugupalli
*Pramana Inc, India

Background & objectives: Cytopathology smears have 3-D cell clusters spread across the Z plane. The current standard best focus image yields suboptimal WSI with focus errors. Here, we used volumetric scanning with dynamic Z stacks to generate in-focus WSI similar to traditional microscopy
Methods: Thirty PAP smears were volumetrically scanned using Pramana Spectral HT scanner with a fixed stacks of five and later with dynamic Z stacks at AOI level to accommodate varying cell cluster thickness. Post image acquisition, final WSI were generated after Z stacks fusion. Pathologists evaluated both the cohorts (fixed and dynamic Z stacks) to assess smear suitability for clinical reporting.
Results: For all the 30 Pap smears, images with dynamic Z stacks had better image quality in comparison to fixed Z stack layers images as per Pathologist evaluation. The finer subcellular details for thick cellular smears (eg keratohyaline granules) were better appreciated in smears with dynamic Z stacks. Number of stacks required for dynamic Z stacks at the AOI level were determined by focused content spread across the Z stacks and it varies with thickness of 3-D cell cluster. In fixed Z stack layers images, most of the cellular details were in focus except few AOIs where thick cellular clusters shows wider spread of cellular details across the Z stacks.
Conclusion: Dynamic Z stacks based volumetric scanning at the AOI level generates good quality in-focus images at par with traditional microscopy. It also helps to overcome the limitation of current standard best focus image by facilitating the capture of granular details spread across the Z stack layers for thick 3-D cell clusters, thus paving the way for mainstream adoption of digital cytopathology as the primary mode of clinical reporting

E-PS-17-026

Bridging the translation gap in computational pathology: an exploratory case study

O. Baly, S. Kammerer-Jacquet*, R. Cavalcante, P. Richard, C. Eloy, N. Rioux-Leclercq, F. Kletz
*Rennes University Hospital, France

Background & objectives: In real life settings, artificial inteIligence (AI) tools often fail to meet their promised organizational impacts. Our work aims to bridge that gap between theoretical and real-life impacts of assistance AI-based algorithms through an exploratory case study for prostate cancer.
Methods: Our inquiry comprised 27 semi-structured interviews involving pathologists, clinicians, lab technicians, hospital managers, computer engineers from french university hospital and private laboratory and portuguese cancer institute and AI societies. We coded interview transcripts to assess the organizational impacts and then analysed causal relations between codes to identify the causes that affected the performance of evaluated tools in real life settings.
Results: Our results point to three categories of factors, which may influence the real-life organizational impacts of AI tools for cancer diagnosis: (1) learning models allowing for large-scale double-loop interactions between humans and machines, (2) interoperability with local information systems, and (3) users' profile in terms of expertise and trust in AI output.
Conclusion: These exploratory findings open new research avenues in the field of computational pathology, by proposing a set of easily testable hypotheses to uncover the design and organizational factors that need to be addressed for the potential benefits of AI tools to materialize in real life practice.

E-PS-17-027

Deep learning-based early detection of oesophageal adenocarcinoma in histopathological images

A. Kazemi*, H.Q. Nguyen, J. Horstmann, J. Slotta-Huspenina, M. Quante, P.J. Schüffler
*Institute of General and Surgical Pathology, Technical University of Munich, Germany

Background & objectives: Barrett's oesophagus (BE) is the known precursor of oesophageal adenocarcinoma (EAC), which is one of the

most rapidly increasing cancers in Western countries. This study aims to detect EAC among BE patients using deep learning based on whole-slide images (WSI).
Methods: A slide-level weakly supervised model was applied on 1284 WSI from the BarrettNet cohort, a multi-centre BE cohort in Germany. An attention-based multiple-instance learning (MIL) model was developed for EAC detection. The model took advantage of the attention-based pooling function to aggregate patch-level features into slide-level representation and subsequently compute the class probability based on the importance of each patch.
Results: The findings showed that MIL methods are promising in detecting EAC in an imbalanced dataset of histopathological images. After fine-tuning, the model achieved an area under the receiver operating characteristic curve (AUC-ROC) of 0.85 and an accuracy of 0.92 in the test set.
Conclusion: In this study, we used deep learning techniques to automatically detect EAC among BE patients. The findings of the study support the feasibility of accurately detecting EAC based on biopsy histopathological images using a weakly supervised model. The finding demonstrated the potential of attention-based MIL for EAC detection among patients with BE, with promising performance.

E-PS-17-028
Automatic precision cut lung slice analysis with few annotations using a two-stage deep learning approach
F. Kock, T. Nicke*, N. Artysh, A. Prasse, H. Hoefener, A. Schenk
*Fraunhofer Mevis, Bremen/Lübeck, Germany

Background & objectives: Effectiveness of antifibrotic drugs in a long-term culture of precision cut lung slices (PCLS) can be assessed by measuring shrinkage of the slices. We present the results of a two-stage deep learning (DL)-based approach to overcome time-consuming, and manual analysis.
Methods: To measure area changes, coarse tissue segmentations were manually created on 33 microscopic PCLS images. A DL algorithm was trained to detect the initially segmented tissue. To reduce time spent on fully manual annotations, an expert refined the DL predictions, if necessary, on 416 images. A subsequent 2D U-Net was trained using the corrected masks.
Results: To evaluate the impact of expert refinements, the Dice score and surface distance between reference and network output is measured on 700 unseen PCLS time series. After expert refinement, the Dice score increases from 0.92 to 0.95. The root mean square distance decreases from 10.79 to 7.68. Qualitative analysis reveals that the refined network can handle reflections and other artifacts in the microscopic images.
Furthermore, time spent by the expert to manually analyse 3 cases with 6 timepoints is compared to the time used by the DL software. Analyzing the tissue with ImageJ takes 118 seconds per case on average while the DL software needs 0.32 seconds on average.
Conclusion: Using DL to automate and replace manual image analysis can be an effective way to reduce workload and improve robustness and efficiency. Rough and time-efficient segmentation masks are used to train a segmentation network which already shows suitable performance for PCLS analysis. Refining the output and retraining the algorithm results in an increase of robustness and performance metrics.

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E-PS-17-030
Digital preservation of historic pathology collections and integration of digital reconstruction into pathology educational system: experience of local pathology centre
M. Kupryte*, L. Poškienė
*Lithuanian university of health sciences, Lithuania

Background & objectives: Digital reconstruction is implemented into pathology for morphology documentation and analysis. Recent demand for professional online platform optimization induced progress of historical pathology collection digitalization into education. Aim is to determine pathology collection digitalization tendencies in preservation and online education.
Methods: 262 macrosamples and 58 histoslides of pathology teaching collection (13 organ system categories) were selected. Digital reconstruction of macrosamples was performed by manual 3D scanner device (0.05 mm scanning accuracy), integrating digital data into CAD/CAM software to manufacture 3D macrosample models. Histoslides were scanned by 3D Histech Pannoramic MIDI (H+E scanning profile). Digitized pathology samples were characterized by descriptive statistics.
Results: 92 3D digital macromodels (35.11% of macrocollection samples, 11 categories of organ systems) and 58 scanned histoslides were uploaded into online educational platforms successfully. Predominant representative digital 3D models were of respiratory (n=18, 19.57%), gastrointestinal (n=17, 18.48%), and cardiovascular systems (n=15, 16.30%) with the highest digital reconstructive index of respiratory system (78.26% of macroscopic respiratory samples selected for the study). The majority of scanned histological slides were of neurological (n=10, 17.24%), respiratory (n=8, 13.79%), and gastrointestinal systems (n=7, 12.07%).
Conclusion: The majority of organ systems categories were digitally reconstructed for long-term preservation and implemented in pathology online teaching platform, with the highest reconstructive parameters for respiratory and gastrointestinal systems, serving as an accurate and powerful tool for standardized and practical application-focused pathology education organized in online platforms.

E-PS-17-031
Efficiency of statistical prognostic model with artificial dynamic learning ability in oncopathology practice
M. Kupryte*, K. Merkevicius, M. Adomaityte, A. Cizauskas, R. Paukstaitiene, L. Poškienė
*Lithuanian university of health sciences, Lithuania

Background & objectives: Complex data is obtained during morphologic analysis of histological images. Statistical prognostic model with artificial dynamic learning ability processes data with complex classification principles required to establish diagnoses. Aim is to determine processing efficiency of statistical prognostic models in oncopathology.
Methods: 416 cases of histologically verified uterus endometrioid carcinoma were selected to create statistical prognostic models of criteria system and artificial neuronal network (ANN). Prognostic potential of statistical model was evaluated by ROC curve, AUC parameter, Cohen's kappa coefficient (k>0.4 – moderate and higher correspondence to pathology diagnosis), model sensitivity and specificity. Pathology report was set as reference data ($p<0.05$).
Results: Statistical analysis of applied prognostic models determined that prognostic model of criteria system was less sensitive and more specific compared to ANN model (0.487 and 0.957 vs. 0.656 and 0.924, correspondingly). Significantly higher AUC value was typical for ANN model compared to model of criteria system (0.908 vs. 0.722, correspondingly). Cohen's kappa coefficient for both models detected moderate correspondence to pathology diagnosis: model of criteria system – 0.507 (CI: 0.411 – 0.603) vs. ANN model – 0.594 (CI: 0.504 – 0.684).
Conclusion: Overall, results of ANN model's prognostic efficiency determined results close to the established standards of medical testing method, demonstrating increasing prognostic impact of models with artificial dynamic learning ability in oncopathology.

E-PS-17-032
Microenvironmental tendencies in non-small cell pulmonary carcinoma (NSCLC) model: digital approach to morphometric analysis
M. Kupryte*, P. Skučaitė, V. Martinkutė, V. Ankudavičius, M. Žemaitis, L. Poškienė

*Lithuanian university of health sciences, Lithuania

Background & objectives: Microenvironmental cytotoxic T lymphocytes play a critical role in NSCLC progression. However, results of studies investigating microenvironmental cytotoxic T lymphocytes and NSCLC remain controversial. Study's objective is to apply digital approach to morphometric analysis optimizing microenvironmental studies in NSCLC model.
Methods: Immunohistochemical reactions (DAKO monoclonal mouse anti-human CD8 antibody, clone C8/144B) were performed for CD8+ cytotoxic T lymphocytes in 79 selected NSCLC cases. Samples were scanned with „Pannoramic Viewer (3D Histech)", CD8+ T lymphocytes were counted in three annotated 304 558 μm2 microscopic fields per sample in "Slide Viewer" digital microimaging analysis software. Statistical analysis (Mann-Whitney, Kruskal-Wallis's tests) was applied ($p<0.05$).
Results: Median of 78 (interquartile range-110) CD8+ T lymphocytes was identified in NSCLC microenvironment. Median of CD8+ T lymphocytes was similar in adenocarcinoma vs. squamous cell carcinoma NSCLC types (79, interquartile range-95 cells vs. 72, interquartile range-145 cells; $p>0.05$) and G2 vs. G2/3 vs. G3 differentiation grades of NSCLC (79, interquartile range-137 cells vs. 114, interquartile range-113 cells vs. 76, interquartile range-86 cells; $p>0.05$).
Conclusion: Accurate cytotoxic (CD8+) T lymphocyte status of immune microenvironment in NSCLC model was characterized by digital microimaging analysis technique, optimizing morphometric analysis of NSCLC microenvironment via digital approach. Similar count of CD8+ T lymphocytes was detected in different NSCLC histological types and grade differentiation groups, demonstrating potential application scope of digital morphometric analysis method in practical setting of pathology diagnostics.

E-PS-17-033
Biomechanical bases of forecasting occurrence of carotid atherosclerosis
Y. Kuzyk*
*Danylo Halitsky Lviv State Medical University, Ukraine

Background & objectives: The main problem in developing atherosclerosis is damage to the endothelium in response to hemodynamic stress. Wall shear stress and focal areas of reduced wall shear stress in the area of the carotid bifurcation can stimulate smooth muscle cell proliferation.
Methods: Two software modules were used: ANSYS CFX for simulating blood flow and Structural (Mechanical) for simulating the stress-strain state of the walls. Geometric models of vessels were built based on healthy and diseased vessels cast in the CAD system SolidWorks.
Results: The stress-strained state of different histological structures' atherosclerotic plaques (AP) was studied. Thus, soft AP is significantly different from hard, which creates conditions for the rupture of plates under the influence of arterial pressure and shear stress. The difference in tension between a hard plaque and a healthy vessel in carotid stenosis creates additional flows and eddies, which leads to an increase in the plaque and the development of wall thrombosis. The turbulence of the flows and the formation of a stagnant place in the ampoule of the internal carotid artery contribute to further plaques. For both types of AP, the stress-strain state of the vessel generally coincided.
Conclusion: The main difference is the distribution of the effective load on the plaque at the carotid bifurcation due to the different hardness of the plaque. The increased level of effective stresses at the junction of areas of a healthy vessel and areas affected by soft AP creates conditions for plaque detachment and subsequent thrombosis. Analysis of hemodynamic force distribution shows weak points in the carotid ampulla and bifurcations that should be included during reconstructive surgery.

E-PS-17-034
Automated classification of tuberculosis slide images using deep learning models at low magnification
J. Lee*, J. Lee
*Department of Forensic Medicine, National Forensic Service, Republic of Korea

Background & objectives: The standard tuberculosis (TB) diagnostic method entails labor-intensive examination of slides at 1000x magnification post Ziehl-Neelsen staining. We assessed nine deep learning models for detecting mycobacterium tuberculosis in low-resolution 400x magnification images.
Methods: Samples from fourteen TB-infected lungs and twenty-six normal lungs were collected at the National Forensic Service Headquarters. Patch-based dataset construction created 224x224x3 patches from whole slide images scanned at 400x magnification. Nine TB-infected lungs were used to train seven convoluted neural network architectures and two vision transformer models in classifying mycobacterium tuberculosis slide images into detection and non-detection categories.
Results: Out of 351,875 positive spots, 47,017 contained TB bacteria. From 3.1 million negative spots, 47,017 were randomly selected, constructing a dataset of 98,034 patches. Considering only informative negative slides, NASNet-A Large achieved 99.978% patch detection accuracy, and Densenet169 reached 99.820%. NASNet-A Large classified positive and negative slides with 90% accuracy, while Densenet169 scored 100%. Across thresholds (0.5, 0.6, 0.7, 0.8, 0.9), false positives outnumbered false negatives on positive slides. NASNet-A Large demonstrated consistent error rates, regardless of the threshold, indicating minimal threshold impact on performance.
Conclusion: In our study, nine deep learning networks were assessed for classifying low-resolution slide images at 400x magnification. NASNet-A Large attained 99.978% accuracy, while Densenet169 reached 100%. These models provide rapid and precise assessments, potentially shortening diagnostic time and improving TB diagnosis efficiency. Future endeavors involve enlarging the training dataset to refine methodology and enhance TB diagnostics.

E-PS-17-035
Why is virtual H&E imaging technology not needed? Rapid intraoperative margin assessment in breast cancer surgery: evaluation of the true H&E-based PATHOscope
Y. Lee*, H. Lien, M. Wang, C. Huang, P. Wu, B.J. Borah, Y. Chen, C. Sun, Y. Liao
*Department of Pathology, National Taiwan University Hospital, and National Taiwan University College of Medicine, Taipei, Taiwan

Background & objectives: Breast-conserving therapy is favoured for early-stage breast cancer due to superior survival rates over mastectomy. Despite its time-consuming nature, frozen sections (FS) are standard for intraoperative margin assessment. We explored PATHOscope, artifact-free alternative, assessing its applicability in breast cancer cases.
Methods: The PATHOscope (mesoView, Taiwan) assessed fifty tissues, including cancer and pericancerous normal tissues from sixteen patients with various breast cancer types. A rapid whole-mount tissue H&E staining protocol was applied to fresh breast tissues. Equipped with third-harmonic-generation and two-photon excitation fluorescence modalities, it captured images by detecting signals from H&E dyes, with blinded evaluation against respective formalin-fixed paraffin-embedded (FFPE) pathology.
Results: The total detection time required for each fresh tissue, including rapid H&E staining and PATHOscope imaging, was less than 10 minutes. By utilizing real-time 2D mosaic-stitching technology, the PATHOscope can digitally display a 1 cm2 area in less than 120

seconds, adhering to global whole slide imaging standards for digital resolution. The artifact-free PATHOscope images could present true-H&E histopathological characteristics, including irregularly infiltrating nests and nuclear pleomorphism in cancer tissues, and terminal duct lobular units, adipocytes, and fibrocollagenous stroma in normal tissues. In the initial blinded evaluation, pathologists achieved a 100% accuracy in distinguishing cancer from normal tissues, demonstrating both sensitivity and specificity in cancer detection at 100%.
Conclusion: The rapid fresh digital pathology scope (PATHOscope) offers true H&E-based imaging, artifact-free results, and operates four times faster than conventional FS. By utilizing True H&E imaging technology, pathologists require no extra training. Freshly excised breast tissue can undergo subsequent FFPE staining directly without the contamination issue by non-H&E dyes. As a result, the PATHOscope offers a rapid, reliable alternative to FS, promising improved intraoperative margin assessment for breast-conserving therapy.

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E-PS-17-036
AI-driven quality control for immunohistochemistry: automated detection and exclusion of artifacts for downstream analysis in digitized pathology slides
K. Lingelbach*, M. Bauw, A. Schmidt, A. Baxendale, L. Ruff, S. Ruane, M. Alber
*Aignostics GmbH, Germany

Background & objectives: Immunohistochemistry (IHC) is pivotal for diagnosis and research, offering molecular specificity. Artificial Intelligence (AI) increasingly automates analysis but artifacts can cause incorrect predictions. We present a scalable IHC Quality Control (QC) model for filtering out artifacts amidst high staining variability.
Methods: 86 IHC-stained samples were annotated and used to develop a stain-agnostic deep learning segmentation model. These comprised 3 IHC stains including PD-L1 and two proprietary markers and were distributed across 5 indications (Non-Small Cell Lung Cancer, Colorectal Cancer, Hepatocellular Carcinoma, Head and Neck Squamous Cell Carcinoma, Urothelial Carcinoma). 40 comparably distributed slides were separately annotated as a hold-out evaluation set.
Results: The model was designed to separate "valid tissue" from artifact regions which compromise the accuracy of downstream analysis and should be excluded from further analysis. These include artifacts arising from slide preparation (e.g. folds, contamination, dust, bubbles, specimen marking dye, unspecific stain, and pen marks) and image acquisition (e.g. blur). Across all IHC stains, the model achieved a mean F1 score of 0.96 (0.96 precision, 0.97 recall) for discriminating "valid tissue" from all other classes. The model performed comparably across all three IHC stains.
Conclusion: A robust QC model is essential for artifact elimination in automated digital analysis, enhancing the integrity of results. The developed model eliminates time-consuming and potentially error-prone manual assessment. This facilitates faster and more accurate downstream analyses for tasks such as cell classification, biomarker scoring, and spatial analysis in the tumour microenvironment amidst high IHC staining variability. Additionally, statistics on artifact presence can inform slide preparation and scanning protocols. Future research will extend this model to more IHC biomarkers and tissues.

E-PS-17-037
Improving histopathological screening of colorectal polyps using deep learning
A. Ljone Henriksen*, F.M. I. Julbø, M. Pradhan, E.K. Lindstrøm, L. van der Schee, M. X. Isaksen, A. Manet, O. Skrede, S. De Raedt, H. A. Askautrud, Ø. Holme, D. J. Kerr, M. M. Lacle, M. Novelli, A. Kleppe
*Institute for Cancer Genetics and Informatics, Oslo University Hospital, Norway

Background & objectives: Few polyps harvested during colonoscopy warrant surgery or additional surveillance. Automatic identification of polyps that are low risk would reduce the workload on pathologists. We aimed to develop such a marker by applying deep learning to analyse histopathological section images.
Methods: The DoMore-v1 network was modified to perform attention-based pooling and trained to classify histopathological section images as 1)normal tissue, 2)tubular adenoma low-grade dysplasia, 3)sessile serrated lesion or hyperplastic polyp, 4)high-grade dysplasia or adenocarcinoma, or 5)other. It was developed using 11601 histopathological section images from 2361 patients from United Kingdom and externally tested on 469 images from 295 patients from the The Netherlands.
Results: In the external test, 58 (54.2%) of 107 histopathological section images labelled as tubular adenoma low-grade dysplasia were correctly classified and 1 (0.3%) of 301 images labelled as high-grade dysplasia or adenocarcinoma was misclassified as normal tissue or tubular adenoma low-grade dysplasia, further collectively called low-risk polyps. Three pathologists independently and blindly reviewed this misclassified image, and two of the pathologists classified it as tubular adenoma low-grade dysplasia. For the remaining 61 images in the external test dataset, the biomarker correctly classified 59 (96.7%) of them as not being low-risk polyps.
Conclusion: External testing of a new deep learning marker indicated that more than half of the low-risk polyps can be automatically identified without incorrectly identifying polyps with high-grade dysplasia or adenocarcinoma as being of low-risk type. Allowing pathologists to not assess the automatically identified low-risk polyps will make bowel cancer screening more cost-effective and feasible by substantially reducing the workload for pathologists classifying colorectal polyps.

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E-PS-17-038
Ex-vivo fusion confocal microscopy for an enhanced intraoperatory frozen section diagnosis
S. Lopez-Prades*, M. Gispert-Ruiz, A. Carrasco Lorenzo, C. Miralles, D. Salas Díaz, M. Romero-Sanchez, C. Fuentes, M. Rus, M. Hernández, Y. Duque-Jaimez, D. Martinez, E. Sanfeliu, M. Cuatrecasas Freixas, B. Gonzalez-Farre
*Pathology department. Hospital Clinic. University of Barcelona. Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Spain

Background & objectives: Intraoperative frozen section diagnosis implies tissue waste, time investment, and often poor-quality sections. VivaScope 2500-G4 ex-vivo Fusion Confocal Microscopy (eFuCM) provides real-time, Hematoxylin-Eosin-like images without tissue loss and fast diagnosis. We compared intraoperative diagnosis with eFuCM and gold-standard frozen sections.
Methods: Ninety-one intraoperative biopsies, from 10 different pathology areas, were prospectively recruited. Samples were diagnosed by frozen section, then properly prepared and scanned with eFuCM and finally routinely processed for conventional microscopy. Diagnostic agreement and the technical time between frozen sections and eFuCM images was compared.
Results: An 87.5% concordance was observed between both methods. Among discordances: six cases, correctly diagnosed as positive for carcinoma by frozen section, eFuCM failed to easily confirm malignant cells and one case was a false negative by frozen but not with eFuCM. Interestingly, eFuCM allowed intraoperative diagnosis of one small core biopsy and in five cases with abundant fat tissue content in which a representative frozen section was impossible to be obtained. The average time for eFuCM image acquisition was 7.24 minutes, and 16.47 minutes for frozen technical process. Image quality, especially

with fat and small samples, was better with eFuCM, with no folded areas or tissue loss.
Conclusion: Ex-vivo Fusion Confocal Microscopy is a promising tool which allows a real-time histological diagnosis. It is faster than current gold standard method for intraoperative samples and allows diagnosis in selected cases where frozen sections are difficult. This new method avoids freezing or trimming, and preserves the sample for definitive paraffin diagnosis. In addition, the whole tissue section is visualized. As limitations, technical skills are needed for tissue scanning, and there is a learning curve adaptation to the eFuCM images.

E-PS-17-039
Comparison of the efficiency and costs associated with the use of digital pathology versus conventional microscopy for the diagnosis of biopsies in a Spanish anatomical pathology laboratory
J. Echeveste, L. Álvarez, D. Carcedo, Y. Soto, M.D. Lozano*
*Clinica Univ de Navarra Serv Anatomia Patologica DNI 18015373W, Spain

Background & objectives: Digital pathology (DP) encompasses the digitization of processes related to the acquisition, storage, transmission and analysis of pathological data, contrasting with conventional methodology (CM) using optical microscopes. This study evaluates the efficiency of DP versus CM in a Spanish laboratory.
Methods: This retrospective study compares biopsy samples from 2021 (cases diagnosed using CM) and 2022 (using DP). Covariables analysed were the pathologist who made the diagnosis, the number of slides and the area of the case. Efficiency variables were turnaround-time (TaT), pending cases and pathologist workload. A significance level of 5% was established. Also, a cost analysis was performed.
Results: 11,922 cases were analysed, 6,086 diagnosed with CM (cases of 2021) and 5,836 with DP (cases of 2022). Mean TaT for CM-diagnosed cases was 10.52 (SD 7.12) days compared to 6.85 (SD 5.13) days for DP-diagnosed cases, a reduction of 3.67 days (95%CI: 3.45–3.90; $p<0.001$). This reduction persisted irrespective of the pathologist who made the diagnosis, number of slides, or case area (dermatopathology, gastrointestinal/hepatobiliary pathology, gynaecology and uropathology). Using DP, the average reduction of pending cases over a year was around 25 cases, with peaks of 100 fewer pending cases in some months of high workload. Total costs over a 5-year horizon were higher with DP.
Conclusion: Our study is the first in Spain to compare the efficiency and costs of DP and CM. Our results show a statistically significant reduction in the laboratory TaT with DP compared to CM, which is maintained independently of the covariates analysed. Despite the higher cost, DP contributes to reduce the pathologist's workload. These findings underscore the potential of DP to increase efficiency and streamline the diagnostic process in pathology laboratories, representing a significant advancement in diagnostic technologies within Spanish settings.

E-PS-17-040
Innovation for fast diagnostics in thyroid nodules. A pilot study combining instant digital pathology and fully automated real time PCR testing
G. Maricchiolo*, v. morano, A.M. Naciu, c. taffon, A. Palermo, A. Crescenzi
*Operative Endoscopic Department, Fondazione Policlinico Universitario Campus-Biomedico, Rome, Italy

Background & objectives: Fine needle aspiration (FNA) is a mainstay for evaluation of thyroid nodules, sometimes supported by molecular profile. Instant digital pathology is an emerging tool to speedup morphological assessment. Herein, we combined digital appraisal with molecular analysis to improve patient management.
Methods: Fresh unfixed FNA samples were loaded on polymeric scaffolds and visualized with confocal laser scanning microscope (FCM) to assess cellular adequacy and to provide a diagnostic category. After imaging, a cellular spot was scraped by a scalpel and prepared for molecular analysis using Biocartis IdyllaTM Cartridge. Remaining specimen was formalin fixed and paraffin embedded for permanent histology and NGS sequencing.
Results: Comparing FCM evaluation with diagnosis on permanent cellblock sections, sample adequacy resulted correctly stated, and a diagnostic category was reliable in most cases. All FNA samples loaded onto IdyllaTM cartridges yielded valid results, according to NGS analysis on final cellblock. Study included DNA testing for BRAF and NRAS mutations. Results demonstrated high sensitivity and specificity, affirming the adequacy of the proposed workflow using IdyllaTM platform on fresh cytological material immediately after sampling. Quality and quantity appraisal of thyroid lesional cells, as showed in instant digital imaging, supported the effectiveness of fast molecular analysis. Furthermore, full concordance was observed with paired formalin fixed and paraffin embedded samples analysed by NGS.
Conclusion: To reduce timeframe in responding to clinical needs is essential in modern medicine. In thyroid cytology, molecular profile is used in different contests: stratification of risk of malignancy in indeterminate lesions, to plan surgical extension for small nodules and in predicting therapy response in anaplastic or high-grade carcinomas. This rapid innovative approach that combines FCM fast digital imaging with fully automated real time PCR-based molecular testing, is expected to significantly improve patients' management.

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E-PS-17-041
Continous IHC quality control using an AI-supported system
J. Raffler, C. Herbst, J. Warkotsch, C. Wengenmayr, T. Schaller, B. Märkl*, R. Huss Ralf
*UK Augsburg, Germany

Background & objectives: In order to maintain consistent quality and accuracy in laboratory processes, standardization efforts have been made in recent years. In this regard, we propose a workflow that is supported by artificial intelligence (AI) to continuously monitor quality parameters of IHC.
Methods: Antigen-specific cell lines are applied to the slide as standardized reference samples and stained using an automated staining platform. The stained slides are then scanned with high resolution (Philips UFS). Images and relevant metadata are extracted and aggregated from the LIS. These data are uploaded to the Qualitopix® web suite (Visiopharm A/S) where they are analysed in near real time.
Results: A total of 545 quality tests have been carried out almost continuously. Since June 2023, a systematic evaluation of the test results for HER2/Neu, Ki-67 and PD-L1 has also been carried out with the help of a standardized reference sample (total $n = 178$). Due to the cloud-based software Qualitopix®, deviations could be detected early and usually eliminated at a very reasonable time (e.g. through early batch replacements or changing the position in the staining device). There were also noticeable quality fluctuations due to a combination of two otherwise non-critical reagents or batches, the analysis of which would otherwise have been much more time-consuming and cumbersome.
Conclusion: Thanks to an AI-supported quality control workflow using Qualitopix® from Visiopharm, it is possible to recognize relevant quality fluctuations at an early stage in histopathological routine operations. The standardized evaluation of a large number of relevant parameters enables early root-cause research and problem-solving.

E-PS-17-042

Quantifying mismatch repair immunohistochemistry using digital pathology in colorectal specimens

M. Menard*, N. Grinrod, M. Cecchini, B. Wehrli
*Schulich School of Medicine and Dentistry, Canada

Background & objectives: Immunohistochemistry(IHC) is commonly employed to detect colorectal tumours with loss of mismatch repair(MMR) protein. However, interpretation is subjective, and potentially compromised by tissue fixation time. This study aims to set a clear MMR protein expression threshold for reliable interpretation.
Methods: Immunohistochemical staining results for MMR proteins on the initial biopsy and the subsequent resection of 49 colorectal cancer specimens were analysed using QuPath software to determine comprehensive cell detection, tumour-stroma classification, and for the quantification of the chromogen 3,3′-diaminobenzidine (DAB) staining intensity in tumour and stromal components.
Results: Cases with intact MMR protein expression exhibited an average ratio of DAB staining intensity in tumour to stroma of 3.76, while cases with loss of MMR proteins showed an average ratio of 0.40. There was a significant decrease in DAB staining intensity of all four MMR proteins from biopsy to resection ($p<0.05$). Fixation times ranged from 46-289 hours, but did not significantly impact DAB intensity when comparing biopsies to resections. A proposed objective cutoff value of <1 indicates loss of MMR expression, while >1 suggests intact expression, with a potential equivocal range.
Conclusion: Establishing a quantitative threshold for MMR staining in colorectal cancer holds significant clinical implications, facilitating more objective and standardized interpretation of immunohistochemistry results. Integration of this approach into semi-automated workflows has the potential to streamline MMR testing, ensuring more consistent and accurate identification of cases with MMR deficiencies, thus enabling tailored therapeutic strategies and enhanced management of colorectal cancer patients.

E-PS-17-043

Comprehensive digital pathology platform offering reliable digital evaluation of predictive and prognostic biomarkers

T. Micsik*, V. Jonas, B. Wichmann, R. Paulik, A. Jakab, L. Fonyad, A. Fintha, B. Molnár

*Semmelweis University Budapest, Hungary

Background & objectives: Besides histological diagnosis, pathological signing-out needs precise prognostic and predictive biomarker assessment directly influencing patients´ treatment and posing legislation consequences. Manual assessment suffers from tumour heterogeneity and interobserver variabilities, which might be solved with digital pathology algorythms involving machine learnig.
Methods: Biomarkers were evaluated on immunohistochemical and hematoxilin-eosin (HE) slides with 3DHistech`s (Budapest, Hungary) digital platform and Machine learning algorithms. MembraneQuant was used for HER2 and PDL1 slides in breast and lung cancers, whereas NuclearQuant for estrogen (ER), progesterone receptors (PR) and Ki67 proliferation indices for breast and neuroendocrine tumours. PatternQuant Tumour stroma evaluator processed HE-slides of colorectal cancers.
Results: Previous manually derived data were compared to the automatic data derived by machine learning algorythms. Breast markers showed substantial agreement with ER (n=174, Quadratic weighted Kappa=0,909-0,973), PR (n=174, Quadratic weighted Kappa=0,939-0,982), HER2 (n=174, Quadratic weighted Kappa=0,876-0,951) and Ki67 (n=100, Pearson Correlation Coefficient= 0,803-0,858). GastroenteroPancreatic NeuroendocrineTumour Ki67-grading application on 60 cases yielded also high correlation with Cohen`s Kappa of 0.972. The Tumour Stroma evaluator delivered robust prognostication (n=185, Hazard Ratio=2,005) on colorectal cancers. PDL1-application was validated on 130 non small cell lung cancer cases resulting Cohen`s Kappa of 0,88-0,92.
Conclusion: The tested methods were validated with good performance and delivered robust prognostications with breast, lung, colorectal cancers and neuroendocrine tumours, and thus offer reliable applications for evaluation. The investigated algorithms fit well in routine diagnostic workflow of the digital pathology platform and can efficiently lower our routine workload and decrease the effects of intratumoural heterogeneity and interobserver variability. In conclusion, pathologist can benefit from digital image analysis applications offered by 3DHistech´s digital pathology platform in their everyday practice.

E-PS-17-044

Decision Tree-based rapid digital pathology - molecular diagnostic service

Y. Molchanov, C. Mayer, I. Barshack*
*Sheba MC, Israel

Background & objectives: The emergence of next-generation sequencing (NGS) enables the identification of cancer-driving genomic changes, albeit with time constraints. This study aims to explore how AI algorithms workflow implementation can expedite patient selection for real-time PCR tests, thereby dramatically optimizing treatment timelines.
Methods: "decision tree" including: tumour morphology, tissue sub type, micro diagnosis, tissue size, AI algorithm results, Real-time PCR verification, was used for all NSCLC cases. AI software analyses the WSI H&E, flagging samples carrying alterations for pathologist to assist in their analysis prioritization. If one of the biomarkers found to be positive, it verified by the Real-time PCR platform.
Results: The time to treatment of NSCLC patients shortened from 3 weeks in the regular workflow which includes NGS to hours after implementation of "decision tree" based clinical workflow in form of Rapid digital-molecular diagnostic service.
Conclusion: Turnaround time is critical factor in the diagnosis and treatment of cancer. Clinical workflow implementation of AI algorithms in combination with rapid molecular techniques can help to streamline the analysis and management of cancer patients and reduce the time required to generate actionable results. AI algorithms in combination with rapid molecular techniques can provide clinicians with actionable insights that can dramatically reduce time to treatment. Its cost-effective method can improve the quality of care and risk management in cancer patients.

E-PS-17-045

New integrated approach to reduce timeframe in lung cancer patients' management. A pilot study combining instant digital pathology and fully automated EGFR molecular testing

V. Morano*, G. Maricchiolo, S. Stigliano, L. Frasca, D. Biasutto, P. Crucitti, A. Gradilone, G. Giannini, F.M. Di Matteo, A. Crescenzi
*Unit of Endocrine Organs and Neuromuscolar Pathology, Fondazione Policlinico Universitario Campus-Biomedico, Rome, Italy

Background & objectives: EUS/EBUS FNAB is became the standard sampling method for advanced lung tumours. Molecular profile is required in non-small-cell lung carcinoma (NSCLC) for planning target therapy. Study's aim is testing a new protocol for combining instant digital pathology with molecular analysis.
Methods: Fresh unfixed EUS/EBUS samples were loaded on polymeric scaffolds and visualized with confocal laser scanning microscope (FCM) to assess cellular adequacy and to provide a diagnostic hypothesis. Via imaging, identified tumour cellular spot was scraped by a scalpel for molecular analysis using Biocartis IdyllaTM System

cartridge. Remaining specimen was formalin fixed and paraffin embedded for permanent cellblock and NGS sequencing.
Results: Comparing FCM evaluation with diagnosis on permanent cellblock sections, sample adequacy resulted correctly stated, and preliminary diagnosis was confirmed in cases. All cytological samples loaded onto IdyllaTM cartridges yielded valid results, according to NGS analysis on final cellblock. Study engaged DNA testing for EGFR mutations. Results demonstrated high sensitivity and specificity, both in positive and negative outcomes, affirming the adequacy of the proposed workflow using IdyllaTM platform on fresh cytological material immediately after sampling. Quality and quantity of lung cancer cells, as showed in instant digital imaging, allowed the feasibility of fast molecular analysis. Furthermore, full concordance was observed with paired formalin fixed and paraffin embedded samples analysed by NGS.
Conclusion: To reduce timeframe in responding to clinical needs is essential in modern medicine. In advanced NSCLC, molecular profile is mandatory to plan targeted therapy since they may increase overall survival and improve quality of life. This rapid innovative approach that combines FCM fast digital pathology imaging with fully automated real time PCR-based EGFR molecular testing, significantly cut the timeframe from EUS/EBUS sampling until to treatment choice and is expected to meaningfully improve patients' management.

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E-PS-17-046
Quantitative analysis of bile duct morphology and spatial distribution in nonalcoholic fatty liver disease / steatohepatitis liver biopsies across disease stages
P. Moulin*, L. Ducor, C. Sempoux
*Lausanne University Hospital, Switzerland

Background & objectives: Non-alcoholic fatty liver disease evolves from steatosis to inflammation and fibrosis. Histopathology confirms the disease and assesses its stage. Our study introduces an automated detection of hepatic progenitor cells and ductular reactions in liver biopsies, critical for evaluating progression risk.
Methods: Liver biopsies from 40 patients with NAFLD/NASH stained by HE, Trichrome, and Cytokeratin-7 were digitised. Fibrosis extension and texture were quantified from trichrome-stained images. Bile ducts and isolated CK7-expressing cells were segmented from CK-7-stained whole-slide images. Their morphological and densitometric characteristics, spatial distribution, and embeddings in the graph neural networks were inserted into a high-dimensional data mining pipeline.
Results: The study identified over 8,000 CK7-positive cells and classified them into three distinct categories: main bile ducts, hepatic progenitor cells, and ductular reactions. We conducted an in-depth analysis of these cells' numerical density and spatial distribution in relation to fibrosis within the liver tissue. This analysis employed kernel density estimators and graph neural networks to explore the intricate spatial relationships among the categorised cells and surrounding fibrotic areas. Additionally, we investigated variations in CK7 staining intensity, examining how the staining intensity of these isolated cells varied depending on their microenvironmental context, including proximity to fibrosis, main bile ducts, and ductular reactions.
Conclusion: This study introduces an innovative approach for detecting hepatic progenitor cells and ductular reactions in liver biopsies and extracting detailed morphological and topographical information from these structures, which play a crucial role in the progression of NAFLD/NASH. A precise and unbiased characterisation of these elements enhances our understanding of the pathophysiology underlying the progression from steatosis to inflammation, regeneration, and fibrosis. Furthermore, this high-granularity data is poised to reveal digital biomarkers crucial for disease prognosis and patient stratification.

E-PS-17-047
Applicability of a Ki67 image analysis breast algorithm on gastrointestinal and hepatopancreaticobiliary neuroendocrine neoplasms
A. Mukherjee*, G. Raghuram, L. Inge, S. Dance, G. Hyland, I. Parker, D. Sculthorpe
*University of Nottingham, United Kingdom

Background & objectives: Grading of gastroentero-pancreatic (GEP) neuroendocrine neoplasms (NENs) is usually performed by manual microscopic Ki67 stain assessment for prognostication. This study assessed whether an automated Ki67 algorithm for an unrelated tumour type (breast) may be applied effectively for grading GEP NENs.
Methods: GEP NEN sections were stained for Ki67 and H&E, digitised on Ventana DP200 scanners, and uploaded on Navify Digital Pathology platform (Roche). Regions of Interest (ROIs) were determined by histopathologists; manual Ki67 assessed, followed by automated assessment with uPath Ki-67 (30-9) image analysis, Breast algorithm (Roche; research use only). Manual versus automated grading (per 2017/2019 WHO classification) concordance was evaluated.
Results: Of 119 cases, 106 were analysable, discounting cases with underestimation of total cells by the algorithm (n=13; 10.9%). Of 203 ROIs analysed, 169 were rectangular and 34 freehand, indicating the platform's flexibility for area shape selection within resections, biopsies or cyto-blocks. Grading matched between manual vs digital assessment in ~86% cases (91/106) and ~88% ROIs (179/203). Of a random sample scored by a second histopathologist, grade match between manual vs digital assessment was observed in ~83% cases (19/23) and ~88% ROIs (38/44). Within this sample, the two pathologists' grade agreement through manual assessment was ~73% versus ~83% for digital assessment. There was also relative economy of time (~200seconds/case).
Conclusion: The uPath Ki-67 (30-9) image analysis, Breast algorithm, performed satisfactorily for grading GEP NENs, showing good concordance with manual assessment. ROI shaping tools helped tailor analysis to specimen type and a time advantage was also gained. In a small proportion, total tumour cell number was misjudged, likely due to differential size or staining quality of NENs. Results illustrate that existing tissue-specific digital algorithms for common stains have potential to expand usage to other tumour types with further fine-tuning.

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E-PS-17-048
Convolutional neural network classifier for pT1colorectal carcinoma detection
E. Musulen*, P. Cano, K. Saez de Gordoa, M. Daca-Álvarez, M. Pellisé, M. Cuatrecasas, D. Gil
*Pathology Department, Hospital Universitari General de Catalunya-Grupo QuironSalud and Josep Carreras Leukaemia Research Institute (IJC), Spain

Background & objectives: pT1 colorectal carcinomas are submucosal invasive cancers that harbor risk of lymph node involvement. Digitization of histopathological images allows their analysis using artificial intelligence (AI) methods. The objective is to design an AI algorithm to detect pT1 colorectal carcinomas.

Methods: A pretrained ResNet convolutional neural network (CNN) was used as backbone network for the extraction of visual features from 256x256 windows cropped from tissue samples. The ResNet 2048 features were the input to a classification neural network with one hidden layer with 1024 neurons. The classification network was trained from scratch for 100 epochs using a weighted cross-entropy loss.
Results: The system has been tested for the detection of high-grade dysplasia (HGD) and invasive cancer components in histopathological images. Pathologists annotated positive (HGD and invasive cancer) and negative tissue samples on whole slide images from 82 patients from two hospitals. A total of 9649 256x256 windows were cropped from the annotated samples to test the algorithm in a 10-fold cross-validation. A window was considered positive if there was more than 50% of dysplastic and infiltrated tissue. Specificity was 81.5% (95% confidence interval – CI – 71%,92%) and sensitivity 87% (CI 83%,91%) with an average AUC of 0.85.
Conclusion: Our convolutional neural network classifier is a useful tool for identifying pT1 colorectal carcinomas. The digitization of histopathological images will allow the incorporation of AI tools to assist pathologists in their daily work and will potentially be in widespread use in the coming years.

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E-PS-17-049
Utilizing deep learning model for assessing melanocytic density in resection margins of lentigo maligna
J. Siarov, D. Kumar, J. Paoli, J. Mölne, N. Neittaanmäki*
*Department of Laboratory Medicine, Institute of Biomedicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

Background & objectives: Surgical excision with clear histological margins is the preferred treatment for lentigo maligna (LM). We evaluated the capabilities of a deep learning algorithm for automated assessment of LM margins and the recurrence risk.
Methods: In total, 353 whole slide images were collected for the study. The deep learning algorithm was trained with 3,973 pixel-wise annotations on 729 training regions. The AI's evaluations of the 58 test regions were compared to those of five blinded pathologists, who performed their evaluations first without AI and, and again, assisted by AI.
Results: The AI model demonstrated excellent performance, achieving an area under the receiver operating characteristic curve (AUC) of 0.84 in discriminating margins with low and high recurrence risk cutoff ($\leq$25 melanocytes in an area of 0.5 mm in the resection margin serving as the cutoff for low risk of recurrence and $\geq$26 for high risk) . Immunohistochemistry (SOX10) served as the reference standard. The AUC for dermatopathologists ranged from 0.72 to 0.90 for comparison. Additionally, the AI improved the performance for some of the pathologists, enhancing the AUC from 0.72 to 0.85 (p=0.029).
Conclusion: In conclusion, the deep learning AI model showed excellent accuracy in detecting high-risk versus low-risk resection margins of LM. The utilization of such an automated tool could aid pathologists in the assessment and/or pre-screening of LM excisions.

E-PS-17-051
Development of virtual models for surgical specimens — application in pathology
G. Nogueira Fontinha*, V. Almeida, L. Veloso, J. Pimentel, N. Sousa, E. Santos, L. Bastião, L. Carvalho, V. Sousa
*nstitute of Anatomical and Molecular Pathology, Faculty of Medicine of the University of Coimbra, Coimbra, Portugal

Background & objectives: In recent years there have been major technological developments in the diagnostic field, such as digital pathology and the development of Artificial Intelligence algorithms. The teaching of Pathology can also benefit from technological developments, particularly online, remote, and interactive methodologies.
Methods: In partnership with the Center for Graphical Computation (CCG) and BMD Software, the Institute of Pathological Anatomy and Molecular Pathology of the Faculty of Medicine of the University of Coimbra is implementing the PathoBox platform within the scope of the iPATH project, which allows to manage virtual slides data and apply and develop AI algorithms.
Results: A new project is underway in partnership with BMD and CCG, financed by the PRR (C644937233-00000047) in the HfPT (Health From Portugal) consortium, with the aim of developing interactive tools using augmented reality applied to surgical specimens and virtual histological slides, with a view to developing new pre- and postgraduate teaching methodologies.
Conclusion: Surgical specimens scanned and virtualized using LIDAR may be the target of various interactions in a simulation environment. The aim is to develop surgical specimen's virtualization tools and augmented/mixed reality and interactivity approaches applied to virtual slides to promote effective communication in professional contexts linked to medicine and medical teaching. These tools will be developed to support interface through consumer-grade mobile platforms, thus maximizing the proper inclusion of target audiences.

E-PS-17-052
Multimodal fusion of pathological lung specimen based on 3D-printed cone-shaped phantoms
P. Nolte*, C.J. Gröger, M. Brettmacher, M. Stammes, C. Rußmann, C. Dullin
*HAWK Goettingen, Germany

Background & objectives: Histology - the standard of pathological tissue assessment – is a specific but intrinsically 2D method, while microCT provides unspecific 3D imaging. Combining both would be highly beneficial, which we achieved using 3D printed phantoms to ease the registration process.
Methods: All rhesus macaque lung samples were stained with phosphotungstic-acid, fixed and embedded in methyl methacrylate-based agents together with cone-shaped phantoms. These phantoms were created from a novel specialized resin-iodine mixture and printed using stereolithography. After hardening defined regions-of-interest marked in an Synchrotron-MicroCT scan were isolated using a modified pathological saw and laser microtomy. Finally, both modalities were spatially registered.
Results: Our proprietary resin-iodine mixture in combination with stereolithography allows for the creation phantoms characterized by a high spatial resolution, which can be segmented from the embedding matrix. Furthermore, the resulting cut-sections can be identified in histological imaging, thus severely simplifying the multimodal fusion of microCT and histological imaging. Serial sectioning was realized through laser microtomy, thus allowing for the contact-less generation of adjacent slides from one specimen. This significantly limits the deformations present in sections produced with a microtome. The matched sections were considered as seed points for the color transfer into microCT volume. Based on the fused histological and microCT image data, the segmentation of higher-dimensional features is possible.
Conclusion: Based upon the newly developed phantoms the matching of corresponding microCT and histological data was realized. The developed resin is compatible with classical stereolithography and the resin-based embedding required for the cutting-grinding technique. In comparison to other markers, our phantoms take the height of the cut into account, thus allowing for the automatized correlation of both modalities. Due to the compatibility with similar tissue samples, the

potential for the generation of multimodal datasets for applications in digital pathology is significant.

E-PS-17-053

A cutting-edge software technology to automatically quantify brightfield multiplex immunohistochemistry in penile carcinoma

R. Peraino*, T. Franceschini, F. Ambrosi, A. Grillini, E. Franchini, E. Demaria, A. Gherardi, A. Bevilacqua, M. Fiorentino, M. Mottola
*University of Bologna, Italy

Background & objectives: Penile squamous cell carcinoma is classified as either HPV-associated or HPV-independent and its prognosis differs due to the tumour microenvironment (TME) evaluated by brightfield multiplex immunohistochemistry (BF-mIHC). Our aim is to develop and validate a software for automated BF-mIHC quantification.
Methods: TME is characterized by five stained markers: CD4(green), CD8(dab), FOXP3(yellow), CD68(purple), and CD163(teal) and, as the reference standard, markers' counting is performed in hotspot regions, manually segmented by an expert pathologist. We developed a procedure for automatic quantification of stained markers based on Hue Saturation Intensity (HSI) color-spectra analysis. Automatic counting is validated through Bland-Altman and t-test of differences (α=0.05).
Results: This study includes 10 BF-mIHC whole-slide images of penile cancer, undergoing comparison between manual and automatic marker counting. CD68 and CD163 resulted completely co-expressed thus allowing a paired counting of CD163 and CD68 (i.e., CD68+CD163). Hotspot regions measured on average 0.22±0.05 mm2 (mean±standard deviation). Bland-Altman analysis, carried out on percentage counting of single markers expression, reports the equivalence of manual and automatic counting for all CD4, CD8, FOXP3, CD68+CD163 markers, with mean percentage differences of -0.60% for CD4, 1.54% for CD8, -0.03% for FOXP3, and -0.90% for CD163+CD68. t-Test accepts null hypothesis of equivalence with p-value=0.68 for CD4, p-value=0.20 for CD8, p-value=0.90 for FOXP3, and p-value=0.32 for CD68+CD163.
Conclusion: This preliminary study highlights the role of software technologies in improving pathological reading of BF-mIHC whole-slide images, thus enhancing standardization and reproducibility of measurements. Moreover, automatic BF-mIHC quantification is incredibly faster than manual counting, thus being compliant with real-time analyses. In addition, our methodology is based on a general-purpose approach, resulting easily portable for the TME characterization in different cancers too. This will help endowing the pathological routine with cutting-edge technologies improving accurateness and repeatability of reports.

E-PS-17-054

Computer-aided diagnosis in digital dermatopathology: automatic detection of malignant lesions

A. Nivaggioli, R. Peyret*, N. Pozin, M. Sockeel, S. Sockeel, S. Mazellier, C. Lefebvre, V. Rouleau, A. Gauthier, S. Kammerer-Jacquet
*Primaa, France

Background & objectives: Most malignant dermatopathological lesions are basal cell carcinomas (BCC), squamous cell carcinomas (SCC), or melanomas. The automatic detection of such lesions, along with automated measurement of lesion thickness and margins, could assist pathologists in establishing faster and more accurate diagnoses.
Methods: We collected and annotated 1795 digitized slides containing malignant, benign lesions, and healthy tissues. Using Deep Feature Learning, we trained a classifier on 20x zoom patches to identify melanoma, BCC, or SCC. Computer vision methods then automatically measured lesion thickness and surgical margins, therefore enhancing diagnostic speed and accuracy.
Results: The test dataset includes 392 slides of the most common malignant lesions, as well as 500 slides of healthy tissue or benign lesions. The F1-score of our classification model for detecting malignant lesions is 0.892. The balanced accuracy of our model in predicting the diagnosis of melanoma, BCC, or SCC is 0.965. At the patch-level, it can detect a malignant lesion with a precision-recall area under the curve (AUC) of 0.946. Lesions and sample measurements are consistent with medical practice, and a clinical validation study is currently ongoing.
Conclusion: We propose the first algorithm capable of locating and identifying cutaneous malignant lesions in histopathological whole slide images, while also automatically measuring the thickness and margins. Ongoing developments are expected to further improve the results. The detection of benign lesions, the classification of subtypes of malignant lesions, and the automatic detection and counting of mitosis are also subjects of research.

E-PS-17-055

Morphometric assessment of cardiac muscle fibers density depending on age

I.E. Plesea*, M.S. Șerbănescu, V.T. Grigorean, L. Iovan, I.D. Avramescu, L. Eftimie, R.M. Pleșea
*"Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

Background & objectives: Aging and diseases, with their subsequent lesions, cause cardiac wall remodelling consisting of its components' structural and functional changes. The authors compared the variations of muscle fibre-MF amount-% between the different cardiac wall regions while patients are ageing.
Methods: Five epicardium-to-endocardium cross sections (left ventricle anterior-LV_AW, lateral-LV_LW and posterior-LV_PW, interventricular septum-IVS and right ventricle-RVW) from 95 patients with different ages (0-24 years-AP_01, 25-44 years-AP_02, 45-64 years-AP_03 and >64 years-AP_04) autopsied in the hospital, were processed, stained with Picro-Sirius_Red and slides were digitized. The myocardiocytes amount was measured with an "in-house" designed software. Average values-AV were compared using Pearson's test.
Results: The FM percentage is the lowest in childhood and adolescence, increases significantly during young adulthood to decrease then smoothly until the old age. The FM amount is the highest in the LV_W decreases from LV_AW toward the IVS and is the lowest in the RV_W in all periods of life, excepting AP_01 where it is the highest in the RV_W and AP_04 where it is higher in the LV_LW than in LV_PW. FM values are also higher in men than in women in all cardiac wall regions and their decrease from LV_W to RV_W is more pronounced in women than in men.
Conclusion: This remodeling process of the cardiac wall along its regions and with aging is following the same decreasing pattern of FM percentage in both sexes, generally with higher values in men than in women.

E-PS-17-056

Multi-class and multi-institutional supervised learning classifier characterises colon cancer and enables clinicopathological biomarker implementation

M. Polack*, N. Coudray, B. Liu, A. Claudio Quiros, T. Sakellaropoulos, S. Crobach, R. Tollenaar, K. Yuan, H. van Krieken, W. Mesker, A. Tsirigos
*Dept. Surgery, Leiden University Medical Center, Leiden, The Netherlands

Background & objectives: Hematoxylin-and-eosin-stained colon cancer whole-slide images (WSIs) can be analysed with a supervised

deep learning tool, categorizing small image patches (tiles) into tissue types. Subsequently, visualization of tissues can support pathologists' assessments, including automated biomarker determination like the tumour-stroma ratio (TSR).
Methods: A convolutional neural network (CNN)-based classifier was trained on 100 extensively detailed, QuPath-annotated WSIs from the AVANT-study, validated and tested on 1113 AVANT WSIs. An additional external validation cohort will comprise the TCGA-colon adenocarcinoma (N=435 WSIs) and UNITED-study (N=932 WSIs). Our classifier categorizes all WSI tiles into tissue types, forming heat maps. Clinicopathological predictions and TSR calculations are currently running.
Results: Supervised learning for segmentation was used based on 12 annotation types: tumour epithelium, tumour stroma, necrosis, erythrocytes, immune cells, mucin, fatty tissue, muscle tissue, healthy/dysplastic colon epithelium, healthy stroma, artifacts and background. Maintaining a train-validation-test split on the patient level (70%-15%-15%), preliminary 5-fold cross-validation resulted in a micro-average 0.98 (0.97-0.99) Area Under the Curve. Biomarkers like the TSR can be automatically assessed and calculated with this classifier by implementing cut-offs on the selected regions of interest and/or hotspots, e.g. determining stroma-high tumours, while also facilitating colon cancer characterization, for instance in the distinction of poor-undifferentiated or mucinous tumours, establishing a supportive, adaptable tool for routine pathology diagnostics.
Conclusion: Harnessing the well-established, multi-institutional AVANT, TCGA and UNITED cohorts, our high-performing supervised deep learning multi-class segmentation model already accurately classifies WSI tiles into tissue types. Moreover, visualization of these categorized tiles in automatically created, intuitive WSI heat maps, facilitates tumour characterization and enables biomarker determination, like TSR, ultimately resulting in a reproducible, unbiased and pathologist-friendly tool. Implementation of our CNN classifier can support future clinical decision-making, including steps toward improved tailored treatment strategies for colon cancer patients.

E-PS-17-058
Computational evaluation of uninvolved lymph node morphology predicts outcomes in locally advanced head neck cancer
S. Gazi, N. Seshadri, T. Bameta, A. Sharma, S. Ghosh-Laskar, A. Sethi, A. Patil, N. Mittal, K. Rabade, M. Bal, S. Rane*
*Tata Memorial Centre-Actrec, India

Background & objectives: Host immune response plays a vital role in cancer progression. While tumour-infiltrating lymphocytes (TILs) have been studied extensively, the role of the immune response in the regional nodes is not widely studied.
Methods: We perform a computational analysis of uninvolved cervical lymph node morphology in upfront operated cases of advanced (T3-T4, N2-N3) oral squamous cell cancer using computationally derived metrics of lymph node response using a deep learning-based segmentation of germinal centres modified from our previous work in breast cancer(https://doi.org/10.1002/path.6088). An interim analysis of 75 out of 500 total patients is being presented.
Results: The mean(SD) age was 45.8±9 years; M:F ratio was 5:1. All patients underwent surgery followed by either adjuvant RT (n=54) or CTRT (n=20) with curative intent. The median DFS was 18.84 months. A mean(SE) of 14(1.45) uninvolved nodes per patient was studied. Mean(SE) of 9.6 (0.78) GC per node (1-32.5) were noted. GC count/node, GC area, GC distance from node capsule, area proportion occupied by GC were all associated with better DFS. K-M analysis revealed better DFS at 1yr for patients with ≥13 average GC count/node (65%vs38%; $p = 0.013$) & for patients with GC farther away from the node capsule (≥median 754μm) (57%vs34%, $p = 0.021$).
Conclusion: In this interim analysis of 75 advanced oral cancer patients, systemic immune response, as manifested by the extent of secondary follicle formation in the regional lymph nodes, is significantly associated with better disease-free survival. We further show that DL based segmentation of GC is a reliable method to identify, segment and quantify host immune response in regional nodes. We intend to complete a more comprehensive analysis of 500 patients and present it at the meeting.

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E-PS-17-060
Integrating spatial vessel analysis into tumour microenvironment characterization
S. Renne*, Ö. Mintemur, G. Grion, F. Colella, K. Roufail, C. Matteo, V. D'amato, M. Meroni, R. Frapolli, L. Morosi, G. Martano, F. Cananzi
*Humanitas University, Italy

Background & objectives: Tumour microenvironment characterization is critical for targeted therapies. Diverse cellular components can be studied with an increasing number of technologies; however, integration with spatial vessel analysis is often overlooked. We aim to create a pipeline to segment and analyse vessels.
Methods: Leiomyosarcoma model slices were stained with immunohistochemistry for an endothelial marker (CD31). TIFF whole slide images were acquired. Tiling was performed with Groovy and QuPath for visual image checking. Tiles were converted from RGB to HSV and the H channel was used for segmentation in Python. Vessels were detected using morphological operations. Vessels' mask image and individual characteristics were generated.
Results: For each vessel, our pipeline generated the following measurements: a centroid (i.e. location), section area, major (M) and minor (m) axis, eccentricity (m/M), and orientation. Measurements were then used to generate density maps. These maps allowed easy visualization of the features and can be used in spatial analysis. A proof of concept analysis using drug distribution data showed the feasibility of this spatial approach. Exploiting Bayesian data analysis and Gaussian processing, we were able to estimate the effect of spatial changes in vascularization on drug distribution.
Conclusion: This novel pipeline allows seamless integration of spatial vessel analysis into tumour microenvironment characterization. We showcased the potential for integrating spatial vascular data with other spatial information, paving the way for improved understanding of tumour biology and targeted therapy design.

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E-PS-17-061
Enhancing precision in HER2 in situ hybridization quantification in breast cancer: integration of a cancer cell classification model using deep learning
I. Rienda-Martínez*, J. Pinto, C. Eloy, A. Polónia
*Hospital La Fe, Spain

Background & objectives: In the context of breast cancer diagnostics, achieving high precision in HER2 assessment is essential. This study aims to assess the impact of integrating a cancer cell classification model on a validated HER2 in situ hybridization (ISH) quantification system.

Methods: We trained a cancer cell classification model using a DenseNet-based semantic segmentation from HALO software (Indica Labs) with 798 annotations in 18 whole slide images (WSI) of breast cancer. The performance of the HER2 ISH quantification, with and without integration of the cancer cell classification model, was evaluated using 20 distinct WSI from breast cancer (10 HER2-negative and 10 HER2-positive).
Results: After the validation phase, the cancer classification model achieved a precision of 0.846, a recall of 0.844, a F1-score of 0.845, a sensitivity of 0.66 and a specificity of 0.91. A positive predictive value (PPV) of cancer cells reached a value higher than 0.95 when at least 72% cancer cell cellularity was present. The integration of the cancer classification model significantly increased the HER2 and CEP17 copy numbers ($p<0.001$), as well as the HER2/CEP17 ratio ($p=0.003$). The increase in HER2 copy numbers was higher in HER2-positive cases compared to HER2-negative cases (average of 0.44 copies/cell and 0.06 copies/cell, respectively). Lastly, the HER2 ISH group classification remained unchanged in all cases.
Conclusion: The implementation of our DenseNet-based cancer cell classification model for breast cancer enhances cancer cell selectivity in a validated HER2 ISH quantification system, leading to significantly higher HER2 and CEP17 copy numbers. This achievement may impact borderline cases where slight variations in HER2 copy numbers and/or HER2/CEP17 ratio affect the HER2 final ISH group classification. Finally, high PPV can be achieved only in high cancer cellularity cases showing the importance of pathologists in the selection of appropriate cancer regions.

E-PS-17-062
Evaluating the utility of large language models for cross-linguistic pathology reporting
T. Romagnoli*, S. Lin, A. Bychkov, L. Cima, E. Munari, S. Rasmussen, A. Sharma, R. Singh, E. Ullah, B. Wehrli, M. Cecchini
*London Health Sciences Centre, Canada

Background & objectives: Large language models (LLMs) demonstrate potential for improving pathology text translation, offering a tool for better cross-border collaboration. This study evaluates the translational capacity of LLMs in pathology compared to traditional methods.
Methods: Ten pathology cases were prepared in English and translated into Italian by two pathologists including diagnosis and commentary. These were then translated back into English using GPT-4, Gemini (1.0) and Google Translate. Five English-speaking pathologists evaluated the translations for medical terminology, report structure and contextual comprehension using a 5-point Likert scale. Their suitability for clinical use was also assessed.
Results: GPT-4 demonstrated significantly better performance in medical terminology and report structure compared to Gemini and Google Translate. Contextual understanding was similar across the three translation methods. The majority of pathologists rated GPT-4 translations as acceptable for clinical practice (62%), exceeding Gemini (40%) and Google Translate (36%). Notably, only 8% of GPT-4 translations were deemed unacceptable as compared to Gemini (38%) and Google Translate (26%).
Conclusion: This study offers preliminary insights into the potential of LLMs for improving pathology text translation. The ability of LLMs to grasp the nuanced medical context holds promise. As LLMs rapidly evolve, future studies with larger datasets and a wider range of languages will be needed to fully explore their capabilities. LLMs could play a role in breaking down language barriers in pathology thereby facilitating global collaboration and potentially driving standardization in reporting.

E-PS-17-063
Immunosoppression in primary and recurrent colorectal cancer: prediction of response to therapy and prognosis
G. Sabella*, E. Daveri, l. Sorrentino, V. Lagano, M. Salvi, O. Pennisi, F. Molinari, G. Centonze, M. Milione
*Switzerland

Background & objectives: The estimation of risk of recurrence for colorectal carcinoma patients must be improved. A robust immunoscore quantification is needed to introduce immune parameters into cancer classification. The aim of the study was to assess the correlation between immunoscore and prognosis.
Methods: Tumour samples from 30 patients with colorectal primary tumours stage I–III operated by upfront surgery, were collected between 2010 and 2019. Dedicated image-analysis software were used to quantify the density of CD3+ and CD8+ T-cell effectors in the tumour and its invasive margin and to determine the standardised immunoscore assay. Associations with clinicopathological features and survival data were evaluated.
Results: Hematoxylin normalization of 30 samples was performed to standardize the staining intensity across the whole slide images, enhancing the contrast between DAB and hematoxylin, thus ensuring more consistent and reliable results in the subsequent nuclear segmentation. Sum of peritumoural lymphocytic reaction and tumour-infiltrating lymphocytes was calculated as overall local lymphocytic score (LLS) for each sample; association with perineural invasion (PNI) was detected. Kaplan-Meier curves showed that patients with low LLS and high PNI tended to have lowest disease free survival (long rank $p=0.0098$). Moreover, an high LLS correlated with an high CD3+ cell density ($p=0.0009$) and the absence of PNI was associated with an high CD8+ tumour density ($p= 0.009$).
Conclusion: Our preliminary results suggested that perineural invasion, regardless of local lymphocytic tumour density, could be an independent negative prognostic factor in primary colorectal cancers.

E-PS-17-064
The development and validation of machine learning algorithms for accurately determining the nuclear grade of breast cancer inroutine morphological diagnostics
A. Semenova*, V. Galkin, A. Artemieva, Y. Andreeva, Y. Vishnevskaya, N. Savelov, D. Voronkina, K. Botashev, V. Shatalov, Y. Andryukhina
*Moscow State Budgetary Healthcare Institution "Moscow City Hospital named after S.S. Yudin, Moscow Healthcare Department", Russia

Background & objectives: Most commonly used grading system of the breast cancer is the Nottingham combined grading system based on nuclear pleomorphism evaluation. We offer a deep learning neural network-based segmentation method for automated scoring for nuclear pleomorphism reduce hallenges in criteria establishment.
Methods: We did whole slide image (WSI) segmentation using a convolutional neural network. Our labeled training dataset of 300 slides was independently processed by two pathologists, who highlighted areas with homogeneous nuclear pleomorphism scores. This markup was refined using our general tumour segmentation model and used to train the separate nuclear pleomorphism segmentation model.
Results: Our model was evaluated using the test dataset of 118 whole slide images (WSI) introduced in [1]. It outperformed the regression-based method reported in the original report, achieving a higher Cohen's quadratic kappa score of 0.545 compared to the original score of 0.526 computed in comparison with 4 experienced pathologists. The

use of segmentation in marking up the entire slide allows us to obtain a comprehensive distribution of pleomorphism of cell nuclei over the entire area of a breast tumour. The resulting model eliminates the differences when working with different types of scanners and samples, which provides fast and reliable diagnostics within a few minutes
Conclusion: We introduce a vision-based automated approach for evaluating nuclear pleomorphism in whole slide images (WSI). Our deep learning model, utilizing a 6-class segmentation approach, delivers competitive metrics surpassing the existing patch-based regression method. It achieves efficient inference time and grading results consistent with interobserver agreement among four independent pathologists. This approach holds significant potential, providing an unbiased perspective on nuclear pleomorphism grading, and potentially assisting pathologists in achieving reliable diagnostic decisions.

Funding: This research is implemented within the Grant "The development and validation of machine learning algorithms for supporting medical decision-making in the routine morphological diagnostics of breast cancer".

E-PS-17-065
The development of machine learning algorithms for decision-making support to help evaluate HER2/new-status in breast cancer diagnostics
A. Semenova*, V. Galkin, Y. Andreeva, Y. Vishnevskaya, N. Savelov, V. Shatalov, Y. Andryukhina, I. Kondratenko, D. Voronkina, V. Pirogova, L. Polyvanov, A. Artemieva
*Moscow State Budgetary Healthcare Institution "Moscow City Hospital named after S.S. Yudin, Moscow Healthcare Department", Russia

Background & objectives: HER2 is an important biomarker used to predict breast cancer outcome and to prescribe a suitable target therapy. Patients with ultra-low HER2 expression have new therapeutic options available with an "absolute 0" score as a critical criterion for such therapy.
Methods: We propose a new approach to HER2 status evaluation, categorizing as absolute 0, 0, 1+, 2+, and 3+ in both the region of interest (ROI) and the whole slide image (WSI). At first we segment the tumour area and then classify every small piece of the tumour pathwise to determine the percentage of each class.
Results: The study evaluated metrics such as accuracy, precision, and reproducibility in categorizing ROI segments. The classification between HER2-low (abs 0, 0, 1+) and HER2-high (2+, 3+) resulted in 97% accuracy, 97.1% precision, and 96.2% reproducibility. The classification between abs 0 and 0 gave 87.2% accuracy, 85.9% precision, and 87.4% reproducibility. Additionally, the study examined the classification between 1+ and 2+ to assess its impact on the FISH application decision, resulting in 93.3% accuracy, 92.4% precision, and 88.7% reproducibility. The study addressed the challenges of distinguishing carcinoma in situ from the invasive component, which significantly affects the HER2 evaluation results on WSI.
Conclusion: We are excited to introduce a new automated solution for standardizing HER2-score assessment using computer vision technology. Our deep learning model, which utilizes an ensemble architecture approach, has shown competitive metrics on both ROI and WSI. The scoring algorithm provides a high-precision separation of the absolute 0 and 3+ classes, which are key parameters for prescribing targeted therapy. This approach has significant potential, providing unbiased full slide assessment that could increase the reproducibility of diagnostic decisions.

Funding: This research is implemented within the Grant "The development and validation of machine learning algorithms for supporting medical decision-making in the routine morphological diagnostics of breast cancer".

E-PS-17-066
Utility of digital pathology in the evaluation of liquid-based PAP tests
M.İ. Şengör Aygün*, S. Erdogan-Durmus, C. Comunoglu, O. Yalcın
*Pathology Department, Prof. Dr. Cemil Tascioglu City Hospital, Istanbul, Turkey

Background & objectives: Digital whole slide imaging (WSI) techniques have become common. WSI is frequently used in surgical pathology, however, its use in cytopathology is still limited. We aimed to compare the cytopathological evaluation of thin-layer slide smears with that of the WSI.
Methods: Sixty consecutive thin layer slide smears (SurePath) examined in one day at Prof. Dr. Cemil Tascioglu City Hospital Department of Pathology were included. Slide smears were evaluated by 2 pathologists under a light microscope and 1 pathologist on WSI. Bethesda system was used. Nonneoplastic findings are also listed. The results of evaluation by light microscopy and WSI were compared.
Results: By light microscopy, the rate of epithelial cell abnormality (ECA) was 6.7%. One case was evaluated as ASC-US, 2 cases as LSIL, and 1 case as HSIL. The ECA rate was found 10% in evaluation via WSI (4 cases as ASC-US and 2 cases as LSIL). Concordance between the pathologists was 95%. Discordance was detected in 3 ECA cases. Two of the discordant cases were evaluated as negative on light microscopy, whereas ASC-US on WSI. One case, which was evaluated as HSIL on light microscopy, was evaluated as ASC-US on WSI.
Conclusion: The concordance between light microscopy and WSI is high in cervical cytological evaluation. However, focusing problems due to thick cell groups, overlapping cells, and the presence of fibrin in evaluation with digital imaging methods in cervical cytology constitute the limitations of digital imaging scanning. The limitations of our series are the small number of cases and the absence of glandular cell abnormality in the series.

E-PS-17-067
AI for advanced cancer diagnosis: a CAD System empowered by a novel vision transformer network for histopathology analysis
A. Shakarami*, L. Nicolè, S. Ghidoni
*Intelligent Autonomous Systems Laboratory (IAS-Lab), Department of Information Engineering, University of Padova, Italy

Background & objectives: Digital pathology transforms practice with innovative tools. Accurate diagnosis of various cancers is crucial for determining appropriate treatment strategies. Our study introduces a CAD system using Whole Slide Images to diagnose cancer.
Methods: The CAD system, based on our novel Vision Transformer Network, enhances adaptability. Its flexible architecture enables efficient processing of varied cancer data, achieving superior histology classification. Supported by Transformer Blocks' self-attention mechanism, the network accurately understands histopathological image patterns, enhancing feature identification and classification accuracy.
Results: Our CAD system detects Breast Cancer, Non-Small Cell Lung Cancer (NSCL, distinguishing between lung adenocarcinoma and lung squamous cell carcinoma), Skin Melanoma, Colon Adenocarcinoma, Gastric Carcinoma, Hepatocarcinoma, and infiltrative gliomas (distinguishing from each other: Glioblastoma, Astrocytoma, and Oligodendroglioma). Trained on a 512,271 annotated histological images dataset, the network achieved an impressive 98.12% overall accuracy on the test set at the patient level. The validation of the CAD on two separate datasets also revealed high diagnostic sensitivities of 94.11% and 92%, respectively.
Conclusion: The proposed CAD system is a valuable tool for bridging the gap between AI engineering and clinical research in cancer diagnosis. It enhances predictive accuracy and facilitates a deeper understanding of medical images by capturing diverse information and refining

feature representation. This offers potential benefits for research and clinical practice.

E-PS-17-069

Quality control of AI-assisted cervical cancer screening diagnosis

X. Sun*, J. Wang, H. Li
*Landing Med, China

Background & objectives: To explore the quality control of AI cervical cancer screening diagnosis.
Methods: From September 2022 to December 2023, cervical samples from 5,267,030 women in China's Hubei Province were prepared by liquid based methods and stained by Pap solution. All samples were scanned by Landing Med's digital pathology slide scanners (WSI scanner) and analysed using Landing Med's proprietary cervical cytology (LBC) AI analysis system.
Results: Among 5,267,030 women, cervical samples were diagnosed as 4,956,172 cases (94.1%) NILM, 209,310 cases (3.97%) ASCUS, 58,706 cases (1.11%) LSIL, 23,617 cases (0.45%) ASC-H, 8,012 cases (0.15%) HSIL, and 5,836 cases (0.11%) AGC. Among these screened women, 61,903 underwent cervical biopsy, revealing 34,545 cases of cervical inflammation, 19,917 cases of CIN I, 6,817 cases of CIN II+, and 624 cases of invasive cancer through histopathological diagnosis. Comparing the concordance rates between cytology and histology, the agreement rates for diagnosing CIN II+ in ASCUS, LSIL, ASC-H, HSIL, and AGC were 4.75%, 9.56%, 26.58%, 63.42%, and 4.83%, respectively.
Conclusion: 1. Compared to conventional cytology, AI cervical cancer screening has slightly increased the diagnostic rate of ASCUS.
2. Implementing quality control for AI cervical cancer screening can achieve a level comparable to manual cervical cancer screening.
3. AI screening technology is applicable for large-scale population-based cervical cancer screening, especially in developing countries.

E-PS-17-070

Validating an AI-based analytic tool for IHC staining QA: precision studies of the digital pathology pipeline

J.M. Tuthill*
*HFHS, USA

Background & objectives: Standardization of immunohistochemistry staining quality assessment is critical for diagnostic accuracy. Pathologists currently assess stain quality subjectively, comparing control sections to patient tissue. Qualitopix (Visiopharm, Denmark), a cloud-based artificial intelligence platform for uses quantitative analysis for scoring stained slides.
Methods: Glass slides were produced from two 4-core standardized cell-line blocks (Histocyte Laboratories, Newcastle, England) with epitopes for estrogen receptor (ER) and progesterone receptor (PR) of increasing intensities, stained using Ventana Benchmark Ultra and scanned on DP 200 and HT scanners (Roche, Basel, Switzerland). An intra-scanner precision study was performed by comparing Qualitopix-derived H scores of ER and PR slides.
Results: Intra-scanner precision studies demonstrated consistent reproducibility using both scanners:
%CV for ER cores were 0%, 10.7%, 2.3% and 0.3% for cores 1 [0 +/- 0.003], 2 [0.3 +/- 0.25], 3 [2.4 +/-1.4] and 4 [79 +/- 0.65] respectively.
% CV for PR cores were 0%, 0.6%, 0.4% and 0.1% for cores 1 [0 +/- 0.01], 2 [29 +/-4.5], 3 [65+/-2], and 4 [94+/-2] respectively.
Concordance studies revealed tight agreement.
ICC for ER cores were 0.64 (moderate), 0.95(excellent), 0.95(excellent) and 0.68 (moderate) for cores 1, 2, 3 and 4 respectively.
ICC for PR cores were 0.64 (moderate), 0.87(good), 0.96(excellent) and 0.68 (moderate) for cores 1, 2, 3 and 4 respectively.
Conclusion: Quality assurance is essential to the use of digital pathology, particularly to the application of AI. Studies of precision, reproducibility, and accuracy are lacking in the literature. This study demonstrates the precision characteristics of one vendor's digital pathology product line.

E-PS-17-071

Comparison of conventional mismatch repair protein (MMR) expression analysis with QuPath positive cell count algorithm

M. Üner*, K. Yılmaz, A. Üner
*Department of Pathology, Hacettepe University, Turkey

Background & objectives: Machine learning-based biomarker algorithms provide detailed and accurate results in tumour analysis. Particularly, open-source softwares (QuPath etc.) stand out in biomarker analysis due to versatility for development and accessibility. Herein, we compared QuPath with conventional assessment of MMR protein analysis.
Methods: MLH1, PMS2, MSH2, and MSH6 proteins were evaluated manually and using QuPath software on virtual tissue microarray slides comprising 75 lymphoma cases. Spearman's Rho correlation test was applied to assess the parameters scored manually (positive tumour cell percentage, staining intensity, modified H score) and those scored via QuPath (positive tumour cell percentage, H-score, Allred proportion and Allred intensity scores).
Results: The highest correlation was obtained for H-scores. When manually scored modified H scores were compared with QuPath's detailed H scores for MLH1, PMS2, MSH2, and MSH6, Spearman correlation coefficients were 0.89, 0.78, 0.85, and 0.81 respectively. Additional correlation results for MLH1, PMS2, MSH2, and MSH6, respectively, were as follows:
Conclusion: In this study, we observed that for objectively defined parameters like H-score, there was a high correlation between QuPath and manual scoring. However, for more subjective parameters like intensity evaluation, there was lower correlation between manual and QuPath based analysis. Digital applications can help pathology practice in biomarker research, where tissue microarrays are frequently used, and machine learning/artificial intelligence algorithms come to the fore in this field. QuPath is an open-source, improvable image analysis platform which pathologists can easily use.

E-PS-17-072

Introducing the MONKEY challenge: machine-learning for optimal detection of inflammatory cells in the kidney

D. Van Midden*, L. Studer, F. Ayatollahi, A.B. Farris, J. Kers, L. Hilbrands, J. van der Laak
*Radboud University Medical Center, The Netherlands

Background & objectives: The Banff classification remains the gold standard for diagnosing rejection in kidney transplant biopsies. Since the scoring suffers from subjectivity and is time consuming, development of automated biopsy assessment holds great potential to reduce pathologist's workload and increase scoring consistency.
Methods: MONKEY is an AI competition for developing a machine learning solution that automates the detection of lymphocytes and monocytes in Periodic acid-Schiff (PAS) stained kidney transplant biopsies. The dataset consists of annotated regions from a multi-centric cohort of 120 biopsies. To ensure reliable annotations, the slides are re-stained with antibodies against CD3, CD20, and PU.1 to identify lymphocytes and monocytes.
Results: The challenge is planned to open during summer 2024 and will run on the Grand Challenge Platform (monkey.grand-challenge.org) with leaderboards for individual tasks. During the first phase (validation phase), participants are required to submit the output of their algorithms. It will result in a best performing algorithm to detect

lymphocytes and monocytes. Algorithm performance will be evaluated on a separate test set during the second phase (test phase). The final, best performing algorithm will be accessible for the research community and will be further incorporated in AI for automated Banff lesion scoring. The MONKEY dataset will remain publicly available for research purposes.
Conclusion: Several of our previous challenges (CAMELYON, PANDA and TIGER), where similar wisdom-of-the-crowd approach was applied for urgent clinical applications, have produced highly successful algorithms, sometimes even surpassing experienced pathologists. The MONKEY challenge is highly ambitious as it aims to differentiate between lymphocytes and monocytes. As 10 out of the 17 lesion scores of the Banff Classification focus on the presence of inflammatory cells in different compartments, this brings us a step closer to automated Banff lesion scoring.

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E-PS-17-073
Unlocking the potential of deep learning-based detection and quantification of tumour infiltrating lymphocytes in gastric cancer
Y. Weeda*, D. Wessels, A. Mkundan, E.J. Bekkers, O.J. De Boer, W. Song, L. Kodach, S. Meijer
*Department of Pathology, Amsterdam University Medical center, The Netherlands

Background & objectives: Automated tumour infiltrating lymphocytes (TILs%) detection in breast and lung cancer holds promise for guiding personalized immune-based treatment selection. This study investigates the novel application of deep learning for TILs% quantification in gastric adenocarcinoma (GA).
Methods: A U-Net tissue segmentation and yollov3 cell-detection model, initially trained on breast cancer slides, was employed. Whole slide images were tiled and fed to both models. Tumour bulk and stroma segmentations, combined with lymphocytes and plasma cells detections were used for TILs% quantification. This model was applied on 60 TCGA-STAD slides assessed by two expert pathologists following TILs working-group guidelines.
Results: The Pearson correlation between the model's prediction and the pathologists for whole-slide TILs% equaled 0.72. Muscle and necrotic regions were frequently mislabeled as stromal tissue, while benign and metaplastic areas were incorrectly identified as malignant. Areas of inflammation, characterized by dense aggregation of plasma cells and granulocytes presented a challenge, particularly due to the unwanted inclusion of granulocyte count in the final TILs% score.
Conclusion: Despite lacking prior exposure to GA slides, the breast cancer-trained TILs% model exhibited a strong correlation with pathologist assessment. Misclassification were attributed to specific digestive tract tissue features. Future improvements involve training the model on GA slides and in particular on regions covering benign tissue, necrosis and metaplasia. Using antibody supervision, the model will be extended for inclusion of both plasma cells and granulocytes. This model promises a more standardized, reproducible and less time-consuming method for TILs assessment in GA.

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E-PS-17-074
Creating a valuable decision tree from a knowledge graph: emphasizing topology over content
M. Legnar, S. Porubsky, Z. Popovic, A. Dendooven, S. Leh, C. Weis*
*Institute of Pathology Heidelberg (IPH), University Hospital Heidelberg, Germany

Background & objectives: Histological diagnoses require well-defined criteria, often scattered in texts. Knowledge graphs could gather such information, but manual extraction is needed for diagnostic algorithms, like decision trees. This research proposes machine learning for diagnostic tree generation, using datasets of different topology.
Methods: The initial step involves knowledge graph generation by means of computer linguistics. Subsequently, two distinct methodologies are evaluated: firstly, a concept-frequency-based approach, and secondly, the application of the MINDWALC algorithm. To further improve MINDWALC's ability to utilize the knowledge, stored in the present knowledge graph, we introduce additional mind-walking strategies.
Results: Employing Pokémon datasets as a meticulously curated toy dataset with either flat, hierarchical or combined topology, we can demonstrate through artificial gradual graph degradation by removing nodes and edges that the complexity of the resultant decision trees correlates with the increasing deterioration of the graph. In addition, we can show that MINDWALC takes advantage of knowledge graphs as it uses also information in the depth of the graph, while the just frequency-based approach uses only the direct neighbouring elements. In this context, MINDWALC can also used for different graph topologies (flat topology versus hierarchical topology like SNOMEDCT or KBC), however the walking strategies need to be adapted to the topology.
Conclusion: We can show that the MINDWALC algorithm takes advantage of data stored in a knowledge graph, since it produces comprehensive diagnostic algorithms in the form of decision trees. By adding new walking strategies, we can adapt it to different graph types, especially with hierarchical topologies like used for entities in classification systems like used in the WHO books, SNOMEDCT or in our data set KBC.

E-PS-17-075
AI case triaging of digital dermatopathology cases: a second pair of eyes in a digital workflow
J. Weldon*, M. Morrissey, R. Sykes, M. Colleluori, J. Fitzgerald, C. Durnin-White, S. Carmody, M. Rafferty, P. Moulin, A. Power, D. O'Shea, N. Mulligan, R. Chetty, C. Girleanu
*Deciphex, Ireland

Background & objectives: Our aim is to alleviate pressure points to improve patient management of dermatopathology cases that, based on benign clinical impressions, may have been deemed non-urgent by implementing a dermatopathology AI classification model within a digital pathology workflow.
Methods: We are developing an AI-empowered digital pathology system for AI case triaging of skin cases. Prediction data and masks can be incorporated into the case information as digital H&E slides are sent to the cloud-based platform. A proprietary, weakly supervised learning classifier for slide-level dermatopathology biopsy classification was created and applied in a digital pathology workflow.
Results: The AI model successfully triaged 1,000 digitised clinical cases according to their diagnosis. Cases were accurately classified into routine (normal / non neoplastic pathology) or urgent (basal cell carcinoma / squamous cell carcinoma and melanocytic lesions) categories based on their histopathological features. This categorisation was based on consultation with senior pathologists who deemed the urgent and routine classifications that would be most beneficial. Annotations by expert pathologists were used for both training and testing of our AI models. Feedback from pathologists gave rise to tile blending which was performed to improve the AI mask with readability of the tissue beneath.
Conclusion: In summary, developments herein provide AI case triaging for pathologists which will support skin diagnosis and treatment. There is applicability of this dermatopathology AI for both case triage and as a 'second pair of eyes' or double read. This AI can be seamlessly

deployed within a digital pathology platform that connects laboratories worldwide to an international network, where subspecialty pathologists can apply their expertise to clinical cases.

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E-PS-17-076

Feasibility study of invasive breast carcinoma detection on HER2 immunohistochemistry and dual in-situ hybridization image

T. Ohnishi, N. Bakoglu, D. Ross, Y. Yagi*
*Memorial Sloan Kettering Cancer Center, USA

Background & objectives: For a smooth workflow in human epidermal growth factor receptor 2 (HER2) amplification assessment, this study aims to detect invasive breast carcinoma on HER2 immunohistochemistry (IHC) or dual in-situ hybridization (ISH) images using an AI-based image analysis algorithm.
Methods: Our AI model detects the invasive area from only the unmixed hematoxylin component. We obtained 79 datasets containing whole slide images of H&E, IHC and Dual ISH slides scanned by PANNORAMIC 1000 or PANNORAMIC 250 Flash III (3DHISTECH Ltd., Hungary). As ground truth, pathologists annotated the invasive areas on the H&E images.
Results: 13 H&E images were randomly selected as training dataset and two IHC or three dual ISH images were used as test dataset. The trained AI model was tested on H&E, IHC and dual ISH images. Although some misdetections were observed on in-situ area, invasive areas were sufficiently visualized even on dual ISH image. In addition, the in-house image analysis application for dual ISH was tested on invasive areas detected by the proposed algorithm. We confirmed that the HER2 status of the invasive areas determined by our algorithm was the same as that determined by the pathologist's manual assessment.
Conclusion: We developed an AI model for invasive breast carcinoma detection with only hematoxylin component. This study demonstrated it works on immunohistochemistry or in-situ hybridization image without H&E image. We will integrate the proposed algorithm into in-house IHC and dual ISH analysis applications for more automation.

E-PS-17-077

Optimal whole slide image formats for artificial intelligence training in digital pathology

M. Yook*, C.K. Jung, S.K. Yoon, I.Y. Choi
*Department of Medical Informatics, College of Medicine, The Catholic University of Korea, Republic of Korea

Background & objectives: The diversity in file formats of WSI presents significant challenges in preparing data for AI training in DP. This study aims to identify the best WSI file formats that facilitate the creation of AI learning datasets for large-scale DP operations.
Methods: A comprehensive review of the literature on digital pathology image file formats was conducted. This involved examining the characteristics of each format and suggesting a standardized format that can replace the proprietary formats used by different scanner manufacturers.
Results: Our research shows that the use of the DCM format is increasing, especially in Picture Archiving and Communication Systems (PACS) for digital pathology. The Digital Imaging and Communications in Medicine (DICOM) standard used in PACS now supports extensive, multi-layered images, making the DCM format more suitable. While the DCM format is good for interoperability within medical systems, the generic tiled TIFF format can be beneficial for developing AI algorithms outside of traditional medical environments due to its simplicity and adaptability.
Conclusion: Adopting the DCM format for scanning and processing WSIs enables improved interoperability, supporting both clinical diagnostics and digital pathology research. On the other hand, for AI-driven research initiatives that do not require integration with PACS, the TIFF format offers greater convenience and flexibility. This dual-format approach enables a customized application based on specific operational and research requirements, proposing a clear path toward standardized, efficient digital pathology systems that enhance AI capabilities.

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E-PS-17-078

Improving urothelial carcinoma diagnosis with enhanced MIL approach and sub-centre arcface loss

G. Hwang, D. Jeong, W.J. Cho, H. Yoon*, G.Y. Gong, N.H. Cho, Y. Chong
*Deepnoid Inc., Republic of Korea

Background & objectives: Developing a diagnosis system for urothelial carcinoma is challenging due to its difficulty to accurately annotate the lesions. We propose Fixed Feature Space (FFS)-MIL with Sub-centre Arcface loss to enhance classification accuracy in Clustering-constrained Attention Multiple Instance Learning (CLAM) models.
Methods: We remove noise, obtain significant foreground areas, and extract features using a pre-trained ResNet50 on our limited WSI dataset. We utilize Sub-centre Arcface loss to create a feature space with pronounced intra-class distinctions and inter-class separations. The similarity score from above is used as a weighting mechanism to emphasize patches with distinctive features, which are then aggregated for slide-level classification.
Results: To compare the performance of conventional Multiple Instance Learning (MIL) approach and FFS-MIL, we used dataset including 2,235 negative and 226 positive WSIs for urothelial carcinoma. In addition to the WSI-level labels, we collected 10 positive and 10 negative patch image and label pair to use as the standard patches to calculate the similarity. Our method shows improved performance over the CLAM model. CLAM model shows result of Area Under the Curve (AUC) of 0.9699 and accuracy (ACC) of 91.58%, and our method shows AUC of 0.9875 and ACC of 92.06%, highlighting the benefit of Sub-centre Arcface loss in feature space construction and the use of similarity scores for weighting.
Conclusion: Our study demonstrates that the Fixed Feature Space (FFS)-MIL method, utilizing Sub-Sub-centre Arcface loss and minimal number of patch labels, significantly enhances the classification accuracy of cytopathology WSIs for diagnosing urothelial carcinoma. By incorporating a pre-trained ResNet50 model and employing similarity scores as a weighting mechanism, our study shows the effectiveness of our method in improving diagnostic precision in diagnosing urothelial carcinoma with cytopathology WSIs.

E-PS-18E-Poster Session Head and Neck Pathology

E-PS-18-003

Clear cell renal carcinoma's initial metastasis to the oral cavity

V. Almeida*, J. Lourenço, L. Carvalho
*Institute of Anatomical and Molecular Pathology, Faculty of Medicine of the University of Coimbra, Coimbra, Portugal

Background & objectives: Clear cell renal (CCR) carcinoma seldom metastasizes to the head and neck, rendering oral cavity involvement highly uncommon. We present a 95-year-old male with CCR carcinoma metastasis to the alveolar ridge, his first metastatic manifestation, seven years post-diagnosis.

Methods: In overall good health, the patient, with a history of Meniere's disease, hypertension, and dyslipidemia, sought Stomatology consultation for a 3 cm ulcerated exophytic lesion in the oral cavity's second quadrant. Clinical assessment indicated a potential pyogenic granuloma.
Results: Surgical biopsy unveiled neoplastic infiltration characterized by compact nests and sheets of cells with clear cytoplasm, distinct membrane, and a network of arborizing vessels. Immunohistochemistry confirmed metastatic CCR, ruling out other clear cell carcinomas of the oral cavity. Following histopathological results, the patient's medical history revealed prior nephrectomy for CCR in 2015, staged pT2N0M0 at another hospital. Three months post-diagnosis, the lesion enlarged, and PET imaging indicated bone invasion, coinciding with the development of multiple pulmonary lesions. Palliative radiotherapy was proposed, yielding pain relief and lesion size reduction. The patient also receives palliative care in nephrology.
Conclusion: Metastatic RCC to the oral cavity presents a diagnostic challenge due to its rarity. Routine excision and histopathological examination of oral lesions, alongside clinical integration, are vital for case comprehension. Unfortunately, prognosis for metastatic renal cell carcinoma is typically poor, often signaling widespread disease upon oral cavity metastasis.

E-PS-18-004
Tonsillar synovial sarcoma: a rare presentation in head and neck region - case report
S. AlOmari*, M.M. Al-Sheyab, S.M. Al-Khatib
*Jordan University of Science and Technology, Jordan

Background & objectives: Synovial sarcoma commonly occurs in adolescents and young adults, predominately in extremities. However, its occurrence in the head and neck, particularly the tonsils, is exceptionally rare. We present a case of tonsillar synovial sarcoma, highlighting its diagnostic challenges and management.
Methods: A 33-year-old previously healthy male presented with globus sensation, dysphagia, odynophagia, and frequent choking. He underwent comprehensive clinical evaluation including detailed history-taking, physical examination, and fiberoptic laryngoscopy. Subsequently, histopathological assessment was performed following right tonsillectomy, involving gross examination and microscopic assessment of hematoxylin and eosin-stained slides. Immunohistochemistry and fluorescence in situ hybridization (FISH) were performed for additional characterization.
Results: Clinical examination revealed significant right-sided neck swelling. Fiberoptic laryngoscopy identified marked enlargement of the right tonsil with posterior extension. Subsequent right tonsillectomy was performed. Gross examination of excised specimens revealed multiple fragments of brown firm tissue with homogeneous, tan cut surfaces. Histopathological assessment demonstrated a biphasic tumour with gland-like spaces lined by atypical cells and spindle cell areas arranged in a fascicular pattern. Immunohistochemical analysis revealed positivity for Epithelial Membrane Antigen (EMA), Pancytokeratin and Cytokeratin 7 immunohistochemical markers in the epithelial component and for BCL-2 and CD99 in the spindle cell component. FISH analysis identified the characteristic SYT gene rearrangement confirming the diagnosis of synovial sarcoma.
Conclusion: Tonsillar synovial sarcoma represents a diagnostic challenge, requiring a high index of suspicion and comprehensive evaluation. With only twenty previously published cases documented in the literature, awareness of this rare presentation is crucial for prompt diagnosis and appropriate management. Treatment involves surgical resection with adjuvant therapies tailored to individual patient and tumour characteristics. Collaboration among multidisciplinary healthcare teams and ongoing research efforts are essential for optimizing diagnostic accuracy, treatment efficacy, and patient outcomes in this rare malignancy.

E-PS-18-005
MAML2 rearrangement in mucoepidermoid carcinoma of the salivary glands with oncocytic features
A. Ambrosini-Spaltro*, F. De Paola, C. Ravaioli, M. Costantini, P. Rinaldi, M.P. Foschini
*Pathology Unit, Morgani-Pierantoni Hospital, AUSL Romagna, Forlì, Italy

Background & objectives: MAML2 rearrangement is a marker of mucoepidermoid carcinoma and has recently been described in its morphological variants. Our aim was to describe MAML2 rearrangement in mucoepidermoid carcinoma of the salivary glands with oncocytic features.
Methods: Cases of mucoepidermoid carcinoma with oncocytic features were searched in the Archives of the Pathological Units of three different Hospitals. All cases were reviewed in a common platform: https://my.pathomation.com/share/collection/F3xpO93RPPy4bJNhqPkW .
MAML2 rearrangement was detected by FISH using the MAML2 dual color break apart probe (Zytovision, Germany). A case was considered rearranged when more than 12% of nuclei were positive.
Results: A total of 5 cases was collected. All diagnoses were confirmed as mucoepidermoid carcinomas with extensive oncocytic features (in more than 50% of the neoplastic cells). Patents were: 3 females, 2 males, with ages ranging from 48 to 81 years. Three cases were from major salivary glands (2 submandibular, 1 parotid), whereas two cases were from minor salivary glands (1 base of the tongue, 1 upper lip). FISH detected MAML2 rearrangement in 3/5 cases (60.0%), with the percentage of positive cells varying from 20% to 30% of neoplastic cells. Rearranged cases were N. 1, N. 3, and N. 4. Positive cells were found particularly in and around mucoid cells.
Conclusion: MAML2 rearrangement detected by FISH, when present, may represent a valid tool to support the diagnosis of mucoepidermoid carcinoma, even in cases with extensive oncocytic features. This may be particularly useful for small biopsies and/or cytological samples, to correctly define cases with diffuse oncocytic features.

E-PS-18-007
NTRK3-EML4 rearranged spindle cell tumour (diffusely infiltrating smooth muscle and soft tissues) of the oral cavity: a case report
G.G.M. Attanasio*, G. Broggi, L. Salvatorelli, G. Angelico, G. Tinnirello, G. Magro
*Italy

Background & objectives: This case report unveils the first NTRK3-EML4 rearranged spindle cell tumour discovered in the oral cavity, emphasizing the critical importance of identifying rare neoplasms in uncommon sites. It highlights the unique morphological characteristics that guide targeted therapeutic interventions.
Methods: A 54-year-old presented with a non-tender, firm growth in the maxillary left posterior gingiva. Diagnostic assessments included imaging and an excisional biopsy, followed by extensive histopathological, immunohistochemical, and molecular analysis. This comprehensive approach aimed to delineate the lesion's nature and its genetic underpinnings.
Results: Histological analysis revealed bland spindle cells arranged either randomly or in intersecting fascicles, interspersed with keloid-like collagen bands. Despite occasional nuclear pleomorphism, the mitotic rate was low, with no necrosis observed. Immunohistochemically, cells were positive for CD34, vimentin, and S-100, but negative for SOX-10 and melanocytic markers, aiding in the exclusion of melanoma and MPNST. The identification of a novel NTRK3 exon 14-EML4 exon 2 fusion via RNA sequencing established the diagnosis of an NTRK3-EML4-rearranged spindle cell tumour. This distinctive

molecular and immunohistochemical signature, combined with the infiltration pattern, characterizes its unique pathology. Post-surgical follow-up showed no recurrence or metastases after 48 months.
Conclusion: Unveiling an NTRK3-EML4 rearranged spindle cell tumour in an uncommon site such as the oral cavity underlines the imperative of a meticulous approach to the diagnostic process. By integrating clinical observations with detailed histological, immunohistochemical, and molecular analyses, this case contributes significantly to the spectrum of NTRK fusion-positive tumours. It underscores the potential for precision medicine in identifying and treating rare, aggressive neoplasms based on their unique pathological profiles.

E-PS-18-008
Expect the unexpected: uncommon head and neck sites harboring pulmonary carcinoma metastases
L. Banias*, A. Iacob, B. Bögözi, Z. Kovacs, T. Mezei, S. Gurzu
*Romania

Background & objectives: Metastases from lung cancer in unusual anatomical sites pose diagnostic challenges due to their rarity and diverse clinical presentations. We aimed to present two consecutive cases of metastatic pulmonary carcinomas in unexpected head and neck locations.
Methods: A 64-year-old female patient (case 1) and a 68-year-old male patient (case 2) were admitted to the Oral and Maxillofacial Surgery Department for a mandibular lesion which raised suspicion of osteoperiostitis/tumour (case 1), and a preauricular tumour of the parotid region (case 2). Biopsies were taken from both lesions and submitted for histopathological examination.
Results: Case 1: histopathological evaluation revealed large, cohesive, focally clear tumour cells that infiltrated the bone and surrounding soft tissues. They focally expressed CK7, NapsinA, and TTF1, and were negative for Estrogen-Receptor, Mammaglobin, CD10, RCC, CK5/6, CK20, suggestive of adenocarcinoma with most likely pulmonary origin. Case 2: microscopic analysis showed discohesive, small, atypical cells with reduced cytoplasm, hyperchromatic nuclei and high mitotic rate, infiltrating the parotid gland and adjacent soft tissues. These cells expressed CK-AE1/AE3, TTF1, CD56, Synaptophysin, and Chromogranin. A diagnosis of a small cell carcinoma metastasis, likely originating from the lung, was established. Imaging studies confirmed the pulmonary origin of the primary tumours in both cases.
Conclusion: Metastases from lung carcinomas should be considered in the differential diagnosis of unusual tumoural lesions, even in anatomical sites like the jawbone or parotid gland. Comprehensive histopathological evaluation is crucial for accurate diagnosis and optimal patient management, especially in cases with atypical clinical presentations. IHC determinations proved to be indispensable for highlighting the primary tumour location.

E-PS-18-009
Inhibition of platinum-induced BCL2 upregulation overcomes chemoresistance in head and neck squamous cell carcinoma through resensitisation to cell death
A. Becker*, F. Klauk, T. Freitag, D.F. Strüder, B. Schneider, A. Zimpfer, C. Maletzki
*Institute of Pathology, Rostock Medical Center, Germany

Background & objectives: The survival of head and neck squamous cell carcinoma (HNSCC) remains poor with high recurrence rates. Resistance to chemotherapy negatively affects response rates. The anti-apoptotic protein BCL2 has been implicated in apoptosis resistance and tumour cell invasion/migration.
Methods: BCL2 immunostatus was correlated with the response to chemoradiotherapy in a uniformly treated HNSCC cohort. The combination therapy of ABT-199, a BCL2 inhibitor, and cisplatin was evaluated in vitro using corresponding patient-derived cell lines. Colony formation and the mode of cell death were analysed in-depth.
Results: Patients with BCL2-positive tumours (17%) prior to treatment (either radiation, cisplatin monotherapy or both) had shorter overall and progression-free survival (log-rank; p=0.048) and a higher rate of tumour relapse (Fisher's exact test; p=0.0032). BCL2 inhibition alone had no effect on cell functions in our triple panel of cisplatin-sensitive cell lines. BCL2 inhibition enhanced cisplatin-induced effects. Rates of autophagy and cell death, including methuosis, were doubled, while epithelial-mesenchymal transformation was inhibited.
Conclusion: Selective inhibition of BCL2 is available and standard of care in other malignancies. In HNSCC, immunohistochemical assessment of BCL2 could help personalise therapy by identifying a subpopulation that can overcome chemoresistance, particularly in locally advanced HNSCC.

E-PS-18-010
Middle ear neuroendocrine tumour: a new case report and a review of the literature
K. Ben Lazreg*, A. Bellalah, A. Ben Mabrouk, S. Ben Hammouda, D. Beltaifa, A. Zakhama, M. Njima
*Fattouma Bourguiba University Hospital, Monastir, Tunisia

Background & objectives: Middle ear neuroendocrine tumours (MENET) is a rare neoplasm showing epithelial and neuroendocrine differentiation. This nomenclature included benign adenomatous neoplasm,adenoma, adenoma with neuroendocrine diferentiation, carcinoid tumours and neuroendocrine adenoma. Herein, we report a new case of this misleading diagnosis.
Methods: A 55-year-old man with no medical history, presented with a left ear discharge and left peripheral facial paralysis (PFP). He underwent computed tomography scans and an endoscopic exploratory tympanotomy.
Results: The computed tomography scans showed chronic cholesteatoma otitis. On the endoscopic exploratory tympanotomy, we discovered a polypoid lesion of the external auditory canal (EAC) originating from the tympanic cavity. Histological examination of the polypoid lesion showed a proliferation of solid sheets of small cells within an endocrine stroma. Tumour cells had monomorphic nuclei without mitosis. There was no necrosis or perineural invasion. Tumour cells were positive for neuroendocrine markers, AE1/3, and negative for CK7 and PS100. The proliferation index (Ki67) was less than 1%. A paraganglioma was ruled out and the diagnosis of grade1 MENET was retained.
Conclusion: The MENET is an epithelial neoplasm arising from the middle ear mucosa with prominent neuroendocrine features. It's thought that it originates from an undifferentiated pluripotent endodermal stem cell. Like our observation, it occurs in the fifth decade of life. The PFP is rarely seen as a result of neural compression. The MENET rarely extends to the EAC. The MENET can mimic a cholesteatoma, paraganglioma, acoustic neuroma, and meningioma. The histologic and immunohistochemical features help to distinguish it from other entities.

E-PS-18-011
A case report of an ameloblastic carcinoma
C. Benallal*, A. Jaifi, H. Rais
*Morocco

Background & objectives: This work aims to provide an overview of the histopathological characteristics of ameloblastic carcinoma in a 63-year-old patient.
Methods: This involves a 63-year-old patient with no significant medical history, who presented with an ulcerated and budding lesion in the retro-molar trigone extending to the palate, non-bleeding upon contact, associated with a non-inflammatory maxillary budding lesion. A facial CT scan was performed, revealing a tumoural process in the retro-molar trigone with bone lysis. The biopsy excision was performed.

Results: The specimen, weighing 2 grams and measuring 1.2-1.5 cm, displayed a beige coloration and firm consistency. The microscopic analysis revealed a normoacanthotic squamous epithelium with orthokeratotic lamellar keratosis and an invasive carcinomatous proliferation in lobules and solid masses. The tumour cells exhibited large, anisocaryotic nuclei, numerous abnormal mitoses, and moderately vacuolated cytoplasm. The reactive stroma demonstrated fibroinflammatory characteristics, along with the presence of vascular emboli and perineural sheathing. Immunohistochemical examination indicated diffuse cytoplasmic expression of CK19 and nuclear expression of P63, with no expression of CK5/6, thereby confirming the diagnosis of ameloblastic carcinoma.
Conclusion: Due to their rarity and potential for aggressive behaviour, accurate histopathological diagnosis of ameloblastic carcinoma is essential. Differential diagnosis should consider other odontogenic tumours, primary intraosseous squamous cell carcinoma, and metastatic malignant tumours.

E-PS-18-012
High grade non-intestinal type sinonasal adenocarcinoma with micropapillary pattern and Pan-Trk immunohistochemistry positivity
B. Binici*, L. Cinel
*Turkey

Background & objectives: Non-intestinal type sinonasal adenocarcinomas are rare neoplasms that include heterogeneous morphology and divided as subgroups;low and high grade.They are seen in sixth decade,high grade tumours are more common in male.They are located in the nasal cavity,ethmoid sinus and cause obstruction,bleeding,pain.
Methods: A 60-year-old male patient was admitted to the clinic with epistaxis for three months.On examination,vegetating mass was observed in posterior right nasal passage.It was learned that the patient had a biopsy diagnosed as sinonasal adenocarcinoma in the same localization in 2018 and received radiotherapy for recurrent mass in 2021.
Results: Current imaging revealed a 32x23 mm contrast enhancing expansile mass in the sphenoid sinus and ethmoid sinus. Biopsy revealed a papillary and micropapillary pattern,moderate to severe atypia,necrosis and stromal inflammation.Immunohistochemical examination shows Cytokeratin 20,CDX-2,SATB2,mammoglobin,DOG1,PAX-8 and GCDFP-15 were negative while p40 and p63 staining was observed only in the basal cells. Cytokeratin 7,S100,panTRK were diffuse positive.Ki-67 proliferation index was 40%.With these findings,the case was evaluated as high grade non-intestinal sinonasal adenocarcinoma.
Conclusion: Non intestinal sinonasal adenocarcinomas are rare,constitute 10-20% of sinonasal tract malignancies, high grade neoplasms have worse prognosis and distant metastasis in 30% of cases. There are only two high grade non intestinal sinonazal adenocarcinoma cases with PanTrk positivity in the English literature.Treatment options include complete surgical excision,radiotherapy, and targeted therapies in cases with mutations.Due to the positivity of panTRK immunohistochemistry,our case may be considered for targeted therapy.

E-PS-18-013
Salivary gland oncocytic cystadenomas, how should we name them? Two case reports and literature discussion
B. Binici*, L. Cinel
*Turkey

Background & objectives: Oncocytic papillary cystadenoma is a rare benign salivary gland neoplasm with a higher incidence in women, usually affecting elderly patient and mostly located in the parotid gland. It consists of well-circumscribed, cystic spaces lined with columnar-cuboidal oncocytic cells and intraluminal papillary proliferation.
Methods: Two cases are presented to draw attention to rarity and different nomenclatures used in the literature.56-year-old male patient presented with a six-year history of swelling in the neck. He stated that the mass had been enlarged and painful for last 3 months. The other patient,85-year-old woman presented with a swelling of her neck for 1.5 months. For both cases surgical excision was performed.
Results: In the first case 3x2.5x1.5 cm multicystic lesion was observed. In the second case 4.5x2.5x2.5 cm, multicystic but well circumscribed lesion was observed. Microscopic examination for both cases cystic spaces lined by columnar to cuboidal oncocytic cells, cystic cavities surrounded by a fibrous capsule, containing secretions in lumen and papillary formations was found. First case also had basal cell adenoma. While these lesions were scattered in the first case, they were well circumscribed in the second case. First case was diagnosed as multiple oncocytic cyst in 2019.Second case was diagnosed as papillary oncocytic cystadenoma in 2024.The first case was not followed up in our hospital for 5 years, in the second case, routine follow-up was recommended by the clinic after diagnosis.
Conclusion: Cystadenoma which develops from the ductal cells, was previously classified as a subtype of monomorphic adenomas, but now classified as a single entity and has two subtypes:papillary and mucous. It has also been diagnosed as"cystic duct adenoma, Warthin tumour without lymphoid stroma, intraductal papillary hyperplasia, oncocytic cystadenoma". Recurrence is rare after complete surgical excision and infrequently show malignant transformation. Today,it is described under the title of oncocytic papillary cystadenoma in WHO blue book of head and neck tumours. The differential diagnosis includes intraductal papilloma, Warthin tumour, oncocytoma, sclerosing polycystic adenoma.

E-PS-18-014
Adamantinoma-like Ewing sarcoma of the nasal cavity: a challenging diagnosis
L. Bouzidi*, M. Mellouli, F. Kolsi, S. Makni, M. Meddeb, S. charfi, T. Sellami Boudawara
*Department of Pathology, Habib Bourguiba University Hospital, Sfax, Tunisia

Background & objectives: The Ewing sarcoma family of tumours (EFT) of the head and neck are rare and may be difficult to diagnose as they display significant histologic overlap with other more common undifferentiated small blue round cell malignancies.
Methods: We report a case of sinonasal adamantinoma-like EFT with complex epithelial diferentiation with particular focus on diferential diagnosis and tumour classifcation.
Results: The patient was a 46-year-old male who presented with epistaxis and seizures. MRI of the facial area showed a nasal tumour with intracranial extension. A biopsy of the nasal mass was performed. Histological fndings revealed a round blue cell tumour infltrating in solid sheets and lobules embedded in a fbrous stroma. Focal areas showed pseudopapillary pattern indicating epithelial diferentiation. The neoplastic cells were hyperchromatic and demonstrate brisk mitotic activity. On immunohistochemistry analysis, tumour cells were positive for CD99, pan-cytokeratin, p40 and NKX2.2. The tumour was negative for myogenin, MyoD1 and chromogranin. The diagnosis of adamantinoma-like EFT was made and confirmed by FISH assays that showed EWSR1 and FLI1 rearrangements.
Conclusion: Our case reinforce that a subset of head and neck EFT may show epithelial diferentiation with strong cytokeratin and p40 expression, and thus indistinguishable from more common true epithelial neoplasms. Thus, CD99 should be included in the immunopanel of a round cell malignancy in the nasal cavity regardless of epithelial diferentiation or cytokeratin and p40 expression, and a strong and diffuse CD99 positivity should prompt molecular testing for the presence of EWSR1 gene rearrangements.

E-PS-18-015

Clinico-pathological characteristics and molecular profiling of sinonasal inverted papillomas: a 5-year period institutional retrospective case series

M. Bronte Anaut*, S. Fernández Solé, A. Moreno Ibérico, S. Saez Álvarez, J. Arredondo Montero
*Hospital General Rio Carrion, Spain

Background & objectives: Sinonasal Inverted papillomas (SIP) are benign, locally aggressive neoplasms with a risk of malignant degeneration (7%–15%). Different subsets have been identified based on genetic data. We aimed to analyse the correlation between SIP molecular alterations and various clinical variables.
Methods: Clinical data and histological slides from 31 patients diagnosed with SIP were reviewed. For the identification of HPV strains amplified products were hybridized with the CLART® HPV Kit. In other cases, HPV DNA was hybridized with the captures on the 1.0 chip. For the detection of EGFR and KRAS mutations DNA was analysed with COBAS Z4800 KRASMT and Idylla MT.
Results: Four women and 27 men (87.1%) were identified, with a mean age of 57.8±12.2 years. 16 patients (including all women) presented single SIP (55.2%). Eighteen patients had right SIP (58.1%) and 1 patient had bilateral SIP (3.2%). Seven patients (22.6%) presented at least one recurrence. Two of them (6.5%) presented mild atypia. Regarding the genetic study, 6 (21.4%) presented EGFR mutation, HPV was documented in 4 (16%), and 2 (7.1%) presented KRAS mutation. Patients with multiple SIPs were significantly younger than patients with single SIPs (53.4±13.5 vs 62.6±8.7)(p=0.01). Although the analysis did not reach statistical significance, a lower mean age was observed in EGFR+ patients (53.3±6.9 vs. 59.1±11, p=0.13).
Conclusion: The present series demonstrates the presence of EGFR and KRAS mutations and documents the presence of HPV strains in several patients with SIP, alterations associated with squamous carcinomas of the nasal cavity (CNC). However, the low prevalence of the documented alterations in the present series prevents the establishment of a solid causality between these alterations and the development of SIP. New prospective series with larger sample sizes are needed to better understand the clinicopathological implications of the underlying molecular alterations.

E-PS-18-016

Extracutaneous Merkel cell carcinoma: two case reports

K. Bulut*, S. Erkılıç
*Department of Pathology, Medical Faculty, Gaziantep University, Gaziantep, Turkey

Background & objectives: Merkel cell carcinoma (MCC) is a neoplasm with neuroendocrine differentiation most commonly found in sun-exposed areas of the skin. Here we present two cases of primary Merkel cell carcinoma of parotid and mucosa, which are rare sites of presentation.
Methods: Our first case was a 75-year-old woman who presented to our hospital with a mass in the right parotid gland. Fine needle aspiration cytology was initially performed. The diagnosis was reported as a neuroendocrine tumour and the parotid gland was excised. The second case was a 59-year-old woman with a mass in the nasal cavity.
Results: In the first case, the tumour in the parotidectomy specimen appeared 2 cm in diameter, yellowish-white, irregularly circumscribed and with nodular expansion. Microscopically, the tumour consisted of small mononuclear cells, arranged in sheets. The tumour cells were round to polygonal in shape with hyperchromatic nuclei and a scant cytoplasm. Immunohistochemically, these cells were dot-like positive for pancytoceratin and CK20, positive for synaptophysin and chromogranin. In the second case, the specimen was fragmented. Microscopically, there were monotonous basophilic cell nests in the submucosa with marked necrosis. These cells had nuclei with dense, finely granular salt-and-pepper chromatin and sparse rim of eosinophilic cytoplasm. The immunohistochemical profile was similar to the first case.
Conclusion: Both cases were reported as extracutaneous Merkel cell carcinoma. Since there were no skin lesions that could be primary, both cases were accepted as primary. Extracutaneous MCC is a rare neuroendocrine neoplasm that occurs in the mucous membranes and salivary glands of the head and neck. It has an aggressive behaviour and is associated with a high risk of local recurrence and metastasis. It should be considered in the differential diagnosis of mucosal lesions in this area.

E-PS-18-017

MDM2 amplification in HMGA2 altered pleomorphic adenoma: a basis for malignant transformation?

K. Burghout*, G. Breimer, S. Koppes, H.M. Hazelbag, M. Ooft, M. Raicu, A. Cleton-Jansen, T. van Wezel, R. van Eijk, D. Terlouw, S. van Egmond, N. Rupp, D. Cohen
*Department of Pathology, Leiden University Medical Center, Leiden, The Netherlands

Background & objectives: We present an index case, highlighting a locally recurring in situ carcinoma ex pleomorphic adenoma with a *HMGA2::WIF1* fusion and *MDM2* amplification. The primary aim of this study is a case series analysis of *MDM2* analysed *HMGA2* altered PA.
Methods: A comprehensive literature review was performed on the current knowledge of *HGMA2* and *MDM2* amplifications in PA and CXPA. *HMGA2* altered cases were collected from literature and added to our case series analysis.
Results: In 31 *HMGA2* altered neoplasms, *MDM2* amplifications were found in 31% of the PA and 73% of the CXPA (P = 0.04), highlighting a substantial increase in *MDM2* amplifications in malignant lesions. Cases with *MDM2* amplification often showed a more cellular morphology and more prominent cytonuclear atypia.
Conclusion: In *HMGA2* altered salivary gland lesions there is a significant increase in *MDM2* amplification in CXPA compared to PA, implicating a risk of malignant transformation in *HMGA2* altered PA with *MDM2* amplification. Larger prospective studies with long term follow-up are necessary to further establish the consequences of *MDM2*, and potentially other gene amplifications (e.g. *CDK4*), to guide clinical strategies to a tailored treatment for this patient population.

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E-PS-18-019

Immunohistochemical analysis of R-loop burden in a cohort of Oropharyngeal Squamous Cell Carcinomas (OPSCC) with a poor prognosis

H. Crane*, K. Hunter, S. El-Khamisy
*University of Sheffield, United Kingdom

Background & objectives: OPSCC has two clinical subtypes: HPV-associated and HPV-independent, and if tumour recurrence occurs it can be difficult to treat clinically. R-loops are three-stranded DNA:RNA hybrids which can be a source of genomic instability, however their expression in OPSCC is unknown.
Methods: To assess R-loop burden across a cohort of OPSCC with a poor prognosis (n=17), immunohistochemistry was undertaken using an antibody which detects DNA:RNA hybrids, known as S9.6. The specificity of this technique was confirmed by pre-treatment with RNAse H. Following S9.6 immunohistochemistry, a representative area of each slide was analysed in QuPath to provide an S9.6 H-score for each case.

Results: DNA in-situ hybridisation was carried out on each case to confirm HPV status, which revealed 10 tumours were HPV-associated and 7 were HPV-independent. Comparison of S9.6 tumour H-score across the cases revealed that HPV+ tumours had a higher S9.6 H-score (p=0.0154). However, there were no significant differences in S9.6 H-score between gender, T-Stage, N-Stage, smoking status or alcohol consumption. The cohort was comprised of primary tumours, soft tissue metastases and bone metastases and analysis showed that there was significantly higher S9.6 expression in the bone metastases when compared to primary tumours (p=0.0425) and primary/soft tissue metastases (p=0.0077).
Conclusion: In this cohort, we observed a higher S9.6 expression in the tumours which had metastasised to bone compared to primary tumours or soft tissue metastases. However, the limitations of this study are the relatively small and retrospective cohort, therefore confirmation of these findings on a larger cohort, including paired samples, would be valuable. These findings warrant further investigation to determine if the high level of R-loops in bone metastases may represent a potential therapeutic target.

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E-PS-18-020
Kaposi sarcoma of the parotid gland: a rare presentation
Y. Dhouibi*, I. Chelly, A. Zehani, A. Ayari, A. Khadhar, K. Bellil, S. Haouet
*Department of Pathology, Rabta University Hospital, Tunisia

Background & objectives: Kaposi sarcoma (KS) is a vascular neoplasm associated with human herpes virus 8 (HHV8). It typically manifests as cutaneous lesion in immunocompetent individuals. However, primary involvement of the parotid gland is exceedingly rare, with about 10 cases reported in the literature.
Methods: Herein, we present a case of a classic KS localized to the parotid gland, highlighting its unusual presentation and diagnostic challenges.
Results: We report a 52-year-old male patient with a history of ischemic stroke resulting in right hemiparesis.He presented , six months ago, a left preauricular swelling, progressively enlarging. Ultrasound revealed a 25mm superficiel parotid left mass. MRI indicated parotid lesion with significant enhancement after gadolinium injection, suggestive of a primary salivary gland neoplasm. Left exofacial parotidectomy was performed. Pathological examination revealed nodular and diffuse spindle cell tumour proliferation with elongated cells, hyperchromatic nuclei, eosinophilic cytoplasm, cytonuclear atypia, and mitoses. Hemorrhage was noted between tumour cell bundles. Immunohistochemical study using HHV8 showed diffuse nuclear positivity in tumour cells with this antibody.
Conclusion: Primary KS involvement of the parotid gland is exceptionally rare and poses diagnostic challenges due to its unusual presentation. This case underscores the importance of considering KS in the differential diagnosis of parotid masses, particularly in immunocompetent individuals.

E-PS-18-021
Malignant thyroid teratoma: clinical and pathological insights
Y. Dhouibi*, S. Kamoun, Y. Houcine, M. Driss
*Department of Pathology, Rabta University Hospital, Tunisia

Background & objectives: Thyroid teratomas are rare neoplasms. They are composed of mature or immature tissue derived from all three germ cell layers. Graded by neuroectodermal tissue presence, they're classified as benign, immature, or malignant. Less than 40 malignant teratoma cases were reported.
Methods: In this paper, we reported a 17-year-old female patient diagnosed with malignant thyroid teratoma in salah azaiez institution.
Results: A 17-year-old female with Xeroderma Pigmentosum presented at Salah Azaiez hospital with a thyroid goiter, exhibiting a 5cm left paramedian anterior basicervical swelling. Ultrasound revealed a multinodular goiter classified as EU TIRADS 3, with benign fine needle aspiration. Total thyroidectomy uncovered a tumour proliferation in the left lobe, comprising rhabdomyoblastic, immature neuroepithelial, and malpighian epithelial elements within a myxoid stroma. Tumour cells displayed marked atypia with 13/2 mm2 mitoses and thrombi in adjacent vessels. Immunohistochemistry indicated pancytokeratin positivity in epithelial and chromogranin/synaptophysin positivity in neuroblastic components. Immature neuroepithelial infiltration was found in removed cervical lymph nodes. Adjuvant chemotherapy successfully treated the disease, with no recurrence at the 6-month follow-up.
Conclusion: Malignant teratoma of the thyroid is a rare and challenging diagnosis that requires a multidisciplinary approach for optimal management.

E-PS-18-022
Middle ear Neuroendocrine Tumours (MeNET): our single-centre experience with this infrequent and unpredictable pathology over the last 35 years
G. Escuer-Albero*, E.P. Sánchez López, S. Quinones, E. Ruiz-Bravo
*La Paz University Hospital, Spain

Background & objectives: The term "Middle ear NeuroEndocrine Tumour" (MeNET) has been proposed to describe neuroendocrine neoplasms of the middle ear, a rare cause of tumour pathology with a poorly defined grading system and unpredictable prognosis. We describe and reclassify three cases.
Methods: A retrospective analysis was performed of neuroendocrine neoplasms with biopsy in our centre over the last 35 years. Immunohistochemical techniques were used to confirm neuroendocrine differentiation and for grading (ki67) according to the updated proposed WHO 22 grading system. In terms of clinical follow-up, we reviewed the patients' electronic medical records.
Results: The three cases of MeNETs diagnosed in our centre since 1985 showed similar histological features: a trabecular-glandular pattern composed of cuboidal to columnar cells with oval nuclei and "salt and pepper" nuclear chromatin positive for synaptophysin, chromogranin-A and focally for pancytokeratins.
At diagnostic biopsy, two cases were reclassified as Well-differentiated Neuroendocrine Tumours, Grade 1 (NET G1), and the other one was reclassified as Grade 2.
The two recurrent cases with clinical follow-up, NET G1 and NET G2 initially, were located in the surgical bed and in the brain, respectively, and also presented with initial extension beyond the middle ear and incomplete resection.
Conclusion: Although most MeNETs are classified as indolent, the important recurrence rate (25%) and the lack of a well-established grading system make difficult to assess the prognosis. We suggest that there is a strong correlation between the recurrence extension and complete surgical removal.

Given the diverse range of histological grades showed in our recurrence cases (NET G1 and G2), we emphasize the need for additional research with larger simple sizes to better elucidate any correlation.

E-PS-18-023
Expression of p16INK4a, FLOT2, and EGFR in laryngeal carcinoma, prognostic significance and correlation with clinicopathological characteristics
R. Gajanin*, D. Djokanovic, O. Jovic Djokanovic, V. Gajanin, I. Sladojevic, Z. Gojković, Z. Gajanin

*University of Banja Luka, Faculty of Medicine, Republic of Srpska, Bosnia and Herzegovina; University clinical centre Republic of Srpska, Republic of Srpska, Bosnia and Herzegovina

Background & objectives: Various factors can affect the survival of patients with laryngeal cancer. We assessed the expression of protein p16INK4a, Flotillin2 (FLOT2) and epidermal growth factor receptor (EGFR), and prognostic value of other clinicopathological features for this type of cancer.
Methods: We collected patient data on demographics, clinicopathological characteristics, treatment patterns, and outcomes. Histologically and by immunochemistry staining we determined the expression of prognostic factors and molecular biomarkers. The primary endpoints were overall survival (OS), disease-specific survival (DSS), and disease-free survival (DFS). The survival was assessed using the Kaplan–Meier method and Cox regression model analyses of potential prognostic parameters.
Results: After a median follow-up of 78 months, the median OS was 75 months, with an event recorded in 51.9% of patients. Median DFS was 68 months, 23 patients (29.9%) had disease relapse. The DSS survival rate was 71.6% with a median survival not reached. Out of the previously mentioned molecular biomarkers, only EGFR impacted OS with statistical significance (p=0.034). Recurrence and the supraglottic sublocation of laryngeal carcinoma were identified as independent prognostic factors for DSS. Supraglottic sublocation, recurrence, smoking, and treatment modality were independent prognostic factors for DFS.
Conclusion: This research is a comprehensive analysis of the clinicopathological characteristics of these patients, which is additionally combined with knowledge about the biomarker expression of p16INK4a, FLOT2, and EGFR. Based on these results, we get a larger picture of this cancer and based on that we create plans for adequate treatment of these patients and improve survival.

E-PS-18-024
Laryngeal atypical lipomatous tumour: a case report of a rare entity
I. Gorostiaga*, A.M. Cordovilla-Moreno, A. Onaindia, L. Pagalday Gaztañaga, A. Viana-Cora, S. Fernández Solé
*Pathology Department, Osakidetza, Araba University Hospital, Spain

Background & objectives: Liposarcoma is an adipose cell originated malignancy, rarely found in the head and neck (2-9%). Atypical lipomatous tumour / well-differentiated liposarcoma (ALT/WDLPS) is the most common subtype. We present the case of a 81 year-old male with pharyngeal discomfort.
Methods: CT scan showed a solid mass located in the left aryepiglottic fold that occluded the pyriform sinus and imprinted the laryngeal base of the epiglotis and posterior pharyngeal wall. It measured 26 x 26 x 16 mm. Partial resection of the lesion was performed and a polypoid mass of 4,5 x 4 cm was sent to our pathology department.
Results: Grossly, the tumour was a solid yellow to grey-white coloured and lobulated mass covered by intact mucosa on cut surface. Microscopically, a biphasic mesenchymal neoplasm comprised of intermingled fibroblastic and lipomatous components was observed. Adipocytes showed variable size and hypercromatic enlarged nuclei, and rare lipoblasts were identified. Irregular fibrous septa entrapped the adipocytic component and showed atypical stromal cells, some of which were multinucleated. Immunohistochemistry (IHC) tests showed positivity for CD34 in the stromal cells and scattered mastocytes were evinced with CD117. Fluorescence in situ hybridization (FISH) for MDM2 was performed and amplification of the gen was observed. Finally, a diagnosis of ALT was rendered.
Conclusion: Most liposarcomas of the head and neck are commonly low-grade and harbour better survival rates than liposarcomas from other sites. ALT/WDLPS of head and neck represent a locally aggressive tumour, surgical resection with widely negative margins is generally curative and staging is not required as it not clinically relevant in this subtype. Lastly, spindle cell or pleomorphic lipoma should be ruled out in the differential diagnosis by searching for MDM2 amplification by IHC or FISH.

E-PS-18-025
Expanding the spectrum of low-grade sinonasal adenocarcinoma with biphasic seromucinous differentiation and activating HRAS/AKT1 mutations
V.S. Hadnagy*, M. Körner, M. Rössle, P. Dubach, G. Pabst, A. Kutolova, S. Weder, R. Seifert, E.J. Rushing, D. Holzmann, M. Hüllner, S.N. Freiberger, N. Rupp
*Department of Pathology and Molecular Pathology, University Hospital Zurich / Faculty of Medicine, University of Zurich, Switzerland

Background & objectives: Low-grade non-intestinal-type sinonasal adenocarcinoma (LGSNAC) is a rare heterogeneous and poorly characterized group of tumours, distinct from intestinal-type and salivary-type neoplasms. Therefore, further characterization is needed for better biological understanding and classification.
Methods: Clinical, histological and molecular characterization of four cases of biphasic, low-grade adenocarcinomas of the sinonasal tract was performed. All patients were male, between 48 and 78 years, who presented with polypoid masses in the nasal cavity.
Results: Microscopically, virtually all tumours were dominated by tubulo-glandular biphasic patterns, microcystic, focal (micro)papillary, oncocytic or basaloid features. Immunohistochemical staining confirmed biphasic differentiation with an outer layer of myoepithelial cells. Molecular profiling revealed HRAS (p.G13R, p.Q61R) mutations, and concomitant AKT1 (p.E17K, p.Q79R) mutations in two cases. Two cases showed potential in situ / precursor lesions adjacent to the tumour. Follow-up periods ranged from 1 – 30 months, with one case relapsing locally after > 20 years.
Conclusion: This study further corroborates a distinct biphasic neoplasm within the group of LGSNAC. Although morphological and molecular features overlap with salivary gland epithelial-myoepithelial carcinoma, several arguments favour a distinct tumour entity originating from local seromucinous glands, i.e., a sinonasal biphasic seromucinous adenocarcinoma.

E-PS-18-027
Mucinous cystadenoma: rare entity presenting as oral cavity lesion
S. Jakkulwar*, A. Bashir, N. Gangane, N. Oza
*Histopia Lab, India

Background & objectives: Cystadenoma is a benign entity that originates in the minor salivary glands as a cystic growth with papillary projections into lumen without lymphoid element. It is classified into two variants by WHO as the papillary and mucinous forms of cystadenoma.
Methods: We report a case of a 80-year-old male patient with an incidentally detected buccal mucosal lesion, gradually increasing in size. The patient was subjected to excision and was diagnosed as mucinous cystadenoma.
Results: An 80-year-old male presented with buccal mucosal swelling which on palpation was very soft and non-tender. USG revealed well-defined oval hypoechoic lesions in the subcutaneous layer measuring 1.2 cm in the right cheek. Histological examination reveals non keratinizing stratified squamous epithelium with underlying stroma showing well circumscribed lesion comprising of multiple varying sized cysts lined by 1-3 cell layer thick mucinous columnar epithelium with uniform basally placed nuclei, pale cytoplasm, interspersed in a fibrous connective tissue stroma. Intraluminal mucinous secretion noted. No significant nuclear atypia seen. By immunohistochemistry, the basal cells are highlighted by p63. Immunostain for CDX2 is negative. On follow up, patient is disease free and doing well.

Conclusion: Most cases of cystadenomas, including our case, are treated by simple surgical excision. Regular follow-up of the patient is necessary for early identification of recurrence, which may occur due to incomplete excision. High index of suspicion is necessary.

E-PS-18-028

Salivary gland carcinosarcoma arising in the palate from an adenoid cystic carcinoma: case report

J. Jiménez Almonacid*, A.B. Enguita Valls, L. Iglesias Docampo
*Hospital Universitario 12 de Octubre, Madrid, Spain

Background & objectives: Salivary gland carcinosarcoma is an aggressive and rare neoplasm that arises de novo or, in most cases, from a pleomorphic adenoma. The most frequently described sarcomatous component is chondrosarcoma.
Methods: We present the case of a 64-year-old man with a large tumour mass on the palate that on facial CT occupied a large part of the maxillary sinus and nasal fossa with lytic characteristics and calcified bone matrix.
Results: In the histopathological study, a tumour lesion of 9 cm was observed with areas of adenoid cystic carcinoma with a tubular (less than 5%) and solid pattern, along with areas of high-grade adenocarcinoma NOS and other areas with a mixed component with tumour epithelial nests on a stroma of atypical cells with osteoblastic features on an osteoid matrix. These latter cells were positive with vimentin and SATB2 and negative with cytokeratin AE1-AE3. Irregular bone trabeculae were observed. The patient presented lymph node and bone metastases of the epithelial component that was formed by adenoid cystic carcinoma and adenocarcinoma NOS. The immunohistochemical study of MYB showed positivity in these areas.
Conclusion: We present the first case of carcinosarcoma originating from an adenoid cystic carcinoma with a heterologous component of osteosarcoma. These tumours present great morphological and molecular heterogeneity with a very poor prognosis.

E-PS-18-029

Sinonasal teratocarcinosarcoma - a single institution experience from South India

E. Joy*, A. Mathews, J. K, T. Somanathan, A. K R, I. S Nair, R. Kumar R
*Regional Cancer Centre, Thiruvananthapuram, India

Background & objectives: Sinonasal teratocarcinosarcoma (SNTCS) is an aggressive malignant sinonasal neoplasm with fewer than 150 documented cases globally, and less than 35 cases reported from India. Our aim was to review the clinicopathological features which help in diagnosing this challenging entity.
Methods: This retrospective study conducted in our department included 9 consecutive cases of SNTCS reported between 1 st January 2008 to 31 st December 2023 (16 years). Slides were retrieved from the archives and case files were collected from the medical records. The histopathologic features were reviewed, and clinical details including follow-up details were updated as of February 2024.
Results: The mean patient age was 38 years (range 15 to 65) with M:F ratio of 8:1. All patients presented with nasal obstruction and epistaxis (average duration- 6.3 months). Nasal cavity and sinuses were the involved sites. Tumours showed an admixture of epithelial, mesenchymal, and neuroepithelial elements except in one case which showed only neuroepithelial elements initially and was reported as olfactory neuroblastoma, subsequent cervical lymph node biopsy showed other components. Treatment included surgery, radiotherapy, or chemotherapy depending on stage. Four patients had recurrent disease, and one of them succumbed to the disease. Out of eight patients, six are alive by the end of follow-up, two patients were lost to follow-up.
Conclusion: SNTCS remains a rare and aggressive malignancy, often presenting diagnostic challenges due to its complex histological features, especially with limited biopsy material. Sometimes all three components are not present and according to the predominant component, either olfactory neuroblastoma or carcinoma can be differentials like in one of our challenging cases. Overlapping immunoprofile with close differentials adds to the diagnostic difficulty. Despite the aggressive nature of SNTCS, cases of prolonged survival underscore the significance of accurate diagnosis.

E-PS-18-030

Nodular fasciitis in the buccal region - perspectives on definitive diagnosis using cytological samples

T. Kawasaki*, K. Kanemoto, S. Kanno, K. Kuba, R. Sato, M. Katoh, T. Yamazaki, M. Nakahira, Y. Ebihara, M. Hirasaki, T. Torigoe, Y. Yazawa, T. Muramatsu, T. Tashima, J. Ichikawa
*Saitama Medical University, Japan

Background & objectives: Nodular fasciitis is a benign mesenchymal neoplasm consisting of fibroblastic/myofibroblastic proliferation, but it is difficult to differentiate this lesion from cancers. We first report a buccal nodular fasciitis in which the USP6 gene rearrangement was detected in a cytologic specimen.
Methods: The patient was a 37-year-old premenopausal Japanese woman who visited our department for detailed examination of a malar mass that had been growing for about a year. The tumour was suspected to have become adherent to the surrounding skin.
Results: On cytological examination, although cellularity was low, clusters of short-fusiform atypical cells with irregular nuclei were identified in the myxoid background. The diagnosis was spindle cell tumour (Papanicolaou classification: Class III). Since the possibility of a malignancy was also considered, tumourectomy was performed for both definitive diagnosis and treatment. The cut surface of the excised specimen contained a glossy, grey-whitish to tan tumour, measuring 26x21x17 mm, with relatively well-defined margins. Histologically, plump and/or immature spindle-shaped cells proliferated in fascicles, accompanied by feathery tissue culture-like areas with extravasated erythrocytes and lymphocytic infiltration. FISH verified rearrangement of the USP6 gene. Based on these pathological findings, we diagnosed this lesion as nodular fasciitis.
Conclusion: Nodular fasciitis should be included in the differential diagnosis of a mass lesion showing enlargement in the head and neck region. In this case, subsequently, the split signals of the USP6 were also demonstrated in the cytologic specimens, creating the potential for making a definitive diagnosis at this stage.

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E-PS-18-031

Epistaxis as a first symptom of metastatic breast carcinoma

D. Koumoundourou*, P. Bosgana, S. Lygeros
*Department of Pathology, University hospital of Patras, Rio, Greece

Background & objectives: A 70-year-old woman was referred to our clinic due to unilateral left nasal blockage accompanied by proptosis, pain, blurred vision and eyelid edema of the left eye (LE). She also complained of headache, weakness and reported an episode of epistaxis.
Methods: Nasal endoscopy revealed a fleshy mass at the area of middle meatus in the left nostril, blocking the drainage of the ethmoids, maxillary and frontal sinus. Sinus CT scan and MRI showed a

heterogeneous, well-defined mass in the ethmoid cells of the left nasal cavity, invading the retrobulbar orbital fat and extraconal space near the frontoethmoidal suture.
Results: The patient underwent an endoscopic biopsy of the mass under general anesthesia. In the pathology lab we received multiple red-coloured tissue specimen with a soft consistency. Microscopically a malignant tumour was recognized consisiting of neoplastic cells with hyperchromatic nuclei and a small amount of eosinophilic cytoplasm with no glandurar or squamous differentiation. Differential diagnosis included nasopharyngeal, basaloid and sinonasal carcinoma as well as nut and neuroendocrine carcinoma. Immunohistochemically the tumour cells expressed AE3, CK8/18 Gata3, p63, E-Cadherin+++ ER and PR and were negative for 34BE12, p40, CD56 andCK7. Because of ER and PR positivity a breast carcinoma was suspected. The patient's mammography revealed an ill-defined mass of the left breast.
Conclusion: We must always have in mind that breast cancer can mimick many other neoplasms.Breast carcinomas tend to metastasize in many different sites as well as in the central nervous system including leptomeninges and eyes. In this case, epistaxis was the first sign of this unusual breast cancer presentation. The clinical suspicion existed because of the fact that the patient had also axial proptosis and a temporal and downward displacement of the left globe.

E-PS-18-032
Genetic profiling of HPV-associated and –independent head and neck squamous cell carcinomas by conventional NGS and liquid biopsy
J. Laine*, P. Pakkanen, A. Silvoniemi, J. Hagström, M. Tamminen, K. Aro, L. Bäck, L. Aaltonen, H. Irjala
*Turku University Hospital, Department of Pathology, Finland

Background & objectives: The aim of the study was to assess the utility of liquid biopsy (LB) in the genomic profiling of squamous cell carcinoma of the head and neck area.
Methods: Thirty-four patients with head and neck squamous cell carcinoma were enrolled in this prospective study. The genetic profiles of the tumour and cell-free DNA by LB with two independent methods were performed. HPV status by p16 immunohistochemistry and HPV in situ hybridization were obtained at the time of diagnosis.
Results: The mutations in the TP53 gene were the most common in the tumours (22/31) and in LBs (17/29). The mutations of TP53 were more common in the p16 negative (HPV-independent) than in p16-positive (HPV-associated) cases (21 vs 4).The mutations in the genes CDKN2A and MLL2 were also more common in HPV-I cases. PIK3CA-mutations were as common in both groups. There were 6.5 mutations in average in the tumours (total number 202) and 3.38 mutations in the LBs (total 98). The number of mutations that were present both in tumours and in LBs were 54.
Conclusion: The differences observed in genomic profiling between tumour tissue and liquid biopsies could be explained mainly because the amplifications and losses could not be detected in the LBs. Other differences and the possible rationale of the phenomenon are discussed in this paper further on. The liquid biopsy is relatively easy to obtain and gives a valuable information of the mutation status of head and neck tumours, but the limitations, especially in the amplification status should be taken into consideration.

E-PS-18-034
TIM-3- and TIGIT-expressing tumour infiltrating lymphocytes predict poor outcome in sinonasal mucosal melanoma
S. Ledderose*, F. Klauschen, C. Ledderose, A. Sendelhofert, G. Ledderose
*Institute of Pathology, Faculty of Medicine, LMU Munich, Germany

Background & objectives: Sinonasal mucosal melanoma (SNMM) has a poor prognosis. Treatment with common immune checkpoint inhibitors (ICIs) has shown limited efficacy. The co-inhibitory receptors TIM-3, LAG-3 and TIGIT may represent new therapeutic options. Expression data of these ICI-targets in SNMM are lacking.
Methods: Immunohistochemical staining for TIM-3, LAG-3 and TIGIT was performed on tumour tissue samples from 27 patients with primary SNMM. The grade of infiltration with immunoreactive tumour-infiltrating lymphocytes (TILs) was determined semi-quantitatively. Associations between high and low immunoreactive TIL-grade and AJCC tumour stage, overall survival (OS) and progression free survival (PFS) were retrospectively analysed.
Results: High-grade infiltration with LAG-3+, TIM-3+, or TIGIT+ TILs was observed in 4 (14.8%), 14 (51.9%), and 17 (63.0%) tumours, respectively. No significant associations were found between age or gender and the expression patterns of co-inhibitory receptors ($p>0.05$). High infiltration with TIM-3+ or TIGIT+ TILs was more likely among tumours categorized as T4 stage ($p=0.033$ and $p=0.046$, respectively). Low infiltration with TIM-3+ TILs was significantly linked to OS of 5 years or more (OR=20.8, CI 95% 2.0 – 211.8, $p=0.004$) and significantly improved 5-year OS rates were observed for tumours with low numbers of TIGIT+ TILs (OR=17.5, CI 95% 2.4 - 129.5, $p=0.004$).
Conclusion: Our results indicate that high densities of TIM-3+ and TIGIT+ TILs are robust negative prognostic biomarkers for survival in SNMM as they are significantly associated with shorter OS and advanced tumour stages. Our results provide a rationale for innovative co-inhibitory receptor-based ICI treatment strategies in this rare malignancy. Prospective studies with larger case numbers are warranted to confirm our findings.

E-PS-18-035
Periglandular halos in salivary gland adenoid cystic carcinoma: a potential histomorphological criteria for the diagnosis
R. Limani*, Z. Limani, L. Kondirolli, E. Bajraktari, S. Reçica
*Albania

Background & objectives: Adenoid cystic carcinoma accounts for 7.5% of all salivary gland carcinomas being more frequent in minor salivary glands. Periglandular halos are a morphological feature seen in several epithelial carcinomas, such as prostate, breast, basal cell carcinoma, etc.
Methods: 30 tumours morphologically diagnosed as adenoid cystic carcinoma and the adjacent non-neoplastic salivary gland tissue were evaluated for the presence and the extent of periglandular halos. Periglandular halos were graded as a percentage of gland circumference separated from stroma in three groups: less than 50% of circumference and more than 50%, in less or more than 50% of examined glands.
Results: Our study confirms that periglandular halos are significantly more extensive in adenoid cystic carcinoma of the salivary gland than in the adjacent non-neoplastic salivary tissue ($p<0,001$). This confirms that periglandular halos are a histomorphological feature of malignancy in adenoid cystic carcinoma of the salivary gland tissue.
Conclusion: Periglandular halos in adenoid cystic carcinoma of the salivary gland could be a potential histomorphological criterion to support adenoid cystic carcinoma diagnosis. Utilizing this feature effectively may increase the diagnostic confidence in limited tissue samples, where classical features are not easily discernible.

E-PS-18-036
Sinonasal hamarthomas: a rare entity with a challenging diagnosis - how an accurate diagnosis impacts clinical and therapeutic management
L. López Vilaró*, A. Prat, D. Piñol, L. Catasús, S. Bagué Rosell, M. Casasayas, J.R. Gras Cabrerizo, J. Szafranska
*Department of Pathology. Hospital de la Santa Creu i de Sant Pau, Spain

Background & objectives: Sinonasal hamartomes (SNH) are benign lesions included in the 5TH edition of WHO classification of the head and neck tumours. Their diagnosis is mainly histological with few useful additional studies and with the treatment being exclusively surgical.
Methods: We reviewed clinicopathologic features of patients diagnosed of SNH between 2017 and 2023 (n=10). Additionally, we reviewed inflammatory polyps (IP) diagnosed in our institution since 2015 (n=97); we applied the diagnostic criteria of SNH and reclassified 2 IP accordingly.
Results: The study included 12 patients, 6 with REAH, 4 with SH, 1 with NCMH and 1 with inverted papilloma with SNH (IP with SNH). Out of 6 REAH, 5 patients were men, 57 years, all lesions were located in nasal cavity,3 in lamina cribosa and 2 in middle meatus, 3 were bilateral. Out of 4 SH, 3 patients were men, with a mean age of 72 years, all were in nasal cavity, 1 was bilateral. NCMH was a unilateral polypoid mass diagnosed in a 22years-old woman. PCR amplification shown tumoural DICER 1 mutation (NM_030621.4: c. 5125G>A p.(Asp.1709Asn). IP with SNH was observed in a 70years-old woman with unilateral polypoid lesion.
Conclusion: It is important to recognize REAH and SH due to their similarities with inverted papilloma and low grade sinonasal adenocarcinoma; all of them having further different medical and surgical treatments. In addition, NCMH is associated with germinal DICER1 mutation. It is now recommended that all patients with NCMH should be genetical tested because all germinal DICER1 mutation carriers have a predisposition for development of various tumours, most commonly pleuropulmonary blastoma, thyroid, kidney and ovary cancers.

E-PS-18-037
Gnathic chondroblastic osteosarcoma - our institutional experience
J. Yin, S. Amer, D. Zenezan, A. Lazim, R. Kuklani, D. M Proca*
*Temple University, USA

Background & objectives: Osteosarcoma (OS) occurring in the maxillofacial region is exceedingly rare, accounting for 0.5-1% of facial mass tumours. The atypical clinical presentation of jaw OS, distinct from its counterpart in the long bones, adds a layer of complexity to clinical diagnosis.
Methods: Chondroblastic osteosarcoma (COS), a distinctive histopathological subtype of OS, is characterized by an abundance of chondroid matrix with osteoid formation. Chondrosarcoma (CS) is in the differential diagnosis, as an unusual malignant neoplasm known for its locally aggressive behaviour. A delayed diagnosis of any of these entities may lead to metastases, significantly impacting patient outcome.
Results: We outline 3 rare COS identified at our institution over a span of 10 years.
Case 1: 30yo male with a lesion associated with a vital tooth. The lesion showed cartilage with lacunae containing cells with pleomorphic multinucleated cells, osteoid irregular spicules and spindled cells with hyperchromatic nuclei. Mitotic figures were rare.
Case 2: 68yo male with a hard nodule in the maxilla with cellular bone trabeculae and osteoid haphazardly admixed with myxoid chondroid tissue. Hyperchromatic nuclei were noted, but mitotic figures were rare.
Case 3: 59yo male with a lesion at the extracted site of a vital tooth with pleomorphic bizarre cells admixed with malignant cartilage and osteoid.
Conclusion: The rarity of gnathic OS poses challenges for individual institute studies. It is critical to incorporate OS into the differential diagnosis for osseous lesions in the jaw, particularly with the added complexity of chondroid matrix indicating CS. In our series, 2 of 3 patients were older than the average OS age, increasing the likelihood of CS. This underscores the need for heightened awareness of both COS and CS, and consideration of both when encountering a malignant neoplasm with chondroid matrix.

E-PS-18-038
Gli-1 altered tumour: a case report
S. Merino Baamonde*, M. Rubiera Valdés, E. Higueras Mora, C. González Rodríguez, C. Fuente Díaz, F.J. Pérez Rastrollo, M.P. González Gutiérrez, B. Vivanco Allende
*University Hospital of Asturias, Spain

Background & objectives: GLI-1 alterations have been found in soft tissue tumours of varied morphological features, immunohistochemical profile and clinical behaviour. We present a case report of a GLI-1 altered tumour.
Methods: GLI-1 altered tumours are malignant mesenchymal tumours that frequently present with a nested, epithelioid morphology; an elaborate capillary network and multinodular growth. They have an inconsistent and non-specific immunophenotype. They are more often found in the head and neck region. Their behaviour and clinical outcome is uncertain.
Results: Our patient is a 45 year-old male presenting with a lesion in the anterior third of the tongue. An incisional biopsy was performed, and informed as positive for malignancy of mesenchymal origin, recommending total excision of the lesion. Extension studies were carried out, and negative for the presence of metastasis. An anterior partial hemiglosectomy was performed. At the microscopic examination we observed a proliferation of neoplastic cells, with an epithelioid morphology forming nests and cords; with pleomorphism and atypia. The immunohistochemical study revealed positivity for GLI-1 and CD10. The rest of mesenchymal markers including S100 were negative. The FISH study showed a GLI-1 translocation.
Conclusion: GLI-1 altered soft tissue tumours are rare neoplasms, conforming a new pathologic entity. They can present with both translocations and amplifications of the GLI-1 gene. It is necessary to keep in mind that these tumours are of uncertain malignancy, most of them have an indolent clinical course but some cases have presented recurrences and even distal metastasis. This highlights the importance of a correct clinical follow-up to ensure complete remission. Our patient is currently healthy and without recurrence or metastasis.

E-PS-18-039
Ewing sarcoma and adamantinoma-like Ewing sarcoma of the head and neck region in adults: a tertiary care cancer centre series
N. Mittal*, S. Rane, K. Rabade, P. Panjwani, M. Bal, B. Rekhi, A. Patil, M. Ramadwar
*Tata Memorial Center, India

Background & objectives: Ewing sarcoma (ES) is a common extremity tumour in children. However, occurrence in head neck (HN) region in adults is rare, frequently misdiagnosed and poorly understood. Adamantinoma-like Ewing sarcoma (ALES) has HN predilection and an unclear relationship to classical ES.
Methods: Retrospective single centre cohort study of Adult (>/=18 years) HN ES (AES) and Adult ALES(AALES) of 10 years duration (Jan2014-Jan 2024) with available clinical and histological material for review. A total of 40 cases of ES (Mean age 30.1)and 14 cases of AALES (mean age 43.4 years) were evaluated, which include 5 previously published cases of AALES (PMID: 35025056).
Results: M:F ratio of 1.1:1vs6:1, sinonasal site predilection in 52%vs50%, and 60%vs92.9% soft tissue origin characterized AES and AALES respectively. Histologically, 55%vs100% epithelioid histology, 80%vs100% cases with cellular monotony, 20%vs42.9% cases with stromal sclerosis, 17.5%vs14.3% cases with rosettes, mitoses >10/2mm2 in 20%vs30% cases defined AES and AALES respectively. Immunohistochemically, AE1/AE3 in 36.8%and100%, p40/p63 in 0%and100%, membranous CD99 and NKX2.2 positivity in 100%and100% were noted. FISH for EWSR1 gene rearrangement was

positive in all cases of ES(n=9)and AALES(n=8). All patients were treated with multimodality therapy. Recurrence/metastases were seen in 47.2%of AES compared to 16.7%in AALES. With a mean follow-up of 33months and 12months respectively, 50%of ES and 85.7%of AALES patients were disease-free.
Conclusion: AES has a different sex ratio, similar sinonasal involvement and soft-tissue origin, comparable epithelioid, monotonous histology, lower positivity for epithelial and squamous markers and a higher incidence of nodal and/or distant metastases than AALES in this largest single centre study of Adult HNES. Relative lack of round cell histology, and frequent large nested architecture in HNregion distinguishes it from extremity ES. p63 positivity,p40 negativity in AALES is hitherto unreported. Multimodality therapy is the treatment of choice for classical cases.

E-PS-18-040
A case report of a sinusal NK/T-cell lymphoma, nasal type
W. Mokni*, S. Yacoub, S. Bentekaya, D. Chiba, A. Benabdelkader, M. Mokni
*Department of Pathology, Farhat Hached University Hospital, Sousse, Tunisia

Background & objectives: Extranodal NK/T-Lymphoma, nasal type (ENKTL) is an aggressive rare non-Hodgkin lymphoma, associated with Epstein-Barr virus (EBV). Its clinicopathological features can be confused with inflammatory processes, rendering the diagnostic difficult. We review the epidemiology, histology and differential diagnosis of this entity.
Methods: It is a case report of a sinusal ENKTL, diagnosed at our laboratory.
Results: A 69-year-old man presented with right pansinusitis, complicated by orbital cellulitis. The biospy involved some bone fragments and a largely ulcerated respiratory type mucosa, replaced by large foci of fibrinoid necrosis or granulation tissue. The latter contained atypical cells of small to medium size with a lymphoid appearance. The nuclei were notched and irregular, finely nucleolated, showing numerous mitoses. These tumour cells were arranged in a diffuse sheets and around the vessels. On immunohistochemistry, the cells stained positive for CD3, CD2 and TIA1, and were negative for CD4, CD8, CD56 and Pancytokeratin, displaying a cytotoxic T phenotype. The in situ hybridization study with the EBBER probe turned positive.
Conclusion: ENKTL is more prevalent among East Asians and Latin Americans. Paranasal sinuses are the second most involved site, after the nasal cavity. Paranasal tumours may mimic chronic sinusitis. Histologically, it is composed of atypical lymphoid proliferation, exhibiting an angiocentric growth pattern, with angiodestruction and geographical fibrinoid necrosis. The intense inflammatory infiltrate associated with tumour cells can be confusing. A proof of EBV infection is compulsory for the diagnosis. The treatment is currently based on chemotherapy and radiotherapy.

E-PS-18-041
Kaposi's sarcoma of the larynxin an HIV-negative patient (a case report)
W. Mokni*, N. Abdessayed, D. Chiba, A. Benabdelkader, M. Mokni
*Department of Pathology, Farhat Hached University Hospital, Sousse, Tunisia

Background & objectives: Among laryngeal malignancies, sarcomas remain infrequent. Primary Kaposi sarcoma of the larynx is exceedingly rare, especially without a history of immunodeficiency. This case report will discuss the characteristics of laryngeal Kaposi sarcoma, emphasizing the main diagnosis challenges on biopsy.
Methods: We report the case of a 59-year-old man, without a past medical history who consulted for dysphonia evolving from 3 months. Direct laryngoscopy revealed a swelling of the left vocal cord that was removed.
Results: Histologically, it was made of spindle cell proliferation expressing CD34, and TLE1. The diagnosis of monophasic spindle synovial sarcoma was established and the patient was referred to our hospital for additional management. Two months later a wide resection of the mass was performed. Microscopic examination revealed histological and immunohistochemistry features (positive staining of CD34 and HHV8) supporting Kaposi sarcoma. Further investigations for the immune status such as HIV serology were negative. Post-operative CT scan didn't show any residual tumour and the patient is free from recurrence to date.
Conclusion: Four clinicopathological subtypes of KS are well known: classical KS, African-endemic KS (AEKS), iatrogenic KS, and epidemic AIDS-related KS. The AEKS often appears as a multifocal pigmented cutaneous nodules. However, larynx involvement is uncommon, especially in the setting of immunocompetent patients. Its diagnosis is challenging, particularly on small samples. Recurrence is the major complication that requires a strict follow-up.

E-PS-18-042
Tumour-like amyloidosis of the parotid: a case report
M. Nadia*, M. Hamdani, M. Walha, K. Bel Haj Ali, I. Cherif, A. Khabir
*Habib Bourguiba University Hospital of Medicine,Tunisia

Background & objectives: Tumour-like amyloidosis or amyloidoma is a nodular lesion related to abundant amyloid deposits that clinically mimics a malignant tumour.Its etiologic diagnosis requires searching for an underlying infection,a connective-tissue disorder or a lymphoma.Parotid amyloidoma is exceptional.Only three cases heve been reported.
Methods: We report the case of a 60-year-old female with a history of diabetes and hypertension. She presented with an isolated swelling of the right parotid region without facial paralysis or palpable lymphadenopathy. A right superficial parotidectomy with a frozen section examination was performed.
Results: In the Immunohistochemical study, amyloidosis was subtyped AA. The diagnosis of tumour-like amyloidosis associated with the Gougerot-Sjögren syndrome was retained.
Conclusion: An association of parotid amyloidoma and the Gougerot-Sjögren syndrome is a rare condition. The histologic diagnosis may be difficult in this case. Therefore, it is necessary in case of amyloidoma to confirm the diagnosis and carry out an etiological investigation to search for an underlying pathology.

E-PS-18-043
Papillary neoplasm of head and neck: beyond morphological and immunohistochemical analysis
M. Narváez Simón*, C.E. Chamorro Santos, O. Preda, B. Rueda Villafranca, R.M. Ríos Pelegrina
*Upigap-Hospital de Baza-Huvn, Spain

Background & objectives: We report a case of a patient with a history of papillary thyroid carcinoma and a new onset nodule in the scar area of a facial aesthetic procedure. This case was a diagnostic challenge between primary or metastatic lesion.
Methods: A fine needle aspiration puncture was performed. The smears were moderately cellular, revealing a neoplasm with papillary pattern made up of cells with round nucleous with evident nucleolus and vacuolated cytoplasm. The cells were immunoreactive for GATA3 and CKs and negative for TTF-1 and PAX8.Molecular tests were not available, and a diagnosis of secretory carcinoma was suggested, considering salivary gland over as thyroid origin.

Results: Radiological study located the nodule in the parotid gland. Macroscopically, it was a well-defined lesion within the gland. Microscopically, it was a non-encapsulated neoplasm with a cystic and papillary pattern and the same cytological characteristics described above. ETV6::NTRK3 fusion was demonstrated by FISH. A diagnosis of Secretory carcinoma of the salivary gland was made.
Conclusion: Salivary gland and thyroid secretory carcinoma with a papillary pattern share immunophenotype, and it is in these cases that molecular assays are essential for accuracy diagnosis.

E-PS-18-044
Unexpected diagnosis of thyroid tuberculosis: a case report of two patients
H. Belhadj-Miled, Z. Nfikha*, J. Houas, T. Tlili, I. Bahri, M. Abdelkefi, M. Mokni
*Department of Pathology, University Hospital of Farhat Hached, Tunisia

Background & objectives: Thyroid Tuberculosis is very uncommon with often an incidental diagnosis. We report two cases of thyroid tuberculosis and study the clinical, anatomopathological, and evolutive features of this surprising localization.
Methods: We report two cases of tuberculosis involving unexpectedly the thyroid gland.
Results: We report the cases of a 52-year-old male and a 47-year-old female admitted to the Otorhinolaryngology Department for surgical management of thyroid disorders. The male patient presented with clinically and ultrasound benign multinodular goiter and underwent total thyroidectomy, while the female patient had a left thyroid nodule associated with ipsilateral lymph node, leading to total thyroidectomy with lateral neck dissection. Histopathological examination revealed granulomatous epithelioid and giant-cell necrotizing thyroiditis in the first patient's multinodular goiter and, in the second patient, a 0.3 cm right lobar papillary carcinoma concomitant with granulomatous epithelioid thyroiditis and seven lymphadenopathies, showing necrotizing epithelioid and giant-cell lymphadenitis. Both patients showed favourable outcomes under antituberculosis therapy.
Conclusion: Thyroid tuberculosis, though uncommon, should be considered as a potential diagnosis when evaluating a thyroid lesion. Definitive diagnosis typically relies on histopathological examination.

E-PS-18-045
Cementoblastoma of the mandible: about 2 cases
L. Njim*, D. Beltaifa, A. Ben Mabrouk, S. Mabrouk, S. Ben Hammouda, A. Bellalah, M. Njima
*Fattouma Bourguiba University Hospital, Monastir, Tunisia

Background & objectives: Cementoblastoma is an uncommon, benign odontogenic mesenchymal tumour, associated with and attached to the roots of teeth. It is considered to be the only true neoplasm of cemental origin. Herein, we present a clinico-pathologic features of two cases of cementoblastoma.
Methods: We reported two cases of cementoblastoma, diagnosed at the University Hospital of Monastir. Clinical information including anatomical location, patient history, and radiographic appearance was assessed. Regarding pathological features, gross and histopathological aspects were evaluated. Histologic confirmation of lesional tissue continuous with cementum of the tooth root was verified in every case.
Results: A 32-year-old man and a 26-year-old woman, both without any significant medical history. The man had pain in his lower left first molar, while the woman felt discomfort in her upper left second premolar. Radiographs of the specimens displayed a radiopaque mass attached to the mesial root of the teeth, measuring respectively 1.6 and 2 cm. Macroscopically, the tumours were creamish-white. Histologycally, the tumours were continuous with the root cementum. They exhibited abundant irregular trabeculae of basophilic mineralized tissue with prominent reversal lines, indicative of cementum. These features were interspersed with fibrovascular connective tissue. Toward the periphery of the hypocellular mineralized tissue, cementoblasts and osteoclastic multinucleated giant cells were seen.
Conclusion: The cementoblastoma is a benign tumour arising from neoplastic cementoblasts. This tumour primarily affects adults with a mean age of 20.7 years and a higher predilection for males. The mandible is more involved than maxilla. Because of the possibility of recurrence if lesional tissue remains after initial surgery, appropriate treatment should consist of removal of the lesion, along with the affected tooth or teeth, followed by thorough curettage or peripheral ostectomy. Differencial diagnosis includes osteoblastoma, osteoma and odontoma.

E-PS-18-046
Extraosseous ameloblastoma - a rare entity and a pitfall for squamous cell carcinoma
P. Carreira, R. Oliveira*
*Capgs, Portugal

Background & objectives: Ameloblastoma is a odontogenic neoplasm most common in bone. Its extraosseous variant is rare, and may occur in the gums, buccal mucosa or oral floor. We aim to describe an extraosseous ameloblastoma that mimicked a squamous cell carcinoma in biopsy.
Methods: Man, 71 years old, diagnosed with squamous cell carcinoma (on biopsy) of the right retromolar triangle, underwent right hemimandibulectomy and lymph node dissection. The macroscopic study revealed an ulcerated lesion on the alveolar ridge, consisting of white tissue, limited to soft tissues, without bone infiltration.
Results: The histological study revealed a lesion with expansive growth, with compression of the oral epithelium and ulceration. The lesion had cystic areas, with basaloid cells, arranged in a peripheral palisade and reticular axis. There was no bone or lymph node involvement. The immunohistochemical profile revealed positivity for CK5/6, P40, P16 and CK19. A review of the biopsy was performed, which was superficial and showed only the basaloid component, without evidence of the reticular axis. The staining for P40 and P16 supported the diagnosis of squamous cell carcinoma, in line with the clinical suspicion, making the diagnosis of ameloblastoma in biopsy extremely difficult.
Conclusion: Although rare, extraosseous ameloblastoma can mimic squamous cell carcinoma. As it is benign and does not require lymph node emptying, its diagnosis must be taken into account in differential diagnoses or the oral cavity.

E-PS-18-047
Intestinal metaplasia as evidence of field cancerization in patients with intestinal type adenocarcinoma of the sinonasal region
A. Orsatti*, M.V. Altavilla, P. Farneti, G. Sollini, A. Tosoni, E. Donini, E. D'Angelo, P. De Benedittis, L. Raffi, A. Camagni, P. Galli, E. Pasquini, G. Fellegara, M.P. Foschini
*University of Bologna School of Medicine, Bologna, Italy

Background & objectives: Sinonasal-Intestinal type adenocarcinoma (ITAC) is related to inhaled carcinogens, which can favour the development of "field cancerization" (FC). Aim is to evaluate if Intestinal metaplasia (IM) can be evidence of sino-nasal FC.
Methods: The study is based on 8 ITAC cases, completed with resection margins. Cases were reviewed according to the WHO 2022 criteria. IM was diagnosed on hematoxilin-eosin (H&E) according to previously described criteria (Franchi A, et al. Virchows Arch. 2015; 466(2):161-8. doi: 10.1007/s00428-014-1696-1). When no clear IM features were seen, immunohistochemistry with CK 20 and CDX2 antibodies was applied.

Results: IM was present in 8/8 cases in the mucosa adjacent to the main neoplastic lesion. In 2 cases IM was detected histologically on H&E stained slides. In the remaining 6 cases, IM was evidenced by immunohistochemical stainings, that highlighted the presence of CDX2 and/or CK20 positive cells, intermingled with normal respiratory epithelium.
Conclusion: The present data support the hypothesis that IM in the sinonasal mucosa is more frequent than expected when searched for with immunohistochemical markers. Even if more cases should be studied to better understand the prognostic impact of IM, its presence could be related to multiple ITAC foci.

E-PS-18-048
Artificial neural network renders cribriform adenocarcinoma and polymorphous adenocarcinoma of salivary gland two entities, and more!
B.K. Othman*, A. Skálová
*Faculty of Medicine in Pilsen, Charles University, Czech Republic

Background & objectives: The use of artificial neural network (ANN) algorithms has been applauded for classifying chronic renal diseases, and lymphoepithelial lesions. Using conventional neural network rendered computational models with higher classification accuracy. We propose an ANN-based classification model for salivary gland carcinomas (SGCs).
Methods: The genetic alterations of salivary gland carcinomas were retrieved from literature underpinning reporting next-generation sequencing information on diagnosing SGCs, PubMed, OMIM and Genecards databases and AS' registry (n=212). All SGCs were annotated at the subordinate level, following the 2022's taxonomy of the WHO. Eligibility criteria included primary SGCs with NGS data, and IHC workup. Sinonasal salivary-type neoplasms were excluded.
Results: After performing ANN analysis at the subordinate level, For example, intercalated duct-like intraductal carcinoma (not only the superordinate designation intraductal carcinoma), the weighted number of links and total interactions score values were exported and processed. The distance on the visualization charts suggested that (a) cribriform adenocarcinoma and polymorphous adenocarcinoma of salivary gland are too heterogenous to be clustered under the same entity. (b) intercalated intraductal carcinoma differs from the other variants remarkably. (c) squamoglandular differentiation in acinic cell carcinoma and adenoid cystic carcinomas warrants special attention. (d) gene mutations arising secondary to canonical fusions may represent high-grade transformation at the molecular level.
Conclusion: Published studies featuring next-generation sequencing data on SGCs present promising sources for data mining that can enhance the validity of research findings when compared to standard real-time registries. While IT-based pathological knowledge complements WHO classifications, it does not supplant them; instead, it opens up new avenues for research with valuable insights. Furthermore, the significance of chimeric fusion proteins and secondary mutations (alterations) should not be underestimated, as they may explain SGCs oncogenesis, cytodifferentiation, or transformation within SGCs.

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E-PS-18-049
Cutaneous metastasis on scalp of renal cell carcinoma: a case report and review of literature
A.V. Pagliari*
*U.O. Otorinolaringoiatria - ASST Crema, Italy

Background & objectives: Renal cell carcinoma accounts 2-3 % of adult malignancies. At recent incidence of renal cell carcinoma increased in conjunction with improvements in image device. Skin metastasis is a rare entity 3 to 6% of cases and more uncommon scalp localization.
Methods: A 83 year old man was referred to us with a enlarging scalp nodule. On observation the lesion was 2,5 cm red-violet nodule with firm consistency not adherent to deep planes. The lesion was extremely sore and painful. There were no palpable lymph nodes regionally. The patient was submitted to computed tomography. An excisional biopsy under local anaesthesia was performed
Results: The computed tomography revealed a right occipital vascularized lesion localized in subcutaneous tissue, exophytic with no bone invasion. Histopathological examination revealed alveolar, tubular and tubulocystic formations of cells with clear cytoplasm and central round nuclei. Immunohistochemistry showed lesion positive for cytokeratin, vimentin and pax8 and negative for S-100 and leucocytre common antigen.
Conclusion: Reviews studies on metastatic renal cell carcinoma to the skin include less 100 reports and little more 20 with scalp metastasis. A total of 80-90% of patients with skin metastases have prior diagnosis of renal cell carcinom and 10-20% are diagnosed before primary lesions is identified. Renal cell carcinoma skin metastasis is often a poor prognostic indicator and expected lifespan is less than six months. The treatment approach for single isolated skin lesions is surgical removal of the lesion only.

E-PS-18-050
Respiratory epithelial adenomatoid hamartoma: a diagnostic challenge in sinonasal lesions
A.V. Pagliari*
*U.O. Otorinolaringoiatria - ASST Crema, Italy

Background & objectives: Respiratory epithelial adenomatoid hamartoma is a benign tumour of the sinonasal tract often misdiagnosed as nasal polyps or various sinonasal malignancies. Wenig and Heffner first described nasal hamartoma with only 13 cases describe in literature at that time.
Methods: A 68 year old male with a history of nasal congestion presented to us. On a endoscopic exam was seen a polypoid mass anterior and medial to the middle turbinate. A computed tomography show bilateral polypoid soft tissue masses within the bilateral olfactory recesses with no evidence of bony remodelling.
Results: The nasal masses were removed endoscopically under general anaesthesia performing a bilateral ethmoidectomy and antrostomy. The exised masses were elastic a smooth surface. The patient postoperative course was uneventful. Histological examination of a haematoxylin and eosin stained slide demonstrated focal glandular hyperplasia round to oval in shape separated by stroma and glands distended by mucus. Basement membrane is invariably thickened with oedematous stroma with no metaplastic or atypical changes. Immunohistochemistry shows staining positive for CK 7 and negative for CH20, CDX-2 and S-100. The basal cells are p63 positive
Conclusion: Respiratory epithelial adenomatoid hamatoma is an uncommon nasal mass that is becoming increasingly recognized within the literature often mimicking other nasal pathology making diagnosis difficult. Histologically respiratory epithelial adenomatoid hamatoma is characterized by glandular proliferation of ciliated respiratory epithelium. The glands are often round to oval shape separted by respiratory epithelium. In conclusion when a patient is identified with bilateral sinonasal masses without identificable bone erosion on imaging respiratory epithelial adenomatoid hamatoma should be high on the differential diagnosis.

E-PS-18-051
Clinicopathologic features of chronic lymphocytic leukemia/small lymphocytic lymphoma of the Waldeyer's Ring: a twenty-five-year experience from a single institution

A. Pasco Peña*, I. Fernandez, E. Carracedo, A.S. DE OLIVEIRA GOMES, L.M. Ruiz, A. Panizo
*Hospital Universitario de Navarra, Spain

Background & objectives: Most lymphomas involving Waldeyer's ring (WR) are DLBCL, however, primary low-grade lymphomas are exceptional. Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLLL) of Waldeyer's ring is extremely rare. Our aim was to investigate the detailed clinical and morphologic features of WR CLL/SLLL.
Methods: A retrospective study was performed to identify CLL/SLL of the WR diagnosed between 1998 and 2023 at our department. Inclusion criteria were: (1) involvement of WR; and (2) lymphoma satisfying the diagnostic criteria for CLL/SLL based on WHO classification. Demographic, clinical, and follow-up data were obtained from electronic medical records. Pathological data were obtained after reviewing WR biopsies.
Results: 13 cases were identified: 9 males and 4 females, aged 30-77 years (median 67). Tumours involved palatine tonsil (n=7), pharyngeal tonsil (n=5), and lingual tonsil (n=1). Nine (69,2%) and 4 (30,8%) patients had unilateral and bilateral lesions, respectively. Eleven cases had a previous diagnosis of CLL/SLL, only 2 (15,4%) cases the diagnosis was made primarily on WR tissue. On histologic evaluation, all but one cases showed the interfollicular areas expanded by a diffuse proliferation of small lymphocytes. Median follow-up of patients was 39 months (range, 5 to 237 months): 7 alive in progression (follow-up time 16-237 mos.; median 44) and 6 died of disease progression (5-62 mos.; median: 18 mos.).
Conclusion: WR CLL/SLL is exceedingly rare and we report the largest series to date. Most WR CLL/SLL patients present like acute tonsillitis or unilateral tonsillar enlargement. Proper diagnosis require a high index of suspicion, knowledge of previous CLL/SLL history and, occasionally, ancillary studies.

E-PS-18-052
The necessity of morphological and molecular integration: two cases of head and neck mucoepidermoid carcinomas and literature review
J.P. Pereira De Castro*, G. Miranda, C. Perez Duque, P. Dias, M. Jácome
*IPO-Porto, Portugal

Background & objectives: Mucoepidermoid carcinoma is a head and neck neoplasm, sometimes with challenging differential diagnoses. We present two cases to discuss the importance of morphology, the risk of certain pitfalls and the value of molecular studies.
Methods: The first case is a 74-year-old man that developed a mandible mass. Histology was consistent with mucoepidermoid carcinoma. FISH was negative for CRTC1-MAML2 rearragement, but the subsequent NGS study identified CRTC3-MAML2 fusion. The second case is a 63-year-old woman with a base of tongue tumour. The coexistence of squamous dysplasia and adenosquamous phenotype led to FISH analysis, revealing CRTC1-MAML2 rearrangement.
Results: The mandible neoplasm was composed of mucinous and squamoid cells, forming cystic and solid patterns, compatible with intraosseous mucoepidermoid carcinoma. Although FISH analysis did not reveal the most typical genetic alteration, because of the confidence in its morphological features, the initial diagnosis did not change. Subsequent studies with NGS reported a less common rearrangement involving MAML2. The tongue neoplasm was also a mucinous and squamoid tumour, without keratinization or intercelullar bridges. The intimate involvement of the mucosal surface and presence of adjacent squamous dysplasia favoured the hypothesis of adenosquamous carcinoma. However, MAML2 translocation confirmed the diagnosis and the case was signed out as mucoepidermoid carcinoma.
Conclusion: Even in the absence of typical molecular alterations, morphology evaluation remains the most accurate tool for a correct diagnosis. Nevertheless, the non-recognition of two unrelated synchronous tumours and an overly dogmatic vision of certain histological clues may also be misleading, requiring the aid of complementary molecular studies. In such cases, the definitive diagnosis must follow a global integration of all tumour features.

E-PS-18-053
Histone H3K9 methylation in odontogenic tumours
E. Phattarataratip*, A. Lam-Ubol
*Chulalongkorn University, Thailand

Background & objectives: The study aimed to investigate the expression of H3K9Me3 histone modification and its associated enzyme, SETDB1, in odontogenic tumours.
Methods: Paraffin-embedded tissues, which had been diagnosed as adenomatoid odontogenic tumour and ameloblastoma, 30 each, and 15 cases of dental follicle, were included in the study. The tissue was immunohistochemically stained for H3K9Me3 and SETDB1. The intensity and distribution of staining were evaluated as H-score. Statistical analysis was performed to assess differences among groups and related factors that affect protein expression.
Results: The odontogenic epithelium of the dental follicle showed strong and diffuse expression of H3K9Me3. The level of H3K9Me3 was significantly higher than those of adenomatoid odontogenic tumour and ameloblastoma. Adenomatoid odontogenic tumour demonstrated the lowest H3K9Me3 expression. No expression of SETDB1 was detected in all lesions tested.
Conclusion: H3K9Me3 histone modification could potentially play a role in the pathogenesis and behaviour of odontogenic tumours.

E-PS-18-054
HPV-associated multiphenotypic sinonasal carcinoma. Tumour with indolent behaviour? A case-control study
D. Piñol Ballús*, L. López, S. Bagué, A. Gonzalez, A. Holgado, J.R. Gras, J. Szafranska
*Hospital de la Santa Creu i Sant Pau, Barcelona, Spain

Background & objectives: HPV-associated multiphenotypic sinonasal carcinoma (HMSC) is a rare neoplasm, associated with high-risk papillomavirus (HPV), recently included in the 5th edition of WHO classification. HMSC is considered to have more favourable outcome compared to the other types of sinonasal carcinomas.
Methods: 10 cases of HMSC diagnosed between 1990 and 2019 were revised and compared with 7 HPV-negative sinonasal poorly differentiated carcinomas (HSPDC). HMSC cases included 8 men with mean age of 55,3 and follow-up of 93 months, during which, 2 patients died and 2 developed metastatic disease. Adenoid cystic carcinomas, squamous cell carcinomas, neuroendocrine carcinomas and NUT-carcinomas were excluded.
Results: HMSC tumours were predominantly located in ethmoid sinus at early stages (pT2/pT3), with mean size of 25 mm and no metastasis to lymph nodes.
HSPDC cases included 5 men with mean age of 68,6 and follow-up of 37,8 months, during which, 5 patients died. Tumours were mostly located in nasal cavity at later stages (pT4), with a mean size of 38 mm and evidence of metastatic disease to lymph nodes.
Both groups showed microsatellite stability. Patient age, tumour size, location, margin status, perineural invasion, lymph node metastasis and PDL1 expression showed no statistical differences between groups ($p>0,05$). Kaplan-Meier analysis revealed a slightly more favourable outcome of HMSC group ($p<0.05$).
Conclusion: HMSC cases showed a more aggressive behaviour than expected when compared to the cases reported in the literature,

nevertheless, we confirmed that patients with HMSC tend to be younger, have better prognosis and longer survival rates when compared to patients with HSPDC. Our study also observed that tumour stage at the time of diagnosis may be a potential predictor for patient survival. These results should be interpreted with caution due to limited knowledge regarding the treatment for this rare neoplasm.

E-PS-18-055

Heterotopic secretory carcinoma arising on neck lymph node

G. Querzoli*, C. Liberale, A. Altimari, G. Molteni, M.P. Foschini
*Pathology Unit, IRCCS Azienda Ospedaliero Universitaria di Bologna, Bologna, Italy

Background & objectives: Salivary gland neoplasms arising from heterotopic sites are rare and in most of the cases constituted by mucoepidermoid carcinoma. Here, a case of secretory carcinoma (SC) arising from a salivary gland heterotopia in a latero-cervical lymph node is presented.
Methods: A 66-year-old male presented with a left neck mass. Imaging failed to reveal patodieal involvement, while the mass was located in the latero-cervical area. fine needle aspiration cytology was perfomed and suggested the diagnosis of benign/low-grade malignancy neoplasm of possible salivary gland origin. After multidisciplinary discussion, radical surgery was planned. Excision of the mass together with superficial parotidectomy were performed
Results: On histology the tumour showed the typical features of SC. Salivary ducts located within a lymph-node presented features of in situ SC. Molecular analyses showed ETV6-NTRK3 fusion gene. No tumour involvement of the parotid tissue was evidenced. Therefore, the diagnosis of SC arising from salivary gland heterotopia in a latero-cervical lymph node was performed. Salivary gland tumours arising in salivary gland heterotopia are rare and in most of the cases constituted by mucoepidermoid carcinoma or pleomorphic adenoma. One case only of SC arising in heterotopic salivary gland tissue has been reported.
Conclusion: SC is a rare low-grade malignant salivary gland tumour that typically occurs in the parotid gland, displaying specific histological features. The primary treatment for SC is surgery, with a favourable prognosis in most cases. The occurrence of SC on heterotopic salivary gland tissue is rare. This case emphasizes the importance of considering different histopathological entities in unusual locations.

E-PS-18-056

Malignant transformation in patients affected by hyperkeratosis and oral dysplasia

G. Querzoli*, M. Petrocelli, E. Bariani, A.M. Baietti, D.B. Gissi, A. Gabusi, L. Montebugnoli, A. Tarsitano, M.P. Foschini
*Pathology Unit, IRCCS Azienda Ospedaliero Universitaria di Bologna, Italy

Background & objectives: Oral epithelial dysplasia (OED) is a spectrum of eptihelial alterations indicating a risk of malignant transformation to oral squamous carcinoma (OSCC). Aim of the present study is to define the rate of OED malignant transformation after a long follow-up interval.
Methods: All cases presented with a first diagnosis of OED histologically diagnosed between 1992 and 2003 were reviewed according to the WHO 2022 criteria. Clinical charts were reviewed, and eventual malignant transformation was registered.
Results: Ninety-nine cases were retrieved (53 hyperkeratosis, 46 OED) comprising 58.6% males with a mean age of 58.4 years (SD±14.7). Mild, moderate, and severe OED were observed in 15, 15 and 16 cases respectively. Tongue was the most affected site for hyperkeratosis and OED (40 cases, 40.4%). OSCC arose in 2 cases of hyperkeratosis (3%) and 15 cases (15.20%) of OED. Specifically, 4,4,7 cases of mild, moderate, and severe OED respectively developed OED. All OSCC arose in the same site of the hyperkeratosis and OED. A higher rate of malignant transformation in patient with OED compared to hyperkeratosis ($p<0.001$) was observed.
Conclusion: Hyperkeratosis and OED are precursors of OSCC. The present data confirm the significant risk of malignant transformation of these lesions, although variable among the subgroups. OED bears a higher risk of cancer transformation than hyperkeratosis. Our data suggest the importance of a careful follow-up in these patients to early detect the development of OSCC.

E-PS-18-057

Head and neck lymphoepithelial carcinoma of non-nasopharyngeal sites - a case series

K. Rabade*, A. Patil, N. Mittal, S. Rane, M. Bal
*Tata Memorial Centre-Actrec, India

Background & objectives: Lymphoepithelial carcinoma (LEC) of the head and neck region is a rare undifferentiated carcinoma involving the nasopharynx more often than other sites. We present clinicopathological features of head and neck LEC involving the non-nasopharyngeal sites diagnosed at our institute.
Methods: This is a retrospective study of twenty patients diagnosed with head and neck LEC between January 2014 and December 2023, including a review of pathology reports, H-E and immunohistochemistry slides, and medical records. The nasopharyngeal primary site was excluded in all patients by detailed radiologic examination.
Results: The age range was 19-80 years (median-51.5) and showed male preponderance (4:1). 65% of patients belonged to endemic regions of India. The sites included Parotid (10), Submandibular gland (1), Larynx (4), Oropharynx(3) and Oral cavity(2). Thirteen patients(68.5%) showed metastatic regional nodes at presentation. Immunohistochemistry shows positive staining for EBV-LMP1 in 6/12 cases. 13/19 patients underwent surgery out of which one received Neoadjuvant chemotherapy. Twelve patients received adjuvant therapy (Radiotherapy-6 and chemoradiation- 6). Rest of the patients received chemotherapy (3), radiotherapy (1) and chemoradiation (2) as their primary mode of treatment. Follow-up (3-82 months, median 26.5 months) was available in 15 patients of which 25% showed recurrence and 21% distant metastasis.
Conclusion: LEC at non-nasopharyngeal sites is rare and is associated with a favourable prognosis. As previously reported, our series also showed more frequent Epstein-Barr virus association in patients from endemic regions of our country and the commonest sites of distant metastasis were lung and bone. Despite the higher incidence of nodal metastasis and distant metastasis in our series, none of the patients died of the disease.

E-PS-18-058

Co-existence of papillary and medullary thyroid carcinoma: reports of three cases

A. Rais*, Y. Houcine, I. Mallek, S. Kamoun, S. Dellagi, M. ALAYA, A. Lahmar, M. Driss, S. Ben Slama
*Pathology department, Salah Azaiez Institute, Tunisia

Background & objectives: Medullary thyroid carcinoma (MTC) and papillary thyroid carcinoma (PTC) are two different types of tumour. Their concomitant existence is rare and occurs in less than 1% of thyroid tumours .Herein we analyse the clinicopathological, immunohistochemical features and prognosis of these tumours.
Methods: We describe three cases of synchronous PTC and MTC that illustrate the clinicopathological features, immunohistochemical and outcomes of this entity with a review of the literature.
Results: Our case series included two women and one man. The average age of diagnosis was 65 years.The physical examination and Ultrasonography revealed thyroid nodules. Fine needle aspiration was

performed in two cases, showed atypical nuclei and was suggestive of only papillary carcinoma . Histological and immuno histochemical analysis of the tumours demonstrated a mixed carcinoma in two cases and a collision tumour in one case. All patients were treated appropriately with total thyroidectomy with bilateral lymph node dissection. Post-surgical radioactive iodine ablation was added only in the first case. The co-existence of these tumours requires a different clinical approach in treatment and follow-up, depending on which type is dominant.
Conclusion: Synchronous MTC-PTC is a very rare event. PTC and MTC originate from follicular and neuro endocrine parafollicular C cells, respectively. The molecular pathways responsible for their co-occurrence are not completely understood. The most widely accepted theories include stem cell, collision effect and hostage theories. Pathologists should keep in mind the possible co-existence of these tumours because prognosis depends on the medullary component that worsens the outcome of patients.

E-PS-18-059
Follicular dendritic cell sarcoma of the nasopharynx mimicking a meningioma: a case report
A. Rais*, Y. Houcine, S. Kamoun, M. ALAYA, S. Ayadi, M. Driss
*Pathology department, Salah Azaiez Institute, Tunisia

Background & objectives: Follicular dendritic cell sarcoma(FDCS) is a rare entity.It is mainly located in lymph nodes, with extranodal involvement seen more occasionally.The head and neck sites are extremely rare location.Herein,we report a case in the nasopharynx and we describe its clinicopathological features.
Methods: We report the case of a 77-year-old man who presented with a 3-month history of persistent obstruction of the nasal cavity. Magnetic resonance imaging revealed a nasopharyngeal mass centred on the right Rosenmüller fossa, obstructing the pharyngeal umen, with lateral extension towards the parapharyngeal space.Nasal endoscopy examination showed a large nasopharyngeal mass prolapsing into the oropharynx. Nasopharynx biopsy was performed.
Results: Microscopic examination revealed a tumour with a massive architecture, consisting of polygonal cells with a moderate amount of eosinophilic cytoplasm and round vesicular nuclei presenting marked nuclear atypia. The tumour was highly infiltrated by lymphocytes with sometimes storiform architecture. Immunohistochemistry showed that the tumour cells were positive for CD23 and CD21, confirming the diagnosis of FDCS. Staining was negative for PS100, excluding the diagnosis of meningioma. Tumour cells were also negative for other markers of lymphoma: CD3, CD20, CD56, CD4, CD5, CD8, CD45, ALK, and CD30.
Conclusion: Follicular dendritic cell sarcoma is a rare tumour characterized by strong heterogeneity in clinicopathological features and immunohistochemistry, making it highly susceptible to misdiagnosis. Numerous studies have suggested that the occurrence of FDCS may be caused by EBV infection. Most of those cases were found mainly involving the liver and spleen and are considered a distinct entity: EBV-positive inflammatory FDCS. The association between EBV and FDCS of the head and neck is still unclear and warrants further investigation.

E-PS-18-060
Immunohistochemical expression of p16 in tongue squamous cell carcinoma
A. Rais*, W. Khemiri, S. Kamoun, Y. Houcine, M. Alaya, W. Sleimi, M. Driss
*Pathology Department, Salah Azaiez Institute, Tunisia

Background & objectives: The tongue is a common site for squamous cell carcinoma(SCC)within the oral cavity. Human Papillomavirus is recognized as an etiological factor in oropharyngeal SCC.However,its role in oral cavity remains unclear.We aimed to assess the frequency of p16 in tongue SCC.
Methods: This retrospective study analysed 52 cases of tongue SCC diagnosed between 2012 and 2022. Formalin-fixed paraffin-embedded tumour tissue blocks were collected, and p16 immunohistochemistry was conducted. Positive staining was defined as nuclear and cytoplasmic p16 expression in ≥70% of tumour cells.
Results: The study cohort comprised 23 males and 29 females, with a mean age of 61 years (range 42-83). Only three cases were observed in patients aged ≤45. Alcohol and tabacco intoxication were noted in 11% of cases, with stage T2 being the most common. Tumour size ranged from 10 to 45mm with a mean size of 28mm. Positive p16 expression was detected in 34% of tongue SCC cases. However no significant association was found between p16 positivity and clinical factors.
Conclusion: Various studies have reported p16 expression in oral SCC, with rates ranging from 10% to 57%. Our results are in line with the literature. Flowing this study we plan to complete this work with HPV investigation using other tools, such as PCR or in situ hybridization.

E-PS-18-061
Next-generation sequencing - its role in head and neck sarcomas
G. Sadeghian*, D. Sinha
*University College Hospital, United Kingdom

Background & objectives: 40% of sarcomas are misdiagnosed. NGS may provide more accurate diagnosis and hence better treatment. The study aims to provide the first results of a dedicated head and neck sarcoma multidisciplinary team regarding utilizing NGS in the diagnosis and treatment.
Methods: Between January 2023 and April 2024, patients with a histologically verified head and neck sarcoma, who had NGS, were included in the study. Demographic data, anatomic site, morphology data, multidisciplinary team recommendation, details of treatment, and their outcomes were obtained from electronic patient records and analysed retrospectively. Prior to 2023, NGS hasn't been requested for head and neck sarcoma cases.
Results: Among 162 cases of verified head and neck sarcomas,12 patients were included in the study, with a mean age of 36 years. These cases have been diagnosed with ultra-rare sarcoma types. The NGS panels include RNA fusion and RMH200 DNA. Oncogenic variants were found in 4 cases and RNA fusions were detected in 4 cases. The reports of NGS have helped with the diagnosis in 4 cases and potentially advised on the type of chemotherapy treatment by excluding NTRK rearrangement in most cases; however, the overall MDT approaches or surgical strategies have not been affected by the NGS report, and in some cases the reports received after starting the treatment.
Conclusion: While NGS can alter systemic treatment, it does not change surgical management. The small number of head and neck sarcoma cases and tumour heterogeneity in a complex anatomical area warrants NGS on every case would help better define this subset of the population and ultimately may lead to a better outcome.

E-PS-18-062
The role of podoplanin and MMP9 on the multifaceted signalling pathways in squamous cell oral cancer
A. Santoro*, G. Scaglione, D. Arciuolo, G. Angelico, N. D'Alessandris, M. Valente, B. Padial Urtueta, F. Addante, N. Narducci, P. Tralongo, A. Mulè, I.S. Di Stefano, M.C. Pedicillo, G. Pannone, G.F. Zannoni
*Institute of Pathology, Università Cattolica del Sacro Cuore, Rome, Italy

Background & objectives: Podoplanin and MMP9 have been associated with metastasis in oral squamous cell carcinoma (OSCC). We aim to evaluate lymphatic angiogenesis and matrix breakdown in OSCC by

Tissue Microarray (TMA) including samples from both OSCC Superficial and Deep Invasion (SI, DI).
Methods: We collected 90 patients with OSCC, with a long-term follow-up of 8 years. Immunohistochemistry for D2-40 and MMP9 monoclonal Abs was performed by automated technique (Ventana Benchmark®) and analysed using CellSens V1.9® Olympus software. Lymphatic microvessel density (LMD) was expressed as the average of 4 × 200 field counts of podoplaninpos cells for each spot. Pearson's test were performed.
Results: Our results suggested that podoplanin is upregulated and overexpressed in stage IVB OCSS ($p<0.001$), especially in advanced local disease. The study revealed a statistically significant linear correlation between Podoplanin expression and the metastatic tissue microenvironment. Strong evidence was found indicating an association between LMD and MMP9pos cells within the tissue, and a correlation of Podoplanin and MMP9 expression in cancer cells was observed, suggesting a potential regulatory relationship. LMD increased significantly from superficial invasion to deep invasion of primitive tumours ($p<0.05$). Moreover, we have found a positive correlation between tumour grade, LMD and DI.
Conclusion: High levels of podoplanin have been associated with increased cancer invasion and promotion of the growth and creation of new lymphatic vessels within and around the tumour. Recognizing the importance of podoplanin in cancer invasion and lymphangiogenesis is essential for the development of strategies to prevent cancer metastasis. Additionally, podoplanin expression has been identified as a potential biomarker to predict OCSS prognosis and guide treatment decisions. On going analysis of additional samples will futher refine our results.

E-PS-18-063
A rare encounter: ectomesenchymal chondromyxoid tumour
A. Sert*, G. Esendagli
*Gazi University Faculty of Medicine, Turkey

Background & objectives: Ectomesenchymal chondromyxoid tumour is an uncommon type of mesenchymal tumour characterized by a fusion gene called *RREB1::MRTFB.* The lesion is usually located on the anterior of tongue and tends to have a slow-growing nature with occasional local recurrence.
Methods: A 27 years old woman presented to our hospital with a mass on her tongue that had been present for 5 years, with recent growth. On gross examination and sectioning, the mass appeared as a well-defined, soft, flesh-colored nodule, about 1 cm in diameter.
Results: Histologically, the tumour showed typical features, comprising spindle and polygonal cells in a chondromyxoid stroma. There were no atypia, no necrosis or increased mitotic figures. Tumour cells were diffuse, strongly positive to Vimentin. GFAP and S100 were also positive. There was no expression of SMA, cytokeratin 5/6, CD117, p63, OSCAR. Ki67 proliferative activity is generally low (<5%). Since the tumour was close to the surgical margin, it is advisable to monitor the patient closely for possible recurrence.
Conclusion: Ectomesenchymal chondromyxoid tumour is a rare soft tissue tumour with an uncertain origin. Regular monitoring is recommended due to its tendency for recurrence.

E-PS-18-064
Correlation of quantitative indicators of tissue tryptase and chymase with morphological and clinical characteristics of oropharyngeal cancer
I. Sertakov*, I. Moshurov, M. Olshansky, V. Shishkina, S. Stikhina, A. Fedortsov, S. Akulshina, A. Filin
*Voronezh State Medical University, Russia

Background & objectives: Mast cells are one of most important components of tumour microenvironment. The aim of the study is to evaluate the relationship between proteases produced by mast cells (tryptase and chymase) and the morphological characteristics and stage of the oropharynx cancer.
Methods: The group included 20 patients with locally advanced unresectable oropharyngeal cancer of stage III, IVa. The material examined: biopsies. Immunohistochemical staining: antibodies to tryptase and chymase. During the evaluation of staining, 30 fields of view were analysed with a recalculation of the distribution of mast cells per 1 mm^2. Statistical analysis was performed using Microsoft Excel and Statistics 23.0.
Results: The number of tryptase (+) cells in carcinoma tissues (per mm^2) was inversely correlated with the degree of tumour cell differentiation (non-keratinizing/low-differentiated – 26,72 [12,55;40,89]; moderately differentiated – 21,44 [6,96;35,92]; highly differentiated – 13,47 [6,92;20,02]). Similarly for chymase (+) cells: (non-keratinizing/low-differentiated – 2,44 [0,96;3,92]; moderately differentiated – 2,31 [-0,85;5,48]; highly differentiated – 2,09 [0,61;3,56]). The number of tryptase-positive cells per square millimeter in carcinoma tissues was directly proportional to the clinical stage: stage III – 19,56 [4,33;34,78]; stage IV – 22,92 [13,37;32,47]. The number of chymase-positive cells was inversely correlated with the clinical stage of the disease: stage III – 3,07 [0,71;5,42]; stage IV – 2,43 [1,18;3,68].
Conclusion: This study demonstrates a connection between the quantitative levels of tryptase and chymase in mast cells and the morphological and clinical characteristics of the tumour in locally advanced squamous cell carcinoma of the oropharynx. Clinical studies may reveal that high levels of tryptase and chymase are associated with more extensive tumour process, the presence of lymph node metastases, and lower overall patient survival. Therefore, quantitative determination of these enzymes could be useful for prognostic assessment and planning of antitumour treatment.

E-PS-18-065
The relationship between age-related changes in the thyroid gland and nodular pathology
I. Sertakov*, A. Goryacheva, A. Filin, E. Verbitskaya, E. Chupandina, A. Bobrovskikh, M. Bobrovskikh, V. Pozhidaeva, S. Selyavin, A. Tishchenko
*Voronezh State Medical University, Russian Federation

Background & objectives: With age, the processes of atrophy and sclerosis predominate in the thyroid gland. But the volume of the thyroid gland increases with age, and about 90% of people over 70 years have thyroid nodules. Level of thyroid hormones changes slightly.
Methods: Standard survey staining with hematoxylin, eosin, staining with iron hematoxylin according to Weigert, Karatzi hematoxylin, immunohistochemical method. Using digital processing programs for calculations, construction of three-dimensional models.
Results: In the process of aging, pronounced involutive changes occur in the structure of the thyroid gland. In adolescence the proportion of follicles (65%) prevails over the stroma, the follicles located compactly. In elderly people conversely and small follicles predominate. As we age, the thyroid gland shrinks in size but levels of the thyroid hormone triiodothyronine change little. The volume of the thyroid gland and the number of nodules increase with age, and according to mortality statistics, about 90% of people over 70 years of age have thyroid nodules. Considering the increase in its prevalence with age, nodular colloid goiter is often considered as an age-related transformation of the thyroid gland.
Conclusion: Due to the fact that atrophic changes in the background tissue of the thyroid gland occur with age, but the level of hormones in clinical blood tests changes slightly, there may be a relationship between this phenomenon and an increase in the number of nodular (often hormone-producing) pathologies over the years. Which indicates the advisability of studying the morphofunctional restructuring of the thyroid gland that occurs with age.

E-PS-18-066

Warthin-like mucoepidermoid carcinoma of the parotid gland, a challenging diagnosis in disguise: a case report and a literature review

A. Sifre-Ruiz*, M.M. Buda, C. Esquina Rodriguez, A.M. Cordovilla Morneo, I. Etxebarria Fernandez, M.V. Alarcón-Amaya, S. Fernandez Sole, M. Bronte Anaut
*Clinical Department Unit of Pathological Anatomy, OSI Araba, Araba University Hospital, Vitoria-Gasteiz, Alava, Spain

Background & objectives: Warthin-like mucoepidermoid carcinomas (WL-MEC) are an extremely rare subtype of salivary gland neoplasms characterized by the presence of WL lymphoid stroma. We present the case of an 89-year-old female with a left face palpable mass of months of evolution.
Methods: Microscopic haematoxylin-eosin sections of the parotidectomy specimen were reviewed along with those of the previous core needle biopsy. Sociodemographic and radiological data were also collected. A formalin-fixed paraffin embedded (FFPE) tissue block together with its respective slide were sent to another institution for molecular testing by FISH. A literature review was also performed.
Results: After a first radio-pathological diagnosis of Warthin's tumour, the patient underwent surgery. Gross and histological tissue sectioning revealed a well-demarcated, nonencapsulated lesion with a solid-cystic architecture consisting of oncocytic and mucoserous cells conforming pseudoglands within a variably dense lymphoid stroma. A conventional MEC was found in the centre of the lesion. The morphological findings could suggest a single tumour entity or a collision tumour, so it was decided to study the status of the MAML2 (11q21) gene in both components. Confirmation of genetic rearrangement supported the diagnosis of a WL-MEC. Published cases showed an adult female predominance, preferably on the left parotid gland. Most cases presented CRTC1-MAML2 gene fusion.
Conclusion: WL-MEC is a newly-described subtype of MEC. It is a diagnostic challenge, especially when differentiating it from a Warthin's tumour with mucinous and squamous metaplasia particularly in small-sized biopsies. Demonstration of MAML2 rearrangements and the presence of a conventional MEC area and lack of classic bilayered, oncocytic epithelium serve as a final diagnostic clue. Our findings are consistent with the scarce reports published in the literature.

E-PS-18-067

Riedel's thyroiditis with noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP): a case report about an unusual association

S. Ben Tekaya*, D. Chiba, W. Mokni, I. Bahri, H. Yoni, N. Ouini, A. Ben Abdelkader, B. Sriha, M. Mokni
*Department of pathology, Farhat Hached University Hospital, Sousse, Tunisia

Background & objectives: Riedel's thyroiditis (RT) is a very rare disease. No previous cases of its coexistence with noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) have been documented. We present such a case, detailing its histopathological characteristics alongside a literature review.
Methods: A 63-year-old male patient, with no medical history, who underwent a thyroidectomy following clinical suspicion of thyroid abscess.
Results: Macroscopically, the specimen appeared heterogeneous, whitish to brownish, and exhibited firm fibrous tissue infiltrating adjacent muscles. Additionally, a whitish nodule measuring 0.8cm was present within the left lobe. Microscopically, the thyroid gland displayed diffuse and extensive fibrosis, with marked infiltration of chronic and acute inflammatory cells, extending beyond the thyroid into adjacent muscle tissue. The extensive fibrosis also caused damage to blood vessels. Within the left lobe, the identified whitish nodule was found to be encapsulated, consisting of small vesicles lined by cells displaying nuclear atypia characteristic of papillary carcinoma. There were no papillae observed, nor vascular invasion or capsular rupture. The diagnosis of RT associated with NIFTP was retained.
Conclusion: The diagnosis of RT poses significant challenges due to the lack of typical clinical symptoms or imaging features. Clinicians and pathologists should be aware of RT to differentiate it from other disorders, especially malignant lesions. Its incidence is extremely low, with nearly 200cases documented in literature. The etiology remains unclear, though the systemic autoimmune hypothesis, particularly IgG4-related disease, is the most supported. Further research is mandatory to establish the best method of diagnosis and treatment of this condition.

E-PS-18-068

Novel BCOR mutation in pharyngeal sarcoma patients: a case report

W.J. Sung*, J. Hong, M.J. Song
*Daegu Catholic University, Republic of Korea

Background & objectives: Pharyngeal sarcomas are rare. The group of undifferentiated small round cell sarcomas is categorized into four types, including sarcoma with BCOR genetic alterations. We identified a novel BCOR mutation in the tissues of patients with pharyngeal sarcoma.
Methods: A 21-year-old male patient presented with sudden hemoptysis, experiencing cough-induced hemoptysis and difficulty breathing. Neck CT and MRI revealed a 6.5x3.6x2.7 cm protruding mass in the posterior wall of the oropharynx and hypopharynx. Laryngoscopy revealed an ulcerative submucosal mass. An excisional biopsy was performed due to suspicion of malignancy, followed by microscopic examination, immunohistochemistry, and mRNA sequencing.
Results: The specimen was fragmented into multiple small pieces. Microscopic examination revealed diffuse proliferation of primitive small round cells within delicate vascular networks. Numerous mitoses (over 10/10 HPF) and tumour necrosis were observed. Tumour cells exhibited diffuse nuclear BCOR positivity but were negative for cytokeratin, smooth muscle actin, desmin, and S100 in immunohistochemistry. Sequencing analysis identified twelve Cytosine-2,760-deleted reads out of 68 total BCOR reads, resulting in a truncated protein with 667 amino acids, approximately 1,000 amino acids shorter than the reference sequence (NM_017745). RT-PCR of BCOR showed various additional truncation mutant sequences. After 6 cycles of VDC/IE chemotherapy, the patient showed no residual tumours on biopsy or radiologic examination.
Conclusion: Until recently, a significant subset of Ewing-like sarcomas in children or young adults remained unclassified. The broad application of next-generation sequencing to undifferentiated round cell sarcomas has led to the identification of an increasing number of novel genetic abnormalities. We found a novel BCOR mutation in tissues from a patient with pharyngeal sarcoma. Further molecular studies using mutant clones from cell lines are needed to elucidate the details of the molecular mechanism underlying this novel BCOR sarcoma in the pharynx.

E-PS-18-069

Microsecretory adenocarcinoma of salivary glands: case report with literature review

A.M. Tomic*, D. Kablar, N. Tomanovic
*Institute of Pathology, Faculty of Medicine, University of Belgrade, Belgrade, Serbia

Background & objectives: Microsecretory adenocarcinoma of salivary glands is a recently described entity, with specific morphological, immunohistochemical and molecular characteristics. Since its initial report in 2019, less than 30 cases of microsecretory adenocarcinoma in salivary glands have been documented in the literature.
Methods: We present a case of an 80-year-old female with a large hard palate tumour invading the pterygopalatine fossa. Literature was obtained in PubMed Database search concluded with April 2024.
Results: On biopsy, tumour showed a diffuse, mostly tubular and microcystic growth, focally with basophilic secretion in the tubules. Parts of the tumour tissue were necrotic and covered in granulation tissue. Tumour cells were uniform, with an oval, hyperchromatic nucleus, embedded in a scarce fibromyxoid stroma. There was no sign of lymphovascular or perineural invasion. On immunohistochemistry, tumour cells showed positivity for CK7, S100, p63 and SOX10, while they were negative for p40, Calponin, SMA and Mammaglobin. Proliferative index was 5%. Dual break apart FISH probe showed rearrangement is SS18 gene.
Conclusion: Microsecretory adenocarcinomas usually arise from minor salivary glands in the oral cavity, and are generally considered low-grade, without propencity for recurrence and metastases. Several cases corresponding to the microsecretory adenocarcinoma have been reported in the skin and external auditory canal. Rarity of this tumour requires that all diagnosed cases be reported, in order to better understand its nature and behaviour.

E-PS-18-070
Thyroid gland sclerosing mucoepidermoid carcinoma with eosinophilia
K. Tsomaia*, I. Jikia, M. Jangavadze, N. Goishvili, N. Gabidzashvili, B. Arabuli
*TSU Aleqsandre Natishvli Institut of Morphology, Georgia

Background & objectives: Thyroid gland sclerosing mucoepidermoid carcinoma with eosinophilia (SMECE) is rare thyroid tumour. SMECE occurs mostly in females in the mid-50's. Extrathyroidal extension and regional lymph node metastasis is seen in about a half of cases.
Methods: Case Report. We report a case of a 41 year old women with an 16 mm hypoechoic thyroid nodule discovered on a routine ultrasonography. Fine needle aspiration was consistent with BSRTC V. The patient underwent total thyroidectomy, with central neck dissection. Post-operative histology was primarily reported as SMECE confined to the thyroid with 0/22 lymph nodes.
Results: Histopathological examination revealed a heterogeneous tumour in the background of autoimmune thyroiditis. The tumour exhibited extensive sclerosis in the stromal part with significant presence of eosinophils infiltrating, tubular-glandular and chordal structures composed of tumour cells showing squamous and mucinous differentiation, consistent with a diagnosis of mucoepidermoid carcinoma with eosinophilia. Mitotic figures were rarely observed, and there was no lymphovascular or perineural invasion. No metastatic lesions were found in the examined lymph nodes. CK5 and p63 confirmed squamous cells differentiation; CK7 and CEA were positive in mucinous cells and TTF1 positive in tumour cells.
Conclusion: To our knowledge this case presents the first SMECE of thyroid gland in Georgia. With this report we aim to raise awareness of this rare tumour, emphasize the importance of considering SMECE as a differential diagnosis for thyroid nodules, also provide additional helpful immunohistochemical marker for reaching the diagnosis.

E-PS-18-071
Extranodal follicular dendritic cell sarcoma: a case report and review of the literature
P. Vlachou*, N. Stavrinou, E. Spiteri, A. Therapontos, E. Athanasiou, E. Gioti
*Deparment of pathology, Evaggelismos General Hospital , Athens, Greece

Background & objectives: We present the case of a 56-year-old male with an extranodalfollicular dendritic cell sarcoma (FCCS). The aim of this abstract is to remind us of the fact that because of its rarity, FCCS is often misdiagnosed for another entity.
Methods: A 56-year-old male was operated in our hospital for a mass in the tonsils. Upon gross examination, the tumour was a well-circumscribed, solid lesion of 5.3cm in greatest diameter. Hematoxylin/eosin staining was used in the submitted sections. Immunohistochemistry for CD35, CD23, D240, p40, Clusterin, CD21, CK8.18, AE1/AE3, MelanA, HMB-45, CD68, SMA, S100, CD34, LCA, Calretinin, Desmin, ERG was also performed.
Results: The neoplastic cells were organised in whorls or solid pattern. They showed a spindle, ovoid or epithelioid morphology and medium to prominent cytologic atypia, with a moderate amount of eoshinophlic cytoplasm. The nuclei were oval or elongated with vesicular chromatin and sometimes exhibited a distinct eoshinophilic nucleoli and intranuclear pseudo-inclusions.Multi-nucleated forms were also noted. Finally, there was a mild perineoplastic lymphochytic infiltration. Immunohistochemistry showed diffuse and strong cytoplasmic expression of CD35, CD23 and D2-40. Medium to strong cytoplasmic expression of Clusterin and CD21 was also noted, while the rest of the markers were negative.
Conclusion: Based on both phenotypical and immunohistochemical findings the tumour was characterised as extranodal follicular dendritic cell sarcoma. FCCS is a rare malignant neoplasm arising from follicular dendritic cells, normally found in germinal centres and it can be misdiagnosed.Therefore, it is important to have the existence of this neoplasm in the back of our minds and use the appropriate panel of immunohistochemical markers to reach the diagnosis.

E-PS-18-072
Calcifying fibrous tumour of submandibular gland clinically mimicking malignancy - a clinicopathology review and updates
B. Wang*, N. Kandiyil, Y. Haidar
*UC Irvine School of Medicine, USA

Background & objectives: Calcifying fibrous tumour (CFT) is a relatively new entity, considered as a pseudotumour. The pathogenesis of this mass forming is unknown. We report the first case of CFT as an expansile hard mass involving submandibular gland, clinically masquerading as malignancy.
Methods: Case of a 70-year-old woman, who presented with a fist sized rock-hard upper neck mass, which was slowly growing. Occasionally, she felt pain and pressure. Recently, she noticed the mass getting bigger. Radiological impression was a malignant tumour of submandibular gland. Fine Needle Aspiration Cytology and biopsy of the mass reported atypical cells. The patient was referred to Otolaryngology Surgery.
Results: The patient underwent submandibular mass resection. At surgery, intraoperative frozen sections reported a fibrous tumour with extensive calcification. Excised mass was 5 cm in size, with lobulated, white, firm, and non-encapsulated tumour texture. Microscopic examination of submandibular mass demonstrated a fibrous mesenchymal tumour with dense hyalinized stroma and massive islands and nests of dystrophic calcification. The unique morphology was striking for numerous varying sized psammomatous calcifications. A panel of immunohistochemical studies revealed a benign fibrous tumour without features of malignancy identified. After correlation of clinicopathology review and imaging study, the pathological diagnosis was finalized "a CFT of submandibular gland".
Conclusion: A few studies reported that CFT can affect extremities, gastrointestinal tract, chest wall, trunk, and axillary soft tissue. To the best of our knowledge, this is the first described CFT of submandibular gland, clinically mimicking a malignant tumour. Clinical and radiological differentials could be challenging. We report its characteristics to

clarify diagnostic features for distinguishing benign from malignant tumours, in order to avoid potential clinical pitfalls for best treatment management.

E-PS-18-073

Nasopharyngeal amyloidosis: a rare encounter within nasopharyngeal carcinoma

M. Zghal*, S. Hidouri, M. Sellami, O. Boudaouara, C. Chaari, I. Charfeddine, T. Sellami Boudawara, R. Kallel
*Department of Pathology, Habib Bourguiba University Hospital, Sfax, Tunisia

Background & objectives: Tumour-associated amyloid is well known and has been seen in several tumours. The association of amyloidosis with nasopharyngeal carcinoma (NPC) is extremely rare and poorly documented. We present an exceptional case of localized amyloidosis in NPC to highlight this entity.
Methods: A 57-year-old man, with no significant medical history, presented with unilateral nasal obstruction and progressive hypoacusis over several months. Nasal endoscopy showed a polypoid mass involving the posterior wall of the nasopharynx. The patient underwent a biopsy of the nasopharyngeal mass. Two tissue fragments were sent for histopathological assessment.
Results: Histopathological analysis revealed a poorly differentiated tumour proliferation arranged in sheets and exhibiting a syncytial appearance. The tumour cells showed enlarged round nuclei, prominent nucleoli, and moderate cytoplasmic content. The stroma exhibited a lympho-plasmacytic inflammatory infiltrate, interspersed with tumour cells. Immunohistochemically, tumour cells expressed pankeratin. This confirmed the epithelial origin of malignant cells. Deposits of eosinophilic, granular, and fibrillary material were present in both the extracellular and intracellular components. This material stained pink with Congo red and showed apple green birefringence under cross-polarized light, consisting with amyloid deposits. In tumour cells, the deposits appeared as acidophilic hyaline areas distending the cytoplasm. The final diagnosis was localized amyloidosis within undifferentiated NPC.
Conclusion: Nasopharyngeal amyloidosis is a rare condition, with approximately forty documented cases in the literature. The rarity of this condition, along with its sporadic association with NPC, underscores the importance of clinical recognition and histopathological confirmation. Only a few reports of localized amyloidosis in NPC had been described. The nature of amyloid deposits in NPC is unclear, and a neoplastic origin is suggested. Further research is needed to better understand this rare association and develop precise diagnostic and treatment guidelines.

E-PS-19E-Poster Session Molecular Pathology

E-PS-19-001

Utility of massive sequencing (Ngs) in the identification of biomarkers in biliopacreatic cancer

I.C. Abitei*, T. Pereda Salguero, P. Gaspar López-Cózar, E. Fernández Torres, M.D. Bautista de Ojeda
*Hospital Universitario Costa del Sol, Spain

Background & objectives: In recent years, the development of new molecular biology diagnostic techniques has made it possible to understand the main genetic alterations involved in the development of pancreatobilliary cancers and to identify certain biomarkers that are predictive of response to treatment.
Methods: We performed NGS on 35 samples from patients with biliopancreatic neoplasms diagnosed in our service between 2020 and 2024, using the technology Ion Torrent (ThermoFisher). This methodology allows the simultaneous detection of up to 52/161 relevant hotspots, single nucleotide variants (SNVs), insertions, deletions (INDELs), copy number variations (CNVs), fusions and complete exonic sequence coverage from DNA and RNA obtained.
Results: Of the 22 cholangiocarcinoma samples analysed, 2 presented a genetic alteration currently known as biomarker: IDH1- R132C, whose prevalence is 3% in extrahepatic tumours and 10-20% in intrahepatic tumours, has one approved drug and five in development. Of the 13 samples of pancreatic cancer analysed, 1 presented amplification of ERBB2; 1 presented mutation BRAF – V600E and 2 cases presented KRAS-G12C, with approved targeted therapies. Other mutations with therapeutic potential like BRCA2, PIK3CA-G914V, BRAF- L597V, KRAS-Q61H, KRAS-G12, ERBB2-T862A, ERBB2-S310F were discovered in 13 of the analised cases.
Conclusion: Thanks to the massive sequencing study (NGS) that allows us to detect a high number of possible alterations with a single test that requires little tissue material, 17% of our patients could benefit from targeted treatment and and 37% could access available clinical trials.

E-PS-19-002

Comprehensive molecular genetic profiling: homologous recombination deficiency as a targeted therapeutic option for solid tumours

I. Adamik*, Z. Melegh, T. Strausz, L. Báthory-Fülöp, A. Simon, Z. Küronya, E. Soós, E. Tóth
*National Institute of Oncology, Hungary

Background & objectives: Homologous recombination deficiency (HRD) is a genomic signature that can predict the therapeutic response to PARP inhibitor therapy, and can be identified by comprehensive genetic profiling (CGP). Appropriate patient selection is inevitable to identify those who would benefit the most.
Methods: 232 NGS-based Oncomine Comprehensive Assay Plus panel tests were performed at our institute over two years (2022-2023). The combined HRD score was introduced in January 2023. Prior to this, HRD status was predicted by individual scores of LOH, LST and TAI (98 patients) and was later retrospectively reassessed. After January 2023, HRD was assessed by HRD score only (134 patients).
Results: In the pre-January 2023 cohort, 45 tumours were predicted to be PARP inhibitor-sensitive. Sixteen patients received olaparib; treatment improved overall survival (OS) to 14.84 months from 12.61 months. In the post-January 2023 cohort, 13 tumours with high HRDs (HRD >16) were identified. Six patients received olaparib; treatment improved OS to 12.07 months from 5.59 months. The largest histological cohort with high HRDs was high-grade serous ovarian carcinoma (HGSOC, 10 patients); 6 patients received olaparib, and the OS increased to 12.78 months from 10.35 months. Nine patients with other histologies had high HRDs and 3 received therapy. Treatment improved OS to 17.64 months from 10.61 months.
Conclusion: There was an improvement in OS when patients received PARP inhibitor therapy based on individual scores, although the improvement was more prominent when therapeutic decisions were based on HRD scores. Patients with all histologies, including HGSOC and other histologies, equally benefited from olaparib therapy. We therefore believe that genomically instable non-HGSOC tumours could also benefit from PARP inhibitor therapy, while individual scores could be partly used as a substitute to predict therapeutic response.

Funding: The project was implemented with the support from the National Research, Development and Innovation Fund of the Ministry of Culture and Innovation under the National Laboratories Program (National Tumor Biology Laboratory (2022-2.1.1-NL-2022-00010))) Grant Agreement with the National Research, Development and Innovation Office.

E-PS-19-003

High tumour mutation burden assessed by comprehensive molecular genetic profiling as a targeted therapeutic option for solid tumours

I. Adamik*, Z. Melegh, T. Strausz, L. Báthory-Fülöp, E. Csernák, Z. Küronya, E. Soós, E. Tóth
*National Institute of Oncology, Hungary

Background & objectives: The tumour mutation burden (TMB) is an agnostic biomarker of the response to immune checkpoint inhibitor therapy. We assessed the TMB across multiple solid tumour types by comprehensive genetic profiling (CGP) via next-generation sequencing (NGS).
Methods: 232 Oncomine Comprehensive Assay Plus panel tests were performed between January 2022 and December 2023 on a Thermo Fisher Ion S5 platform at our institute. Genomic DNA and total RNA were extracted from formalin-fixed paraffin-embedded tissue blocks. In addition to the TMB status (high TMB defined as more than 10 mutations/megabase), we also assessed microsatellite instability and POLE mutation.
Results: Twenty-seven patients had high-TMB tumours. The mean age of the patients with a high TMB was 59 years (from 20 to 77 years). High TMB status was most common in patients with high-grade neuroendocrine tumours and gastrointestinal carcinomas (18.5% each). Eight patients received immune checkpoint inhibitor therapy (7 pembrolizumab and 1 atezolizumab). Immune checkpoint inhibitor therapy improved OS to 14.01 months from 5.4 months. The average progression-free survival (PFS) in the medicated group was 13.5 months. Progression was the main reason why patients discontinued immune checkpoint inhibitor therapy. Regarding the molecular alterations associated with high TMB, 3 tumours were microsatellite instable, and 2 patients had pathogenic somatic POLE mutations.
Conclusion: TMB status determined by CGP was found to be an effective method for predicting the response to immune checkpoint inhibitors; both PFS and OS improved markedly for patients who received therapy. In our experience, TMB status, along with microsatellite instability and POLE mutation status, can be used as a predictive biomarker for therapeutic response in a wide range of histologies.

Funding: The project was implemented with the support from the National Research, Development and Innovation Fund of the Ministry of Culture and Innovation under the National Laboratories Program (National Tumor Biology Laboratory (2022-2.1.1-NL-2022-00010))) Grant Agreement with the National Research, Development and Innovation Office.

E-PS-19-005

BRAF mutation in colorectal cancer: experience of the pathology department of Mohammed VI University Hospital Centre, Marrakesh, Morocco

O. Ait Ouhssain*, C. Dabaj, H. Rais, B. Zinbi
*Pathology department of the Mohammed VI University Hospital Center of Marrakesh, Morocco

Background & objectives: Colorectal cancer ranks among the most prevalent malignancies worldwide, with mortality rates reaching approximately 33% in developed countries. Detecting the BRAF gene mutation contributes to the diagnosis of sporadic colorectal cancers and the development of anti-BRAF treatments.
Methods: This retrospective study involved 170 cases of colorectal cancer, where BRAF gene mutation screening was conducted between 2016 and 2023 at the Pathology Department of the Mohammed VI University Hospital Centre of Marrakesh, using internationally validated tests.
Results: The average age was 55 years, with a male-to-female sex ratio of 1.25. Biopsies accounted for 54.6% of the received samples. Colorectal cancer mainly manifested as Lieberkühn adenocarcinoma (85% of cases), followed by mucinous adenocarcinoma. Evaluation of differentiation revealed that colorectal cancer was predominantly moderately differentiated (60% of cases). BRAF gene mutation was found in 8 cases, accounting for 4.7% of the total.
Conclusion: Approximately 10% of colorectal cancer patients exhibit BRAF gene mutations. Colorectal cancers with BRAF V600E mutations display specific histopathological characteristics and are often associated with lymph node and peritoneal progression. BRAF mutation presence is also linked to sporadic microsatellite instability (MSI) in 20 to 40% of cases, underscoring the importance of MSI phenotype screening for effective therapeutic approaches. BRAF mutation analysis should be contextualized within the molecular landscape to fully leverage its predictive, prognostic, and therapeutic potential in colorectal cancers.

E-PS-19-007

A simple and cost effective patient derived ex vivo 3D spheroid culture as a promising tool for functional based cancer therapy predictions purpose

A. Ambekar*, A. Banerjee, P. Pawar
*ACE Diagnotics, India

Background & objectives: Breast cancer therapy is based on hormone receptor status. However, due to unavailability of any predictive functional therapeutic platform, pathological complete response rates remain poor. To establish method to develop ex-vivo 3D spheroid to mimic in vivo tumour pathology
Methods: By the mechanical and enzymatic tissue dissociation process, in vitro tumour spheroids were generated in a scaffold 96 well plate format. These were compared by immunohistochemistry with parental tumour derived HE. IHC markers used were Pan cytokeratin, GATA 3. SMA and ER PR and Her2neu
Results: Data suggests, out of five tested samples four resulted in successful generations of spheroids and three of them (one having insufficient slices for complete IHC evaluation) exhibited correlating with above mentioned IHC marker expressions.
Conclusion: The data suggests, ex vivo 3D spheroids could be useful to recapitulate parental tumoural homology and could be a valuable resource for functional based personalized cancer therapy prediction purposes. Furthermore, gene expression data (tumour immune microenvironment) and ex vivo chemotherapy-based drug response analysis is currently under evaluation.

E-PS-19-008

TIM3 expression in human cancer: a tissue microarray study on 16,458 patients

S. Büyücek, S. Etebar Farinani, N. Schraps, T.S. Clauditz, M. Lennartz, F. Lutz, M. Kluth, N. Gorbokon, E. Bady*, F. Viehweger, S. Steurer, K. Möller, R. Simon, G. Sauter, T. Krech
*Institute of Pathology, University Medical Center Hamburg-Eppendorf, Germany

Background & objectives: TIM3 is an inhibitory immune checkpoint mainly occurring in subsets of lymphocytes and macrophages in tumours, and a target of immune checkpoint inhibitor cells. TIM3 can also occur on cancer cells but available data is sparse.
Methods: To comprehensively assess the prevalence of TIM3 expression in cancer, a tissue microarray containing 16,458 samples from 134 different tumour types and subtypes was analysed by immunohistochemistry. TIM3 expression of tumour cells and macrophages was recorded semi-quantitatively.

Results: TIM3 positivity on tumour cells was predominantly seen in clear cell (61.9%) and papillary (62.5%) renal cell carcinomas (RCCs) but also several mesenchymal neoplasms (up to 16.0%), Hodgkin's (25.0%) and non-Hodgkin's lymphomas (up to 9.1%), epithelial thymomas (6.9%), endometrioid (1.4%) and serous high-grade ovarian carcinomas (0.7%). In clear cell RCCs, high TIM3 expression in tumour cells was linked to low grade ($p<0.05$), low pT ($p=0.0014$), and absence of nodal metastases ($p=0.028$). Across all tumour entities, TIM3 positivity on macrophages was linked to increased infiltrating lymphocytes ($p<0.0001$), unfavourable tumour parameters in clear cell RCC and breast cancer but to favourable parameters in colon cancer.
Conclusion: Tumour cell TIM3 expression is a frequent feature of RCCs where high expression is associated with parameters of aggressive disease. TIM3 expression in tumour associated macrophages is abundant and its clinical significance is tumour type dependent.

E-PS-19-009
Novel recombinant monoclonal antibodies for G protein-coupled receptor (GPCR) research and disease characterization
A. Ball*, Y.L. Hsieh, C.K. Huang, S. Huang, S.R. Wu, J. Liu, P.S. Peng, C.Y. Lin
*GeneTex, Inc., USA

Background & objectives: Recombinant monoclonal antibodies (rAbs) are preferred tools for research and diagnostic applications as they offer reproducible performance and consistent supply. Ongoing efforts strive to create new rAb reagents against challenging proteins for which there are few or no reliable products.
Methods: G-protein coupled receptors (GPCRs) are seven-pass transmembrane domain proteins involved in a plethora of physiological and pathophysiological processes. Approximately 30-40% of all prescribed drugs modulate GPCR activity, and other GPCRs could be targeted if better antibodies were available. GeneTex is leveraging its rAb production platform and enhanced validation techniques to develop specific GPCR antibodies for research and possible diagnostic use.
Results: GeneTex's rAb production workflow employs a multiparameter FACS-based methodology to select antigen-specific IgG+ memory B cells from an immunized rabbit (Starkie, 2016). The heavy and light chain variable region genes from single cells producing the GPCR-specific IgG are cloned and co-expressed in mammalian cells to generate the functional antibody. Antibody characterization involves knockout/knockdown (KO/KD), differential expression comparison in cells and tissues, cell fraction enrichment, application-specific testing (e.g., immunohistochemistry), and other methodologies. Presently, specific antibodies for the dopamine D2 receptor (DRD2), retinoic acid-induced protein 3 (RAI3), chemokine receptors CXCR2, CXCR4, and CXCR7, melanocortin receptor 1 (MC1-R), CD97, GLP1R, mGluR5, and AGTR1 (among 20 total GPCR proteins presently) have been developed.
Conclusion: The described antibody manufacturing and assessment approach has resulted in the production of well-validated monoclonal rAbs for 20 human GPCRs. GeneTex's goal is to create rAbs against almost all of the ~360 human GPCRs that are not visual, olfactory, or taste receptors, including perhaps 140 GPCRs considered to be orphan receptors of which little is known. The overarching vision is that these novel reagents will accelerate both academic research as well as clinically relevant diagnostics development and human disease characterization.

E-PS-19-010
Detection of circulating HPV-DNA in liquid biopsy compared to histology in a large tumours spectrum
N. Ben Othman*, V. Euzen, D. Vasseur, C. Smolenschi, J.Y. Scoazec, M.A. Bani
*Department of Medical Biology and Pathology, Morphological pathology laboratory, Gustave Roussy Cancer Campus, Villejuif, France

Background & objectives: Human papillomavirus (HPV) associated tumours are a big burden in healthcare. Detection of viral circulating DNA is a new described biomarker for these tumours. Our work aimed to evaluate the accuracy of this biomarker in a large spectrum of tumours.
Methods: This retrospective analysis included patients with positive circulating HPV DNA (ctHPV-DNA) identified in our institution between 2021 and 2023. The liquid biopsy was analysed by FMI in the clinical trial STING. Clinical features for each patient were obtained from the medical files. We reviewed the localization of different tumours, the histologic type, p16 status and the HPV-in situ hybridization results(HPV-ISH).
Results: A total of 5179 patients have had a liquid biopsy, among which 89 patients had a positive ctHPV-DNA. P16 was positive in 71 cases, among which, two patients had negative HPV-ISH (uterine endometrioid carcinoma and high grade serous carcinoma of the ovary). Positive HPV-ISH was found in squamous cell carcinomas in 96% of cases. They were localized in the cervix (n=23), head&neck (n=21), anal canal (n=12), rectum (n=6), vagina (n=4), oesophagus (n=2) and vulva (n=1). The tumour burden was high in 8 cases (between 20 and 64 Mut/10MB). All p16 negative cases (n=6) were also negative by HPV-ISH including a large spectrum of HPV non associated tumours.
Conclusion: Our results suggest that ctHPV-DNA is a promising prognostic biomarker with a high sensitivity and specificity. However, there are conflicting results whether ctHPV-DNA can be found in blood from patients with pre-malignant lesions or non associated HPV tumours ; further studies are needed to fully elucidate this question.

E-PS-19-011
The structure of germline variants in neuroendocrine tumours in Moscow patients
T. Yanova, A. Danishevich, N. Bodunova*, M. Byakhova, M. Makarova, S. Gadzhieva, D. Isaeva, I. Khatkov
*Moscow Clinical Scientific Center named after A.S. Loginov, Russian Federation

Background & objectives: Neuroendocrine tumours (NETs) are often related with MEN-1, MEN-2 syndromes. The lack of data on the prevalence of hereditary forms and unclear disease pathogenesis complicate the personalized approach of monitoring. Therefore, genetic testing is a relevant method for studying NETs.
Methods: Blood samples from 81 patients with the following localizations of NETs were analysed: pancreas (60/81), colon (9/81), stomach (8/81), small intestine (2/81), lungs (1/81) from The Loginov Moscow Clinical Scientific Center. All patients underwent medical and genetic counseling, as well as psychologist's consultation. The study included whole genome sequencing (WGS), all detected genetic variants were validated by Sanger sequencing.
Results: According to the data of our study, pathogenic/likely pathogenic variants were detected in 19.7% (16/81). In our study, mutations were detected in the group of patients with pancreatic NETs (93.7%) and colorectal NETs (6.3%). Mutations in MEN1(chr11:g.64807677A>G, chr11:g.64808006T>A) gene were detected in two patients with pancreatic NETs. Pathogenic variants in NTHL1 (chr16:g.2046238G>A), WRN (chr8:g.31087830A>T), BRCA2 (chr13:g.32340301delT), SDHA (chr5:g.251439 C>T), and of uncertain clinical significance in BLM (chr15:g.90761227delCTT), PMS2 (chr7:g.5987497G>C), CHEK2 (chr22:g.28695752C>G, chr22:g.28725099A>G), FANCI (chr15:g.89314612G>A), BRCA2 (chr13:g.32398608delinsGAA

TTATATATCT), PLA2G2A (chr1:g.19978380C>T). A variant of uncertain clinical significance in BRCA2 (chr13:g.32340527T>A) gene was identified in colorectal NET. The proportion of hereditary forms of NET in the study group was 1.2% (1/81).
Conclusion: According to literature data, the most frequent localization of NETs is gastrointestinal tract (60%), the predominant localization is blind intestine (17.1%), rectum (16.3%). In our study, pancreatic NETs was in 74,1%. The results of WGS show causative variants in pancreatic NETs. The detected pathogenic variant in MEN1 gene substantiates the necessity of additional examination of the patient to detect neoplasms of new localizations. The significance of other genes in the development of NETs should be further studied.

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E-PS-19-012
A retrospective evaluation of the occurrence of MAPK and PI3K/Akt alterations implicated in anti-EGFR treatment resistance in patients with left-sided colorectal cancer (ls-CRC)
M. Byakhova*, T. Antonova, I. Pokataev, M. Ivanov, A. Lebedeva, V. Mileyko, A. Semenova, C. Babadzhanova, A. Tryakin, M. Fedyanin, V. Galkin
*City clinical oncology hospital No. 1, Russia

Background & objectives: Recent findings from the PARADIGM and PRESSING studies highlight the need for further clarification of the role of hyperselection of CRC patients for anti-EGFR therapy.
Methods: RAS/RAF-wt (as by PCR - performed in various laboratories) ls-CRC patients who were treated at City clinical oncology hospital #1 in 2019-2022 were retrospectively studied by NGS (Solo-test Atlas Pro panel). NGS was performed centrally on the patients' FFPE samples. Study was supported by a grant from the Moscow centre of innovative technologies in healthcare (№2102-2/23).
Results: Out of 118 patients, 44 (37.3%) harbored at least one mutation associated with anti-EGFR resistance. A total of 27 patients had RAS mutations (KRAS common, n=14 (12%); KRAS uncommon, n=10 (8.5%); NRAS, n=3 (2.5%)), 8 patients had BRAF mutations (classI, n = 4 (3%); class II/III - 4 (3%)). All RAS-positive by NGS samples were verified as positive by PCR in a central laboratory. Among RAS/BRAF-negative patients (n=83), mutations associated with anti-EGFR resistance were found in the following genes: ERBB2 (n=3, 2.5%), PTEN (n=3, 2.5%), PIK3CA (n=2, 1.7%), FGFR1 (n=1, 0.8%), ERBB3 (n=1, 0.8%). Single patient was found to be MSI-positive. Any somatic mutation was identified in 100 (86%) patients.
Conclusion: Wide spectrum of PCR-test systems used across various laboratories may result in 14% false-negative results on RAS-mutation testing in ls-CRC. The use of a comprehensive NGS panel may facilitate the elimination of false-negative results and identify an additional 14.5% of ls-CRC patients with non-RAS/RAF mutations who are unlikely to benefit from anti-EGFR therapy. Prospective study was initiated to validate this hypothesis (NCT06226857).

Funding: This research is implemented within the Grant "Optimizing the methodology for selecting first-line therapy for the treatment of patients with metastatic or locally advanced colorectal cancer".

E-PS-19-013
Blood MSI dynamics as a predictive biomarker of immune checkpoint inhibitor therapy efficacy in colorectal cancer (CRC): preliminary results from an observational trial
M. Byakhova*, E. Veselovsky, V. Yudina, O. Kuznetsova, D. Kravchuk, A. Lebedeva, E. Belova, A. Taraskina, T. Grigoreva, A. Kavun, V. Nikulin, V. Mileyko, A. Tryakin, M. Fedyanin, M. Ivanov
*City clinical oncology hospital No. 1, Russia

Background & objectives: Microsatellite instability(MSI) is a biomarker of ICI-therapy benefit in colorectal cancer(CRC). Mutational dynamics in liquid biopsy(LB) have been proven to be predictive of therapeutic outcomes. The dynamics of MSI in LB(bMSI) has not been evaluated for monitoring response to ICI.
Methods: Patients with MSI+ (any method) CRC who were candidates for ICI were recruited. Previous use of ICI was not allowed. LB samples were collected before (BL) and 2 and 4 weeks (2W, 4W) after the start of ICI, and at every follow-up. LB samples were analysed via NGS (Solo Atlas Pro panel; 34 genes, 71 STRs for MSI).
Results: Nine CRC patients completed treatment. Patients with localized disease (n=7) received neoadjuvant treatment with prolgolimab (anti-PD-1) (2 CR, 4 PR, 1 death); 2 patients with advanced/metastatic CRC received nivolumab (1 SD, 1 PD). Among the 9 BL LB samples, 7 (77%) were MSI+; and 7 samples had at least one mutation. The dynamics of bMSI and VAF of the observed mutations were consistent through the course of treatment (pearson 0.89). Patients who had OR/SD had undetectable bMSI at first follow-up, while patients with PD or deceased had an increase in bMSI (at least 2x) at follow-up or earlier.
Conclusion: MSI can be evaluated quantitatively via LB to trace patients' dynamics through the course of treatment. Dynamics of bMSI correlated with the mutational dynamics and treatment outcomes. bMSI was undetectable at follow-up in patients with OR/SD.

Funding: Study was supported by the Russian Science Foundation (grant № 22-75-10154)

E-PS-19-014
IDH 2 - a new gene for personalized therapy in pulmonary adenocarcinomas – reports of two cases
L. Carvalho*, A.F. Ladeirinha, A. Alarcao, M. Reis Silva, T. Ferreira, M. Viseu, M.A. Santos, G. Nogueira Fontinha, J. Pimentel, V. Almeida, V. Sousa
*1. Institute of Anatomical and Molecular Pathology, Faculty of Medicine of the University of Coimbra, Coimbra, Portugal 2. CIMAGO – Research Center for Environment, Genetics and Oncobiology, Faculty of Medicine, University of Coimbra, Coimbra, Portugal 3. Pathology Service, University Hospital Anatomical Pathology Coimbra – Portugal

Background & objectives: Exon/genome sequencing have uncovered potential additional genomic alterations to be targeted such as KRAS G12C, ERBB2, MET mutations and RET, NTRK1/2/3 translocations. IDH1/IDH2 mutations already known in acute myeloid leukemia/diffuse gliomas/cholangiocarcinoma/chondrosarcoma, have been reported in pulmonary carcinomas - 0.4%-1.1% incidence.
Methods: Case 1 – Man 69 years old; solid adenocarcinoma of the lung.
Case 2 – Female 60 years old; solid adenocarcinoma of the lung.
Tumour cells manual macrodissection and nucleic acid extraction were carried out with MagMAX FFPE DNA/RNA Ultra Kit. Mutational search was performed by next-generation sequencing with Oncomine Precision Assay Panel on Genexus (Thermo Fisher Platform).
Results: Case 1 – Missense mutation p.Arg140Gln in IDH2 gene, according to ClinVar - no data submitted for somatic clinical impact and for oncogenicity; germline level described as pathogenic/liked pathogenic. No common mutations for current therapeutic targeted genes were identified.
Case 2 – Missense mutation, p.Arg140Trp in IDH2 gene, according to ClinVar - no data submitted for somatic clinical impact and for oncogenicity; germline level described as uncertain significance. MET-MET.M13M15.1 variant - corresponds to MET exon 14 skipping targeted therapy available (MET TKIs); nonsense mutation p.Arg196Ter in TP53 gene, according to ClinVar, no data submitted for somatic clinical impact and for oncogenicity; and germline level described as pathogenic.

Conclusion: Known under low incidence – mutations require research for 0.4% to 1.1 in pulmonary adenocarcinomas, IDH1/2 inhibitors prescription due to high prevalence of lung carcinoma worldwide. Mutations in IDH1/2 gene may be branching drivers leading to lower subclonality evolution with predictable benefit of IDH1/2 inhibitors.The accumulation of more known cases with IDH1/2 mutations is necessary to elucidate clinicopathological characteristics/clinical evolution after target therapy, in order to reforce the new interpretation of malignant tumours postponed survival through conversion of cell cycle.

E-PS-19-015

Pulmonary adenocarcinoma: EGFR exon 19 insertion – report of 3 cases

L. Carvalho*, A. Alarcao, A.F. Ladeirinha, M. Reis Silva, T. Ferreira, M. Viseu, M.A. Santos, J. Pimentel, G. Nogueira Fontinha, V. Almeida, V. Sousa
*1. Institute of Anatomical and Molecular Pathology, Faculty of Medicine of the University of Coimbra, Coimbra, Portugal 2. CIMAGO – Research Center for Environment, Genetics and Oncobiology, Faculty of Medicine, University of Coimbra, Coimbra, Portugal 3. Pathology Service, University Hospital Anatomical Pathology Coimbra – Portugal

Background & objectives: EGFR exon 19 insertions comprise rarer mutation in pulmonary adenocarcinoma (0.11% of lung carcinomas). Patients have been effectively treated with sequential EGFR tyrosine kinase inhibitors (TKIs), still without effective clinical definition due to few described cases in literature.
Methods: Case 1 - DNA sequencing was performed with Sanger sequencing (2014).
Cases 2 and 3 - DNA/RNA sequencing in next-generation sequencing (Genexus, Oncomine Precision Assay Panel, Thermo Fisher Platform). Manual macrodissection was performed and nucleic acid extraction was carried out with the MagMAX FFPE DNA/RNA Ultra Kit.
Results: EGFR exon 19 insertions were as follow:
Case 1 - p.Lys739_Ile744dupLysIleProValAlaIle by Sanger sequencing;
Case 2and 3 - p.Ile740_Lys745dup by Genexus.
Conclusion: The sequenced adenocarcinomas presented predominant acinar pattern as well as solid, papillary/micropapillary and lepidic patterns, respectively, without relevance for the mutational status. Multiple parallel sequencing (MPS) allows accumulation of tumoural mutational knowledge overtaking concise standardized mutational equipment. Considering effective lab costs, clinical decisions for therapeutic available options and MPS is now the more advisable method.

E-PS-19-016

Pulmonary adenosquamous carcinoma - case series for mutational status

L. Carvalho*, A.F. Ladeirinha, A. Alarcao, M. Reis Silva, T. Ferreira, M. Viseu, M.A. Santos, G. Nogueira Fontinha, J. Pimentel, V. Almeida, V. Sousa
*Portugal

Background & objectives: Pulmonary adenosquamous carcinoma (0.4%-4% of pulmonary carcinomas) have poor prognosis beyond controversial therapeutic/genetic profile characteristics. Adenocarcinoma/epidermoid carcinoma separated differentiation or defined by immunohistochemistry co-infiltrated tumour cells, present similar EGFR-driver and other rarer mutations. A case series recalls this knowledge.
Methods: Following WHO 2021 classification criteria for pulmonary adenosquamous carcinoma, two Groups were compiled: 1–5 cases with separate patterns and 2–10 cases with integrated cellular immune-expression CK7/CK5.6/TTF1/mucin production (PAS-D). Mutational research by next-generation sequencing (Genexus, Oncomine Precision Assay Panel, Thermo Fisher Platform), after manual macrodissection, was performed and nucleic acid extraction, followed MagMAX FFPE DNA/RNA Ultra Kit, manufacturer instructions.
Results: Group 1 – 2 women and 3 men; ages ranging between 49/74; 3 bronchial/transthoracic biopsies and 2 lobectomies-surgical specimens. Group 2 –3 women and 7 men; ages ranging between 56/75; 3 bronchial/5 transthoracic biopsies and 2 surgical specimens.
The mutational status was as follows:
- Group 1 – of the five cases, two presented with mutations in the MET gene, one of which concomitant PI3KCA mutation.
- Group 2 – there were mutations in EGFR, KRAS, ALK, PIK3CA, TP53, FGFR1, RET, HER2 and NTRK3, found in 8 of the 10 included cases, indicating special diversity; three cases had particular concomitancy: PIK3CA, TP53, FGFR, RET, HER2, EGFR amplification and NTRK3 mutation.
Conclusion: Massive parallel sequencing and personalized therapeutic targets for personalized mutational status might allow patients with adenosquamous carcinomas to improve survival at the different levels of progression. Adapted criteria in the classification recognized by WHO 2021, which tumoural cellular level sub-classification might be a particular sub-typing with particular outcomes as exemplified in the present mutational exercise. This small series, defined after routine IHC classification correlated with tumoural heterogeneity/clonality previewed for adenosquamous carcinoma.

E-PS-19-017

Harnessing the potential of Next-Generation Sequencing (NGS) to unravel the molecular landscape of lung cancer: a case report on a middle-aged patient with two synchronous lung adenocarcinomas harbouring two distinct actionable pathogenic genetic variants

N. Chiote*, G. Carrola, D. Sá, T. Santos, C. Vilasboas, J.R. Vizcaíno, N. Jorge Lamas
*1. Institute of Anatomical and Molecular Pathology, Faculty of Medicine of the University of Coimbra, Coimbra, Portugal 2. CIMAGO – Research Center for Environment, Genetics and Oncobiology, Faculty of Medicine, University of Coimbra, Coimbra, Portugal 3. Pathology Service, University Hospital Anatomical Pathology Coimbra – Portugal

Background & objectives: Comprehensive molecular testing plays a significant role in the optimized treatment of cancer. The presence of specific genetic mutations has the prospect to provide effective patient-targeted therapies, with less side effects and substantial gains in survival and quality of life.
Methods: We report the case of a 64-year-old woman, with smoking habits, harbouring two left lower lung nodules on positron emission tomography (PET). Biopsies were directed at both nodules, however, significant biological material was only retrieved from the most superficial lesion, revealing a lung adenocarcinoma. A left lower lobectomy was performed, the two tumours identified and submitted for histological evaluation.
Results: Macroscopic examination of the surgical specimen revealed two well-defined, non-capsulated, solid whitish lesions, one of 3.5x3.4x1.8cm and the other of 1.5x1.5x1.2cm. Upon histological analysis, both lesions had characteristics of adenocarcinoma, but one displayed tubular (40%), micropapillary (30%), solid (20%) and papillary patterns (10%), whereas the other consisted of solid (90%) and tubular patterns (10%). The neoplastic cells were TTF1-positive in both tumours. Next-Generation Sequencing (NGS) testing was performed for each tumour, showing a pathogenic EGFR p.E746_A750del mutation in the 3.5 cm neoplasia and a pathogenic KRAS p.G12C mutation in the 1.5 cm neoplasia, suggesting the presence of two synchronous lung adenocarcinomas.
Conclusion: In this case we found two actionable mutations in two synchronous lung adenocarcinomas, highlighting the utmost importance of

thorough molecular testing in lung cancer. The ability to perform NGS in both tumours helped to define their synchronous nature and also to expand the possibilities regarding a tailored and an effective treatment.

E-PS-19-018

Analytic concordance of a novel pan-tumour HRD signature biomarker between AVENIO tumour tissue CGP Kit V2 and FoundationOneCDx

J. Choi*, H. Lo, N. Zhang, R. Chien, M. De Vos, S.E. Trabucco, T. Wieland, S. Wang, J. Jungmann, R.S. Huang, A. Schrock
*Roche Diagnostics Solutions, USA

Background & objectives: Homologous recombination deficiency (HRD) is found in many cancers. Existing HRD biomarkers have been developed for limited tumour types. AVENIO® Tumour Tissue CGP Kit V2 (AVENIO CGP, For Research Use Only) introduces a pan-tumour HRDsignature (HRDsig), adopted from FoundationOne®CDx (F1CDx).
Methods: HRDsig is a scar-based approach that utilizes >100 copy number features to detect genomic and non-genomic mechanisms of HRD. HRDsig was implemented on AVENIO CGP and compared with F1CDx for 317 Formalin-Fixed Paraffin-Embedded Tissue clinical samples. Using a previously established cutoff of 0.7 (range 0-1), Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) and Pearson correlation (R) were assessed.
Results: Of the 317 samples tested on AVENIO CGP assay, 99.1% had reportable HRDsig status. We show the analytical concordance between AVENIO CGP and F1CDx for HRDsig with R of 0.95. Additionally, using a previously established cutoff of 0.7 to indicate HRDsig positivity, we find a concordance of 92% between the two assays. This includes not only samples of ovarian and fallopian tube tumour origin (92% PPA and NPA, n=25), but also breast (100% PPA, 96% NPA, n=32), and other solid tumour types (71% PPA, 100% NPA, n=255). The prevalence of HRDsig positive samples was 18.8% in breast, 54.2% in ovarian and fallopian tube tumours and 1.9% in other solid tumours.
Conclusion: The addition of HRDsig to the AVENIO® Tumour Tissue CGP Kit V2 provides a robust pan-tumour HRD biomarker, with a high degree of concordance to F1CDx, and provides a tissue biopsy CGP solution for translational and research clinical laboratories globally that does not require additional wet lab steps or samples. The high correlation values indicate similar scores by both assays and results in high PPA and NPA for HRDsig positivity across tumour types.

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E-PS-19-019

Pilot study on NGS characterization of pancreatic ductal adenocarcinomas

F.E. Costa*, J.R. Vizcaíno, N.J. Lamas
*Anatomic Pathology Service, Pathology Department, Unidade Local de Saúde de Santo António (ULSSA), Porto, Portugal

Background & objectives: Pancreatic ductal adenocarcinoma (PDAC) is the most common malignancy of the exocrine pancreas. It has an aggressive clinical course and a dismal prognosis, frequently initially presenting as metastatic disease. Its molecular characterization is fundamental to find potential therapeutic targets.
Methods: To understand the molecular landscape of PDAC patients in our reference centre we retrospectively collected cases of both primary and metastatic PDAC from 2018 until 2024, which underwent routine Next-Generation Sequencing (NGS) testing, using middle-sized panels in the MiSeq (Illumina) or the Genexus (Thermo-Fisher Scientific) platforms. Clinically significant pathogenic variants identified were correlated with clinical, histopathological data and patient outcome.
Results: Our pilot study included 16 patients, 8 males and 8 females with a mean age at diagnosis of 61.4 years (±9.6SD), diagnosed with PDAC. Most cases (62.5%) were primarily diagnosed in pancreatectomy specimens. Five cases (31,2%) were diagnosed as distant metastatic disease. Primary tumours had a mean size of 4.3cm (±1.7SD), 60.0% of which had pT2 stage and 70% had lymph node metastases. Eleven (68.8%) patients were still alive. KRAS and TP53 mutations were found in 11 (68,7%) and 12 (75%) cases, respectively, with the majority of cases (75%) presenting more than one mutation. All patients harbouring a BRAF mutation were dead at the end of the follow-up period ($p<0.05$).
Conclusion: In line with what has been published in the literature, KRAS and p53 were the most frequently mutated genes detected in our series. Three quarters of the cases had more than one mutation identified, highlighting the complex molecular scenario of PDAC. We found a correlation between mutated BRAF and death, since all patients with BRAF-mutated PDAC had passed away. This limited pilot study will help to open novel avenues towards the understanding the molecular pathology underlying PDAC.

E-PS-19-020

Molecular analysis in the diagnosis of follicular lymphomas lacking BCL2 and BCL6 rearrangements

M. Cristian*, K.M. Hebeda, P.J. Groenen
*Center for Research and Development of the Morphological and Genetic Studies of Malignant Pathology - CEDMOG, "Ovidius" University of Constanta, Constanta, Romania

Background & objectives: 10-15% of follicular lymphoma (FL) lack BCL2 and BCL6 rearrangements despite a germinal centre phenotype [1]. This report describes two FL cases with unusual morphologic, immunophenotypic, and genetic features that posed challenges in diagnosis.
Methods: Case 1: A 54-year-old female patient presented with lymphadenopathy above and below the diaphragm (cervical, mediastinal, axillar, retropectoral, paraaortic, inguinal) and spleen involvement by PET-CT; Case 2: A 43-year-old female patient presented with localized inguinal lymphadenopathy. One of the cervical lymph nodes (case 1) and the inguinal lymph node (case 2) were biopsied, and these were pathologically evaluated.
Results: Histology of case 1 showed a lymph node with many germinal centres consisting of a mixture of BCL2 negative, BCL6, CD10, Ki67 and CD23 positive centroblasts and few admixed centrocytes, but lacking mantles. Case 2 showed a mainly diffuse proliferation of small, BCL2, BCL6, CD10, CD23 positive B-cells. Despite a suspicion of FL in both cases, FISH for BCL2, BCL6, and MYC showed no rearrangements. Clonal IGHD-IGHJ and IGJK-IGHJ rearrangements and a pathogenic mutation in EP300 (case 1), and pathogenic mutations in CREBBP and STAT6 (case 2) were demonstrated in the tissues.
Conclusion: These cases illustrate how immunoglobulin clonality analysis confirming the presence of a monoclonal B-cell process and mutation analysis, supporting FL diagnosis, can help to solve non-classical FL cases, as FL lacking BCL2 and BCL6 rearrangement and BCL2 expression, or FL with a predominantly diffuse growth pattern, STAT6 mutation, CD23 expression, and often localized inguinal localization [2].

E-PS-19-021

Ten years of assessing the application of somatic NGS testing through external quality assessment

S. Deans*, D. Cregeen, F. Khawaja, W. Gutowska-Ding, R. Goodall, M. Woodcock, J. Matilainen, C. Roos, A. Nair, S.J. Patton
*GenQA, United Kingdom

Background & objectives: GenQA and EMQN deliver global next generation sequencing (NGS) external quality assessments (EQAs) assessing data quality, and accurate detection of somatic SNVs (single nucleotide variants) and indels (insertion/deletions) enabling laboratories to demonstrate accuracy and precision whilst identifying areas for improvement.
Methods: Participants receive tumour DNA for NGS. The EQAs are platform and gene target agnostic and laboratories can submit up to 3 datasets. The data is analysed to generate data quality and variant consensus reports, including evaluating the variant calling against the participant consensus. An overarching summary report summarises the collated data to share findings in support of benchmarking.
Results: Most laboratory submissions (74% in 2023) use one of the Illumina NGS platforms, with Life Technologies Ion Torrent platforms selected by 22%. Commercial library preparation kits were used for 75%. Mean coverage requirements are variable depending on the testing strategy deployed. In-house bioinformatics pipelines are deployed by laboratories performing exome/genome sequencing, whereas targeted panels were more frequently associated with pipelines supplied with the test platform. The quality of NGS will be presented from the ten EQA rounds determined by sensitivity, precision and F-scores. Confidence in reporting NGS results appears to be increasing as orthogonal method confirmation has reduced since 2015.
Conclusion: EQA data demonstrates an improvement in the standard of NGS testing since 2014, however there is variability in the use and application of the different method platforms, bioinformatics pipelines and variant callers which highlights the continued need for EQA to ensure the high standard of somatic NGS testing. Ongoing assurance of accurate NGS requires formal performance monitoring against defined criteria. This is challenging due to the current diverse approach to somatic NGS. The EQA will develop the required performance criteria.

E-PS-19-022
KRAS mutations detection in colorectal cancer: PCR-direct sequencing or Idylla platform?
R. Doghri*, S. Elfekih, H. Douik, A. Khemir, Z. Abdelkafi, I. Nasri, L. Charfi, G. Sahraoui, K. Mrad
*Pathology Department, Salah Azaiez Institute, Tunisia

Background & objectives: Ras mutations in colorectal cancer can be detected by the Idylla platform. The latter has reported invalid cases. Hence, direct sequencing seemed necessary in order to determine the etiology and optimize molecular biology techniques in the definition of mutational profiles
Methods: This was a 6-month experimental study conducted in the pathology department of the Salah Azaiez institute and in the human genetics departmentin the Faculty of Medicine in Tunis. It included 5 invalid cases and 9 genotyped control cases from biopsies and surgical specimens. A molecular study was performed consisting of DNA extraction, PCR, sequence reaction and Sanger sequencing.
Results: During the lysis step, some samples required a longer incubation time at 56°C. The amount of DNA extracted from the five invalid cases was less than 50 ng/µl. Electrophoresis on 2% agarose gel produced small bands with smears. Sequence analysis generated by direct sequencing showed that all invalid cases did not involve any mutation on the 3 exons.
Conclusion: Given that the Idylla platform manufacturer's recommendations were complied with, and that the invalid samples had been subjected to a long fixation time, the invalid results could be due to the pre-analytical conditions, in particular the hyperfixation of the samples.

E-PS-19-023
Developing EQA for HRD testing in ovarian cancer
J. Fairley*, Z.C. Deans
*GenQA, United Kingdom

Background & objectives: Testing for Homologous repair deficiency (HRD) is recognised as part of standard practice for ovarian cancer. Previously this testing was performed centrally but is increasingly being performed within individual centres and there is a need for external quality assessment (EQA).
Methods: Ten DNA samples extracted from ovarian cancers which had been previously tested were distributed along with a clinical case scenario to laboratories located in England. Participants performed testing according to their local protocols and submitted the results in the form of clinical reports. Results were compared to the original test results and benchmarked with those of the other laboratories.
Results: Participating laboratories used variable platforms for testing which utilise different algorithms to determine the HRD score and apply cut-offs to determine whether a sample is positive or negative. Samples which were previously identified to be HRD positive generally gave concordant results between the participating laboratories. However, for those samples which were previously identified as borderline there were discordant results with these being scored as either positive or negative by participants. There were also issues with samples which had previously been identified as negative giving either discordant results or being reported as inconclusive. The content of the reports varied with no consistent format.
Conclusion: The returns from this assessment of HRD testing demonstrate that there are discrepancies in the results and reporting. In order for laboratories to deliver consistent high quality results for HRD testing, there is a need for further harmonisation and education to analyse and report the results. This assessment has developed a successful format to deliver this through EQA.

E-PS-19-024
Beamion LUNG-1, a phase Ia/Ib trial of the HER2-specific tyrosine kinase inhibitor, zongertinib (BI 1810631), in patients with HER2-driven tumours: outcomes according to HER2 aberration type in lung and other tumours
A. Feuersinger*, F. Opdam, J. Heymach, M. Barve, H. Tu, Y. Wu, D. Berz, A.M. Mueller, U. von Wangenheim, J. Serra, K. Yoh, N. Yamamoto
*Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach an der Riss, Germany

Background & objectives: Beamion LUNG-1 (NCT04886804) is a Phase Ia/Ib trial evaluating the HER2-specific TKI, zongertinib, in patients with HER2 aberration-positive solid tumours (Phase Ia) and HER2 mutation-positive NSCLC (Phase Ib). Here, we report data from Phase Ia according to HER2 aberration type.
Methods: Phase Ia enrolled patients with HER2 aberration-positive (by local assessment: gene mutations, rearrangements, amplification, or overexpression) advanced/metastatic solid tumours. Patients received escalating doses of zongertinib BID (≥15 mg) or QD (≥60 mg), guided by a Bayesian model with overdose control. The primary endpoint of Phase Ia was MTD based on DLTs.
Results: As of January 29, 2024, 83 patients received zongertinib (BID n=17; QD n=66). Three patients had DLTs during the MTD evaluation period; MTD was not reached. TRAEs (all/G3/G4/G5): 76%/8%/1%/0% of patients. Confirmed investigator-assessed ORR/DCR rates in evaluable patients/patients with NSCLC (n=74/n=41) were 35%/85% and 44%/93%. Forty-three patients were *HER2* mutation-positive (TKD mutations n=36 [16 had A775_G776insYVMA]; non-TKD mutations n=6). ORR/DCR (regardless of confirmation) in *HER2* mutation-positive patients: 59%/97% (lung: 59%/97%; non-lung 60%/100%). In patients with A775_G776insYVMA, ORR/DCR: 69%/94%. Twenty-three patients had HER2-overexpressing tumours (2+/3+); 17 patients had *HER2*-amplified tumours. ORR/DCR in patients with HER2-overexpressing tumours (+/-amplification): 39%/83%. 3 patients had *NRG1* fusions; ORR/DCR: 33%/100%.

Conclusion: In this preliminary analysis, zongertinib showed promising activity across a broad range of tumour types with different HER2 aberrations, including aberrations that have historically been difficult to treat. Updated data in patients with specific HER2 aberrations will be described in detail at the meeting.

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E-PS-19-025

BRCA1 and BRCA2 NGS data form FFPE tissue in prostatic cancer: where we are and where we aim to go

A. Filosa*, E. Antolini, E. Bartoli, E. Antaldi, M. Santoni, F. Giantomassi, G. Goteri
*Department of Biomedical Science and Public Health, Università Politecnica delle Marche, Italy

Background & objectives: Comprehensive genomic profiling (CGP) has gained an important role in patients with advanced prostate cancer following the introduction of PARP inhibitors. The aim of our study is to elucidate the tissue sample more suitable for performing such genomic profile.
Methods: A cohort of 70 patients with a histological diagnosis of prostatic adenocarcinoma in different clinical setting was analysed. Somatic DNA was extracted from Formalin-Fixed Paraffin-Embedded (FFPE) tissue using MagCore Genomic DNA FFPE One-Step Kit for MagCore System. Tissue somatic DNA libraries were prepared with Myriapod NGS BRCA1-2 panel-NG035 and sequenced in Mi-Seq System.
Results: Among the 70 cases, 20 of the analysed samples resulted wild type for BRCA1 and BRCA2 genes. Mutations of BRCA2 gene were detected in 4 of the sample, while 46 sequencing data cannot be evaluated due to the poor quality and high fragmentation of the DNA obtained (fragmentation index <0,3).
Conclusion: The importance of providing molecular information on the BRCA1 and BRCA2 genes is widely recognized, especially for patients with metastatic prostate cancer. Formaldehyde in FFPE tissue can be considered the main responsible of unsuccessful data, coming from a highly fragmented DNA. the application of alternative and less invasive procedures could be a solution for some cases like liquid biopsy; provide a timely result useful to the therapeutic choice and easily reproducible for prognostic monitoring.

E-PS-19-026

Molecular landscape of endometrial carcinoma – a single institution preliminary study

Ł. Fuławka*, A. Podgórska, K. Seliga, R. Zub, K. Koszucka, R. Łotocka, A. Kuźniar, M. Bidziński, A. Tysarowski
*Cancer Molecular and Genetic Diagnostics Department, Maria Skłodowska-Curie National Research Institute of Oncology, Poland

Background & objectives: Endometrial carcinoma is the most common gynaecological malignancy in developed countries. The role of histological classification was surpassed by molecular subtypes: POLE-mutated (POLEmut), mismatch repair deficient (MMRd), no specific molecular profile (NSMP) and p53-abnormal (p53abn), differing in response to therapy.
Methods: The group of 104 female patients diagnosed with EC were tested for somatic variants using next-generation sequencing (NGS). DNA was extracted from tumour tissue macrodissected from FFPEs. NGS was performed on Ion Torrent S5 with Oncomine Gynaecological Panel or custom Oncomine Tumour Specific Panel. The coding regions of 7 genes were analysed: BRCA1, BRCA2, CTNNB1, PIK3CA, KRAS, POLE and TP53.
Results: Among the group of 104 EC cases, 72 (69%) have at least one variant (pathogenic/likely pathogenic) detected in 7 investigated genes. In the following number of cases (percentage) the variants were detected in the genes: BRCA1 – 2 (2%), BRCA2 - 6 (6%), CTNNB1 – 18 (17%), KRAS - 22 (21%), PIK3CA – 45 (43%), POLE – 7 (7%) and TP53 – 21 (20%).

Conclusion: This study presents preliminary analysis of somatic variants detection in female patients diagnosed with EC. In the next step, we intend to answer the question of whether there is a correlation between specific variants and clinico-pathologic factors. The long-range plans for our research include compiling molecular and pathological data with analysis of survival and response to therapy.

E-PS-19-027

SMARCA4 gene alterations detected by NGS. Presence in lung cancer and implications on evolution and treatment

P. Gaspar López-Cózar*, I.C. Abitei, L. Robles Cabeza, M. Jironda Gallegos, E. Fernández Torres, M.D. Bautista de Ojeda
*Hospital Universitario Costa del Sol, Spain

Background & objectives: SMARCA4 gene is a tumour suppressor gene. Its alterations are classified in: Class I, with loss of function (truncating mutations, fusions, and homozygous deletion), linked to aggressive behaviour and response to immunotherapy, and Class II (missense or unknown significance).
Methods: A search is conducted in our hospital's next-generation sequencing (NGS) database, which utilizes Ion Torrent (Thermofisher) technology. We selected cases studied using the Oncomine Comprehensive Assay (OCA) panel with the aim of identifying tumours exhibiting alterations in the SMARCA4 gene and analysed patient's evolution and treatment responses.
Results: From 284 neoplasms analysed with OCA, 17 exhibited SMARCA4 gene alterations (6%). Tumours were distributed as follows: lung/thoracic (4), colorectal (3), endometrial (3), ovarian (2), and one each in stomach, prostate, skin, breast and salivary gland. Among the lung tumours, 3 mutations were classified as Class I and 1 as Class II. Histology included mucinous colloid-type adenocarcinoma, large cell neuroendocrine carcinoma, poorly differentiated adenocarcinoma, and undifferentiated carcinoma. All patients were male smokers with a mean age at diagnosis of 69 years. Two patients received immunotherapy as part of their treatment and are still alive after 12 months. The other two patients, who never received immunotherapy, died three months after diagnosis.
Conclusion: Currently, there are no specific therapeutic strategies for tumours with alterations in the SMARCA4 gene. Class I alterations are linked to poor outcomes and some studies suggest potential benefits from immunotherapy, as these tumours tend to have a high tumour mutation burden. In our small series of patients with lung cancer carrying alterations in SMARCA4, both aspects seem to be confirmed.

E-PS-19-028

Initial experience of fluorescence in situ hybridization for MDM2 amplification in mesenchymal lesions of uncertain diagnosis

L. González Lorca*, A. Sánchez Espinosa, S. Blasco Muñoz, D. Pérez Parra, C. Capozzi, V. Alonso Aguirre
*Pathology Department. Hospital Santa Lucía, Spain

Background & objectives: In situ hybridization techniques, developed decades ago, remain in use for confirming genetic translocations characteristic of specific pathologies. FISH MDM2, a probe, detects amplification of the MDM2 gene primarily found in mesenchymal tumours, predominantly in adipose and bone tumours.
Methods: Questionable or positive results from immunohistochemistry studies for MDM2 and CDK4 were validated through FISH MDM2 analysis on 4-micron paraffin sections prepared on the same day of

hybridization. The MD-Stainer hybridizer equipment, along with the automatic probe "MAD-010FA" from VITRO S.A., was employed for this purpose. The evaluation was performed using an Olympus BX43 microscope equipped with LED fluorescence technology.
Results: Eight molecular studies have been assessed, including our own cases and cases referred from nearby regional centres, with histologically uncertain diagnosis of mesenchymal lesions. These studies aim to confirm both well-differentiated/undifferentiated liposarcoma, as well as other lesions with a more probable diagnosis (nodular fascitis, fibrovascular polyp among others) but requiring molecular exclusion of altered MDM2. MDM2 amplification by FISH assay yielded a positive and confirmatory result for the sole case suspected of undifferentiated liposarcoma, with negative results in the rest, confirming the suspected diagnosis in 6 out of 7 cases and ruling out adipose neoplasm in the remaining one.
Conclusion: MDM2 amplification assays have allowed distinguishing small biopsy of low grade neoplasms, like lipomas or lipomatosis, from others of higher grade and biological aggressiveness, such as well-differentiated or undifferentiated liposarcoma. The benign result supports a less frequent follow-up and saves on further sampling or even more aggressive surgeries, as well as helping confirm the diagnosis of other pathologies with less clinical impact.

E-PS-19-029
The use of ThyroidPrint® Assay in the study of AUS and FN thyroid lesions: our experience
D. Guerrero*, A. Echegoyen, J. Pineda, A. Gonzalez-Mayorga, E. Anda
*Department of Pathology, Spain

Background & objectives: 20% of thyroid nodules are atypias of undetermined significance (AUS)/follicular neoplasms (FN). Their management includes thyroidectomy, being 75% benign. Gene expression profile contributes to characterize these lesions. We present our experience about the Idylla™ ThyroidPrint® Assay in AUS/FN.
Methods: Six AUS/FN thyroid lesions iwere analysed by the new Idylla™ ThyroidPrint® Assay (RUO) test released into market. This test is a qualitative reverse transcription polymerase chain reaction (RT-PCR)-based assay with real-time detection in the Idylla equipment (Biocartis, Belgium). The assay assesses the gene expression profile based on 10 target genes in FNA and reports a gene expression classifier score.
Results: One of the six cases was not analyzable because tissue sampling was not satisfactory. One of the five analyzable cases was stored at 4ºC in the preservation solution and was processed after diagnosis of AUS by the pathologist. All the reference genes in all the cases were properly amplified; the gene expression score was of low risk for all the cases. The estimation of new thyroid lesions (three cases per month) will also be presented. Our hospital is one of the first centres in Spain to include this new technique in the portfolio of the Molecular Pathology lab in the Pathology Department.
Conclusion: This is our first description about the use of ThyroidPrint® test in our hospital. This is a very easy technique to perform and helps for a clinical decision about the thyroidectomy in AUS/FN thyroid nodules.

E-PS-19-030
Incidence of atypical fish patterns associated with ALK TKI therapy in NSCLC
F.S. Gürevin*, B. Öğüt, M.A. Inan, N. Akyurek
*Turkey

Background & objectives: Anaplastic lymphoma kinase (ALK) rearrangement is reported in 3% to 8% of patients with non-small cell carcinoma (NSCLC). Atypical ALK FISH patterns which carries the great risk of misinterpretation, hence may result in loss of patients eligible for targeted therapy.
Methods: Tissue and cell block samples from 3680 patients with advanced stage non-small cell lung cancer were routinely examined by ALK fluorescence in situ hybridization (FISH) and immunohistochemistry (Ventana ALK-D5F3-CDx assay). FISH was performed with dual-color, break-apart probe (ZytoLight SPEC) on formalin-fixed, and paraffin-embedded tissue.
Results: ALK FISH test was positive in 179 cases (4.3%). One case showed a 3' signal pattern in atypical disseminated isolation. With a significantly reduced size red (3') signal and complete disconnection of the green cleavage, a 5' signal pattern was present in three cases with loss of the 3' red signal. Two cases showed double deletion with complete discontinuation of a combination signal. Whole endowment NGS and ALK IHC confirmed the information that a mixture gene and expressed oncoprotein are normally present.
Conclusion: FISH testing can be technically challenging and difficult to interpret. NSCLC with atypical/abnormal FISH pattern is a rare event that should be considered positive for ALK rearrangement and should benefit from ALK-targeted therapy. This study highlights the continued discontinuation of the use and compatibility of immunohistochemistry as a preliminary screening method or confirmation of atypical cases by alternative techniques such as next-generation sequencing.

E-PS-19-031
Longitudinal monitoring of cell-free tumour DNA with next-generation sequencing in patients with oesophageal cancer
C. Henssen*, T. Steiert, S. Sebens, A. Franke, F. Richter, M. Forster
*Christian-Albrechts-University Kiel, Institute of Clinical Molecular Biology, Germany

Background & objectives: Liquid biopsy is a minimally invasive technique to detect tumour mutations, e.g. from cell-free DNA (cfDNA) circulating in blood. Our objective was to examine the potential of cfDNA analysis for therapy monitoring of oesophageal cancer (EC) patients.
Methods: 21 patients with advanced EC stages (II-IV) were longitudinally monitored and sampled up to six times, from before neoadjuvant therapy until 12 months post-surgery. DNA was extracted from blood samples and targeted next-generation sequencing (NGS) was performed. Circulating tumour DNA (ctDNA) was analysed as a fraction of cfDNA. Leucocyte DNA was analysed to exclude aging mutations and germline variants.
Results: Four patients died, 5 dropped out, 12 completed the study. In all patients, somatic mutations were discovered in ctDNA prior to therapy (median variant-allele-frequency VAF 0.921%). After the first treatment phase (neoadjuvant therapy or surgery), nearly all mutations' VAFs decreased significantly. In 5/21 patients (23.8%) no mutations were detectable, in another 5 patients all mutations and in 11 patients (52.4%) some mutations remained detectable at decreased VAFs. At 12 months post-surgery, in 7/12 patients at least one mutation was still detectable with a median VAF of 0.355% (range 0.0175-17.35%) and 5/12 patients did not have any detectable somatic mutations.
Conclusion: Using liquid biopsy, mutations were detected in all patients. Further, it was possible to detect a decrease in ctDNA at follow-up and monitor remaining mutations over time. This supports the utility of liquid biopsy and NGS of cfDNA for therapy monitoring in EC patients. Longitudinal monitoring may allow early detection of relapses and rapid treatment adaptation. Future studies will unravel the relationship of VAFs and clinical presentation of EC patients at the different therapy stages.

E-PS-19-032
Adaptive homeostasis as a possible non-genetic regulator of BRCA1/2 splicing in ovarian cancer
E. Izycka-Swieszewska*, A. Jasiak, L. Anderson, S. Neumann, K. Buczkowski, M. Stukan, K. Grabowska, B. Wasąg, R. Weeks, L. Walker, G. Wiggins, H. Cunliffe, M. Ratajska
*Medical University of Gdansk Dpt. of Pathology & Neuropathology, Poland

Background & objectives: Previously, we detected several naturally occurring transcripts of BRCA1/2 genes in peripheral blood mRNA of healthy controls, three isoforms had higher levels in the cancer patients blood. The expression of isoforms in ovarian tumours tissue didn't differ from adjacent tissue.
Methods: Peripheral blood mononuclear cells (PBMCs) from healthy donors cohort (biobank repository), which were cultured in conditioned (acquired through a short-term culture of OVCAR-4 cell line) and control media, respectively. Cells were collected at five time points (4h, 8h, 24h, 48h and 72h), total RNA was extracted.
Results: We investigated the expression of BRCA1ΔE11q, BRCA1ΔE11 and BRCA2ΔE3 isoforms to assess variations in the distribution of these transcripts. Next, to explore the potential role of epigenetic mechanisms in altering the level of those isoforms, we examined the expression of primary DNA (DNMT3A) and RNA (METTL3) methyltransferases. However, we did not identify significant differences between the various time points.
Conclusion: In cancer, transcriptomic changes extend beyond the tumour, provoking changes in mRNA splicing of other normal cells. In summary, we propose that an unknown biological mechanism may promote the overexpression of selected BRCA1/2 isoforms in response to neoplasm. However, further studies are required to explain this phenomenon.

E-PS-19-033
Analysis of BARD1 and its isoform beta (β) in paediatric tumours
E. Izycka-Swieszewska*, A. Jasiak, K. Czarnota, K. Buczkowski, J. Gulczynski, J. Stefanowicz, W. Grajkowska, M. Ratajska
*Medical University of Gdansk Dpt. of Pathology & Neuropathology, Poland

Background & objectives: BARD1 (BRCA1 Associated RING Domain 1) is a tumour-suppressing gene involved in cell cycle control and genome stability, which is engaged in biology of several adult-type tumours. The data on BARD1 and its isoform β in childhood cancer is limited.
Methods: FFPE tumour samples and surrounding normal tissue analysed with qPCR method in neuroblastic tumours (91), germ cell tumours (26: teratomas, yolk sac tumours, dysgerminomas), and rhabdomyosarcoma (RMS - 7 cases) with basic patho-clinical data. Expression analysis with BARD1 FL assay (exons 3, 4), BARD1β with TaqMan probes (exons 1,4); in negative cases FISH with BARD1 specific probe was done.
Results: 94% of neuroblastomas expressed BARD1 FL. 73% of the cases expressed BARD1β. Five samples without BARD1 FL were stages 3/ 4, did not show BARD1β, with no deletion of 2q35 by FISH. Higher expression concerned ganglioneuroma and ganglioneuroblastoma compared to neuroblastoma categories. All GCTs expressed BARD1 FL, with significant differences between the BARD1 FL expression in the tumour and adjacent tissue(higher) in the yolk sac tumour (Z=2,19; p=0.024). BARD1β expression was detected in 23 tumours (n=23/24; 96%) and 16 adjacent tissues (n=16/19; 84%).
RMS tumour tissue expressed BARD1 FL and BARD1β (n=7/7; 100%) with higher expression of BARD1β in neoplastic tissue than adjacent healthy tissues (Z=2,36; p= 0.018).
Conclusion: The expression of BARD1β isoform is higher in neoplastic tissues than normal surroundings. There may be a specific BARD1 isoforms pattern in germ cell tumours, rhabdomyosarcoma, and neuroblastoma subtypes. The differences in BARD1 expression depend on the histological type of neoplasm, and the level of maturation in neuroblastic tumours. Our findings confirm the previously described association with oncogenesis of BARD1β not only in the neuroblastic tumours, but also in selected GCT and RMS for the first time.

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E-PS-19-034
Expression of minor spliceosome component U6atac: a pan-cancer study
C. Komarek*, J.A. Rodriguez Calero, A. Augspach, M. Rubin
*Institute of Tissue Medicine and Pathology, Bern, Switzerland

Background & objectives: U6atac, the rate-limiting catalytic component of the minor spliceosome, is overexpressed in tumour cells. Inhibition of U6atac preferentially affects cancer cells compared to healthy cells. To understand where therapy might be most effective, we interrogated U6atac-expression across multiple cancer types.
Methods: mRNA in situ hybridization for U6atac was performed on pre-existing tissue microarrays. The percentage and intensity of expressing cells were assessed. The intensity was classified from no (0) to high (3) expression and multiplied by the percentage of expressing cells to create a U6atac-score, ranging from 0-300. The score was categorized into equally large groups (low, intermediate, and high).
Results: U6atac is expressed in normal urothelium and urothelial carcinoma. Thirty percent of primary urothelial carcinoma demonstrated a high U6atac score. U6atac-score was significantly higher in matched metastatic urothelial carcinoma than in primary urothelial carcinoma and normal urothelium (p<0,001). Fourteen percent of primary breast cancer have a high U6atac score, which correlates with high proliferation rates (MIB>=35%) (p=0,02). In primary pancreatic neuroendocrine tumours (PanNET), 8% expressed a high U6atac-score. U6atac-expression was significantly lower in Primary PanNET compared to urothelial carcinoma (p<0,001) and showed a lower trend compared to primary breast cancer (p=0,186). Visceral prostate cancer metastases showed a higher U6atac expression compared to bone metastasis (p= 0,031).
Conclusion: U6atac shows increased expression in urothelial carcinoma compared to benign urothelium. Breast cancer U6atac expression is significantly higher in tumours with elevated proliferation index, whereas PanNETs, with low proliferation rates, show the lowest U6atac expression. U6atac is overexpressed in metastatic prostate and bladder cancer. Future work will explore the benefit of U6atac inhibition, alone or in combination, as a novel therapeutical target in several cancer types. Pathology can help determine the best tumour types to test.

E-PS-19-035
Next-Generation Sequencing (NGS) for the identification of lung cancer oncogenic fusions: a retrospective study from a Portuguese university hospital centre
N.J. Lamas*, T. Santos, C. Vilasboas, X. Wen, F.E. Costa, J.R. Vizcaíno
*Centro Hospitalar Universitário de Santo António (CHUdSA), Portugal

Background & objectives: Oncogenic gene fusions are caused by genetic rearrangements and frequently drive non-small cell lung cancer (NSCLC) initiation and progression. Pharmacological targeted inhibition of these fusion products has increasingly become an efficient anti-NSCLC therapeutic option once their accurate identification is achieved.
Methods: To thoroughly characterize lung cancer cases positive for oncogenic gene fusions we retrospectively collected primary and metastatic lung cancer cases from April 2022 until April 2024, which underwent routine Next-Generation Sequencing (NGS) testing using lung cancer-directed panels in the Genexus (Thermo-Fisher Scientific) or MiSeq (Illumina) platforms. The identified gene fusions were correlated with clinical-histopathological data, PD-L1 status and patient outcome.
Results: Our pilot study included 36 patients, with a slight preponderance of male patients (n=19, 52.8%) and a mean age of 65.8 years-old (±11.6). The majority of the cases were lung adenocarcinomas

diagnosed in lung biopsy specimens (n=25, 69.4%). Ten patients (28.6%) had passed away at the end of the study. Oncogenic fusions with two well-known fusion partners were present in nearly 90% of the cases (n=32). In the remainder four cases ALK (n=3) or NTRK3 (n=1) expression imbalance were identified. The most frequently discovered oncogenic fusions were EML4-ALK (n=9, 25%), MET Exon14 Skipping (n=7, 19.4%), KLF5B-RET (n=5, 13.8%) and CD74-ROS1 (n=3, 8.3%). PD-L1 expression was positive in 23/36 cases (63.9%).
Conclusion: Our study allowed an initial characterization of the most relevant oncogenic fusions in a small group of Portuguese NSCLC patients. The most frequently identified oncogenic fusions were in line with previous studies in other countries, yet we observed in our cohort a slight relative increase in the frequency of MET Exon14 Skipping cases. Novel studies are needed to further unravel the landscape of oncogenic kinase fusions in Portuguese NSCLC patients, possibly revealing genetic signatures that are unique to this population.

E-PS-19-037
Multilocus inherited neoplasia alleles syndrome (MINAS) in a patient with Lynch syndrome and Gorlin-Goltz syndrome with corresponding MLH1 and PTCH1 pathogenic variants and dual phenotypic expression
E. Mcgrath*, M. Loughrey, I. Freyling, R. Kennelly, D. Winter, K. Sheahan
*St. Vincent's University Hospital, Ireland

Background & objectives: Multi-locus Inherited Neoplasia Allele Syndrome (MINAS) refers to individuals with germline pathogenic mutations in two or more cancer susceptibility genes. Up to 6% of confirmed Lynch syndrome cases harbor a second germline pathogenic variant of hereditary cancer.
Methods: We describe the first reported case of both Lynch syndrome and Gorlin-Goltz syndrome (nevoid basal cell carcinoma syndrome) in a patient with corresponding MLH1 gene and PTCH1 gene pathogenic variants and phenotypic expression of each variant.
Results: This 46-year-old man initially presented at age 11 with features leading to a clinical diagnosis of Gorlin-Goltz syndrome (multiple odontogenic keratocysts, bifid ribs and calcification in the falcx). At age 30 he presented with altered bowel habit and rectal bleeding. A colonoscopy showed a rectal tumour with background proctitis suggestive of ulcerative colitis. Histology showed a moderately differentiated rectal adenocarcinoma with loss of MLH-1 and PMS-2 on immunohistochemistry. The patient underwent genetic molecular analysis (whole exome sequencing) which identified a pathogenic variant in MLH1 gene (MLH1, c.1489dupC; p.Arg497Profs*6, het.), causative for Lynch syndrome and also a co-existent pathogenic variant in PTCH1 gene (PTCH1, c.260dup; p.Leu87Phefs*3, het), causative for Gorlin-Goltz syndrome.
Conclusion: Cases of MINAS are rare though increasing in the reported literature with the more widespread use of next generation sequencing. Some cases show expected clinical phenotypes, while others exhibit unusual tumour characteristics or multiple primary tumours, suggesting complex interactions between MINAS-associated genes. To our knowledge, this is the first reported instance of MINAS with the co-occurrence of Gorlin-Goltz syndrome and Lynch syndrome with corresponding PTCH1 and MLH1 pathogenic variants and an individual clinical phenotype of each variant.

E-PS-19-038
Accurately assessing the quality and quantity of cell-free DNA extractions
F. Moon*, J. Fairley, K. Nahlik, S. Deans
*GenQA, United Kingdom

Background & objectives: GenQA delivered an exploratory pilot to determine the feasibility and robustness of delivering external quality assessment for cell-free DNA (cfDNA) extraction using reference material that closely resembles patient samples to ensure laboratory extractions are efficient and sufficient for clinical testing.
Methods: The exploratory pilot was set up using novel plasma Seraseq® ctDNA Extraction Reference Material at 50ng/ml. Four laboratories that each use a different cfDNA extraction technique participated. The extracted cfDNA was returned to GenQA for analysis. GenQA determined the mass using volume by weight and concentration by ddPCR and the quality was assessed using Agilent's TapeStation cell-free DNA assay.
Results: Four different cfDNA extraction methods were employed; Maxwell RSC/ccfDNA LV Plasma Kit, Nonacus Cell3™ Xtract, Qiasymphony DSP Circulating DNA Kit and Roche COBAS cfDNA Sample Preparation Kit. There was variability in the volume and concentration that laboratories extracted from the reference plasma samples. This ranged from 43-179µl and 0.5-2.25ng/µl, respectively. The total mass of cfDNA extracted by laboratories ranged from 90-110ng. The Tapestation traces indicated the majority of DNA extracted was ~185 base pairs (bp) and a small proportion of DNA fragments at ~320bp, representing cfDNA extracted from patient plasma.
Conclusion: Although there was variability in the volume and concentration of cfDNA extracted using the different methods, laboratories showed sufficient extraction yield for NGS assays. The Tapestation analysis showed consistency between the laboratories, with profiles closely resembling the results of real patient samples.

The methods for determining extraction efficiency of cfDNA by GenQA from commercially available material is robust and a larger pilot EQA will be carried out for laboratories worldwide.

E-PS-19-039
Hemimegalencephaly associated with drug-resistant epilepsy and a rare molecular genetic alteration in the CPA6 gene: a clinical case
D. Murzaeva*, D. Sitovskaya, V. Mochalov, R. Talybov, Y. Zabrodskaya
*Almazov National Medical Research, Tyumen State Medical University, Russia

Background & objectives: Hemimegalencephaly is extremely rare congenital malformation of cortical development (MCD). It belongs to the MCD group of mTOR-related pathologies and can be the result of various genetic disorders. One of the main clinical manifestations of Hemimegalencephaly is drug-resistant epilepsy.
Methods: Herein, we described for the first time a case report of Hemimegaloencephaly associated with drug-resistant epilepsy and a rare molecular genetic alteration in the CPA6 gene. A magnetic resonance imaging was performed. Patient underwent surgical treatment with subsequent histological and genetical examination.
Results: This article describes a clinical case of Hemimegalencephaly in a 4-year-old boy with frequent generalized tonic-clonic seizures and drug-resistant epilepsy; also, he had speech development delay. MRI revealed a Hemimegalencephaly of the right frontal lobe. Stereotaxic laser disconnection of the large cortical dysplasia in the right frontal lobe of the brain was performed. Morphological features of focal cortical dysplasia type IIb (FCD IIb) were reported. No seizures were observed in the hospital follow up after the operation for 14 days. The whole exome DNA sequencing showed the presence of a heterozygous state _000008.10^G68419028del/633del, pGlu212LysfsTers of the CPA6 gene.
Conclusion: A feature of the case is the identified association of Hemimegalencephaly, morphologically represented by FCD IIb, with a previously unknown heterozygous state in the 6th exon of the CPA6 gene. This association allows to expand our understanding of changes in the activation of PI3K/AKT/mTOR pathway as a key link in the pathogenesis of congenital anomaly of cortical development.

E-PS-19-040

Role of the level of IGG fragments in blood serum in case of oesophageal cancer

N. Nizyaeva*, E. Goufman, A. Aleksankin, K. Gershkovich, N. Tikhonova, M. Aksenova, I. Stepanova, V. Aleksankina, V. Bochkov
*Petrovsky National Research Center of Surgery, Russia

Background & objectives: Oesophageal cancer is malignant tumour with low survival rate. Malignant tumours are characterized by an increase in proteolytic enzymes and proteolysis products. The aim was to assess the level of IgG fragments in the serum of patients with oesophageal cancer.
Methods: The study included 63 patients (median age 63) with oesophageal cancer (adenocarcinoma n=5, squamous cell carcinoma (n=38) and healthy donors (n=20). We analysed indicators of hemostasis and the total IgG and the level of IgG fragments in the blood serum (degradation coefficient IgG-LysK). IgG level lysine was assessed using a commercial reagent kit, "anti-plasminogen-ELISA.
Results: As mentioned above IgG-Lys fragments specifically interacted with plasminogen through their C-terminal lysine. The study showed that serum from healthy control donors group had a significantly lower median IgG-LysK value compared to oesophageal cancer group ($P<0.0001$). False-positive IgG-LysK values were detected in 15% of the control group. False negative results were observed in 12% patients with oesophageal cancer. According to ROC analysis, the sensitivity (SN) of the test in patients with oesophageal cancer was 91% and specificity (SP) 85%, and area under the curve (AUC) 0.903.
Conclusion: Assessment of the level of proteolytic fragments of IgG may be used for detected solid tumours. This approach will improve the sensitivity and specificity of cancer diagnosis.

Funding: The study was carried out within the framework of State Assignment No. 123030700104-3

E-PS-19-041

Beyond the crystal globe: unravelling molecular pathology's mixed bag of dreams

M. Olinca (Comanescu)*, R. Pirlog
*Romania

Background & objectives: Molecular pathology has emerged as a cornerstone of modern oncology, promising a new era of precision medicine where treatments are personalised according to patients molecular profile.
Methods: We focused on both expectations for what molecular pathology can achieve and its limitations in clinical practice. We conducted surveys with oncologists and pathologists to assess their perspectives on the use of molecular pathology, focusing specifically on the challenges they face in communication, interpretation of results, and the impact on treatment planning.
Results: In Romania, as in many parts of the world, the integration of this method into clinical practice brings not just hope but also challenges. Our study aimed to evaluate the real-life challenges and opportunities presented by molecular pathology in Romanian oncologic care. We focused on both expectations for what molecular pathology can achieve and its limitations in clinical practice. Preliminary findings suggest that while molecular pathology is recognized for its potential to dramatically improve patient outcomes, the actual benefits are often hampered by poor communication and gaps in understanding of molecular results. This can lead to delays in treatment adjustments, misinterpretations of data, and suboptimal patient management.
Conclusion: The study looked for ways in which these gaps in a "common language" between pathology and oncology can be bridged, emphasising the role of education to enhance understanding, standardization of reporting, and the establishment of regular molecular tumour boards for challenging cases. Molecular pathology holds immense promise for revolutionizing cancer care in Romania, but its potential must be fully unleashed. Addressing this is crucial for turning molecular pathology into the crystal globe we all wished for.

E-PS-19-043

Proteogenomics reveals varying levels of intra-patient heterogeneity in melanoma metastases

B. Szeitz, Y. Hagemeijer, Z. Páhi, Z. Ujfaludi, V. Doma, J. Gil, R. Appelqvist, J. Malm, K. Pavlowski, M. Szász, D. Fenyő, P. Horvatovich, G. Markó-Varga, L. Betancourt, T. Pankotai*
*Hungarian Cencer of Excellence, Hungary

Background & objectives: Metastatic melanoma is one of the most aggressive among the deadliest cancers, with a dismal 5-year survival rate. The aggressiveness of the disease has been linked to the high genomic heterogeneity resulting in a variety of phenotypes.
Methods: In this study, we present the proteomic and RNA-seq-based proteogenomic characterization of 74 late-stage melanoma metastases which were collected postmortem from more than 20 anatomic locations.
Results: Influence of the host tissue on the tumours' proteome was overall weak, but particularly notable in kidney and spleen metastases. 80% of patients exhibited weak intrapatient homogeneity based on the tumours' histopathological and proteomic/proteogenomic data, respectively. Unsupervised clustering revealed proteome-based metastasis groups, mainly driven by mitochondrial processes, extracellular matrix and immune system pathways, but not affected by the patients' treatment history.
Conclusion: A severity score, assembled from survival-associated proteins, was assigned to individual metastases, revealing that average expression of these proteins across the metastases may influence survival, irrespective of within-patient heterogeneity. In summary, our research offers insight into the molecular heterogeneity of late-stage melanoma metastases, emphasizing the importance of personalized therapy development even for late-stage patients.

E-PS-19-044

Molecular characterization of synchronous sporadic colorectal carcinomas

G. Ricciardi*, E. Germanà, W.G. Giordano, M. Ballato, R. Scarfì, M. Santarpia, C. Pizzimenti, V. Fiorentino, M. Martini, A. Ieni, G. Giuffrè
*Department of Biomedical, Dental, Morphological and Functional Imaging Sciences, University of Messina, Messina, Italy

Background & objectives: The study analysed KRAS, NRAS and BRAF status as well as mismatch repair (MMR) protein expression and microsatellite instability (MSI) in synchronous sporadic colorectal carcinomas (sCRC) to assess genomic alterations among lesions in the same patient.
Methods: Sixteen patients (13 males, 3 females) with sCRC were studied. Fourteen patients present two sCRC, while two had three. Tumour samples were formalin-fixed, paraffin-embebbed, processed for DNA extraction and analysed for mutations in KRAS, NRAS, and BRAF as well as for MSI analysis using qPCR. Immunohistochemistry was performed to evaluate the expression of MSH2, MSH6, MLH1, and PMS2 proteins.
Results: Of 34 samples, 19 (55.9%) had KRAS mutations; discordant KRAS status was found in 8 (50%) of 16 sCRC patients. NRAS mutation in codon 61 was found in 1 (2.9%) sample and a discordant NRAS status was observed only in this patient. BRAF mutation in codon 600 was found in 3 (8.8%) samples from the same patient; concordant BRAF status was observed in all patients. Notably, the patient harboring the BRAF mutation displayed dMMR/MSI status in all lesions; concordant MMR/MSI status was observed in all patients.

Conclusion: A discordance of genomic alterations has been documented in 9 (56.25%) of 16 patients. Therefore, molecular characterization should be assessed on each lesion to better define disease management of sCRC patients.

E-PS-19-045

Expression of PD-L1 in lung adenocarcinoma and its cerebral metastasis, and the association with survival

M. Rubiera Valdés*, D. Corte-Torres, A. Vallina, J.C. Celis Pinto, S. Fernández Menéndez, K.M. Piña Batista, I. Fernández Vega
*University Hospital of Asturias, Spain

Background & objectives: Lung cancer, predominantly adenocarcinoma, frequently leads to brain metastases. PD-L1, a protein regulating immune responses, is a crucial target in cancer immunotherapy.
Methods: Twenty-six patients with lung adenocarcinoma and surgically resected brain metastases (2007-2019) were analysed using tissue arrays. Immunohistochemistry (IHC) assessed PD-L1 expression via the H-Score method. PD-L1 positivity was defined as ≥1% tumour expression. Statistical analysis employed SPSSv25 ($p<0.05$).
Results: Significant differences existed between primary tumour and metastasis positivity ($p=0.002$). Approximately half of primary tumour samples were PD-L1 positive, contrasting with 34% of brain metastases. PD-L1 expression in lung adenocarcinoma correlated with worse overall survival (43.13 vs 95.26 weeks; $p=0.013$), disease-free survival (11.52 vs 75.94 weeks; $p=0.024$), and post-metastasis period (32.94 vs 79.41 weeks; $p=0.026$). PD-L1 expression in brain metastases did not affect survival significantly.
Conclusion: Our study reveals underexpression of PD-L1 in brain metastases of lung adenocarcinoma. Evaluation of PD-L1 in lung adenocarcinoma predicts prognosis, with PD-L1 expression indicating poorer outcomes. Thus, PD-L1 expression might serve as a negative prognostic factor in lung adenocarcinoma development.

E-PS-19-046

Clinical implications of next generation sequencing for the classification of endometrial carcinoma

L. Sánchez*, S. Perez-Buira, F. Rojo
*Fundación Jiménez Díaz, Spain

Background & objectives: Molecular classification of endometrial carcinoma defined four subgroups of patients: POLE ultramutated, microsatellite unstable, copy number low and copy number high. Our objetive is to establish the clinical value of this characterization through a panel of genes using next-generation sequencing.
Methods: From patients with FIGO stages IA to IIIB, 97 formalin-fixed, paraffin embedded samples of endometrial carcinoma were studied. Immunohistochemical analysis was performed to detect p53 and repair proteins, in addition to sequencing a panel of 55 genes (Action OncokitDx). Microsatellite instability was determined by a panel of 110 microsatellites. The POLE pathogenic variants were classified according to León-Castillo et al.
Results: The patients were classified based on molecular analysis, and the results showed that 8.24% (8/97) were POLE mutation, 18.5% (18/97) were hipermutated, 39.17% (38/97) were high copy number and 34.02% (33/97) were low copy number. Seven cases present molecular alterations belonging to two subgroups simultaneously: three mutations in p53 and MSI, two with mutations in POLE with MSI and two with p53 and POLE. The concordance between altered expression of p53 and the presente of pathogenic mutations in p53 using the gene panel was 97.3%. Clinical follow-up of the patients identified five of the eight patients with a pathogenic mutation in POLE avoided adjuvant chemotherapy.
Conclusion: Molecular characterization of endometrial carcinoma into subgroups has important implications for prognosis and treatment. Next-generation sequencing is a powerful tool that provides reliable results consistent with surrogate immunohistochemical markers. By performing a molecular profile of patients, NGS can identify important genetic mutations such as p53, POLE and MSI, as well as variants like CTNNB1 that have prognostic value. This information can help clinicians identify patients who may benefit from additional treatment and avoid unnecessary overtreatment.

E-PS-19-047

Comparation between two commercial solutions for homologous recombination deficiency

M. Sánchez Ares*, R. Pérez-Becerra, T. Pereira Ares, I. Lesende Rodríguez, J.R. Antúnez López, J. Cameselle Teijeiro, I. Abdulkader Nallib
*Department of Pathology, Clinical University Hospital of Santiago de Compostela, Health Research Institute of Santiago de Compostela, Galician Healthcare Service (SERGAS), Santiago de Compostela, Spain

Background & objectives: Testing for a homologous recombination deficiency (HRD) in primary high-grade ovarian cancer is crucial for recommending the appropriate therapy. In recent years, several tests have been developed to detect HRD. Comparison between the analytical solutions was performed in this study.
Methods: HRD analysis of 16 formalin-fixed, paraffin-embedded (FFPE) samples of patients with high-grade serous ovarian cancer a minimum of 30% tumour cells was performed using two different solutions, manual SOPHiA DDM™ HRD Solution (Sophia Genetics) and automatized SeqOne HRD assay (SeqOne Genomics). All samples were prepared following the manufacturer's protocol. Sequencing was performed in NextSeq 550 (Illumina).
Results: The concordance in the results were 43.75% (4 cases were discordant between both solutions and 3 were non conclusive for the Sophia DDM™ HRD). All the discordance cases were related with the calculation of the genomic instability; 3 of the 4 samples with discordant results were very close to the threshold in both solutions (Sophia 1.8, -2 , 0,2) (SeqOne 0.22 , 0.74 , 0.32). The estimated tumour content for these cases were 30%, 50% and 60%, respectively. In the fourth case, the result was widely discordant (Sophia -6.9 SeqOne 0.87) the tumour content of 60%.
Conclusion: Automatization library preparation for SeqOne´s solution using the Magnis NGS Prep System can help to reduce operator's errors, which could explain the difference in the non-conclusive results between both solutions. Indeed, workflow automation can be a powerful tool for improving efficiency and saving time. Values close to the threshold should be taken with caution before administering PARP inhibitor therapy to patients according to our results.

E-PS-19-048

Circulating tumour cell culture

S. Sikirić*, S. Seiwerth, I. Kaloper Lovreković
*University of Zagreb, School of Medicine, Institute of Pathology, Croatia

Background & objectives: There is limited understanding of the processes driving metastasis. However, it is believed that the spread of cancer cells from the primary tumour, and the initiation of a secondary tumour, is facilitated by circulating tumour cells present in the bloodstream.
Methods: Only a handful of laboratories have managed to successfully grow viable circulating tumour cells (CTCs) in significant quantities. The aim of our work is to focus on the morphological changes in CTCs of different types of carcinomas over the course of 6 months since the cell isolation.
Results: We observed the initial cluster formation and their subsequent breakage, cell growth, adhesion and changes in viability. We collected

extensive photographic material and established protocols for cell cultivation, formalin fixation and paraffin embedding for preservation and use in immunocytochemistry.
Conclusion: We believe that our findings are a useful source of information for future research in the field of CTCs.

E-PS-19-049
KRAS mutations in pulmonary adenocarcinomas
V. Sousa*, A. Alarcao, A.F. Ladeirinha, M. Reis Silva, T. Ferreira, M. Viseu, M.A. Santos, J. Pimentel, G. Nogueira Fontinha, V. Almeida, L. Carvalho
*ULS Coimbra, Pathology Department; Faculdade de Medicina da Universidade de Coimbra, Portugal

Background & objectives: KRAS mutations are identified in 20-25% of lung adenocarcinomas. Mutated KRAS is a prognostic factor for overall survival, associated with more aggressive clinical phenotype. Several types of KRAS mutations can be found, making this gene an attractive target.
Methods: We present a serial of 71 cases in the last 15 month of KRAS positive mutations in NSCLC. It was performed mutation research by next-generation sequencing (Genexus, Oncomine Precision Assay Panel, Thermo Fisher Platform). Manual macrodissection was performed and nucleic acid extraction was carried out with the MagMAX FFPE DNA/RNA Ultra Kit.
Results: In a total of 71 cases we found: 38 (53,21%) - G12C; 11 (15,49%) - G12V; 10 (14,08%) - G12D; 6 (8,45%) - G12A; 1 (1,4%) - G12L; 1 (1,40%) - G12F; 3 (4,22%) - G13C; and 1 (1,4%) - G13D. We observed, as described in the literature, that mutations in KRAS are more frequent in codon 12 than in codon 13. We observed that 29/71 (40,84%) cases had concomitant mutations in other genes, namely: point mutation in TP53, PI3KCA, ALK, GNAS, MAP2K1, PTEN, FGFR3 and BRAF gene; amplification KRAS, ERBB2, FGFR3, FGFR1 and CD274 gene; MET exon 14 skipping (MET-MET.M13M15.1).
Conclusion: KRAS is an attractive therapeutic strategy due to its high prevalence and its role in initiating and sustaining tumour growth. Approval of KRAS G12C inhibitors in locally advanced or metastatic NSCLC has brought hope to many patients. Studies show that non G12C KRAS mutation are found in 53% of adenocarcinomas. Inhibitors targeting other KRAS mutants are in development. Given that there are so many KRAS mutations, efforts should be made to find new predictive biomarkers that will help modify treatment.

E-PS-19-050
MET and concomitant mutations in pulmonary adenocarcinomas
V. Sousa*, A.F. Ladeirinha, A. Alarcao, M. Reis Silva, T. Ferreira, M. Viseu, M.A. Santos, J. Pimentel, G. Nogueira Fontinha, V. Almeida, L. Carvalho
*ULS Coimbra, Pathology Department; Faculdade de Medicina da Universidade de Coimbra, Portugal

Background & objectives: Anti-MET targeted therapies were developed for MET exon 14 skipping and probably amplifications raising as genetic resistance. In advanced stages, 2%-4% METex14 point mutations or deletions occur predominantly in adenocarcinoma/sarcomatoid carcinomas. RNA-base methodology offers higher sensitivity than DNA-based methodology.
Methods: Mutation analysis by NGS (Genexus, Oncomine Precision Assay Panel, Thermo Fisher Platform) after macrodissection was performed and nucleic acid extraction, carried out with MagMAX FFPE DNA/RNA Ultra Kit. Oncomine Precision Assay Panel search MET DNA Hotspots (SNVs/Indels), CNVs (polysomy/amplification), intergenetic and intra-genetic fusions.
Results: MET alterations revised in the last 15 months consisted on 14 cases. MET exon 14 skipping mutations: 11/14 with MET-MET. M13M15.1; 5/14 with point mutations in MET gene; 1/14 deletion in MET gene. 2/14 with amplification (copy number: 21,57 and 10,34). The most important fact consisted on 8/14 concomitant mutations: TP53, PIK3CA, ALK (point mutation and fusion), ERBB2, PTEN, SMO, EGFR, KRAS (mutation and amplification), CD274.
Conclusion: Oncogenic activation of genes-drivers are responsible for resistance mechanisms either understood has resistance to MET-targeted therapies and as primary resistance. Recently it has been reported that PI3K pathway alteration is common in concomitancy with METex14 and believed that confers primary resistance to MET TKI. Early identification of alterations in MET kinase domain at diagnosis, is crucial for understanding progression and resistance mechanism, to develop novel therapies or to design treatment strategies in order to improve patient outcomes.

E-PS-19-051
The number of CD20+ B-lymphocytes expressing PD-1 is associated with the status of the mismatch repair system in endometrial cancer
L. Tashireva*, A. Kalinchuk
*Russia

Background & objectives: The status of the mismatch repair (MMR) system affects the treatment approach for endometrial cancer (EC) upon progression. This study aims to investigate the PD1-positive immune cells composition of the EC, specifically focusing on MSS/pMMR and MSI/dMMR.
Methods: The study enrolled 44 patients with endometrial cancer. Patients were divided into two groups: MSS/pMMR (n=34) and MSI/dMMR (n=10). The immunophenotype of microenvironment cells and their PD1 expression were evaluated using multiplex TSA-associated immunohistochemistry with Vectra 3.0 (Akoya).
Results: FoxP3+ T-lymphocytes and CD163+ macrophages expressing PD-1 were found to be equally rare and in low numbers in the tumour stroma (MSI/dMMR: 0.00(0.00-0.00)% and 0.00(0.00-0.00)%, respectively; MSS/pMMR: 0.00(0.00-0.07)% and 0.00(0.00-0.13)%, respectively; p=0.1820, p=0.3605). However, patients with MSI/dMMR endometrial cancer exhibited a significant increase in the proportion of CD20+ B-lymphocytes expressing PD-1 (MSI/dMMR: 0.12(0.06-0.40)% and MSS/pMMR: 0.00(0.00-0.01)%, p=0.0003). Notably, the fractions of CD8+ T-lymphocytes did not differ significantly between patients with different statuses of the mismatch repair system (MSI/dMMR: 0.20(0.00-0.63)% and MSS/pMMR: 0.00(0.00-0.14)%, p=0.1609).
Conclusion: MSI/dMMR-positive tumours exhibit elevated quantities of CD20+ B-lymphocytes expressing PD-1. This finding could be significant for immunotherapy employing pembrolizumab (an anti-PD-1 therapeutic antibody) as it may impede immune cells with pro-tumour characteristics. The study was supported by the Russian Science Foundation (grant number 20-75-10033-P).

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E-PS-19-052
Feasibility of fusion detection array in soft tissue tumours by nCounter platform
G. Teixeira*, F. Escremim de Paula, M. Queiroz de Almeida Bonatelli, G. Noriz Berardineli, M. Reis, K. Emília de Sá Rodrigues, L. C van Kempen, R. Manuel Reis
*Barretos Cancer Hospital, Brazil

Background & objectives: Identifying unique gene translocations in sarcomas is important to their classifications. Custom-based mRNA analysis by nCounter can be a feasible method for middle-income countries. We aimed to implement a nCounter custom-based approach in a Brazilian Molecular Diagnostic Laboratory.
Methods: A retrospective series of 56 cases with suspected sarcomas were admitted to Barretos Cancer Hospital. Following RNA isolation from FFPE samples, the fusion detection was done using a previously designed custom-based nCounter platform (NanoString), which detects 174 gene fusion transcripts. The nCounter results were compared with FISH or NGS analysis and histological features.
Results: Most cases were Ewing sarcomas, followed by synovial sarcoma and alveolar rhabdomyosarcoma. Ages ranged from 4 months to 85 years old. nCounter evaluation was conclusive in 55 cases and identified 24 fusions: nine SS18-SSX1, eight EWSR-FLI1, three PAX3-FOXO1, two EWSR1-WT1, one EWSR1-NR4A3, one HEY1-NCOA2 and one CDH11-USP6. FISH analysis was performed in 39 cases and NGS in 17. Two samples exhibited a nCounter negative result, justified by the absence of specific probes for these fusions (EWSR1-FEV and NUMA-NTRK1). In five cases, the nCounter results were negative despite the presence of a target probe. Overall, the comparative methodological analysis showed an accuracy of 82.5%, sensitivity of 76.6% and a specificity of 100%.
Conclusion: The nCounter technique showed its highest diagnostic efficacy for Ewing sarcoma, synovial sarcoma, myxoid liposarcoma, alveolar rhabdomyosarcoma, and desmoplastic small round cell tumours. These results emphasize that the NanoString assay is a rapid, cost-effective, and accurate tool for sarcomas molecular diagnosis. Nevertheless, additional molecular testing may be warranted in nCounter negative results, particularly for rare sarcoma subtypes.

E-PS-19-053
Immunological modulation in wound healing of the rat uterus by Mesenchymal Stem Cell-conditioned medium (MSC-medium) obtained under 10% oxygen content
N. Tikhonova*, V. Aleksankina, A. Milovanov, A. Aleksankin, T. Fokina, E. Kuznetsova, A. Sklifas, A. Temnov
*Petrovsky National Research Center of Surgery, Russia

Background & objectives: We assessed the effect of the conditioned medium obtained by culturing mesenchymal stem cells with low oxygen content (10%) on uterine healing after surgery incision, number of CD68+ cells and mRNA expression of IL1b, IL4, IL6, IL10 in wound healing zone.
Methods: MSC-medium was used to treat uterine surgical incision on Sprague-Dawley rats (treated group=17, untreated=10). Expression of IL1b, IL4, IL6, IL10 in wound healing zone was measured at 5th and 15th days after surgery. At the same samples, there were performed the histological examination with Mallory staining and with aSMA and CD68 immunohistochemical staining. Differences were considered statistically significant at $p<0.05$.
Results: At 5th day, there were lower IL10 expression($p=0.036$) in treated group like the area of wound healing zone was smaller($p=0.012$). At 15th day compared to 5th day, there were lower expression of IL1b($p<0.001$), IL4($p=0.004$), IL6($p=0.038$), IL10($p=0.002$) in untreated group. On 15th day, the treated group had a higher IL1b level ($p=0.021$) and less CD68+cells ($p=0.001$) than the untreated group. In the treated group, there were more CD68+cells at 5th day than at 15th. At 5th ($p=0.012$) and 15th ($p=0.003$) days untreated group had more healing area than treated group. IL1b, IL4, IL6, IL10 levels in treated group for both monitor points were close to parameters of intact uterine horn.
Conclusion: MSC-medium obtained under a reduced content of O2 (10%) influences of the size of the healing area and expression of IL10 in uterine wall after full-thickness surgical incision. Strong decrease the indicators of IL1b, IL4, IL6, IL10 from 5th to 15th days in untreated group and absent significant differences in treated group may indicate on faster and better healing with MSC-medium and modulation of inflammatory response.

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E-PS-19-054
The participation of IGG fragments in inflammation mechanisms for gastric malignancies
E. Goufman, N. Tikhonova*, A. Aleksankin, N. Nizyaeva, V. Bochkov, K. Gershkovich
*Petrovsky National Research Center of Surgery, Russia

Background & objectives: Aim was to study presence of IgG fragments with free C-terminal lysine (IgG-LysK) in serum of patients with stomach cancer, to assess link with the clinical-morphological characteristics of stomach cancer, and its possible role in diagnosing and predicting the disease.
Methods: The study included 68 patients (average age 61) with stomach cancer. The clinical diagnosis was confirmed by a morphological study of the tumour based on the international histological classification (WHO, 2019). The control group consisted of 20 healthy donors. The level of IgG fragments (IgG-LysK) was assessed by ELISA.
Results: According to histological and clinical morphological analysis, most (84%) of patients with stomach cancer were diagnosed with adenocarcinoma. The study found that the serum of healthy control group donors had a lower median IgG-LysK value than the stomach cancer group ($P=0.003$). False positive IgG-LysK values were detected in 15% of control group. False negative results were observed in 32% of patients with stomach cancer.
Conclusion: According to the ROC analysis, the sensitivity (SN) of stomach cancer and healthy people's SN was 68% with specificity (SP) 85% and AUC 0.719. This is higher than similar rates of oncology for these pathologies currently in use.

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E-PS-19-055
Differentially expressed genes in molecular subtypes of high-grade serous ovarian cancer
A. Tregubova*, A. Kobelyatskaya, A. Badlaeva, R. Aleksandra, M. Sannikova, R. Dmitrii, D. Sergei, A. Asaturova
*FSBI «National Medical Research Center for Obstetrics, Gynecology and Perinatology named after Academician V.I.Kulakov», Russia

Background & objectives: Currently the consensus about four molecular subtypes of high-grade serous ovarian cancer (HGSOC) is adopted and these subtypes probably differ in tumour progression manner.The goal of our investigation was to identify the special gene expression pattern for each molecular subtype.
Methods: This study used RNA-Seq data of HGSOC samples from The Cancer Genome Atlas (TCGAOV project). The cohort was divided into four molecular subtypes: differentiated (DS), immunoreactive (IS), mesenchymal (MS), and proliferative (PS). Differential expression analysis was performed in the statistical environment R using the EdgeR package. The MannWhitney (MW) and the quasi-likelihood tests (QLF) were used for statistical analysis.

Results: We identified 357 differentially expressed genes (QLF and MW p-values < 0.05) between the studied subtypes. Most importantly that there were 33 genes with increased expression in the IS, 91 – in the MS, and 137 – in the PS. The DS had a much less clear expression pattern than the other three subtypes with only 4 genes with increased expression. Moreover, there were a number of genes helped to subdivide HGSOC into two subtypes: DS/IS versus MS/PS – 52 genes, DS/MS versus IS/PS – 9, DS/PS versus IS/MS – 31. In total, 96 genes could be noted in one way or another as having increased expression within the DS.
Conclusion: The study showed that differentiated molecular subtype of HGSOC does not have its own clear gene expression pattern, but it can be identified through analysis within the context of the other subtypes. Through this work, we identified 357 genes that were differentially expressed in four molecular subtypes of ovarian cancer.

Funding: International Society of Gynecological Pathologists (ISGyP) Young Member Award (research proposal entitled "ArIStOtel: Artificial intelligent-based system for serous ovarian cancer subtyping")

E-PS-19-057
Lung cancer proteogenomics: the future of precision oncology
I. Vamvakaris*, N. Kontouli-Pertesi, M.L. Petre, O. Boulioglou, G. Vatselas, D. Valakos, G. Liadakis, I. Gkiozos, K. Syrigos, A. Anagnostopoulos
*Sotiria Hospital Athens Greece

Background & objectives: Lung cancer is the leading cause of cancer-associated mortality worldwide. The aim of the study was to investigate proteogenomic approaches in lung cancer, focusing on how elucidation of key proteogenomic features can lead to tangible clinical outcomes.
Methods: This was a literature-based study, adopting a strict methodological approach towards incorporating and analyzing all fundamental lung cancer proteogenomic studies. Key article features including molecular attributes, tumour biomarkers and major hallmarks involved in oncogenesis were taken in consideration. Molecular aspects of the disease have been explored thorough genomic investigations, however several pillar points are still elusive.
Results: Through the examined literature a consensus was portrayed, indicating that proteogenomics is anticipated to fill significant comprehension gaps and aid in the discovery of novel treatment options. Genomic profiling provides evidence of shared driver mutations in lung cancer patients, while the exploration of downstream effect generated by genomic alterations uncoveres variability in transcript and protein correlation. Emphasis is attributed in defining proteogenomic subtypes of tumours belonging to major histological classes, generating potential predictive markers and druggable targets.
Conclusion: Integration of genomic characterisation with in-depth proteomic profiling has introduced a new dimension in lung cancer research called proteogenomics.The present study delivers an up-to-date synthesis of landmark lung cancer proteogenomic studies. Mapping in fields where knowledge is at its infancy can be leveraged against this fatal disease, and will bring us one step closer to the application of personalized medicine for the treatment of lung cancer.

E-PS-19-058
A possible antineoplastic effect of the neuroprotective drug edaravone in ovarian cancer
C. Villa*, E. Duranti, C. Venturin, M. Cadamuro, M. Lavitrano
*Department of Medicine and Surgery, University of Milano-Bicocca, Monza, Italy

Background & objectives: The free radical scavenger edaravone (EDA) is currently used to treat amyotrophic lateral sclerosis. Recent research demonstrated that EDA can exert antitumour effects due to its antioxidant and anti-inflammatory properties, however no studies have explored its effects on ovarian cancer.
Methods: The OVCAR8 cell line was treated with different concentrations of EDA ranging from 25 to 1000 μM for 48 hours. MTT and wound healing assays were used to investigate the effects of EDA on cell viability and migration, respectively. The expression of proteins involved in these molecular pathways was determined using Western blot analysis.
Results: No differences in cell viability were found after EDA treatment at different concentrations (25, 50, 100, 200, 400, 700 and 1000 μM) for 48 hours. Conversely, wound healing assays demonstrated that 48h treatment with EDA significantly reduces OVCAR8 cell motility compared to untreated controls ($p < 0.05$). To investigate the molecular mechanisms supervising OVCAR8 migration, the JNK signaling pathway was explored. Western blot analysis revealed that EDA treatment reduced the expression of p-JNK, possibly reflecting the JNK pathway inhibition.
Conclusion: Our preliminary results suggested that EDA has no effect on cell viability but it can significantly slow migration in the ovarian cancer cell line OVCAR8. However, more extensive research is required to validate the reliability of our findings and to further investigate the molecular targets of EDA and its underlying mechanisms in ovarian cancer.

E-PS-19-059
Validation and workflow optimization of Her2/new assessment - our experience
S. Zeneli*, M. Ikonomi, M. Shyti
*UHC "Mother Teresa", Albania

Background & objectives: Her2 for equivocal cases, that can't be evaluated from only immunohistochemistry, need to be assessed for gene amplification using in situ hybridization probes. SISH is a quite novel assay that has recently been introduced in our laboratory practice.
Methods: For the first time in Albania we used SISH for Her2 status assessment. 120 samples were examined for HER2 protein expression with immunohistochemistry. 50 samples were stained with HER2/SISH (INFORM HER2 DNA Probe). We applied the recommended protocol, kits and reagents on all samples for Her2 gene amplification. After first results, we tried to improve specimen and histopathological technique
Results: Strict quality control standards are necessary for Her2 status assessment. There are many factors that can affect results: proper fixation, tissue processing, reagent quality, probe quality. Achieving good results with archived tissues is more difficult because of effects on fixation and accessibility of DNA. Optimal results were obtained with 24h of tissue fixation and 56°C overnight backing. Results on hybridization efficiency and signal quality were compared on the same group of samples with protocol improvements.
Conclusion: Optimal signal quality was achieved after improving tissue handling, test standardization and experience in interpretations of Her2 results. Establishment of these protocols has increased the success of the assay in our laboratory, especially for samples more than 1 year old. However, the main issue about this study is reaching an effective result in economical restriction situations, where samples of current or recurrent cases need to be reviewed for HER2 status.

E-PS-19-060
Multi-dimensional evaluation of the performance of homologous recombination deficiency detection in China
X. Zhou*, Q. Bai, X. Zhu, Z. Liang, H. Wu
*Fudan University Shanghai Cancer Center, China

Background & objectives: To evaluate the performance of different molecular assays, tumour purity and labs to identify homologous recombination deficiency (HRD) status and discuss the limitations of

HRD detection to provide evidence-based recommendations for optimal HRD detection in China.
Methods: Forty clinical samples from patients with ovarian cancer at Fudan University Shanghai Cancer Center (FUSCC) and Peking Union Medical College Hospital (PUMCH) and six cell line references with different tumour purity (30%; 50%; 80%) were selected. Currently available HRD detection assays in China (illumina, AmoyDx, Burning Rock, Genecast, Geneseeq, Precision Scientific, BGI and Geneplus) were performed in two independent labs.
Results: Among cell line references, one with 30% tumour purity showed HRD negative while 50% and 80% tumour purity showed HRD positive in three molecular assays. For clinical samples, assays for HRD assessment showed a high concordance of HRD score between each other. 77.5% (31/40) had HRD results that were completely consistent with each assay, while 22.5% (9/40) had inconsistent assay results. The concordance of HRD status between different molecular assays and illumina TSO 500 HRD ranges from 95.24% to 100% for PPA, 63.16%-78.95% for NPA and 82.50% to 90.00% for OPA. The correlation coefficients between HRD score detected by the same assays in different labs were high (R: 0.90-0.99).
Conclusion: Different molecular assays had high accuracy for identifying deleterious BRCA1/2 alterations while exhibited a few inconsistent in identifying HRD status.

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E-PS-20E-Poster Session Pulmonary Pathology

E-PS-20-002
Clinicopathological features of non-small cell lung carcinoma with NRAS mutation
A. Ambrosini-Spaltro*, C. Rengucci, L. Capelli, E. Chiadini, C. Bennati, A. Delmonte, S. Vecchiarelli, F. Limarzi, S. Nosseir, G. Gallo, M. Valli, D. Calistri
*Pathology Unit, Morgani-Pierantoni Hospital, AUSL Romagna, Forlì, Italy

Background & objectives: NRAS mutations affect less than 1% of lung adenocarcinomas and have rarely been studied in the literature. This study aimed to analyse the clinicopathological features of lung carcinomas with NRAS mutations, focusing on codon 61 versus other mutations.
Methods: All lung carcinomas that were molecularly examined between 2020 and early 2024 were considered. NRAS-mutated lung carcinomas were retrieved from a molecular diagnostic unit (reference unit for four different hospitals). The samples were both cytological and histological, and analysed using next-generation sequencing. All cases were morphologically reviewed. Statistical analyses included log-rank tests for overall survival (OS) and progression-free survival (PFS).
Results: NRAS mutation was detected in 17/1948 samples (0.87%), obtained from 13 patients. Most mutations (9/13, 70%) involved codon 61, whereas 4/13 were in codon 12 (2 cases), 13, 142. In 5/13 cases, co-alterations in other genes were found. Pleomorphic/sarcomatoid features were detected in 2/8 (25%) cases analysed from histological samples, and in 2/4 (50%) cases analysed from surgical specimens. Follow-up was available in 10/13 cases, and 4 patients deceased. Based on preliminary data, patients with NRAS mutations in codon 61 performed slightly better than patients with other mutations, without statistical significance (p= 0.069 for OS). Data on PFS are currently ongoing.
Conclusion: NRAS-mutated lung carcinomas are rare (<1%) and may exhibit pleomorphic or sarcomatoid features. Codon 61 mutations are associated with a slightly better prognosis than non-codon 61 mutations. Follow-up analyses are ongoing, especially for PFS.

E-PS-20-003
Acute fibrinous and organizing pneumonia in a patient with Von Willebrand disease: a case report
S. Amer*, M.R. Miller, I. Akhtar, M. Mollaee
*Pathology department - Temple University Hospital, USA

Background & objectives: INTRODUCTION: Acute fibrinous and organizing pneumonia (AFOP) is a rare form of lung injury with an acute or subacute presentation. The diagnosis of AFOP is one of exclusion and requires the absence of alveolar hyaline membranes, infectious agents, and significant.
Methods: eosinophilia/neutrophilia ratio to distinguish it from more common lung pathologies. CASE PRESENTATION: A 33-year-old female with past medical history of mild von Willebrand disease, and diabetes mellitus was admitted with diabetic ketoacidosis and small intestinal ischemia requiring small bowel resection. She was re-admitted few weeks later with massive hemoptysis and hypoxia requiring intubation. CT angiogram of thorax showed large dense.
Results: consolidation and ground glass opacities in the right lung. She underwent right lower lobe lobectomy and middle lobe wedge resection. Histological examination showed extensive intraalveolar fibrin with lack of granulomata, and hyaline membrane formation consistent with AFOP. DISCUSSION: AFOP is an underdiagnosed histopathological pattern of lung injury with two different forms of acute, with a poor and subacute form associated with a more favourable prognosis respectively. The etiology of AFOP remains unclear. It is recognized by the presence of intra-alveolar fibrin balls on biopsy. Conditions associated with its development include autoimmune diseases, dermatomyositis, mixed connective tissue disease, systemic lupus erythematosus, immunomodulatory therapies, and environmental exposures to substances such as asbestos,
Conclusion: infectious agents, especially in immunocompromised patients. Definitive diagnosis is made on lung biopsy. Corticosteroids are the mainstay of treatment. Despite poor prognosis in acute form, definite diagnosis and proper treatment improve the outcome. CONCLUSIONS: Bleeding disorders like von Willebrand disease and its potential association with AFOP have not been previously reported in the literature. Having high suspicion and prompt diagnosis are crucial for the treatment as the clinical manifestation is very non-specific.

E-PS-20-004
Relapsing granulomatosis with polyangiitis with lung manifestation in a patient with kidney transplant: a case report
S. Amer*, J. Hassler, M. Mollaee
*Pathology department - Temple University Hospital, USA

Background & objectives: BACKGROUND: Granulomatosis with polyangiitis (GPA) is a relatively rare autoimmune systemic disease with an unknown etiology that is characterized by necrotizing granulomatosis and small vessel vasculitis of the respiratory tracts with accompanying glomerulonephritis. GPA activity and relapse in renal transplant
Methods: recipients is very infrequent. The biopsy remains a gold standard for diagnosis. CASE PRESENTATION: A 77-year-old male with history of end-stage renal disease (ESRD) on dialysis underwent a renal biopsy. Histologic examination revealed GPA with positive c-ANCA (cytoplasmic antineutrophilic cytoplasmic antibody). The

patient received a renal transplant with eventual graft loss secondary to BK virus infection. A few years later,
Results: he underwent a second kidney transplant. Two years after his most recent transplant, he presented with shortness of breath and was found to have acute hypoxic respiratory failure. CT scan of the chest showed a bilateral multifocal ground-glass and consolidative opacities in the lower lobes. Serology was negative for myeloperoxidase (MPO) or proteinase 3 (PR3) ANCA titers. The patient subsequently underwent a bronchoalveolar lavage and transbronchial biopsy. An infectious disease workup and cultures were all negative. The biopsy showed an acute fibrinous lung injury in an early organizing subacute phase, hemosiderin-laden macrophages in air spaces, and patchy fresh blood admixed with intraalveolar fibrin compatible with diffuse alveolar hemorrhage (DAH).
Conclusion: Additionally, increased neutrophils in the pulmonary interstitium suggestive of active capillaritis. Although DAH and capillaritis are non-specific findings, they are highly characteristic of a systemic vasculitis syndrome and support a diagnosis of an active GPA involving the lung in this immunosuppressed patient. DISCUSSION: Relapse in ANCA vasculitis remains a main challenge. Transplant patients should be closely monitored for relapse. Early diagnosis is essential for early treatment by increasing immunosuppression and/or immunomodulation and the pathologist needs to have this in differential diagnosis.

E-PS-20-005
Hyalinising clear cell carcinoma of the lung: a case report
B.B. Ardaya Lopez*, H. Galindo Guzman, M. Cebollero Presmanes, M. García Martos
*Hospital General Universitario Gregorio Marañon, Bolivia

Background & objectives: Hyalinizing clear cell carcinoma (HCCC) of the lung, a rare subset of pulmonary salivary gland-type tumours (SGT), constitutes less than 0.09% of primary pulmonary tumours, with limited clinicopathological data available. Here, we present the case of a 49-year-old non-smoking woman.
Methods: Our case involves a 49-year-old woman who presented with dyspnea, cough, and hemoptoic sputum. Imaging and bronchoscopy revealed obstruction of the right intermediate bronchus, resulting in atelectasis of the right middle and lower lobes. Cryobiopsy suggested a salivary gland-type tumour (SGT), leading to the decision to undergo a right lower lobectomy.
Results: Morphologically, it was an endobronchial, well-defined lesion that histologically corresponded to a well-demarcated, non-encapsulated neoplasia formed by two types of cells: some with eosinophilic cytoplasm and others with clear cytoplasm and hyperchromatic nuclei, without marked atypia, growing in nests and trabeculae on a densely hyaline stroma with myxoid foci. The neoplastic cells showed positivity for CK7, CK5/6, and EMA, with focal positivity for p63 and p40. Based on these findings, and after ruling out other primary lung tumours as well as those of metastatic origin, a diagnosis of HCCC was made. No lymph nodes were affected. Following bilobectomy, the patient experienced a favourable recovery. No tumour recurrence evident presently.
Conclusion: Although the clinical presentation was nonspecific and lacked defining radiological features, understanding the morphological patterns under the microscope and the immunophenotype of HCCC is crucial for the correct recognition of this rare entity. Recently, characteristic genetic alterations such as EWSR1::ATF1, the most common gene fusion, have been recognized, providing another important diagnostic tool. HCCC of the lung generally has a good prognosis, and recurrence is rare. Given its rarity, our case contributes valuable epidemiological data to the understanding of HCCC.

E-PS-20-006
Checkpoint Kinase 1 immunohistochemical expression in pleural mesothelioma
A. Asghari Birbaneh*, C. Meristoudis, V. Panou, O.D. Røe
*Pathology and Anatomy Institute, North Denmark Regional Hospital, Hjoerring, Denmark; Centre for Clinical Research, North Denmark Regional Hospital, Hjoerring, Denmark

Background & objectives: Pleural mesothelioma (PM) is an aggressive, typically chemo-resistant cancer. Checkpoint Kinase 1 (CHEK1) is an embryonal gene involved in DNA repair, with an important role in chemotherapy resistance. We aim to explore the immunohistochemical (IHC) expression of CHEK1 in PM
Methods: Tissue Micro Arrays (TMA) were constructed from retrieved archival material of patients diagnosed with PM, between 1975-2013. The TMA slides were stained with an anti-CHEK1 mouse monoclonal antibody and the histochemical score (H-score) was assessed. Additionally, demographic, clinical and survival characteristics such as sex, age, tumour subtype, treatment choices, and overall survival were retrospectively retrieved from the medical records.
Results: In total, 45 patients were included in the study. CHEK1 was expressed in 43 (95.6%) cases. The H-score ranged between 0-268. It was expressed in both the nucleus and cytoplasm, but with varying intensity. The intensity was higher in the nucleus compared to the cytoplasm for all the subtypes. In the epithelioid subtype, a higher percentage of stained cytoplasm was observed compared to the nucleus. However, this pattern shifted towards more variation between the nucleus and cytoplasm in the biphasic and sarcomatoid subtypes.
Conclusion: The study demonstrates that only 2 (4.4%) patients showed lack of CHEK1 expression. This is in alignment with the literature that shows that CHEK1 expression is typically not expected in normal mesothelial cells and is considered a sign of malignancy, though with low specificity. We are currently including further PM patients to conduct a larger study investigating the potential prognostic and predictive value of CHEK1 expression in PM.

E-PS-20-007
TTF1 is a highly specific marker for pulmonary and thyroidal cancer: a tissue microarray study evaluating more than 17,000 tumours from 152 different tumour entities
K. Möller, T. Gulzar, M. Lennartz, N. Schraps, F. Viehweger, E. Bady*, C. Bernreuther, R. Simon, T.S. Clauditz, G. Sauter, N. Gorbokon, M. Reck, N. Frost, T. Krech, S. Steurer
*Institute of Pathology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

Background & objectives: Thyroid transcription factor-1 (TTF1) is a tissue-specific transcription promoter with a critical role in the development in the thyroid, the lung and the brain. TTF1 immunohistochemistry (IHC) is routinely used for the distinction of primary pulmonary adenocarcinomas.
Methods: To better understand the prevalence of TTF1 expression in human malignancies and the diagnostic utility of TTF1 IHC, a tissue microarray containing 17,772 samples from 152 different tumour types and subtypes was analysed by IHC. Napsin A, Cytokeratin 20, SATB2, FABP1, and Villin IHC data were available from previous studies.
Results: TTF1 staining was seen in 82 of 152 tumour categories, including thyroidal cancers (up to 100% positive), adenocarcinomas (94.0%) and neuroendocrine tumours (67.0%) of the lung, and neuroendocrine carcinomas of various other organs (71.0%-80.0%). Co-analysis of TTF1 and Napsin A for diagnosing pulmonary adenocarcinomas revealed a sensitivity/specificity of 94%/86% for TTF1, 87%/98% for Napsin A, and 97%/85% for the combination of TTF1

and Napsin A. The combined analysis of TTF1 and enteric markers (CK20, SATB2, FABP1, Villin) revealed a positivity for TTF1 and at least one enteric marker in 22% of pulmonary adenocarcinomas but also a TTF1 positivity in 6% of colorectal, 2% of pancreatic, and 3% of gastric adenocarcinomas.
Conclusion: TTF1 is a marker of high sensitivity but insufficient specificity for the distinction of pulmonary adenocarcinomas. A small fraction of (strongly) TTF1 positive gastrointestinal (and other) adenocarcinomas represents a significant pitfall mimicking enteric type pulmonary adenocarcinoma. The combined analysis of TTF1 and Napsin A significantly improves the specificity of pulmonary adenocarcinoma diagnosis.

E-PS-20-008
Application of the 5th WHO guidelines for the diagnosis of small lung biopsies in a tertiary care centre: is insecurity of pathologists for the right diagnosis justified?
M. Beckert*, G. Levidou, T. Papadopoulos
*Klinikum Nürnberg, Germany

Background & objectives: Diagnosing lung cancer (LC) on small biopsies is a daily routine for pathologists. According to the WHO-guidelines, this diagnosis should be made by morphology, using only limited additional testing. However, extensive testing is often conducted.
Methods: A retrospective analysis of 288 lung biopsies diagnosed in our Department was conducted.
Results: Our analysis showed that a comparable diagnostic certainty can be achieved in case of definite primary LC, with a mean number of 1 (SD±1,4) ancillary techniques, reaching a concordance rate of 97,3% compared to extensive testing. Only in cases of metastases (information unknown or not shared), an advantage of the extensive testing is proven, since limited techniques can lead to the diagnosis of a primary non-small cell lung carcinoma no other specified (NSCLC NOS) (14/47 metastases). We also found a comparable expression of p40 and p63 in squamous cell carcinoma, but higher p63 in adenocarcinomas (p<0,001) or NSCLC NOS (p=0,007).
Conclusion: The uncertainty of pathologists regarding the diagnosis of lung cancer in small biopsies is justified where the diagnosis of NSCLC NOS is reached.

E-PS-20-009
Expression of the PDL-1 protein in immunohistochemistry in non-small cell lung carcinomas
C. Benallal*, H. Azal, H. Rachidi, y. Msougar, H. Rais
*Morocco

Background & objectives: The objective of our study was to study the expression of PDL1 and ALK in NSCLC while focusing on the technical requirements in immunohistochemistry and FISH in order to optimize the yield of biopsies and improve patient care
Methods: We carried out a cross-sectional study, spread over 18 months from September 2017 to January 31, 2020 and involving 111 patients collected from the Mohammed VI University Hospital in Marrakech for diagnosis and follow-up. Tumours were analysed histologically and classified according to PDL-1 and ALK expression profile. A correlation with clinical, histological and prognostic factors was also achieved
Results: Adenocarcinoma was the most common histological type in our series with a rate of 75%, followed by squamous cell carcinoma (21.6%) and CBPNC without other indications (2.7%). Of the patients studied, 51.4% had a TPS less than 1%, 25.8% had a TPS between 1% and 49%, and 22.9% had a TPS greater than 50%.The expression of the anti-ALK antibody was positive in only 3 patients in our series (2.9%).
Conclusion: Bronchopulmonary cancers (PBC) are the leading cause of cancer death in the world. In recent years, PBC has benefited from major therapeutic advances, mainly represented by targeted therapies and immunotherapy. Patients with positive anti-PD-L1 antibody expression may benefit from immunotherapy. Crizotinib is a preferred treatment option in patients with a rearrangement of the ALK gene. Adequate and timely management can change the prognosis of bronchopulmonary tumours found in our region and improve survival.

E-PS-20-010
Relationship between clinicopathological parameters and EGFR mutation status in non-small cell lung carcinomas and correlation of PD-L1 expression
S. Cagaptay*, D. Gurel, A. Aysal Ağalar, C. Ulukus, K. Canaslan, V. Karacam, I. Ulugun, K.C. Tertemiz, I. Oztop
*Dokuz Eylul University, Turkey

Background & objectives: Our study aims to investigate clinical and pathological parameters that may be associated with EGFR mutations and ALK and ROS rearrangement and to understand the relationship between PD-L1 expression and driver mutations.
Methods: Between 2015 and 2022, 141 biopsy materials and 97 resection materials were evaluated and the cases diagnosed with NSCLC were included in the study. Statistical analyses were performed using the IBM SPPSS Version 29.0 program and a p value of <0.05 was considered significant.
Results: A significant relationship was found between the presence of EGFR mutation and female gender and non-smoking status (p<0.001). EGFR mutation was found to be significantly higher in adenocarcinomas showing mixed patterns (p=<0.001). No significant relationship was detected between PD-L1 expression (p=0.557) and expression level (p=0.500) and driver mutations. The mean overall survival time in the patient group receiving immunotherapy was statistically significantly longer, including the group with PD-L1 expression level <1% (p=0.041). The average overall survival time was significantly lower in patients with ALK rearrangement (p<0.001) and was found to be an independent poor prognostic factor (HR: 8.6, 95% CI: 1, 9-38, p=0.004).
Conclusion: Targeted therapies provide significant improvements in life expectancy in NSCLC patients. But the relationship between driver mutations and clinical and histopathological parameters is still poorly understood. Analyses for driver mutations should be performed in all patients, regardless of their demographic, clinical, histopathological characteristics and stage. Using other biomarkers that can predict immunotherapy response along with PD-L1 expression status may contribute to predicting treatment response.

E-PS-20-011
An insidious cystic lung lesion causing pneumothorax: a case report
C.Y. Chow*, P.Y. Tang, A. Takano
*Singapore

Background & objectives: Cystic lung disease encompasses a broad range of differential diagnoses based on radiological appearances. Herein, we report a patient who presented with spontaneous pneumothorax and no prior medical history, ultimately found to have cystic metastases of angiosarcoma in the lung.
Methods: An 84-year-old male, never smoker, presented with haemoptysis and shortness of breath. Chest X-ray revealed bilateral pneumothoraces with patchy opacities and a mid-zone 2cm cystic lesion in the right lung. The patient underwent wedge resection of the right lung with pleurodesis and chest tube insertion. His pneumothorax failed to resolve, prompting multiple rounds of talc pleurodesis after the initial procedure.

Results: Histologic study demonstrated intraparenchymal hemorrhage featuring small clusters of atypical cells in the alveolar spaces with increased mitotic activity. Immunohistochemical stains were strongly positivity for endothelial markers. The Ki-67 proliferation index was 30-40%. A diagnosis of epithelioid angiosarcoma was made, with a comment to exclude primary tumour of sun-exposed skin such as that of the head or neck regions. A clinical examination later revealed a nodular tumour at the left fronto-parietal scalp, which was FDG-avid on PET scan. The patient was managed as angiosarcoma of the scalp with metastatic disease to the lung. He was started on chemotherapy regime of paclitaxel but showed disease progression despite one year of treatment.
Conclusion: Angiosarcoma is a rare but highly aggressive vascular tumour that can present in the lung as metastasis. This case underscores the importance of considering rare metastatic malignancies in the differential diagnosis of cystic lung diseases in elderly patients, even in the absence of prior medical history or the absence of visible clinical lesions. Clinicians should be cognisant that metastatic angiosarcoma to the lung can present with recurrent pneumothorax. Comprehensive histopathological assessment is indispensable for accurate diagnosis in such intricate presentations.

E-PS-20-012
Mucous gland adenoma of the lung: a case report from a very rare entity in an unusual location
O.M. Da Rocha Moreira Pedro*, D. Almeida, J. dos Santos, M. Honavar, T. Amaro
*ULS Matosinhos; Escola Superior de Saúde - Instituto Politécnico do Porto, Portugal

Background & objectives: To present a rare case of a Mucous gland adenoma (MGA) located peripherally in the lung, along with a brief overview of its histopathological and clinical characteristics.
Methods: A 68-year-old male with clinical history of hypertension, type 2 diabetes, dyslipidemia and sleep apnea syndrome presented with a parenchimatous peripheral lung mass in the apical segment of the inferior lobe of the right lung, with less than 1 centimeter in size, with no contrast enhancing. Biopsy was performed for histopathological analysis.
Results: Histopathological examination revealed pulmonary parenchyma with focal proliferation of mucinous columnar cells with mild cytology features, without hyperchromasia, pleomorphism, or mitoses. The immunohistochemical profile showed positivity for CK7+ with no expression of TTF1, S100 and P63. Given the histological findings the diagnosis of a mucous gland adenoma was made, a very uncommon entity of the bronchial tree, althoungh there are few reported cases of intraparenchymal location. The patient is in a 3 month CT scan follow up scheme and there were no changes in the size or features of the mass in the first six months post biopsy.
Conclusion: Mucous gland adenomas are challenging to diagnose due to their rarity and can mimic other pulmonary neoplasms. A thorough differential diagnosis study should be done with other rare benign entities (alveolar cell adenoma and mucinous cystadenoma), but the main differential diagnosis should be with malignant lesions (adenocarcinoma and low-grade mucoepidermoid carcinoma) that need a completely different management and treatment. There are no more than 6 cases (according to our research) of a MGA in a periphereal intraparenchimal location.

E-PS-20-013
Immunophenotypic analyses of diffuse idiopathic pulmonary neuroendocrine cell hyperplasia: a brief case series tested with emerging markers INSM1 and POU2F3
B. Del Forno*, F. Fortarezza, F. Pezzuto, F. Lunardi, E. Faccioli, F. Rea, F. Calabrese
*Università di Padova, Italy

Background & objectives: Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH) is a rare entity characterized by an abnormal proliferation of pulmonary neuroendocrine cells. Its role as preinvasive lesion is not well defined. We performed immunohistochemical profiling with particular reference to new NE markers.
Methods: Eight lung resection specimens with multifocal NECH, including a case with associated silicotic nodules, were carefully reviewed. Carcinoids, tumourlets and NECH were histologically diagnosed using WHO criteria. The number of NECH/slide and tumourlet/case was recorded. The expression of chromogranin A, synaptophysin, CD56, Ki67, TTF1, INSM1 and POU2F3 was analysed and graded in all neuroendocrine cells.
Results: We recorded 3-6 NECH/slide and most of them (n=7) were associated with tumourlets. Common neuroendocrine markers (chromogranin A, synaptophysin and CD56) were highly expressed. The percentage of positive cells for INSM1 was >50% in three cases, 20-40% in four cases and focal staining (<5%) was present in only one case. Interestingly, INSM1 was overexpressed only in cases of DIPNECH associated with typical carcinoids. POU2F3 expression was negative in all cases. In the non-idiopathic form (associated with silicotic nodules), 13 NECH/slide and 6 tumourlets were found, with an expression of NE markers similar to that of DIPNECH cases.
Conclusion: POU2F3 was never expressed in our cases, thus supporting its expression in tumourlets and carcinoids is not noteworthy. INSM1 expression was particularly increased in DIPNECH associated with carcinoids. These data could help us to better understand the pathobiology of DIPNECH, allowing, if the data are confirmed in larger case series, to stratify reactive NECH from preinvasive lesions.

E-PS-20-014
Association of EGFR mutation status with morphological, epidemiological, clinical characteristics of lung adenocarcinoma and squamous cell carcinoma
S. Dubencovs*, J. Nazarovs, A. Mežals
*Pauls Stradins Clinical University Hospital, Pathology institute, Latvia

Background & objectives: EGFR mutation in non-small cell lung cancer is associated with female gender, smaller tumour size, TTF-1 expression etc. [Zhang, Katgı] The aim was to evaluate the association of EGFR mutation status with some morphological, epidemiological and clinical characteristics in Latvia.
Methods: A total of 139 cases were identified in Pauls Stradiņš Clinical University Hospital with diagnosed lung adenocarcinoma (AC) and squamous cell carcinoma (SCC), when EGFR mutation analysis was performed in 2022-2023. We evaluated the correlation of EGFR mutation status with patients gender, age, tumour histological type, grade, radiological size and immunohistochemical TTF-1, PD-L1 expression and ALK mutation status.
Results: Mean age of patients was 68.9±SD8.1 years, 101 males and 38 females. Positive EGFR mutation was found in 17 patients (12%), negative in 122 patients (88%). EGFR positivity correlated significantly with female gender (p<0.0001). EGFR positive mutation was found in AC only (n=17), 60 AC were EGFR negative, all SCC (n=62) were EGFR negative. Positive EGFR mutation status correlated significantly with AC vs SCC (p=0.0001) and TTF-1 positivity (p=0.0001). Negative correlation was found between EGFR and PD-L1 (p=0.04). No statistically significant correlation was found between EGFR mutation status and patients age, tumour size, histological grade, ALK mutation (p>0.05).
Conclusion: In our population, the female gender, adenocarcinoma type tumour (vs squamous cell carcinoma) and immunohistochemical TTF-1 positivity were associated with the presence of EGFR mutation. These characteristics can predict the status of EGFR mutation in lung non-small cell carcinoma.

E-PS-20-015

Differential expression of MRPL23 in non-small cell lung cancer and its prognostic implications

J. Durślewicz*, M. Gagat, Ł. Szylberg, D. Grzanka
*Department of Clinical Pathomorphology, Faculty of Medicine, Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Torun, Bydgoszcz, Poland

Background & objectives: MRPL23, essential for mitochondrial function and protein synthesis, shows variable expression in cancers, influencing tumourigenesis. This study investigates its expression in non-small cell lung cancer (NSCLC) to assess MRPL23's potential as a prognostic biomarker for patient outcomes.
Methods: Tissue Microarray (TMA) slides from 120 NSCLC patients and 10 normal tissues underwent immunohistochemical staining for MRPL23, assessed using a modified Remmele-Stegner index. MRPL23 mRNA from the TCGA cohort was analysed for prognostic and treatment outcomes. Complementary investigations included Western blot and quantitative PCR analyses performed on several NSCLC cell lines: A549, H1299, H647, MRC5, and HBEC.
Results: MRPL23 expression was significantly higher in NSCLC compared to normal lung tissues ($p < 0.0001$). Squamous cell carcinoma (SCC) exhibited significantly higher MRPL23 levels than adenocarcinoma (ADC) ($p = 0.01$). Additionally, a significant correlation existed between MRPL23 expression and nodal status (N status, p=0.05). Kaplan-Meier analysis demonstrated that high MRPL23 expression was significantly associated with shorter overall survival (OS) in NSCLC patients ($p = 0.001$). Univariate and multivariate Cox analyses identified high MRPL23 expression as an independent risk factor for poor prognosis (HR 1.67, 95% CI 1.03-2.70, $p = 0.04$). Analysis of the TCGA cohort reinforced these findings, with high MRPL23 expression correlating with significantly shorter OS ($p = 0.017$).
Conclusion: This study demonstrates that MRPL23, crucial for mitochondrial function and protein synthesis, is significantly overexpressed in NSCLC tissues. High MRPL23 expression correlates with advanced nodal status and significantly shorter OS, underscoring its potential as an independent prognostic biomarker. These findings suggest that MRPL23 could be pivotal in understanding NSCLC progression and may guide therapeutic strategies targeting mitochondrial pathways.

E-PS-20-016

Hepatoid adenocarcinoma of the lung with EGFR and TP53 mutation: a case report and literature review

A. Dutta*, S.S. Nayak, N. Karuvandan, O.A. Shetty
*HBCH&RC, Vizag, India

Background & objectives: Hepatoid adenocarcinoma of lung (HAL) is a rare and aggressive type of lung adenocarcinoma with evidence of hepatocellular differentiation. There is limited data on the mutational status, behaviour and treatment strategies of this entity.
Methods: A 43-year-old smoker male presented with a 4-month history of right thigh pain and weight loss. X-ray of right femur showed a lytic lesion in shaft and biopsy (done outside) revealed a malignant epithelial tumour. CECT scan showed an enhancing 8.3 x 5.8 cm lesion in the right lung and metastatic lesions in liver, pancreas and adrenal gland.
Results: The biopsy was reviewed. It showed an epithelioid tumour infiltrating the bone and arranged in sheets, nests and glands. On immunohistochemistry, the tumour was positive for CK7, HepPar1, TTF-1 (cytoplasmic) and negative for Napsin A and CK20. The final diagnosis was metastatic hepatoid adenocarcinoma of primary lung origin. The patient was treated with palliative intent and started on chemotherapy with pemetrexed and carboplatin. Genomic testing detected missense mutations in exon 21 of EGFR and exon 7 of TP53 gene. Thereafter, the patient received oral afatinib. Response CT scan showed partial response. However, one and half months later the patient progressed clinically and died.
Conclusion: HAL poses a diagnostic challenge owing to its rarity and morphological resemblance to hepatocellular carcinoma. A judicious immunohistochemical panel is crucial for accurate diagnosis and subsequent conservation of tissue for molecular testing. This tumour often presents in advanced stage, has poor response to conventional chemotherapy and is usually negative for oncogenic driver mutations. To our knowledge, this is the first report of HAL harboring both EGFR and TP53 mutation, suggesting an important role of molecular profiling-directed therapy in these patients.

E-PS-20-017

Challenges in diagnosis of multiple lung cancers: synchronous double primary lung or intrapulmonary metastasis?

I. El Hadhri*, R. Ayadi, E. Braham, R. Yaiche, I. bouassida, I. Mallek, O. Ismail, S. Ben Slama, A. Ayadi
*Sahloul University Hospital, Tunisia

Background & objectives: Worldwide, lung cancer is the most fatal cancer among multiple types of malignances. In the case of multifocal lung cancers, discriminating multiple primary lung cancers from intrapulmonary metastasis remains a common dilemma in the clinical setting.
Methods: This retrospective study was performed on 7 male and one female patients, aged between 52 and 78, with a mean age of 64 years, diagnosed with multiple primary lung cancers between 2004 and 2023 at our department of pathology.
Results: It was discovered to have two synchronous lung masses on imaging examinations. The diagnosis was made on transparietal biopsy (n=2), surgical biopsy (n= 2) and surgical resection (n=4). Histological and immunohistochemistry examination showed combined carcinoid typic tumour (EMA+, Chromogranin+, Synaptophysin+) and B lymphoma of the marginal zone type MALT (CD20+, CD5 -, EMA + lymph epithelial lesion) (n=1), squamous carcinoma (p40+, TTF1-) and adenocarcinoma (TTF1+, p40-) (n=3), small cell carcinoma (CD5+, TTF1+, P63-), squamous carcinoma (P63+, TTF1-) and adenocarcinoma (TTF1+, p63-) (n=1), and identical morphology of multifocal adenocarcinoma (TTF1+) (n=3). Histopathological and immunohistochemistry examinations led to the final diagnosis of multiple primary lung cancers.
Conclusion: Multiple primary lung cancers are increasingly encountered in clinical practice. clinicopathological characteristics and immunohistochemical study could be helpful in differentiating multiple primary tumours from metastases. Although surgical resection remains the mainly choice for the treatment. Nevertheless, there are still several controversies exist in the diagnosis, classification, and multidisciplinary management strategies of this cancers.

E-PS-20-018

Distinguiching synchronous double primary lung adenocarcinoma from intrapulmonary metastasis based on histological findings and immunohistochemical study

I. El Hadhri*, R. Ayadi, E. Braham, R. Yaiche, I. bouassida, I. Mallek, O. Ismail, S. Ben Slama, A. Ayadi
*Sahloul University Hospital, Tunisia

Background & objectives: Lung cancer is the deadliest cancer worldwide. The incidence of multiple lung cancer in reported clinical series ranges from 1% to 7%. Differentiating synchronous double primary lung adenocarcinoma from interpulmonary metastasis has important therapeutic and prognostic implications.
Methods: Here, we report two cases of a 61-year-old man and a 52-year-old woman found to have two discrete, synchronous lung masses on imaging studies, both with prior carcinoma histories (rectal carcinoma vs breast carcinoma and thyroid carcinoma respectively). The final diagnosis was established through an histological

and immunohistochemical examination at the pathological anatomy department of Abderrahmen Mami Hospital.
Results: The patients underwent wedge and lobectomy resection of the tumours. For woman, the 1,2 cm left upper lobe showed invasive adenocarcinoma papillary predominant (TTF1+, CK7+, CK20-). The 1 cm left lower lobe showed metastatic vesicular thyroid carcinoma (Thyroglobulin +, TTF1-). For man, the 3,4 and 1 cm left upper lobe showed invasive adenocarcinoma lepidic predominant (Thyroglobulin-, TTF1+). The 2 cm right lower lobe showed metastatic rectal adenocarcinoma (TTF1-, CK7-, CK20+).
Conclusion: These two patients remind us of the coexistence of synchronous double primary lung adenocarcinomas and intrapulmonary metastasis. The diagnosis of synchronous malignancies poses challenges for both the diagnosing pathologist and the treating clinician.

E-PS-20-019
Tracheal adenoid cystic carcinoma: an extremely rare malignant tumour involving the trachea
I. El Hadhri*, R. Ayadi, E. Braham, R. Yaiche, M. Affes, I. bouassida, I. Mallek, O. Ismail, S. Hantous-Zannad, A. Ayadi
*Sahloul University Hospital, Tunisia

Background & objectives: Primary tracheal tumours are extremely rare, accounting for 0.2 % of the respiratory system. Adenoid cystic carcinoma (ACC) is the second most common malignancy of the trachea. To better understand this entity, we reviewed clinicopathological data of patients with ACC.
Methods: We report 10 cases of ACC of the trachea, treated in our institution from 1998 to 2023. The clinical features, histopathology findings and treatment are discussed. There were 5 males and 5 females patients, aged between 27 and 54 years with a mean of 44,55 years.
Results: All the patients presented with respiratory symptoms: dyspnea (6), dry cough (6), hemoptysis (3) and dysphagia (2). Chest X-ray showed an endotracheal opacity (2 cases), narrowing of the tracheal lumen (2 cases). Bronchoscopy revealed a budding formation (n=7). The treatment was surgical (n=8) : Tracheal resection and anastomosis (n=7) and pneumonectomy with extended resection to the carina and the trachea (n=1). Endoscopic treatment was performed in 2 cases. Histologically, the tumour is characterized by a predominant compact sheet-like and nested pattern of rounded basaloid cells. Tumour stroma exhibited myxoid characteristics. Immunohistochemically (n=2), the tumour was diffusely positive for CK, EMA and PS100. TTF1, Chromogranin, CD117 and CK20 were negative.
Conclusion: Primary ACC of the trachea are malignant tumours which have to be kept in mind. Diagnosis of this entity is challenging due to its low incidence. A good understanding of the clinico-pathological profile may aid in clinical suspicion and diagnosis at an early stage. ACC has an indolent course and good prognosis. Their treatment is mainly surgical combined with radiotherapy.

E-PS-20-020
Non-small cell bronchopulmonary carcinoma and molecular testing for EGFR, ALK and PDL-1 status, 8 years experience at CHU Mohammed VI
H. El Khadraoui*, H. Rais, B. Benzi
*Anatomopathology department, Morocco

Background & objectives: In non-small cell bronchopulmonary carcinomas have benefited from major therapeutic advances following the emergence of targeted therapies and immunotherapy by targeting the PD1/PDL1 immune response checkpoint, the search for rearrangement of the Anaplastic lymphoma kinase (ALK) and EGFR mutation.
Methods: Our work concerns a retrospective study carried out in the Anatomical Pathology department of the Mohammed VI University Hospital of Marrakech between January 2016 and december 2023. The samples were analysed histologically and classified according to the EGFR mutational profile as well as the PDL-1 expression profile and ALK.
Results: The results showed that adenocarcinoma is the most represented type (75%), followed by squamous cell carcinoma (15%). The EGFR mutation sought in 281 patients found 79 cases mutated. Among these mutations, those involving exon 19 were the most frequent and represented 72% of all EGFR mutations. ALK rearrangement was performed in 201 patients of which 11 cases were positive. The evaluation of PDL-1 status concerned 304 patients including 231 cases affected by lung adenocarcinoma and 73 cases affected by squamous cell carcinoma. The TPS score was less than 1% in 58.69% of patients.
Conclusion: The analysis of theranostic molecular markers EGFR and ALK as well as the advent of immunotherapy have completely transformed the management and prognosis of NSCLC. Therefore, the involvement of pathologists in the molecular testing strategy for bronchopulmonary carcinomas is essential to improve patient care.

E-PS-20-021
Informatics and digital pathology in non-small cell lung cancer: automatic quantification of brightfield multiplex immunohistochemistry
M. Errani*, F. Ambrosi, T. Franceschini, C. Ricci, A. Grillini, E. Franchini, E. Demaria, A. Gherardi, A. Bevilacqua, M. Fiorentino, M. Mottola
*University of Bologna School of Medicine, Bologna, Italy

Background & objectives: Tumour microenvironment (TME) affects the prognosis of tumours, including non-small cell lung cancer, meanwhile digital pathology revealed possibilities in TME quantification, especially using brightfield multiplex immunohistochemistry (BF-mIHC). We aim to develop and validate a software tool for automated BF-mIHC quantification.
Methods: The BF-mIHC included four markers: CD20(purple), CD68(teal), CD8(dab), and CD4(green). A pulmonary pathologist performed markers' counting in three hotspot regions: tumoural front, intratumoural, and intratumoural stroma, respectively, manually segmented. We developed a software for automated BF-mIHC quantification based on Hue Saturation Intensity (HSI) color-spectra analysis. Then, we validated software counts against pathologist through Bland-Altman and a t-test of differences (α=0.05).
Results: The study includes 10 BF-mIHC whole-slide images of tumour, in which the segmented hotspot regions of tumoural front, intratumour, and intratumoural stroma measure on average 0.63±0.39mm2 (mean±std.dev.), 4.20±5.23mm2, and 0.82±0.83mm2, respectively. Bland-Altman analysis of percentage counting of single marker expression reports equivalent CD20, CD68, CD8, and CD4 markers in all regions, with the lowest absolute difference of 0.31% for CD68 in the tumour hotspot and the highest absolute difference of 3.4% for CD4 in the tumoural front hotspot. For all regions, t-Test confirms the statistical equivalence of the manual and software-based automated counts, with overall p-values>0.26 for CD20, p-values>0.11 for CD68, p-values>0.27 for CD8, and p>0.06 for CD4.
Conclusion: Our study improves the current state-of-the-art of digital and computational pathology with ad-hoc developed software for automated BF-mIHC quantification. The automated quantification ensures standardization and reproducibility of measurements, as well as pulling down manual-operator computing time, thus performing basically real-time analysis. Although primarily developed for non-small cell lung

cancer, thanks to the general approach methodology adopted, it will be easily portable for BF-mIHC analysis of different tumours. Finally, our software will help reduce the time spent on pathological reports.

E-PS-20-022

Recognition of two distinct variants of mucin-producing primary lung adenocarcinoma

Y. Tsushima, K. Lami, J. Fukuoka*
*Nagasaki University, Japan

Background & objectives: A subset of pulmonary adenocarcinoma exhibits mucin production. The major histological subtypes include invasive mucinous adenocarcinoma (IMA), however, mucin production can also occur in non-mucinous adenocarcinomas, whose clinical attributes remain poorly understood.
Methods: We examined 142 cases of primary lung adenocarcinoma that had undergone surgical resection. Mucin production status was evaluated by three pathologists. Correlations with pathological diagnoses and clinicopathological parameters were analysed. Survival data were analysed using log-rank tests based on individual pathologist assessments and consensus evaluations by the three pathologists.
Results: Mucin production was identified in 30 patients, categorized into two types: Type A (cytoplasm and airspace; n=6) and Type B (predominantly in airspace; n=24). Type A cases were diagnosed as IMA and were HNF4a positive, while Type B cases were more aligned with invasive non-mucinous adenocarcinomas and were TTF-1 positive. Of the 24 Type B, only one was diagnosed as IMA. The presence of mucin showed no significant correlations with survival, gender, smoking history, or lymph node metastasis. However, mucin-positive cases displayed a significant correlation with the presence of Spread Through Air Spaces (STAS) (P=0.046). Notably, lung adenocarcinomas associated with STAS in our cohort had an unfavourable prognosis (P=0.018).
Conclusion: We identified two distinct morphological variants of mucin-producing lung adenocarcinomas. Mucin observed in both cytoplasm and airspace are HNF4a positive invasive mucinous adenocarcinoma. In contrast, mucin observed predominantly in the airspace, and not in the cytoplasm, was mostly observed in TTF-1 positive non-mucinous adenocarcinomas. Both variants are significantly linked to the presence of STAS.

E-PS-20-023

Mind the gap: molecular testing in lung cancer biopsies and targeted therapy correlation

L. Gallego*, E. Lee
*University Hospital Waterford, Ireland

Background & objectives: The evolving field of molecular pathology refined the understanding of different histologic phenotypes of cancer and provided the development of targeted therapies. Our objective is to understand the use of molecular testing in lung biopsies in UHW and its impact.
Methods: We analysed a cohort of seventy-nine cases using the following criteria: biopsies + coded T-20200 (Lower respiratory tract, NOS) + 2023 and extracted forty-nine cases with a diagnosis of Primary Lung Malignancy. Within this group, we analysed the type of tumour, molecular testing with its result and median turnaround time, cases that required re-sampling, and cases that received targeted therapy.
Results: From a total cohort of forty-nine, four cases were small cell lung cancer and were not sent for molecular testing. Four cases were non-diagnostic and required a second biopsy as the tissue did not survive or there was tumour necrosis. There were forty-one cases of non-small cell lung cancer, of which thirty (73%) were sent for molecular testing. The median turnaround time for in house PD-L1 testing was 16 days and the median turnaround time for external next-generation sequencing testing was thirty-four days. Five (12%) cases required re-biopsy as molecular testing was unsuccessful. Gene mutations were detected in eleven cases, seven of which received targeted therapy.
Conclusion: Molecular testing has become a mandatory component of the non-small cell lung cancer (NSCLC) management. However, there's still a percentage of biopsies that are non-diagnostic, requiring a second biopsy or lavage for molecular testing, and turnaround times are long in the context of advance cancer. Three patients died before having the chance of receiving targeted treatment. It is mandatory to look for a solution as a multidisciplinary team to solve these issues and provide better patient care.

E-PS-20-024

Is the expression of programmed cell death ligand 1 related to histological features in small biopsies of lung adenocarcinoma?

N. Gardic*, A. Lovrenski, S. Glumac, M. Jovanović
*Institute for Pulmonary Diseases of Vojvodina, Serbia

Background & objectives: PD-L1-targeted immunotherapy orchestrates a direct interaction between lymphocytes and tumour cells, revolutionizing lung cancer treatment. The aim was to examin the differences in histological features between the groups based on PD-L1 espression in small biopsies of lung adenocarcinoma.
Methods: The retrospective study included 61 patients diagnosed with lung adenocarcinoma. Based on tumour proportion score (TPS), patients were categorized into two groups: high expression group (HEG, TPS>50%), and negative group (NG, TPS<1%). Examined morphological features encompassed: arrangement of tumour cells, nuclear size and atypia, visibility of nucleoli, presence of necrosis, intracytoplasmic vacuoles, signet ring cells, stroma, presence of inflammatory infiltrate.
Results: The mean age of the patients was 63.61 years. The majority of patients were males (61.67% vs. 38.33%). The mean MPS in HEG was 80.6%, with an IQR of 70-90%. In HEG, cells predominantly had solid arrangement (63.33%), while in the NG, it was dominant in only 20% of the samples ($p<0.01$). Conversely, the dominant arragement of cells in NG was acinar (66.67%vs.30%, $p<0,01$). The lepidic arrangement was present in 10% of NG samples, whereas none were observed in HEG. Tumour stroma and inflammatory infiltrate were qualitatively more abundant in HEG ($p<0.05$). Signet-ring cells were statistically significantly more common in NG (40%), whereas in HEG, they were found in 13.33%.
Conclusion: The logistic regression model based on these distinctive tumour characteristics for predicting group membership was statistically significant, demonstrating accuracy, sensitivity, and specificity of 85%, 80%, and 90%, respectively. There were no statistically significant differences in other histological characteristics. The described differences in histological characteristics between the groups, supported by the results of other studies, could suggest the choice of sample for analysis, and perhaps the adequacy of the sample.

E-PS-20-025

The role of mediastinal transbronchial nodal cryobiopsy in the diagnosis of non-small cell lung cancer

M.J. Gil-Belmonte*, B. Agredano-Ávila, J.J. Cruz-Rueda, H.A. Taveras-Espinal, G. Valdenebro-Cuadrado, F.J. Velasco-Albendea
*Clinical Management Unit of Pathological Anatomy, Torrecárdenas University Hospital, Spain

Background & objectives: Endobronchial ultrasound-guided transbronchial mediastinal lymph node cryobiopsy (EBUS-TBCNB) constitutes a complementary sampling method to endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA). We aim to compare both techniques and the implementation of ROSE regarding ancillary molecular studies in neoplastic pulmonary pathology.

Methods: A retrospective study followed by statistical analysis, including 30 patients (n=30) diagnosed with NSCLC, was conducted. All samples were obtained by either EBUS-TBCNB and EBUS-TBNA, assisted or not by ROSE. The study variables were the size and amount of DNA and RNA of EBUS-TBNA and EBUS-TBCNB specimens as well as their adequacy for biomarker testing.
Results: Cryobiopsies were valid for diagnosis and sufficient for biomarker determination using immunohistochemistry and RT-PCR in 27 out of 30 cases. Their maximum average size (3,28 ± 1 mm), the average amount of DNA (95,53 ± 55,8 ng/μL) and the RNA (22,35 ± 11,8 ng/μL) extracted were significantly higher than those from EBUS-TBNA samples (1,73 ± 1,1 mm, 19 ng/μL ± 15,1 and 6,46 ± 2,9 ng/μL, respectively). Seventeen cases were assisted by ROSE, while 13 were not. Three cases insufficient for biomarker testing had their cryobiopsy sampled without ROSE support. However, no statistically significant differences were found when contrasting the use of ROSE and the molecular testing yield.
Conclusion: EBUS-TBCNB facilitates morphological and histo-architectural examination and optimizes molecular analysis in NSCLC samples accounting for its greater size, which implies more neoplastic cells and tumour genetic material available for ancillary studies. Although no statistically significant differences were found concerning the use of ROSE, all cases found inadequate for biomarker studies (due to necrosis and capsular sampling) might have been redirected with the aid and guidance of the on-site pathologist.

E-PS-20-026
Pulmonary pathology features in methadone-related fatalities
D. Gorelova*, O. Reshetnikova, E. Romanova, A. Ermakov
*Immanuel Kant Baltic Federal University, Russian Federation

Background & objectives: Methadone is widely used in substitution therapy programs for heroin users. However, many aspects of such therapy remain controversial due to the toxic effect of methadone itself. The aim of study was to evaluate lungs injury features in methadone-related deaths.
Methods: Autopsy protocols, results of toxicology evaluations in 116 cases of death associated with toxic effects of methadone were examined. Histological slides of internal organs' samples were studied with a targeted evaluation of lung pathomorphology. The correlation between epidemiological data, medical histories' information and pathomorphological patterns of the lungs was analysed in the aspect of thanatogenesis of methadone-related deaths.
Results: The majority of deaths from the toxic effect of methadone occurred in the age group of 26-45 years, and 84.6% of them were men. Clinical features of the methadone toxicity included various sedation symptoms until severe respiratory depression. Post- mortem examination revealed acute hemodynamic disorders within lungs' parenchyma. Histopathological changes included severe venous congestion; stasis within interalveolar capillaries, accompanied with increased permeability and haemorrhages into alveoli' lumens. Serous exudate in alveoli and interstitial edema were also found in many cases. Chronic pulmonary changes were registered in 67 % of cases with fatal methadone poisoning. Microscopic examination has shown siderophages presence within alveoli; perivascular fibrosis of varying severity with round-cell infiltrates.
Conclusion: The data of present study has contributed the issue that various commodities in opioid addict patients may enhance the methadone toxicity. Pathological changes in the lungs are analysed in terms of their role in the thanatogenesis of deaths caused by the toxic effect of methadone. Methadone prescription should be done by addict medicine professionals with caution to patients at risk for respiratory depression and pulmonary complications.

E-PS-20-027
Lymphangiomatosis, systemic and localised
A. Hadick*, H. Popper
*Medical University of Graz, Austria

Background & objectives: Lymphangiomatosis is characterised by proliferating lymphatics, forming channels lined by primitive endothelial tubules, presenting as systemic or localised disease. Systemic variant presents with albuminaemia and loss of electrolytes. Bone leasions are present. Localised form present with loss of lung function.
Methods: Two cases of systemic and 3 cases of pulmonary lymphangiomatosis were identified in our archive. The age of the patients varied from months to several decades. Formalin-fixed and paraffin-embedded sections from surgical resections were stained by H&E, and antibodies for low molecular weight keratin, smooth muscle actin, CD31, podoplanin, and vascular growth factor receptors.
Results: Cystic lesions were identified in all patient. The cystic lesions formed a network of channels and were lined by flat cells, which were negative for keratin and SMA. A positive reaction was found for CD31, podoplanin, and VEGFR2+3. In one patient bone lesions were found after the pathohistologic diagnosis was submitted. One patient with severe lesions in both lungs was referred to lung transplantation, but due to his overall worse condition dies few days after transplantation. In two patients a differential diagnosis of lymphangiomatosis versus lymphangiectasis was made. The later was most consistent with the clinical evaluation.
Conclusion: The diagnosis of lymphangiomatosis might be complicated if no clinical information is present. Especially in young patients and in lung-only affection several differential diagnosis of maldevelopmental lung diseases have to be considered. However, once the proliferation of lymphatics is recognised, the diagnosis can be made right away.

E-PS-20-028
Prognostic impact of the IASLC grading system of lung adenocarcinoma: a systematic review and meta-analysis
F. Hegedus*, N. Zombori-Tóth, S. Kiss, T. Lantos, T. Zombori
*University of Szeged, Hungary

Background & objectives: A novel grading system for pulmonary adenocarcinoma was proposed by the International Association for the Study of Lung Cancer (IASLC). We aimed to validate the prognostic impact of this grading system on overall survival (OS) and recurrence-free survival (RFS).
Methods: The review protocol was registered in PROSPERO (CRD42023396059). We aimed to identify randomized or non-randomized controlled trials published after 2020 comparing different IASLC grade categories in Medline, Embase, and CENTRAL. Hazard ratios (HRs) with 95% confidence intervals (CIs) of OS and RFS were pooled and the QUIPS tool was used to assess the risk of bias in the included studies.
Results: Ten articles were eligible for this review and altogether 4,923 patients were investigated in the articles included. Regarding OS estimates, grade 1 lung adenocarcinomas had better outcome than grade 3 both in univariate and multivariate analyses (HRuni=0.19, 95%CI: 0.05-0.66, p=0.009; HRmulti=0.21, 95%CI: 0.12-0.38, p<0.001). Regarding RFS estimates, grade 1 adenocarcinomas had favourable prognosis than grade 3 in multivariate analysis (HRmulti=0.22, 95%CI: 0.14-0.35, p<0.001). When focusing on stage I disease, similarly, patients with grade 1 adenocarcinomas had better outcome than those with grade 3 tumours in multivariate analyses (OS: HRmulti=0.17, 95%CI: 0.09-0.33, p<0.001; RFS: HRmulti=0.20, 95%CI: 0.11-0.36, p<0.001).

Conclusion: The literature data and the result of our meta-analysis demonstrate the prognostic relevance of the IASLC grading system. The application of this novel grading system does not require specific skills and it is reproducible. These facts support the inclusion of this prognostic parameter in daily routine worldwide. However, more prospective studies are necessary for the evaluation of the prognostic role of grade 2 category.

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E-PS-20-029

Pleomorphic carcinoma of the lung in young patients-report of two cases and review of the literature

Á. Ilyés*, K. Straub, E. Deé, O. Iurcsuk, E. Kálmán, B. Nagy, S. Csató, A. Burszán-Barabás, A. Dobrică
*Emergency County Hospital Miercurea-Ciuc, Pathology Department, Romania

Background & objectives: Pleomorphic carcinoma of the lung is a rare type of non-small cell lung carcinoma, comprising <1% of invasive primary carcinomas, that occures mainly in older male patients, with strong association of smoking and unfavourable prognosis.
Methods: We present two cases of primary pleomorphic carcinoma of the lung, both occuring in young females, one of a 31 year old, non smoker, investigated for supraclavicular lymphadenopathy and the second one of a 43 year-old, smoker, with treated cavitary pulmonary tuberculosis. We are describing the morphological characteristics, immunohistochemical and molecular profiles, treatment strategies and the clinical evolution of these cases
Results: The tumours were detected by CT-scan, localized peripherically in the left lung associated with mediastinal lymphadenopathies. The surgical specimens were obtained by open thoracotomy. A wedge resection and removal of one diaphragmatic nodule was performed in the first case and an excisional biopsy in the second one. Based on the morphological and immunohistochemical examinations the diagnosis of pleomorphic carcinoma with adenocarcinomatous and high-grade sarcomatous component was made. PDL-1 expression was detected in >50% of TC in both cases. The first patient was treated with Carboplatin-Pemetrexed-Pembrolizumab therapy with a remarkable response in the dimension and extension of disease. In the second case the Paclitaxel-Carboplatin and concomitant radiotherapy is still ongoing.
Conclusion: Primary pleomorphic carcinomas of the lung in young adults are exceptionally rare tumours, with no standard therapeutic approach, most of them diagnosed in an advanced stage of the disease. A definitive histological diagnosis can be made only on surgical resection specimens. Majority of this tumours are refractory to classical chemotherapeutic agents, but new studies are suggesting that immune checkpoint inhibitors can improve the prognosis.

E-PS-20-030

Pleuroparenchymal fibroelastosis: a case series based review regarding its radiological-anatomopathological correlation

J.J. Jiménez Velasco*, N. Fontanil Vior, Y. Guzmán Gómez, S. Alvarez Alonso, J.J. Gómez Román
*Hospital Universitario Marqués de Valdecilla, Spain

Background & objectives: Pleuroparenchymal fibroelastosis (PPFE) being a recently described and rare entity makes it difficult to diagnose for both radiologists and pathologists. We explored the correlation between radiological and anatomopathological findings and compared the concordance and diagnostic criteria.
Methods: A retrospective descriptive study was made of all PPFE cases diagnosed at our service between 2014 and 2023, collecting the medical records and comparing the results of the radiological examinations. A radio-pathological diagnostic classification (Reddy et al.) was also considered in order to clarify the diagnostic criteria of both areas.
Results: Thirty-three patients (18 women, 54.5%) with a median age of 69 (47-86) were included as anatomopathological diagnosis of PPFE. Three (9.1%) were autopsy specimens, one (3%) was an interconsultation and twenty-nine (87.88%) were biopsy specimens. Eighteen (54.55%) patients had smoking history. Six (18.18%) had undergone lung transplants, three (9.1%) kidney transplants and four (12.12%) had connective tissue diseases. Seventeen (51.52%) patients underwent treatments usually associated with PPFE, including radiotherapy, chemotherapy and other interventions. Of all PPFE diagnosis at our service, twenty (60.60%) were classified as inconsistent radiological pattern, three (9.1%) as consistent pattern and six (18.18%) presented a definitive radiological pattern. We had no radiological data of four (12.12%) patients.
Conclusion: While all the patients with a biopsy-based diagnosis of PPFE filled the definitive pattern criteria, only six of them showed radiological concordance. Though it is an entity usually suggested by clinical and radiological features, our series shows that in the vast majority of cases the biopsy findings did not match with those of the radiology; a new revision of the diagnostic criteria for both radiology and histopathology must be developed, since the lack of concordance is patent.

E-PS-20-031

A case report of a pulmonary S100-negative granular cell tumour

D. Jones (Westcott)*, L. D'Sa, M. Goddard, S. Preston
*Addenbrooke's Hospital; Cambridge University Hospitals NHS Foundation Trust, United Kingdom

Background & objectives: Granular cell tumours are rare entities, involving a wide variety of sites. The majority show neural differentiation and express S100 protein. A small subset, known as primitive non-neural granular cell tumours have an unknown lineage and don't express this protein.
Methods: We report a rare case of an incidental pulmonary primitive non-neural granular cell tumour. A 73-year-old male ex-smoker with a history of prostate adenocarcinoma and papillary renal cell carcinoma was found to have a 14mm nodule in the left upper lung lobe on routine CT surveillance. The patient was asymptomatic and radiologically the lesion was in keeping with a metastasis.
Results: A video-assisted thoracoscopic lobectomy was performed with lymph node dissection. Histologically, the peri-bronchial tumour was well-circumscribed and composed of polygonal cells with abundant eosinophilic cytoplasm. There was no necrosis, pleural involvement, lymphovascular space invasion nor lymph node metastases. Mitotic figures were not readily identifiable and the proliferation index was low. On immunohistochemistry, the tumour was positive for CD68, PASD and CD10 and negative for S100. Markers to assess metastatic carcinoma were negative. There was no evidence of a TFE3 gene rearrangement by FISH. The tumour was completely excised and a CT scan 8 months post-operatively showed no tumour recurrence.
Conclusion: As a variety of tumours can show granular cell change, this case highlights the importance of a thorough immunohistochemical panel, especially in a patient with a strong neoplastic history. It adds to the limited knowledge of this rare entity, with only two previously reported cases of pulmonary primitive non-neural granular cell tumours on literature review. It also emphasizes the importance of performing S100 protein immunohistochemistry on granular cell tumours, to identify and enable better characterisation of this rare non-neural subset.

E-PS-20-032

Hepatoid adenocarcinoma of lung: a series of three cases with histopathological, immunohistochemical and predictive biomarkers assessment

M. Jovanović*, N. Tomanovic, R. Jankovic, M. Stjepanović, S. Popevic, N. Nikolić, K. Branković, S. Glumac
*Institute for pathology, MFUB, Serbia

Background & objectives: Hepatoid adenocarcinoma (HAC) of the lung is uncommon primary lung carcinoma with morphological features similar to hepatocellular carcinoma. It is highly aggressive neoplasm, usually diagnosed in unresectable or metastatic stage, which lacks effective treatment and has poor prognosis.
Methods: The histopathology reports of NSCLC analysed in this cross-sectional study are from bronchoscopy and surgery samples procured during the initial diagnostic work-up at the respective Clinics of the University Clinical centre of Serbia between 2022 and 2023. These samples were routinely processed, including immunohistochemical (IHC) analyses, and were subsequently reviewed at the Institute for Pathology, Medical Faculty, University of Belgrade.
Results: In two-year period 7 HACs were diagnosed, representing less than 1% of all NSCLCs. For 3 cases (one from 2022, two from 2023) there was oncology board data with predictive biomarkers testing (PD-L1, ALK), which all were negative. First case is 72-years-old male, unresectible IIIB stage, with direct infiltration of scapular region, died 8 months after the diagnosis. Second case is 71-years-old male, IV stage, lost to follow up two months after the Oncology board. Third case is 57-years-old female, IV stage, died 5 months after the diagnosis. In all 3 cases tumour was positive for CK7, cytoplasmic TTF-1, HepPar-1 and pCEA, while negative for CK20, Napsin A, p40, CD10.
Conclusion: HAC is a special-type adenocarcinoma with hepatocyte-like differentiation, usually occurring in digestive and genitourinary tracts (stomach as the most common location, followed by pancreas, ovary, uterus, bladder), and lungs. Distinguishing HAC from metastatic hepatocellular carcinoma can be challenging, especially in cases with liver masses, when a comprehensive radiologic, morphologic and IHC correlation is needed. Literature highlights, including our own three-patient series, underscore HAL's aggressive nature as a rare form of lung carcinoma with limited treatment options and a poor prognosis.

E-PS-20-033
Glimpses of rarity: 25 cases of salivary gland-type lung carcinomas from a tertiary care centre in South India
E. Joy*, S. Nair P, P. T R, R. P Mony, I. S Nair, L. A L, A. Mathew
*Regional Cancer Centre, Thiruvananthapuram, India

Background & objectives: Primary salivary gland-type lung carcinoma constitutes <1% of lung cancers. The diagnosis can be challenging, requires radiological and clinicopathological findings, especially in core biopsies. Objective: To assess the clinicopathological features of these carcinomas, to enhance diagnostic precision and resource optimization.
Methods: This retrospective study done in our department included 25 cases from 1st January 2013 to 31st December 2023.H&E slides along with IHC and medical records were analysed. Since the medical records of 5 patients were unavailable, clinical data analysis was done in 20 cases only.
Results: The presenting symptoms were cough (70%), dyspnea and hemoptysis. CECT showed homogenous contrast-enhancing growth, causing lung collapse in some with tracheal/bronchial lesions (median size:3.4 cm) in bronchoscopy. Among 25 cases, 18 were mucoepidermoid carcinoma (MEC), 6 adenoid cystic carcinoma (ACC), and one epithelial myoepithelial carcinoma. The diagnosis was given for 20 cases in core needle biopsy and 5 in pneumonectomy. The median age for MEC was 38 years and ACC was 42.5 years. The M: F ratio in MEC was 1:1.3 and ACC was 1:1. Eleven patients underwent surgery and 9 had radiotherapy/chemotherapy. Three margin-positive cases received postoperative radiotherapy. 16 patients are alive now with the median follow-up being 51.5 months.
Conclusion: Primary salivary gland-type carcinomas are considered low-grade and have significantly better outcomes than other types of lung cancers. An accurate histological characterization, especially with small biopsies, is essential for tailored treatment and it helps avoid molecular tests, thus optimizing resources and reducing tissue wastage.

E-PS-20-034
Combined small cell lung carcinoma: case report highlighting important histological, immunohistochemical and molecular features
M. Keyter*, A. Favre-Bulle, M. Brendle, M. Trimech, E. Missiaglia, M. Gonzalez, S. Berezowska
*Department of Laboratory Medicine and Pathology, Institute of Pathology, Lausanne University Hospital and University of Lausanne, Switzerland

Background & objectives: Combined small cell lung carcinoma (CSCLC) is defined as a carcinoma containing small cell (SCLC) and non-small cell (NSCLC) regions. The cell of origin and pathogenesis remain undefined. We report a case highlighting important histological, immunohistochemical and molecular characteristics.
Methods: A 71-year-old man with a strong smoking history, presented with a right upper lobe lung mass and associated haemoptysis. He underwent a right upper lobe lobectomy. Histological, immunohistochemical and molecular analyses (targeted 52-gene next generation sequencing (NGS) panel of both tumour regions) were performed.
Results: An ill-defined tumour measuring 4.7 x 4.1 cm was present in the right upper lobe. At the periphery, an adenocarcinoma with lepidic, acinar and micropapillary growth patterns was seen merging with a centrally located SCLC. The SCLC had classic neuroendocrine morphology and neuroendocrine immunophenotypic expression (synaptophysin, chromogranin and insulinoma associated protein 1; diffuse positive staining). Neuroendocrine marker expression was absent in the adenocarcinoma. RB1 expression was lost within the SCLC and retained in the adenocarcinoma. Identical KRAS c.37G>T (trunk) and TP53 c.818G>A mutations were present in both the adenocarcinoma and SCLC regions of the tumour. In the SCLC, additional RB1 c.1072C>T and PIK3CA c.1633G>A mutations were found.
Conclusion: This case report highlights important features of a CSCLC, with distinct adenocarcinoma and small cell neuroendocrine morphologies and immunophenotypes. NGS of the two regions showed a common clonal origin (KRAS), with divergent differentiation. Mutations in TP53, RB1 and PIK3CA confirm their important role in neuroendocrine differentiation/transformation. In conclusion, this case provides supporting molecular evidence of a common clonal origin with divergent differentiation/lineage plasticity due to additional genomic events and altered signaling pathways.

E-PS-20-035
Angiogenesis in the crossroad of molecular pathways in lung cancer
E. Lampri*, M. Saranti, A. Zikou, I. Tragani, D. Dimou, A. Varouktsi, S. Papadatos, P. Margariti, V. Galani, A. Mitselou
*Department of Pathology, Faculty of Medicine, School of Health Sciences, University of Ioannina, Greece

Background & objectives: In the crossroad of tumourigenesis, angiogenesis plays a vital role in conjuction with proliferation markers and cell adhesion molecules Angiogenesis is a basic requirement for nutrition and oxygenation of tumour cells, cellular proliferation and metastatic spread of lung carcinoma.
Methods: Formalin-fixed-paraffin-embedded tissue specimens from 131 patients (77 surgical material and 54 autopsy cases) diagnosed with lung cancer, were retrieved from the archived material of the Department of Pathology of Hospital "Hatzikostas" and 54 patients from the Department of Forensic Pathology and Toxicology from University of Ioannina. The expressions of VEGF, CD44, E-cadherin, Ki67, p53, and TTF1 were examined immunohistochemically.
Results: VEGF was detected in 46.8% of surgical and 50% of autopsy material, where strong immunoreactivity was detected in 45.9% of squamous cell carcinoma, 53.31% of adenocarcinomas,

100% of large cell carcinomas and 15,4% of small cell lung carcinomas. High Ki67 and p53 expression was observed in 61.8% and 61.06%, respectively. Reduced/negative E-cadherin expression was noted in 69.46%, while CD44 positivity in 44.27% of cases. Survival was associated statistically with E-cadherin and CD44. Reduced E-cadherin was associated with high Ki-67 expression. High VEGF and reduced E-cadherin expression associated with poorly-differentiated tumours. All squamous carcinomas were completely devoid of TTF-1 immunoreactivity, while adenocarcinomas expressed TTF-1 in the majority of the cases (80.85%).
Conclusion: It was investigated the expression of VEGF in lung cancer both in surgical and autopsy material, its association with proliferation markers (Ki-67, p53), cell adhesion molecules (E- cadherin and CD44) and TTF-1. It was revealed a co-existence of high VEGF expression and reduced E-cadherin expression in poorly-differentiated tumours. Moreover, high CD44 and reduced E-cadherin expression proved to be a poor prognostic factor.

E-PS-20-036
Histopathological features of thoracic granulomatosis with polyangiitis
F. Loued*, R. Ayadi, E. Brahem, R. Yaiche, O. Ismail, B. Hamdi, S. Ben Slama, A. Ayadi
*Department of Pathology, Monji Slim Hospital, Tunis, Tunisia

Background & objectives: Granulomatosis with polyangiitis (GPA) is a rare multisystem disease related to the presence of circulating antineutrophil cytoplasmic antibodies (ANCAs). the upper and lower respiratory tract and lungs are frequently affected. We aim to describe the broncho-pulmonary manifestations of GPA.
Methods: This retrospective study was performed on 18 cases of GPA selected from our pathology department from 1997 to 2023.
Results: There were 8 male and 10 female patients with a mean age of 40 years (3-64). Clinically, 9 patients had unspecific pulmonary symptoms and 9 patients were asymptomatic. Imaging findings consisted of nodules, infiltrates and pleural opacities and multiple pulmonary excavated lesions found in 2 cases. The diagnosis was made on transparietal needle biopsy (n=13), surgical resection (n= 5) and tracheal biopsy (n=1). Histological examination revealed parenchymal necrosis in 13 cases taking two forms either neutrophilic micro-abscesses or areas of geographic necrosis. Granulomatous lesions, consisting of micro-abscesses surrounded by giant cells, were identified in 13 cases. Vasculitis were identified in 13 cases. Fibrinoid necrosis was relatively uncommon (2 cases).
Conclusion: GPA should be considered in patient presenting respiratory and general symptoms with multiple bilateral cavitary pulmonary nodules after eleminating infectious and malignant disease. Typical criteria found on histo-pathogical examination of lung nodule in association with ANCA positivity confirm the diagnosis.

E-PS-20-037
Pulmonary alveolar proteinosis: diagnosing a rare lung disease
F. Loued*, R. Ayadi, E. Brahem, R. Yaiche, O. Ismail, B. Hamdi, S. Ben Slama, A. Ayadi
*Department of Pathology, Monji Slim Hospital, Tunis, Tunisia

Background & objectives: Pulmonary alveolar proteinosis (PAP) is a rare lung disease, characterized by an accumulation of a lipoproteinaceous material within the alveoli.it can be idiopathic or secondary. Diagnosis may be based on bronchoalveolar fluid findings, but is frequently made on tissue samples.
Methods: This retrospective study was performed on cases of PAP selected from our pathology department from 1994 to 2023.
Results: There were 4 male and 9 female patients with a mean age of 34 years (3-56). Clinically, patients reported a progressive dyspnea, dry cough and recurrent lung infections. The diagnosis was suggested on chest CT with diffuse infiltrative pneumonia having a classic "crazy paving" appearance (n=13) and on bronchoalveolar lavage fluid (BALF) (n=2). BALF had a milky appearance and increased cellularity. Careful examination revealed foamy macrophages containing eosinophilic granules, with extracellular globular hyaline material found homogeneously positive on PAS. The diagnosis was made on surgical pulmonary biopsy in all cases. Histological analysis showed an intra-alveolar accumulation of a granular eosinophilic and amorphous PAS-positive material. Interstitial fibrosis or inflammation is absent.
Conclusion: Pulmonary alveolar proteinosis is a rare disease that is difficult to diagnose and treat. In general, it is thought that the diagnosis of this entity requires both cytological and histological examination. A multidisciplinary team effort including pathologists and pulmonologists is mandatory to assess the diagnosis.

E-PS-20-038
Hyalinizing clear cell carcinoma: integration of morphology, immunophenotype and molecular features to diagnose the infrequent subtypes of lung cancer
J. Martin-Lopez*, P. Martin Acosta, L. Martin Fragueiro, C. Salas Anton
*Hospital Universitario Puerta de Hierro, Spain

Background & objectives: Hyalinizing clear cell carcinoma (HCCC) are rare salivary gland type tumours accounting for less than 1% of lung tumours with only few cases reported nowadays. Clinically, their behaviour is generally indolent and rarely do they recur or metastasize.
Methods: We report a case of HCCC with hiliar lymph node involvement. To review the entity, we summarize the histomorphologic, immunophenotypic, and molecular features of the case referred to our centre to surgical excision which was previously diagnosed of squamous cell carcinoma on small biopsy.
Results: A 64-year-old male, ex-smoker, presented an incidentally lung nodule in a chest x-ray. CT scan showed a 3,6 cm hilar mass in the upper left lobe with SUVmax 6,48. A small biopsy was diagnosed of squamous cell carcinoma and a lobectomy was performed. Histopathologically a central endobronchial lesion infiltrates as solid sheets, nests, and cords of polygonal cells with abundant pale eosinophilic to clear cytoplasm. Hyalinization and desmoplasia of the stroma separates the clear cells. There was no evidence of necrosis or nuclear pleomorphism. Tumour cells express p40, p63, CK5/6, and CK7 and break-apart FISH revealed a translocation of EWSR1 gene.
Conclusion: HCCC is a rare lung neoplasm which requires the integration of a correct histomorphological evaluation, a differential diagnosis ordering immunohistochemical techniques and a proper molecular testing. ATF1 is the fusion partner most commonly associated with EWSR1 but some authors described other fusion partner with more clinically aggressive course.

E-PS-20-039
HER2 expression and mutation in lung adenocarcinoma: a retrospective unicentric study of 206 patients
A. Mouraire*, M.C. Ferreira, I. Molnar, F. Penault-Llorca, M. Kossaï
*Department of Pathology and Molecular Pathology, Centre Jean Perrin, Clermont-Ferrand, France

Background & objectives: HER2-targeting antibody-drug conjugates have shown promising results in ERBB-2-altered lung adenocarcinoma. We aim to determine the incidence of ERBB-2 alterations in a French cohort of patients with lung adenocarcinoma, and to identify any correlations with clinico-pathological and molecular data.

Methods: This single-centre retrospective study involved 206 patients who underwent first-line surgery for invasive lung adenocarcinoma between 2011 and 2014 at the Centre Jean Perrin in Clermont-Ferrand. All clinicopathological data were reported. Immunohistochemical analysis was performed on formalin-fixed, paraffin-embedded tumour samples with anti-HER2 and PD-L1 antibodies. Next-generation DNA sequencing was realized using a custom-targeted panel of 45 genes of interest.
Results: Only seven mutations (2.9%) in the ERBB-2 gene were identified in all tumour samples. No overexpression or amplification was found. PD-L1 was expressed in 30% of tumours. HER2 expression without gene amplification was observed in 60% of cases (25% HER2-low, 35% HER2 ultra-low). A positive correlation was observed between PD-L1 positive expression (≥1%) and HER2-low expression (p=0.02). Somatic TP53 mutation was significantly associated with HER2-low expression (p=0.002). No correlation between HER2 expression and clinical features and other molecular alteration was found. Due to the small size of the cohort, statistical analysis to show any correlation between clinical or molecular features and ERBB-2 mutation was not possible.
Conclusion: The low incidence rate of ERBB-2 mutations is consistent with the literature. We observed no association between HER2 expression and gene mutation, as described in studies. Relationship between HER2-low expression and PD-L1 positive status in lung adenocarcinoma should be further determined in future studies. TP53 mutation associated with HER2-low expression may be related to its ability to induce HER2 overexpression in cancer cells. We plan to collect a large cohort selected on the ERBB-2 mutation criterion to establish possible correlations.

E-PS-20-040
Reproducibility study on non-small cell lung cancer specimens stained with PD-L1 IHC 22C3 pharmDx (Dako Omnis, GE006)
J. Musser*, G. Toland, C. Roach, S. Tabuena-Frolli, S. Hund
*Agilent Technologies, USA

Background & objectives: PD-L1 IHC 22C3 pharmDx is designed for use in the detection of PD-L1 expression in human tissues. This study establishes inter- and intra-site reproducibility on non-small cell lung cancer (NSCLC) specimens using binary positive/negative endpoint for TPS 1% and 50%.
Methods: A 3-site study included immunohistochemical staining on 60 specimens using GE006 on Dako Omnis and scoring blinded and randomized slides by three observers. Assessment of Negative Percent Agreement (NPA), Positive Percent Agreement (PPA) and Overall Agreement (OA) used pairwise comparisons. The two-sided 95% confidence intervals were computed using percentile Bootstrap method based on TPS cutoffs of 1% and 50%.
Results: Diagnostic agreement was assessed separately for each cutoff. Acceptance criteria (AC) for lower bound two-sided 95% percentile bootstrap confidence interval (LBCI) computed on NPA, PPA, and OA must be ≥85%.
Inter-site reproducibility for TPS 1% cutoff achieved LBCI values of 98.3%, 98.7%, and 99.2% for NPA, PPA and OA respectively. Intra-site reproducibility achieved LBCI values of 98.3%, 98.7%, and 99.2% for NPA, PPA and OA respectively.
Inter-site reproducibility of the assay for TPS 50% cutoff achieved LBCI values of 87.6%, 84.2%, and 88.0% for NPA, PPA, and OA respectively. Intra-site reproducibility achieved LBCI values of 94.1%, 94.7%, and 94.8% for NPA, PPA and OA respectively.
Conclusion: PD-L1 IHC 22C3 pharmDx demonstrates high reproducibility in staining and scoring between different testing sites. High study endpoints were achieved with OA point estimates values of 99.7% for Inter-and Intra-site evaluations using TPS ≥1% cutoff, and Inter-site (92.8%) and Intra-site reproducibility (97.0%) for TPS ≥50% cutoff. This data supports high reproducibility of the assay and is aligned with the high scores in external quality assessments, increasing confidence in clinical use of the device on NSCLC specimens.

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E-PS-20-041
ADAM17, ACE2, TMPRSS2 and TNFAIP2 – comparative immunohistochemical landscape in lungs of fatal cases of SarsCov-19 and AH1N1 influenza infection
R. Neagu*, S. Zurac, M. Balea, L. Nichita, L. Stanciu, S. Niculae, A. Cibotariu, D.M. Marinoiu, A. Bordea, R. Ionescu, C. Dumitru, A. Vilaia, C. Popp
*Department of Pathology, Colentina University Hospital, Bucharest, Romania

Background & objectives: The outbreaks of COVID-19 (2020-2023) and AH1N1 influenza (2009-2010) have led to significant morbidity and mortality. The objective of this study is to acquire a better understanding of the immunohistochemical landscape of these respiratory viral infections at molecular level.
Methods: The most representative paraffin blocks from the lungs of 16 AH1N1 and 8 COVID19 deceased patients were selected.
Immunohistochemical staining for ADAM17, ACE, TMPRSS and TNFAIP were performed in order to assess the presence of these key proteins involved in viral infection and immune response.
Results: We found evidence of severe lung damage in both groups: in patients with AH1N1 the most significant lesion was diffuse alveolar damage, while COVID patients had especially vascular lesions (thrombosis and lung infarction). There were observed notable variations in the expression patterns of ADAM17, ACE2, TMPRSS2, and TNFAIP2 between the two groups. ADAM17 exhibited consistent presence in both AH1N1 and COVID-19 cases, with significantly increased expression in the latter (t-test value: 0.0091). Conversely, ACE2 was sporadically identified in a minority of cases in each viral infection. TMPRSS2 manifested comparable levels of expression in both conditions. Additionally, TNFAIP2 displayed a greater occurrence in COVID-19 cases (t-test value:0.0094)
Conclusion: These observations imply distinct protein signatures in AH1N1 and COVID-19 infections, potentially reflecting diverse mechanisms underlying viral pathogenesis and providing valuable information for the development of targeted therapeutic strategies and interventions.

E-PS-20-042
A lung adenocarcinoma with unusual initial presentation as a right inguinal metastasis
S. Neves*, I. Araújo, D. Sá, N. Jorge Lamas

*Unidade Local de Saúde de Santo António (ULSSA), Portugal
Background & objectives: The majority of lung adenocarcinomas present with locally advanced or with metastatic disease, usually to the nervous system, bone, liver, adrenal gland or respiratory system. Metastases to other body regions, such as the inguinal region has been scarcely reported.
Methods: We present the case of a 67-year old man who was referred to our hospital by his primary care physician due to a right inguinal hernia. The patient underwent hernioplasty surgery and 6 months after, he presented with an ulcerated lesion on the surface of the scar. The patient had no other symptoms. A biopsy of the lesion was performed.
Results: The biopsy revealed fibrous tissue infiltrated by a malignant epithelial neoplasm forming glands with mildly atypical cells, occasionally with mitotic figures and foci of necrosis. The

immunohistochemistry study showed immunoreactivity in the neoplastic cells for CKAE1/AE3, EMA, CK7 and TTF1, without immunoreactivity for CK20, PAX8, NKX3.1, p40, p63, GATA-3 or SOX-10. The diagnosis of inguinal metastasis of adenocarcinoma, favouring the lung as a primary origin site was rendered. The PD-L1 immunohistochemistry showed a strong positive result. The FISH studies for rearrangement of the ALK and ROS genes were negative. The NGS study using a lung cancer-directed panel did not reveal any significant pathogenic variants.
Conclusion: Our pathological result prompted additional studies, including cerebral and thoraco-abdominopelvic CT scans, which revealed a 7.4 cm upper-right lobe lung mass and multiple brain, mediastinal, retroperitoneal, adrenal, and bilateral inguinal metastases. Three weeks later, the patient developed generalized weakness and dysphagia. He was later submitted to cranial and thoracic radiotherapy and immunotherapy. His condition progressively worsened, and the patient passed away nearly two months after performing the inguinal biopsy. This case highlights an extremely unusual presentation of metastatic lung cancer.

E-PS-20-043
Pathologic analysis of 116 pulmonary carcinoid tumours, excised over a 16-year period in a Greek regional cancer centre
A. Nikolaidou*, P. Kousidis, N. Barbetakis, D. Paliouras, G. Panselinas, S. Androniadou, E. Triantafillidou, S. Mavropoulou, V. Christoforidou
*Pathology Department, Theageneio Anticancer Hospital of Thessaloniki, Greece

Background & objectives: Pulmonary carcinoids are uncommon neoplasms among pulmonary malignancies, with differing histology and management. We present an analysis of 116 cases, operated on in our hospital over a 16-year period.
Methods: A comprehensive search was performed for patients with a pathology report compatible with pulmonary neuroendocrine tumours excised over the past 16 years. Reports, tissue slides and immunohistochemistry were reviewed by a different pathologist. For patients with a diagnosis of primary pulmonary typical carcinoid (TC) or atypical carcinoid (AC), patient records were accessed to determine patient characteristics, history and outcomes.
Results: We identified 116 total patients. Among the 73 TC patients, 58 (79.4%) were female and 15 (20.5%) male, while median age at diagnosis was 67 years (IQR 58–72). Median tumour diameter was 17.0 mm (IQR 9-25). Median number of mitoses was 1/2 mm2 (Range 0-1.5). Among the 26 AC patients, 18 (69.2%) were female and 8 (30.8%) male, while median age at diagnosis was 61 years (IQR 57.3–66.8). Median tumour diameter was 19.0 mm (IQR 14.3-25). Median number of mitoses was 2/2 mm2 (IQR 2-3). We also identified 13 TC-AC equivocal cases and 4 AC-NEC equivocal cases. We described and analysed morphologic and immunohistochemical parameters among each subgroup.
Conclusion: Primary pulmonary carcinoids present uncommon yet often encountered tumours in high-volume centres. Histologic categorization is paramount in accurate diagnosis and management. Special attention is required for diagnosing cases with intermediate characteristics.

E-PS-20-044
Thoracic SMARCA4-deficient undifferentiated tumour: a case report series
E.I. Ortega Pinto*, E. Revilla Sanchez, J. Jiménez Almonacid
*Hospital Universitario 12 de Octubre, Madrid, Spain

Background & objectives: Thoracic SMARCA4-deficient undifferentiated tumour (SMARCA4-UT) is a malignant neoplasm, that involves the mediastinum, pulmonary hilum, lung, and/or pleura. Usually, it presents in young to middle-aged male adults. Most patients with this entity are heavy smokers.
Methods: We report two cases diagnosed during the 2021-2023 period. One male and one female, age range between 66 to 75 years. Both patients had history of heavy smoking. The female patient presented a pulmonary nodule and one adenopathy. The male patient had a tonsillar ulcer, several lymphadenopathies, a pulmonary mass, and lesions in the transverse colon and adrenal glands.
Results: The biopsy´s findings were superimposable, showing a neoplastic proliferation of undifferentiated cells that grew diffusely, and was accompanied by tumoural necrosis. The cells presented a high N/C ratio and irregular nuclei, with occasional nucleoli. Frequent mitosis and karyorrhexis were identified. Both specimens were negative for AE1-AE3, SOX10, CD45, P40 and positive for SOX2 and focally C-MYC. The female case was focally positive for TTF1 and synaptophysin, plus intensely positive for SALL-4. The male case was positive for CD34. Both cases presented loss of SMARCA4 and SMARCA2. NGS techniques, showed a MYC mutation in the male case, and a CTNNB1 and TP53 mutations plus an amplification of PIK3CA in the other.
Conclusion: SMARCA4-UT is a rare malignant entity, which has recently been described and has an ominous prognosis. Furthermore, it is fundamental to consider this pathology in the differential diagnosis of rhabdoid-like tumours in the thorax. It is necessary to carry out more studies to understand and better characterize the behaviour and molecular features of these neoplasms.

E-PS-20-045
A tumour whose name is harder to remember than to diagnose – bronchiolar adenoma / ciliated muconodular papillary tumour: report of a case diagnosed in frozen section
M.S. Özlü*, J. Noury Rad Davaji, C. Yüksel, S. Dizbay Sak
*Ankara University Medical School, Pathology Department, Turkey

Background & objectives: Ciliated muconodular papillary tumour (CMPT) is a benign pulmonary tumour. Due to its rarity and underrecognition, diagnosing it can pose challenges, particularly during intraoperative examination. Here, we present a case of CMPT diagnosed via frozen section.
Methods: A 52-year-old male patient visited the cardiology clinic due to dizziness. Vital signs and blood tests were normal. A 15mm spiculated subsolid nodule with pseudocavitation was discovered in the left lower lobe on CT scan. Intra-operative examination revealed a peribronchiolar tumour with double-layered epithelium containing mucinous and ciliated luminal cells.
Results: In the peripheral areas, tumour cells were growing along the alveolar walls suggesting a lepidic pattern. The tumour was diagnosed as CPMT and a wedge resection was performed avoiding a lobectomy. Immunohistochemistry on permanent sections showed tumour cells universally positive for TTF-1, with a basal epithelial layer confirmed by p63, p40, CK5/6, ruling out adenocarcinoma.
Conclusion: In a study consisting of 150 CMPT cases examined with frozen section, it was reported that the diagnosis of "favour CMPT" could be made in 38% of CMPTs and the definitive diagnosis of CMPT could be made in only one case. Being aware of this rare entity, knowing that the lesion is localized around the bronchioles, and looking for two-layered epithelium in frozen sections can help recognizing this entity by frozen section.

E-PS-20-046
Rare, very rare, and even rarer: carcinoid tumour, sclerosing pneumocytoma, and combined carcinoid tumour and sclerosing pneumocytoma
M.S. Özlü*, H. Aknar, B.M. Yenigün, S. Dizbay Sak
*Ankara University Medical School, Pathology Department, Turkey

Background & objectives: Pulmonary sclerosing pneumocytomas (PSP) and carcinoid tumours (CT) are rare tumours. Only five cases

of combined PSP and CT are present in the English literature. Here, clinical and histopathological findings of a combined case of PSP and CT are shared.
Methods: A chest CT scan revealed two distinct nodules in the right upper lobe of a 73-year-old female patient, measuring 17 mm and 9 mm. During the intraoperative consultation, the 17 mm nodule was diagnosed as a carcinoid tumour, and lobectomy was performed. On permanent sections, this tumour showed two intermingled components.
Results: On permanent sections, this tumour showed two intermingled components: one with uniform spindle cells with INSM-1, Synaptophysin, Chromogranin-A, and TTF-1 positivity; and the other with a sclerotic-calcified matrix, showing papillary formations and a solid arrangement Upon immunohistochemical examination, the second component showed weak ER, pronounced PR, CK7, TTF-1, Napsin-A, and EMA positivity. Neuroendocrine markers were negative in the second component. The Ki67 was low in both components. The lesion was diagnosed as a combined carcinoid tumour and sclerosing pneumocytoma. NGS revealed an AKT1 mutation (c.49G>A, p.E17K, VAF: 49%). However, MEN1, EIF1AX, ARID1A mutations that are associated with carcinoid tumours were not present. The 9 mm tumour was a pulmonary hamartoma.
Conclusion: Combined PSP and carcinoid tumour is a very rare entity and its pathogenesis is unknown. This tumour may represent a collision tumour that developed from two separate cells, or both components may originate from a single multipotential cell. In this particular case, a genetic predisposition also comes to mind, because a pulmonary hamartoma was also present.

E-PS-20-047
Pulmonary crystal-storing histiocytosis masking pulmonary extranodal marginal zone lymphoma. A rare entity mimicking lung carcinoma
C. Panayi*, M. Sheaff, M. Grantham, A. Wotherspoon, A. Nicholson, K. Giaslakiotis
*Department of Histopathology, Royal London Hospital, Barts Health NHS Trust, London, United Kingdom

Background & objectives: Crystal-storing histiocytosis (CSH) is a rare disorder characterised by massive accumulation of crystallised immunoglobulins within histiocytes and is commonly associated with lymphoproliferative disorders/plasma cell neoplasms. Pulmonary-CSH is extremely rare. Familiarity with this condition is important to avoid diagnostic pitfalls.
Methods: We present the full diagnostic histopathology work-up of a case of pulmonary-CSH associated with pulmonary extranodal marginal zone lymphoma (p-ENMZL), which was encountered in a thoracic pathology centre as a suspected lung cancer. The histological diagnosis was reached with the use of multiple modalities including frozen section intraoperative consultation, immunohistochemistry, electron microscopy, PCR-based clonality studies, and expert pathology review.
Results: A 65-year-old male patient presented with a non-productive cough and an isolated left lingular nodule, which was suspicious for carcinoma. Intraoperative frozen section consultation suggested histiocytic inflammation and fibrosis. Paraffin-embedded tissue sections revealed a histiocytic proliferation infiltrating fibrotic lung parenchyma, pleura, and blood vessels, and obscuring a lymphoplasmacytic infiltrate with rare lymphoepithelial lesions. The histiocytes contained numerous elongate refractile and non-polarisable crystals, which were further characterised by immunohistochemistry and electron microscopy. PCR studies revealed a monoclonal immunoglobulin heavy/kappa light chain rearrangement. The appearances were consistent with p-ENMZL associated with CSH. No other lesions were detected over a 4-year haemato-oncology clinical follow-up. A review of the literature is provided
Conclusion: This case report demonstrates the typical features of pulmonary-CSH and highlights its propensity to conceal an underlying lymphoproliferative disorder, which may require multiple diagnostic modalities to resolve. The histological diagnosis was notable for integrating complementary frozen section intraoperative consultation, routine histology, immunohistochemistry, electron microscopy, PCR-based clonality studies, and expert pathology review. It is important for pulmonary pathologists to be familiar with this rare condition to avoid diagnostic pitfalls and to prompt when necessary further investigations for possible associated lymphoproliferative disorders.

E-PS-20-048
High endothelial venules in the pleura: MECA-79 expression in mesothelioma, pleuralmetastasis and pleuritis
G. Karpathiou, M. Peoch, M. Mobarki, J. Pascal*, T. Amaamri Seebach
*CHU of Saint-Etienne, France

Background & objectives: High endothelial venules (HEVs) are vessels specialized in the extravasation of lymphocytes from the blood to the tissue implicated in the immune microenvironment of several tumours. Their presence has been never studied in pleural tissue.
Methods: We retrospectively studied 149 surgical pleural biopsies for MECA-79 expression by immunohistochemistry, a marker specifically recognizing HEVs. The tissues included 44 (44%) inflammatory and 105 (56%) neoplastic diseases. The latter corresponded to 34 (22.8%) mesotheliomas and 71 (47.7%) metastases from lung (n=50) or breast (n=21) primaries.
Results: HEVs were present in 102 (68%) of all pleural specimens with a mean number of foci containing HEVs of 13.33 (SD 20.64). Neoplastic pleural pathologies harbored HEVs in 73.3% of the cases compared to the non-neoplastic pathologies which harbored HEVs in 56.8% of the cases (p=0.048). Their presence did not differ between pulmonary or mammary metastasis (p=0.7).
Conclusion: We show for the first time that HEVs are present in the pleural cavity probably participating in the immune microenvironment of inflammatory and neoplastic pleural disease.

E-PS-20-050
A case of endobronchial leiomyoma
I. Petrovic*, M. Jovanović, J. Sopta, J. Stanojevic, S. Popevic, M. Stjepanović, S. Glumac
*Faculty of Medicine, University of Belgrade, Belgrade, Serbia, Institute for Oncology and Radiology of Serbia, Belgrade, Serbia

Background & objectives: Benign tumours of the trachea, bronchi, and lung parenchyma are uncommon, particularly those located in the central airways. We present a rare case of endobronchial leiomyoma, a tumour that develops from the smooth muscle layer of the bronchial wall.
Methods: Routinely haematoxylin-eosin (H&E) stained slide and immunohistochemical analysis of bronchoscopically obtained small samples.
Results: We present a 59-year-old female patient who complained of chronic dyspnoea and cough.During bronchoscopy in the subsegmental bronchus of the right lower lobe, an exophytic, partially occlusive intraluminal mass with a smooth mucosal surface was discovered and sampled. Routine H&E revealed a submucosal tumour growing in a fascicular and lobular pattern, composed of bland spindle cells with vacuolated eosinophilic cytoplasm and long spindle nuclei, without nuclear atypia or mitoses.Those spindle cells were diffusely positive for Vimentin, αSMA, Desmin, and h-caldesmon, while negative for CKAE1/AE3, S-100, and CD34 markers. The Ki-67 proliferative index was 2%. The diagnosis of endobronchial leiomyoma, a primary, benign tumour of bronchial smooth muscle origin, was confirmed.
Conclusion: Benign pulmonary neoplasms are rare and usually present as hamartomas, papillomas, adenomas, and benign mesenchymal tumours. Endobronchial leiomyomas, as the primary benign tumour of

the bronchial tree, have the lowest prevalence among all benign pulmonary tumours. The main differential diagnosis are centrally located malignant neoplasms of the lungs, leiomyosarcoma, and metastasizing uterine leiomyoma, which differ primarily in their

E-PS-20-051
Adenocarcinoma combined with carcinoid/diagnosed on transthoracic biopsy – case report
J. Pimentel*, V. Almeida, A. Ramos, V. Sousa, L. Carvalho
*Centro Hospitalar e Universitário, Portugal

Background & objectives: Combined primary pulmonary tumours with neuroendocrine/non-neuroendocrine components are recognized in WHO classification for small/large cell neuroendocrine carcinomas. The coexistence of adenocarcinoma and carcinoid is rare, with only 11 cases reported. These tumours' pathogenesis is not completely defined.
Results: We present the case of a 44-year old male, smoker (26 pack year); thoracic CT showed a 38x31 mm lobulated mass on the lingula and a transthoracic biopsy was performed. The filiform 13 mm biopsy was composed of two distinct components. An adenocarcinoma component represented by clear cells in acinar, papillary and micropapillary patterns, with CK7 and TTF1 expression. Between areas of adenocarcinoma, a spindle cell component, with short intersecting fascicles, regular nuclei and without mitotic figures or necrosis was identified. Immunohistochemistry study revealed TTF1, CK7, CD56 and chromogranin A expression and a proliferative index below 5% (Ki67).
Conclusion: The combination of adenocarcinoma and carcinoid is unusual, with only 11 cases described. Its pathogenesis is not complety elucidated in the current literature. Therefore, studies are needed on this matter, in order to better understand its prognostic implications and proper management.

E-PS-20-052
Anti-MDA5 antibodies and dendritic cells in dermatomyositis with lung involvement
J. Knirsch*, H. Popper
*Medical University Graz, Austria

Background & objectives: Dermatomyositis rarely involves the lung, but probably was overlooked. In acute disease lymphocytic interstitial pneumonia combined with histolytic granulomas predominate, mixed lymphocyte populations are seen dominated by CD4+Tcells. Fibrosing pneumonia is seen in chronic phase, probably related to anti-melanoma-differentiation-associated-gene5 antibody.
Methods: 19 cases were identified in the lung pathology archive, which had the suspected diagnosis of autoimmune diseases, probably dermatomyositis. From these cases 4µm thick paraffin-embedded sections were cut and subjected to immunohistochemistry with antibodies for different dendritic cells (immature and plasmocytic DC) and anti-MDA5 antibodies.
Results: Out of the 19 cases 6 could be confirmed to be dermatomyositis with lung involvement. All of them expressed anti-MDA5 in the histiocytic cells, which were identified as dendritic cells, many expressing markers for immature and plasmocytic dendritic cell.
Conclusion: If these dendritic cells function and induce immune tolerance cannot be answered from our investigation. However, the presence of immature dendritic cells point to an impaired immune function. Different patterns of fibrosis was present in our cases. Anti-MDA5 antibody reaction might assist in providing clues for the involvement of the lung and progressive fibrosis

E-PS-20-053
Lymphangiomatosis, systemic and localised
A. Hadick*, H. Popper
*Medical University of Graz, Austria

Background & objectives: Lymphangiomatosis is characterised by proliferating lymphatics, forming channels lined by primitive endothelial tubules, presenting as systemic or localised disease. Systemic variant presents with albuminaemia and loss of electrolytes. Bone leasions are present. Localised form present with loss of lung function.
Methods: Two cases of systemic and 3 cases of pulmonary lymphangiomatosis were identified in our archive. The age of the patients varied from months to several decades. Formalin-fixed and paraffin-embedded sections from surgical resections were stained by H&E, and antibodies for low molecular weight keratin, smooth muscle actin, CD31, podoplanin, and vascular growth factor receptors.
Results: Cystic lesions were identified in all patients. The cystic lesions formed a network of channels and were lined by flat cells, which were negative for keratin and SMA. A positive reaction was found for CD31, podoplanin, and VEGFR2+3. In one patient bone lesions were found after the pathohistologic diagnosis was submitted. One patient with severe lesions in both lungs was referred to lung transplantation, but due to his overall worse condition dies few days after transplantation. In two patients a differential diagnosis of lymphangiomatosis versus lymphangiectasis was made. The later was most consistent with the clinical evaluation.
Conclusion: The diagnosis of lymphangiomatosis might be complicated if no clinical information is present. Especially in young patients and in lung-only affection several differential diagnoses of maldevelopmental lung diseases have toi be considered. However, once the proliferation of lymphatics is recognised, the diagnosis can be made right away.

E-PS-20-054
Biopsy interpretation of an unusual mesothelial proliferation in the peritoneum of a male patient
L.S. Punjabi*, C. Chua Ze Xin, X.M. Cheng, W.Q. Leow
*Singapore General Hospital, Singapore

Background & objectives: Well-differentiated papillary mesothelial tumour(WDPMT) is an indolent proliferation with a preponderance for the peritoneum. There are few reports of invasive foci arising from WDPMT, associated with multifocal and recurrent disease but rarely mortality. Hence, distinction from malignant mesothelioma (MM) is crucial.
Methods: Herein we present a diagnostically challenging case of WDPMT with invasive foci. A 44-year-old male with no significant history presented with urinary symptoms. CT urogram revealed peritoneal, mesenteric and omental nodularity with low volume ascites. Diagnostic laparoscopy confirmed punctate disease involving lower abdominal omentum and peritoneum which were biopsied while ascitic fluid was drained.
Results: Peritoneal biopsies showed a multi-focal papillary tumour composed of myxoid to hyalinised fibrous cores lined by single layer of bland epithelioid cells. There were a few foci of tubules and solid nests of epithelioid cells within the hyalinised fibrosis and fat, suggestive of invasion. The cells were immunopositive for CK5/6, calretinin, WT1 and D2-40, supporting mesothelial origin. They were weakly and focally positive for BerEP4, and negative for CD15, ruling out adenocarcinoma. GLUT1 was positive, suggesting a metabolically active proliferation. PAX8 was negative, BAP1 showed heterogenous staining and FISH was negative for p16 deletion. Smears and cell block of ascitic fluid showed bland mesothelial cells in sheets and papillaroid structures.
Conclusion: Distinguishing WDPMT with invasive foci from epithelioid MM with WDPMT-like features is challenging, more so on a limited biopsy. Immunopositivity for L1CAM and PAX8 favours WDPMT, while loss of BAP1 and p16 deletion favours epithelioid MM. Recent studies have demonstrated unique molecular alterations in WDPMT, potentially expanding the diagnostic armamentarium in

future. The patient in this case subsequently underwent surgical resection and findings on resection corroborated the biopsy. The patient remains well with no evidence of recurrence (2 years post-surgery).

E-PS-20-055

Exploring PDL-1 expression, TCD8 lymphocytes, and immunotherapy response in advanced NSCLC patients: a single-centre study

R. Rendon*, L. Lopez Herrera, J. Machuca Aguado, A. López Prieto, M.A. Idoate Gastearena
*Spain

Background & objectives: A cohort of patients diagnosed with genotyped non-small cell lung cancer (NSCLC) exhibiting PDL-1-positive expression (greater than 1%) underwent molecular sequencing. The study aimed to investigate the association between the presence of TCD8 lymphocytes and the response to immunotherapy.
Methods: This single-centre study comprised 50 advanced NSCLC patients who underwent immunotherapy from 2016 to 2021, with a median follow-up of 40 months. Stromal and intraepithelial CD8+ T lymphocytes (TILs) were evaluated and graded using Donnen's classification. Immunohistochemical assessment of PDL-1 expression and molecular analysis via next-generation sequencing (NGS) were conducted. Correlations with treatment response and overall survival (OS) were examined.
Results: The correlation between PDL-1 expression and overall survival exhibited statistical significance (p= 0.03) when patients were categorized into two groups: high PDL-1 (≥50%) and low PDL-1 (<50%). A higher abundance of stromal TILs demonstrated a statistically significant association with OS (p=0.05). Conversely, intraepithelial TILs displayed a discernible yet statistically non-significant relationship. Patient stratification into four subgroups based on PDL-1 expression levels and stromal TILs revealed that those within the high-PDL-1 and high-TILs-CD8+ subgroup exhibited the most favourable overall survival outcomes (p=0.014). Molecular analyses identified alterations including EGFR, TP53, BRAF and KRAS mutations, no statistical correlations were found. Female patients demonstrated superior overall survival compared to their male counterparts (p=0.04).
Conclusion: In conclusion, our study highlights the significant association between PDL-1 expression, stromal TILs, and overall survival in advanced NSCLC patients undergoing immunotherapy. The stratification based on PDL-1 levels and stromal TILs revealed subgroups with distinct survival outcomes. Molecular analyses identified common mutations but lacked statistical correlations with clinical parameters. Notably, gender differences in survival underscore the need for personalized treatment approaches in NSCLC management.

E-PS-20-056

Expression of FOXP3 in the microenvironment of non-small cell lung cancer tissue on the background of the application of immunotherapy

A. Romaniuk*, Y. Moskalenko, A. Baryshok, R. Moskalenko
*Sumy State University, Ukraine

Background & objectives: FOXP3 is mainly expressed in a subset of CD4+ T-cells that play a suppressive role in the immune system. Determining the level of Foxp3 expression in the tumour microenvironment of non-small cell lung cancer tissues against the background of immunotherapy.
Methods: For the study, 16 samples of NSCLC patients treated with immunopreparations were taken. The studied samples had 9 squamous cell carcinomas and 7 lung adenocarcinomas. The tissue of NSCLC was studied using histological and immunohistochemical methods. Antibodies against the Foxp3 receptor were used in the IHC study.
Results: The average age of the patients included in the study from the NSCLC was 58,67 ± 1,55 years, the age range was from 39 to 75 years. Comparison of Foxp3 expression in the tumour microenvironment of squamous cell carcinoma (27.35±3.33) and adenocarcinoma (16.93±3.09) showed a significant difference between these indicators (p<0.05).
Conclusion: Our study shows that in the background of immunotherapy, the presence of immunosuppressive CD4+ T-cells is higher in squamous lung cancer tissue than in adenocarcinoma samples. This may be related to the different effectiveness of immunotherapy in different histological forms of NSCLC.

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E-PS-20-057

Tumour infiltrating lymphocytes characterization in advanced non-small cell lung cancer with first-line immune checkpoint inhibitors treatment

L. Ruivo*, M. Pinho Fialho, D. Baptista, J. Filipe
*Department of Pathology - Unidade Local de Saúde Santa Maria (ULSSM); Instituto Politécnico de Lisboa (ESTeSL), Portugal

Background & objectives: Tumour-infiltrating lymphocytes (TILs) may have impact on prognosis in non-small cell lung cancer (NSCLC) and may affect the efficacy of treatment. Our aim is to characterize TILs in advanced NSCLC with PD-L1 score>50%, treated with first-line immune checkpoint inhibitors.
Methods: We performed a single-centre retrospective study. Patients diagnosed with advanced NSCLC with PD-L1>50%, from 2017 to 2023, were selected. Medical records and histological slides from the primary tumour specimens before treatment were reviewed. Immunohistochemistry for CD20, CD3, CD8 and PD-1 was performed. Tumour and stromal TILs were scored using 0%, 25% and 50% cut-offs.
Results: A total of 34 patients were included. Median age was 64 years and 74% were male. The most prevalent histological type observed was adenocarcinoma (70%). Partial response to therapy was observed in 53% of patients, disease progression was seen in 44% and only 3% had a complete response. All the samples analysed had a lymphocytic inflammatory infiltrate, with CD3+ T lymphocytes being the most prevalent. The type of inflammatory infiltrate was overlapped in all treatment response subgroups. None of the cases showed more than 50% of tumour or stromal PD-1+ inflammatory cells.
Conclusion: Despite therapy with immune checkpoint inhibitors, the majority of patients showed a partial response. It seems that the type of inflammatory infiltrate did not influence therapeutic response. Tumour and stromal PD-1+ inflammatory cells were the least prevalent and PD-1 was not relevant in TILs evaluation. Multi-centre randomized studies would provide more accurate data and allow performing statistical analysis regarding the prognostic value of TILs. A second biopsy could show if there are differences in type of inflammatory infiltrate during treatment.

E-PS-20-059

Non-small cell lung carcinoma with coexpression of TTF-1 and p40: is there new entity on a horizon?

I. Savic*, K. Kundovic, J. Myers
*Institute of Pathology, Faculty of Medicine, University of Belgrade, Belgrade, Serbia

Background & objectives: Non-small cell lung carcinoma (NSCLC) coexpressing TTF-1 and p40 in the same tumour cells is rare. Herein, we present a 61-year-old female, heavy smoker, presented with

malaise, unintentional 30 kg weight loss, and cough with recent onset of hemoptysis.
Methods: CT scan showed an endobronchial, necrotizing left upper lobe mass measuring 6cm in diameter that encircled the pulmonary artery. In the left lower lobe, a smaller mass (4.6cm) was suspicious for a metastatic deposit. Left pleural effusion and atelectasis of the left lung were noted. Mediastinal lymph nodes were enlarged.
Results: Following transbronchial biopsy, histopathological examination showed fragments of bronchial mucosa infiltrated with pleomorphic cells with slightly eosinophilic cytoplasm and nuclear pleomorphism. Immunohistochemistry showed TTF-1 expression, which was coexpressed with p40 in tumour cells. Tumour cells were positive for napsinA and CK7. Diagnosis of adenocarcinoma with aberrant expression of p40, was made. Chemotherapy with Taxol/CBDCA was indicated, but the patient refused it. She died 7 months after initial diagnosis.
Conclusion: Expression of TTF-1 and p40 in NSCLC is usually mutually exclusive. Coexpression of TTF-1 and p40 indicates biphenotypic differentiation. The biological and clinical implications of this unique phenotype are not well known. Further studies are needed this phenomenon to be elucidated.

E-PS-20-060
Prevalence of phenotypic transformation as acquired resistance mechanism in EGFR mutated non small cell lung cancers
R. Sparavelli*, R. Bruno, A. Sbrana, I. Petrini, A. Chella, G. Alì
*Surgical, Medical, Molecular, and Critical Care Pathology Department, University of Pisa, Italy

Background & objectives: Metastatic lung adenocarcinoma (mADC) harboring EGFR activating mutations benefit from first-line osimertinib, but acquired resistance inevitably occurs. Different resistance mechanisms, on- and off-target, have been described. Here, we evaluated the prevalence of phenotypic transformation in a consecutive series of mADC.
Methods: A consecutive 3-year series of non small cell lung cancer (NSCLC) was reviewed according to histological and molecular characteristics. Ninety-three mADC harboring EGFR exon-19 (57 cases) deletion and p.(L858R) mutation (36 cases) were selected. All cases were treated by first-line osimertinib. The prevalence and type of phenotypic transformation was evaluated in patients with available rebiopsy at first-line progression time.
Results: For 27 mADC a rebiopsy was performed, 20 cases had EGFR exon-19 deletion and 7 p.(L858R). Four cases (3 females and 1 male, 67-year median age) underwent phenotypic transformation (14,8%), after about 15 months of osimertinib treatment. All these cases harbored exon-19 deletions and TP53 mutations. Two cases switched to small cell lung cancer histology; in one case a MET amplification was also detected on rebiopsy. One case changed to large cell neuroendocrine and one to sarcomatoid carcinomas. All cases maintained EGFR activating alteration. For 3 cases liquid biopsy was performed at progression time: one was negative, one presented only exon-19 deletion and one only MET amplification.
Conclusion: In our study, phenotypic transformation had a considerable prevalence among EGFR positive mADC treated by first-line osimertinib. Different types of histological changes were detected as the only resistance mechanism, except for one case with an acquired MET amplification. Moreover, all cases harbored TP53 alterations, influencing treatment response. Despite the usefulness of liquid biopsy, rebiopsy should be executed whenever possible. Indeed, rebiopsy remains the only tool to assess the histological transformation, which greatly impacts on prognosis and treatment decisions.

E-PS-20-061
A rare case of typical carcinoid tumour with a component of pigmented carcinoid tumour - case report
E. Stojkoska*, D. Jasar, K. Kubelka-Sabit, V. Filipovski, A. Arsovski, D. Smilevski
*Clinical Hospital Acibadem-Sistina, North Macedonia

Background & objectives: Melanin pigment is found in the neuroendocrine cells of pigmented carcinoid tumours, which are uncommon neoplasms. Our case focuses on the clinical, histological, and immunohistochemical findings of a case involving a typical lung carcinoid tumour that includes a pigmented component.
Methods: After undergoing radiological testing that detected a solitary lung nodule in the lower lobe of the lung and a biopsy sample that confirmed the existence of a carcinoid tumour, a 75-year-old male patient had lobectomy surgery.
Results: The surgically removed material from the left lung lobe had a large, clearly defined oval tumour with a grayish-yellow color. The tumour was 6 cm in size and had a black zone of 3 cm. The overall dimensions of the material were 13cm by 12cm by 5cm. The histology of the tumour showed the presence of neuroendocrine nests with the typical nuclear features of a carcinoid tumour. Additionally, the black area of the tumour displayed discrete neuroendocrine cells containing brown-black pigment inside their cytoplasm. Immunohistochemical labeling showed that all tumour cells had positive neuroendocrine markers. The pigmented zone, on the other hand, had positive melanocytic markers.
Conclusion: The infrequency of pigmented carcinoid tumours, with only a limited number of reported instances, presents difficulties in their diagnosis and emphasizes the importance of distinguishing them from other types of lung cancers, particularly primary or metastatic melanoma. This highlights the importance of interdisciplinary teamwork in optimizing results for these rare lung conditions. This example emphasizes the importance of doing a thorough pathological examination and immunohistochemistry analysis to accurately diagnose and choose appropriate treatment regimens for lung-pigmented carcinoid tumours.

E-PS-20-062
Collagen V is the trigger for pulmonary fibrosis in the systemic sclerosis (SSc) model
V. Elias Contini, A.P. Pereira Velosa, Z.A. de Jesus Queiroz, S. Catanozi, A. Dos Santos Filho, S. de Morais Fernezlian, L. Keren Ramos da Silveira, T. de Matos Lobo, C. Machado Baldavira, D. Frediane Barbeiro, A. Souza Santos, P. Degrava Sampaio Barros, V.L. Capelozzi, W. Paganelli Rosolia Teodoro*
*Division of Rheumatology, Faculdade de Medicina da Universidade de São Paulo, Brazil

Background & objectives: Considering the importance of therapeutic management in patients with SSc and the development of antifibrotics, our proposal was to establish the beginning of the evolution of pulmonary fibrosis in the SSc model.
Methods: The SSc model was induced in C57BL/6 mice via COLV emulsified in Freund's adjuvant (IMU-COLV). Animals were categorized into IMU-COLV15, 30, and 45-day groups, alongside the control groups. Techniques including histology, immunofluorescence, RT-qPCR, and 4-hydroxyproline quantification assessed total collagen, type I and V collagen expression, and COL5α1, COL5α2, Col1a1 genes.
Results: The samples indicated an increase in collagen I in the IMU-COLV45 days compared to the IMU-COLV15 and 30 days. The amount of COLV was significantly higher in the IMU-COLV45 days compared to the IMU-COLV15 and 30days ($p=0.0135$; $p=0.0005$). The IMU-COLV45 days increased total collagen deposition compared to the IMU-COLV15 and 30 days ($p=0.0027$; $p=0.0205$). Col5a1 expression was higher in the IMU-COLV15 and 45days compared to the IMU-COLV30 days ($p=0.0004$; $p=0.0347$). The expression of Col5a2

was higher in the IMU-COLV15 days compared to the IMU-COLV30 days ($p<0.0001$) and IMU-COLV45 days ($p=0.0356$). Col1a1 was more significant in the IMU-COLV45 days compared to the IMU-COLV15 and 30days ($p=0.0027$; $p=0.0027$).
Conclusion: Our results indicate that the SSc model presents activation of Col5a1 and Col5a2 genes for the COLV α1 and α2 chain, after 15 days, resulting in fibrosis of the lung tissue after 45 days, with increased of Col1a1 gene. The IMU-COLV model presents early changes in lung tissue, which will be of great value for studying the pathogenesis of lung involvement in SSc and new approaches for the early treatment of this disease

E-PS-20-063
PD-L1 expression and type-I interferon response in non-small cell lung cancer
C. Thomsen*, C. Meristoudis

*Department of Pathology and Department of Clinical Medicine, Aalborg University Hospital and Aalborg University, Aalborg, Denmark
Background & objectives: Type-I interferons have been suggested as adjuvants to immune checkpoint inhibitors in the treatment of several cancer types. The purpose of this study was to investigate the relationship between PD-L1 expression and type-I interferon response in non-small cell lung carcinomas.
Methods: We examined the immunohistochemical expression of PD-L1 and MxA (type-I interferon-stimulated gene) in tissue microarrays with 106 different NSCLC cases, assessed by both the percentage of positive tumour cells (TPS) and H-score (0-300).
Results: No correlation was found between PD-L1 and MxA, either as TPS vs H-score ($R2=0.06$), or in treatment-relevant categories (<1%, 1-24%, 25-49%, 50%-) that apply in Denmark. 7 out of 16 cases with TPS>50% were MxA-negative.
Conclusion: We found no correlation between type-I interferon response and PD-L1 expression in NSCLC. The identification of a group of patients with high PD-L1 expression but without type-I interferon response may suggests a potentially beneficial effect of interferon-stimulating treatments for this subset of NSCLC patients, but further investigation is required.

E-PS-20-064
Epitheloid hemangioendothelioma in the lung: a case report
S. Turgut*, G. Özbilim, M.Y. Çelik, H. Keskin
*Akdeniz University Hospital, Turkey

Background & objectives: Epithelioid hemangioendothelioma (EHE) is a rare malignant vascular tumour composed of epitheloid endothelial cells within a myxohyalin stroma and uncommon in the lung. Therefore, we aim to present this case due to its infrequency in the thoracic region.
Methods: A 39-year-old female patient, who had been followed for 5 years due to a nodule in her lung. She presented with a complaint of dry cough that had been present for 5 months. The size of the tumour increased in the latest CT scan. The mass was removed with surgery.
Results: Grossly, the material revealed a tumour measuring 0,9 cm in diameter, irregularly bordered, firm, white, attracting attention. In microscopic examination, a tumour with hypocellular- sclerotic centre and cellular periphery, embedded in a myxoid-hyaline stroma, forming nests and small clusters, demonstrating moderate cytological atypia with round-oval nuclei and variable eosinophilic cytoplasm were seen. No necrosis was observed within the tumour, mitoses is 2 per 50 high-power fields. Immunohistochemical staining with CAMTA-1, CD31, CD34, and ERG indicated widespread and strong positivity in tumour cells, while the Ki67 proliferation index was assessed to be approximately 1-2%. Histochemical staining with crystal violet and congo red for differential diagnosis of amyloidosis yielded negative results.
Conclusion: Pulmonary-based EHEs typically present as multiple; however, no other foci were detected in our patient. EHEs associated with CAMTA1, CD31, ERG, CD34 expression but panCK staining is negative in our case. It has been categorized as low-risk group due to the tumour diameter being under 3 cm and the low mitotic count. This case is presented and discussed in the light of literature information.

E-PS-20-065
Pulmonary nodular lymphoid hyperplasia presenting as multifocal mass suspicious for malignancy: a case report
D. Udovicic-Gagula*, E. Delic
*Clinical centre of the University of Saraj, Bosnia and Herzegovina

Background & objectives: Pulmonary nodular lymphoid hyperplasia (PNLH) is a rare non-neoplastic lymphoproliferative disorder often presenting as a mass in the lung. Due to its presentation, it is usually radiologically interpreted as suspected for malignancy.
Methods: Here, we report a case of a 62-year-old woman with previous history of breast carcinoma, presented with repeated episodes of cough and fever. A computed tomography scan of the thorax revealed a spiculated mass and additional smaller area in the same lobe, presentation suggestive for lung primary malignancy although metastasis could not be excluded.
Results: Bronchoscopy was performed but could not reached diagnoses, and the lesion was inaccessible for transthoracic needle biopsy. Subsequently thoracotomy was performed, even atypical resection was planned due to the location of lesion it could not be performed and a lobectomy was done. Histopathologic examination of postoperative specimen showed lymphoid predominant lesion with well-formed follicles, morphology and immunohistochemistry was consistent with PNLH.
Conclusion: PNLH is benign lymphoproliferative lesion whose radiologic presentation often mimicking malignancy, and it should be included in differential diagnose of lung mass-like lesions.

E-PS-20-066
A benign but life-threatening cause of hemoptysis: endobronchial capillary hemangiomas
I. Vamvakaris*, S. Zaneli, N. Anagnostopoulos, G. Liadakis, M. Anagnostopoyloy, P. Tziakou, I. Grypari, A. Bakiri, G. Stratakos
*Sotiria Hospital Athens, Greece

Background & objectives: Capillary hemangioma of the tracheobronchial tree is an extremely rare benign lesion in adults. We present a case of a male patient with endobronchial capillary hemangioma which was diagnosed from bronchoscopic lung biopsy specimen.
Methods: A 58-year-old male presented to the emergency department complaining for hemoptysis. He was an active smoker (30 pack/year), with a history of coronary syndrome that underwent coronary angioplasty with stenting and arterial hypertension. He was under antiplatelet treatment with acetylosalicylic acid, statin and PPIs.
Results: On physical examination, the vital signs were normal and the auscultation did not reveal any remarkable findings. Laboratory tests were also normal. The CT scan revealed limited ground glass opacities in the middle lobe. The patient underwent flexible bronchoscopy and a polypoid endobronchial lesion was found at the superior segmental bronchus of the right lower lobe. The lesion was removed using loop electrocautery. Histologic examination revealed characteristic abnormalities typical for capillary hemangioma. Post bronchoscopy follow up was uneventful.
Conclusion: Endobronchial capillary hemangiomas are rare. However, they must be included in the differential diagnosis of a patient presenting with hemoptysis. Biopsies of such lesions should be performed by experienced interventional pulmonologists using several bronchoscopic modalities since the risk of bleeding is high.

E-PS-20-067

Small cell lung carcinoma subtypes defined by ASCL1, NEUROD1 and POU2F3: an immunohistochemical study

A. Vigdorovits*, G. Olteanu, A. Pascalau, A. Camarasan, M. Muresan, O. Pop
*University of Oradea, Romania

Background & objectives: Recent studies have proposed subtyping small cell lung carcinoma (SCLC) based on differential gene expression of ASCL1, NEUROD1 and POU2F3. Here, we explored the immunohistochemical (IHC) expression patterns of these markers in biopsies of patients with SCLC.
Methods: Biopsies of 51 SCLC diagnosed between 2021 and 2024 were evaluated for IHC expression of ASCL1, NEUROD1, and POU2F3. The cases were reviewed by a thoracic pathologist and H-scores for ASCL1, NEUROD1 and POU2F3 were calculated to subtype SCLC into SCLC-A, SCLC-N, SCLC-P and SCLC-I. Additionally, we evaluated the expression of CD56, Ki67 and the presence of tumour-infiltrating lymphocytes (TILs).
Results: According to predominant marker expression, 35 cases (69%) were SCLC-A (ASCL1 dominant), 5 (9%) were SCLC-N (NEUROD1 dominant), 4 (8%) were SCLC-P (POU2F3 dominant) and 7 (14%) were SCLC-I (triple negative). The dominant marker for each subtype had a significantly higher H-score compared to the other subtypes (pair-wise $p < 0.05$). CD56 H-score was significantly higher in SCLC-A cases compared to SCLC-I ($p = 0.008$). Different median Ki-67 indexes were observed: 90% for SCLC-A and SCLC-N, 85% for SCLC-P and 80 % for SCLC-I ($p > 0.05$). SCLC-P and SCLC-I showed slightly more TILs (mean 12.5% and 8.5%) compared to SCLC-A and SCLC-N (mean 6.4% and 6%) ($p > 0.05$).
Conclusion: Our study confirms the utility of using IHC to determine the novel SCLC subtypes. Significant differential expression of IHC markers was observed. Given the potential therapeutic targets available for each subtype, the use of this classification in routine clinical practice could prove vital for patient management in the near future.

E-PS-20-068

Expect the unexpecting: a new pulmonary nodule in a patient with a history of follicular lymphoma

A. Vilaia*, F. Pezzuto, G. Scapinello, F. Piazza, D. Marino, F. Calabrese
*Colentina University Hospital, Romania

Background & objectives: Pleuro-pulmonary Kaposi sarcoma (KS) is rare among HIV-positive patients and exceedingly scarce in HIV-negative individuals. In sero-negative patients, it usually occurs as a post-transplant complication, with only rare cases of pulmonary involvement reported in patients undergoing immunosuppressive or immunomodulatory treatments.
Methods: We report a case of a 70-years-old woman, previously treated for Non-Hodgkin Follicular Lymphoma with chemotherapy and immunotherapy, in clinical remission, presenting with non-specific symptoms. Comprehensive clinical and imaging assessments revealed a perihilar lesion measuring 25mm located in the left lung, PET-positive, no cutaneous lesions or significant adenopathies. A relapsing lymphoma was considered a and CT-guided biopsy was performed.
Results: Histologic examination revealed a spindle cells proliferation with fascicular growth with anastomosing, slit-like vascular spaces containing abundant blood extravasation and hemosiderin deposits. The cells showed moderate atypia, hyperchromatic nuclei, and scattered mitotic figures. Considering the histological aspects, further immunohistological tests were performed. The tumour cells were positive for vascular markers (CD34, CD31 and ERG), showed strong nuclear positivity for HHV8 antibody, and were negative for cytokeratins, S100, SYT-SSX18, ALK1 actin and lymphoid markers. The final diagnosis was pulmonary KS. The unexpected findings led to further bioclinical testing, which confirmed the patient's HIV-negative status, and a real-time-polymerase chain reaction positive test for HHV8-DNA. Follow-up PET-CT showed rapid progression in tumour's size.
Conclusion: This case is a reminder to never underestimate the occurrence of unusual lesions that may appear in patients undergoing immunosuppressive treatments. Histology and ancillary tools are always the best method to approach peculiar or difficult cases taking into consideration a broad spectrum of differential diagnoses. Otherwise, like in this case, the correct diagnosis could have easily been overlooked.

E-PS-20-069

Clinicopathologic characteristics of pleomorphic carcinoma of the lung in a single Tunisian institution: a series of 8 cases

R. Yaiche*, Y. Houcine, R. Ayadi, E. Braham, O. Ismail, A. Ayadi
*Abderrahmane Mami Hospital, Tunisia

Background & objectives: Pulmonary Pleomorphic carcinoma (PPC) is a rare aggressive type of non-small cell lung carcinoma (NSCLC), accounting for less than 1% of all cases of lung cancer. In this study, 8 cases of PC were reviewed to identify its clinicopathologic characteristics.
Methods: This is a retrospective study, including 8 patients who underwent surgical resection for pulmonary pleomorphic carcinoma. Data were recorded from pathological reports at AbdErrahman Mami Hospital on a period of 14 years, from 2014 until 2023.
Results: The mean age was 62 years (range: 40 to 75 years). There were 6 men among whom 5 were smokers and 2 women. The diagnosis of PPC was confirmed histologically on surgical specimen or biopsies (respectively 5 cases and 3 cases).
¾ of PPC were in the right lung, mostly the upper lobe (5 cases). Of epithelial components, 4 were adenocarcinomas, one was epidermoid carcinoma and three were large cell carcinomas. As for sarcomatous elements, 6 were of spindle cell types, one each of giant cell and combined spindle and giant cell types.
Pleural involvement was observed in three cases. Nodal status was classified as pN0 disease in most cases.
Conclusion: PPC is a highly malignant subtype of sarcomatoid carcinoma. It usually occurs in male smokers and mostly presents as a voluminous necrotic peripheral lesion of the upper lobe of the right lung. Distant metastases are common; hence the prognosis remains poor despite of surgery and adjuvant chemotherapy.

E-PS-20-070

Pulmonary inflammatory myofibroblastic tumour: an unusual condition in adults

R. Yaiche*, E. Braham, I. El Hadhri, I. bouassida, R. Ayadi, I. Mallek, O. Ismail, S. Ben Slama, A. Ayadi
*Abderrahmane Mami Hospital, Tunisia

Background & objectives: Inflammatory myofibroblastic tumour (IMT)of the lung is a rare condition of unknown etiology in adults, representing around 1% of adult lung neoplasms. In this study, we aim to highlight the IMT's variability in terms of clinical presentation and histopathological features.
Methods: We retrospectively investigated patients diagnosed with IM at the Abderrahman Mami Hospital over a period of 10 years from 2011 to 2021. A total of 10 patients were identified. All reviewed patient data were acquired from the medical records and histopathological reports.
Results: Eight males and two females with a mean age of 46 years (range: 41-59 years) were identified. The chief complaint was chest pain in 5 cases, recurrent pneumonia in 2 cases and chronic dry cough in 3 cases. CT-findings revealed well-circumscribed, solitary lung nodules with a predilection for the upper lobes (6/10 cases). Endobronchial

extension was reported in 2 cases. All patients were treated surgically by lobectomies in 5 cases, pneumectomy in 2 cases and wedge resection in 3 cases. The diagnosis of IMT was confirmed by histologic examination. The mean tumour size was 65mm. All cases were immunoreactive to SMA and vimentin. Follow-up was recurrence-free in all cases.
Conclusion: IMT of the lung is a rare benign mesenchymal neoplasm which tends to mimic malignant tumours, therefore it needs to be considered in differential diagnosis of lung masses. The diagnosis is based on histological confirmation. Optimal curative treatment remains surgical resection whenever possible.

E-PS-20-071
Pleural mesotheloma in situ (MIS) mimicking well-differentiated papillary mesothelial tumour (WDPMT): report of two cases of this novel challenging entity
S. Zanella*, S. Fraticelli, D. Rahal, S. Uccella, G. Pelosi, P. Bossi
*Department of Biomedical Sciences, Humanitas University, Milan, Italy; Pathology Service, IRCCS Humanitas Research Hospital, Milan, Italy

Background & objectives: MIS is a rare in situ neoplasm of the serosal membranes, potentially progressing to invasive mesothelioma. WDPMT is a lesion of uncertain malignant potential, more likely benign. We present two cases of MIS mimicking WDPMT, underlining important differential diagnostic criteria.
Methods: A 77 yo man and 85 yo woman, both presenting with unilateral pleural effusion, underwent thoracoscopic biopsy of the parietal pleura. Microscopically, a mesothelial proliferation with large papillae lined by epithelial cells with low cytologic atypia in a mixoid stroma was present in both cases. Thus, an immunohistochemical panel and FISH for CDKN2A were performed, to distinguish MIS from WDPMT.
Results: In both cases, the epithelial cells lining the papillae were positive for WT1 and, focally, for Calretinin. PAX8 was negative. BAP1 was not expressed. FISH analysis showed homozygous deletion of CDKN2A in one case, and no alteration in the other. These findings qualified undoubtedly both lesions as malignant, since BAP1 negativity and/or CDKN2A deletion are seen only in malignant mesothelioma, and not in WDPMT. As no invasion was present, we classified the lesions as MIS, regardless that the morphological appearance was one that may suggest WDPMT. In the 77yo male patient, a second adjacent sample showed a flat atypical mesothelial proliferation with the same immunophenotype, further confirming MIS.
Conclusion: A 2023 paper of Galateau-Salle et al, building on a previous work of Lee et Al of 2018, described a small series of MIS mimicking WDPMT, 3 of which were thoracic and presented with pleural effusion. As in our cases, despite the deceptively bland morphology of the lesions, ancillary analysis revealed their malignant nature. Our report reinforces the need for immunohistochemistry and FISH analysis on WDPMT cases, at least for the ones with suspicious clinical features.

E-PS-21E-Poster Session Thymic and Mediastinal Pathology
E-PS-21-001
Giant cardiac glomus tumour: a rare presentation with rapid progression in an elderly patient
S. Amer*, N. Dioufa, J. Fu, M. Mollaee
*Pathology department - Temple University Hospital, USA

Background & objectives: Glomus tumour is a mesenchymal neoplasm arising from neuromyoarterial structure, the glomus body. Many of them are benign but rarely show malignant features. Glomangiosarcoma usually arises from a glomus tumour. Glomus tumour of the heart is very rare, because
Methods: of the rarity of the glomus bodies in the heart. Only few cases have been reported in the literature. CASE PRESENTATION: An 80-year-old female with a stable pericardial mass since 2013 presented with acute respiratory failure requiring intubation. CT angiogram of the thorax revealed a significant rapid progression of the right pericardial soft tissue mass (11.3 x 10.4 x 6.7
Results: cm) with a significant mass effect along the left ventricle and major vascular structures. There was no evidence of invasion to adjacent myocardial or diaphragmatic tissue. She underwent CT-guided biopsy. Histological examination revealed round to polygonal cells with eosinophilic cytoplasm and round nuclei surrounded by capillary-sized vascular channel. Immunohistochemical analyses of the tumour cells were positive for desmin, smooth muscle actin (SMA), muscle-specific actin (focal), CD34 (focal) and negative for S100, AE1/AE3, WT1, calretinin, CD31, Beta-catenin, STAT6, HMB45, and CD99. The Ki67 proliferation index was 30% supporting the diagnosis of myoid soft tissue tumour with features of glomus tumour variant favouring glomangiosarcoma given the rapidly increasing size of the mass
Conclusion: and high proliferation rate. Patient's clinical condition deteriorated rapidly and she expired in few weeks. DISCUSSION: Glomus tumours and extracutaneous glomangiosarcomas especially in the heart are extremely rare and are often misdiagnosed with other soft tissue tumours. This case emphasizes the importance of having this entity in differential diagnosis for pathologists. The tissue biopsy diagnosis, and immunohistochemistry panel are the keys for the diagnosis. Surgical resection with wide margins remains the mainstay of treatment to minimize recurrence rate and metastasis

E-PS-21-002
Neuroblastoma in a 70 year old woman: case report and literature review
M. De Uribe Viloria*, S. Quinones, E.P. Sánchez López, G. Escuer-Albero, V. Macarrón, R.M. Regojo, I. Esteban-Rodríguez
*La Paz University Hospital, Spain

Background & objectives: Neuroblastoma is an embryonic neoplasm of the sympathetic nervous system, and the most common extracranial solid neoplasm of early childhood. However, neuroblastoma in adults is exceedingly rare, presenting primarily in the mediastinum and retroperitoneal region in this age range.
Methods: We reviewed our files from 2014 to March 2024 encountering a single case of neuroblastoma in an adult patient. The diagnosis was achieved by using Hematoxilin-Eosine and immunohistochemical studies. From the clinical history we obtained the age at diagnosis, symptomatology and radiological studies.
Results: We present the case of a 70-year-old woman, with a history of SIADH associated hyponatremia, presenting with severe hyponatremia and a large mediastinal mass in the CT scan. Said mass was enucleated, showing a tumour displaying variable sized nests, conformed by monotonous round cells with scant cytoplasm, small hyperchromatic nuclei with salt and pepper chromatin surrounded by fibrillary matrix material reminiscent of neuropil. It showed positivity for neuroendocrine markers (chromogranin A, synaptophysin and CD56) and neuron-specific enolase, and was negative for CKAE1/AE3, EMA, CD117, CD5,Tdt, CD99, S100 and vimentin. The expression of ATRX was preserved. The proliferation index (Ki 67) was close to 15%. Necrosis and dystrophic calcifications were present.
Conclusion: Neuroblastoma is extremely rare tumour in adults, with a significantly worse prognosis than in paediatric patients. To date there are less than 30 cases reported in literature. Due to its infrequent nature it poses a diagnostic and management challenge. Our case presents typical pathological findings, in spite of occurring at an older age than these tumours usually present. Further research focusing on this rare malignancy in adults may help address the challenges of this disease.

E-PS-21-003

Posterior mediastinal ganglioneuroma with fat tissue: pathological study of an unusual tumour

I. El Hadhri*, R. Ayadi, E. Braham, R. Yaiche, M. Affes, I. Mallek, O. Ismail, S. Hantous-Zannad, I. Bouassida, A. Ayadi
*Sahloul University Hospital, Tunisia

Background & objectives: Ganglioneuroma (GN) is a rare and benign tumour that arises from the sympathetic nervous system. Most GNs are asymptomatic and are found coincidentally on radiography. Fatty replacement in cases of GN is extremely rare, hence the interest of this study.
Methods: Herein, we present two cases of GN with metaplasia by adipocytes. The highlights in these cases included not only the rare fatty replacement within the tumour, but also the location of the tumour, which resulted in uncertainty in diagnosis and preoperative planning.
Results: We report two cases of GN with fat tissue in a 30-year-old man and a 28-year-old woman, both without prior medical history. They experienced local compression symptoms, including chest and lower back pain. Diagnostic imaging, revealed a parahilar opacity and a solid paravertebral mass with heterogeneous density. Subsequent surgical intervention, based on extemporaneous examination, confirmed the diagnosis of GN. On gross examination, tumours size ranged between 9 and 8cm. They were described as well-defined mass and yellowish-white cut surface. Microscopically, the tumour exhibited a benign mesenchymal proliferation of three cell types: spindle cells, ganglion cells, and adipose cells. Histopathological examinations led to the final diagnosis of GN with fat tissue.
Conclusion: Ganglioneuroma is a rare tumour in the posterior mediastinum; fat tissue containing ganglioneuromas are rarely reported. This type of dumb-bell tumour requires radical resection because it can cause chest pain and severe compression symptoms as the disease progresses.

E-PS-21-004

Hidden in plain sight: an ectopic thymoma

C. Guerin*, A. Robinson, E. O' Neill, A. Fabre, J. Kirby, M. Sabah
*Ireland

Background & objectives: Thymoma arising outside of the anterosuperior mediastinum is a rare occurrence, accounting for only 4% of thymoma cases. We present a case of a large ectopic thymoma arising in the right hemithorax of a man with transient neurological deficit.
Methods: A 52-year-old man presented with transient unilateral jaw weakness, ptosis and diplopia. His symptoms were initially attributed to a transient ischaemic attack (TIA). A chest x-ray was performed which showed an unexpected mass in the right hemi-thorax. Further evaluation by CT scan demonstrated a 10cm right sided thoracic lesion with a wide base abutting the pericardium.
Results: CT guided core biopsy of the lesion was performed. On microscopy, the cores of tissue were infiltrated by hyperchromatic cells with a diffuse growth pattern. Mitotic figures were not seen. There was no evidence of haemorrhage or necrosis. Immunohistochemical stains highlighted an epithelial population, positive for AE1/3 and p63, admixed with CD3, CD5 and TdT positive lymphocytes. Scattered CD20 positive lymphocytes were present. TTF-1 and CK5/6 were weakly positive. CD117, Napsin A, CD56, chromogranin and synaptophysin were negative. Serum anti-titin antibody was also found to be positive. The patient was diagnosed with ectopic thymoma, B2 subtype, with associated paraneoplastic myasthenia gravis.
Conclusion: Ectopic thymoma is a rare entity and can prove a challenging diagnosis. It is believed to derive from thymic tissue which becomes displaced during embryonic development. The morphological findings are the same as those of orthotopic mediastinal thymoma and all subtypes of thymoma can develop ectopically. Tumour cells are CD117 negative, a marker of KIT expression which is positive in thymic carcinoma. In contrast to mediastinal thymoma, ectopic thymoma is less commonly associated with myasthenia gravis, making our case unusual.

E-PS-21-005

A case report of a mediastinal, mixed non-seminomatous germ cell tumour harboring postpubertal teratoma with four types of somatic malignancies

P. Kousidis*, G. Panselinas, S. Androniadou, V. Christoforidou, N. Barbetakis, Z. Zafeiriou, A. Nikolaidou
*Pathology Department, Theageneio Anticancer Hospital of Thessaloniki, Greece

Background & objectives: Extragonadal germ cell tumours (EGCTs) most commonly arise in the anterior mediastinum. Somatic-type transformation of teratomatous component to multiple types of malignancy is rare. We present a case of a 22-year-old male patient and analyse the diagnostic considerations and challenges.
Methods: A 22-year-old male patient was admitted to our Thoracic Surgery Department for thoracic surgical management of an anterior mediastinal tumour, previously diagnosed as a mixed non-seminomatous germ-cell tumour (m-NSGCT) with embryonal carcinoma (EC) and postpubertal teratoma. We extensively reviewed the patient's history, results of prior studies, tissue slides and performed substantial tissue sampling for diagnosis.
Results: The excised specimen was a 4 kg, 28 cm round-to-oval tumour, with smooth surface. During dissection it was found to be mostly solid, with small cysts and with large areas of necrosis. Microscopically, no foci of embryonal carcinoma were identified, possibly due to prior chemotherapy. The postpubertal teratoma exhibited multiple types of epithelium, focally dysplastic. Importantly, a population of glial cells with malignant elements was present, of the type of high-grade glioblastoma. There were also small populations of rhabdomyosarcoma, chondrosarcoma and osteosarcoma. Areas of lung parenchyma adjacent to the tumour were excised showing invasion yet clear resection (R0).
Conclusion: The patient was clinically improving at 2 months postoperatively and was scheduled for surveillance and possible administration of TIP chemotherapy. In conclusion, approach to mediastinal tumours with elements of immature teratoma is challenging. Total excision, with extensive sampling, is a critical consideration in order to accurately diagnose all malignant elements. The number of reported cases and thus the potential for studying and optimizing specific treatments, is rising.

E-PS-21-006

Atypical thymic carcinoid tumour: a case report and novel literature review

P. Kousidis*, V. Christoforidou, N. Barbetakis, S. Androniadou, N. Dimitrellos, E. Triantafillidou, A. Nikolaidou
*Pathology Department, Theageneio Anticancer Hospital of Thessaloniki, Greece

Background & objectives: Primary thymic neuroendocrine tumours (t-NETs) are rare tumours among primary thymic malignancies. They present a heterogenous group, regarding both histology and prognosis, from typical carcinoids to small-cell carcinomas. We present a case of thymic atypical carcinoid in a 61-year-old male.
Methods: A 61-year-old male patient was admitted to our Thoracic Surgery Department for elective resection of a thymic tumour. The patient underwent total thymectomy with wedge resection of part of lung RUL through a median sternotomy. All excised specimens were sent for pathologic examination.

Results: Macroscopic examination of the thymus showed a well circumscribed, 4.2 cm maximal diameter, yellow-tan and white tumour. Microscopically, the tumour was comprised of oval, medium to small-sized cells, with mainly eosinophilic cytoplasm and at areas visible nucleoli. Nuclear atypia was low to moderate. Margins were clear of malignancy (R0). Mitoses were 5/2 mm2. Focal areas of necrosis were present. Extensive immunohistochemistry revealed positivity for Ker8/18, KerAE1/AE3, chromogranin, synaptophysin and CD56, negativity for p63, p40, TTF1, CD20/L26, TdT, CD5 and CD3 and a Ki-67 of 20%. The other specimens were clear of malignancy. We analyse the diagnostic challenges and further appropriate NGS tests for enhancing diagnostic and prognostic accuracy.
Conclusion: The combination of findings led to the diagnosis of a primary t-NET of the type of atypical carcinoid (grade 2 NET). Among primary thymic malignancies, primary t-NETs are a subgroup of tumours requiring specific considerations in macroscopic, microscopic diagnosis and further testing. The field of t-NETs is evolving, with new molecular approaches enhancing our precision in handling these rare tumours.

E-PS-21-007
A rare case of mediastinal cystic seminoma
R. Lyrio*, A. Pestana Lopes, M. Mendes de Almeida
*Hospital da Luz Lisboa, Portugal

Background & objectives: Prominent cystic change of mediastinal seminomas in patients is uncommon and rarely reported, and the ones that are reported usually only show unilocular cystic changes. We, hereby, report a case of a mediastinal seminoma with multilocular cystic changes.
Methods: A 19 year old man presented with odynophagia to the emergency room. Computed thoracic tomography revealed at the anterior mediastinum a 90mm septated multilocular cystic lesion. PET scan showed no abnormal uptake. No distant metastasis were identified. Blood tests showed normal levels of germ cells tumour markers. A thymectomy via robotic approach was performed and the specimen was sent for analysis.
Results: On gross examination, the lesion consisted of a multilocular cyst originating from the inferior pole of the thymus. The cystic wall showed irregular thickness with nodular areas. Microscopically, the cystic wall was lined by normal squamous epithelium, and the nodular areas were characterized by lymphocyte-rich stroma with germinal centres, epithelioid granulomas and a population of polygonal cells with slightly clear cytoplasm and occasional prominent nucleoli. Immunostaining of the lymphoid component was consistent with reactive lymphoid follicular hyperplasia, and the neoplastic cells with clear cytoplasm were positive with PLAP, SALL4, OCT3/4 and CD117, and were negative with CD31. The final diagnosis was mediastinal cystic seminoma.
Conclusion: The pathogenesis of the cystic process in these cases remains unsettled. However, it is important for pathologists and clinicians to be aware that seminomas can give rise to multicystic lesions in the mediastinum, so proper clinical management can be given to these patients in due time.

E-PS-21-008
A case report of a rare and aggressive tumour of the thymus: lymphoepithelioma-like carcinoma
A. Mahmoudi*, A. Bdioui, M. Krifa, Y. Ben Romdhane, S. Mestiri, S. Hmissa
*University Hospital Sahloul, Tunisia

Background & objectives: Thymic carcinomas encompass a variety of rare tumours of the anterior mediastinum. Lymphoepithelioma-like carcinoma (LELC) accounts for 6% of all thymic carcinomas. It's an aggressive entity that's been shown to be associated with Epstein-Barr Virus in most of the cases.
Methods: We report a case of a thymic LELC in a 68 year old man, with no medical history, collected at the laboratory of pathology. The patient presented with anterior chest pain. Chest computed tomography revealed a tumour in the anterior mediastinum. A surgical resection of the tumour was performed.
Results: Histologically, the mass demonstrated infiltrative carcinomatous growth. The cells appeared polygonal and notably atypical, forming syncytial clusters. Mitotic activity was pronounced, and the stroma exhibited inflammation with a prominent plasma cell component adjacent to the tumour clusters, along with abundant sclerotic desmoplastic changes. Lymphatic emboli were observed at a distance. There was no residual thymic tissue, which led us to consider nodal metastasis from a bronchogenic carcinoma. Subsequently, immunohistochemical analysis was made and revealed focal expression of C Kit (CD117), CK7, and P63 in tumour cells, while CK20, synaptophysin, chromogranin, and CD30 were negative. EB-encoded RNA in situ hybridization of the tumour was positive.
Conclusion: The case we report underlines the histopathological and immunohistochemical features of a rare and aggressive type of carcinoma in the thymus.

E-PS-21-009
Lipofibroadenoma: a case report and review of the literature with clinicopathological analysis
D. O'Dwyer*, F. Roberts, H. Pitchamuthu
*NHS GGC, United Kingdom

Background & objectives: Lipofibroadenoma (LFA) is a thymic epithelial-mesenchymal neoplasm morphologically reminiscent of fibroadenoma of the breast. Only 21 cases have been reported in the literature. Here we present a case report of this extremely rare neoplasm and review of the literature.
Methods: We describe the case of LFA in a 62-year-old male alongside a review of the literature with analysis of clinical, radiological, and histological features. Correlation between clinicopathological characteristics is performed using Chi square.
Results: In this case the patient was being investigated in primary care for persistent cough. Subsequent CT imaging was indicative of a teratoma in the anterior mediastinum. Histological evaluation revealed an LFA with background thymic hyperplasia and clear resection margins. The follow-up period has been uneventful. Of the 22 cases reported in the literature, including this case, the majority occur in males (59.1%, n=13). The average age at presentation is 37.7years and the average size is 11.3cm. A significant proportion of cases occur alongside thymic hyperplasia or thymoma (36.4%, n=8), as in this present case. Older age is significantly correlated with concomitant pathology (p=0.05).
Conclusion: LFA is considered a benign thymic epithelial tumour. Of the cases reported in the literature, no adverse clinical events are documented. However, limited follow-up data is available and clinicopathological characteristics are yet to be well-defined. We have analysed this present case alongside those reported in the literature and found a correlation between older age and concomitant pathology - which is something not previously reported. These cases may require additional follow-up however, further characterisation of this rare tumour is required.

E-PS-21-010
Primary neuroendocrine tumour of the mediastinum: a case report and literature review
O. Tzaida*, G. Galanopoulos, P. Bafaloukos, E. Souka, N. Mpolanos
*Metaxa Cancer Hospital, Piraeus, Greece

Background & objectives: Neuroendocrine neoplasms are epithelial tumours with a predominant neuroendocrine differentiation. They are

mostly encountered in the gastrointestinal tract, genitourinary tract, and lungs. Anterior mediastinum is a very rare location site for primary tumours.
Methods: A 57-year-old female patient with a history of multiple endocrine neoplasia type 1 presented with dyspnea and fatigue over the last 4 months. She reported no chest pain or any weight loss. Imaging showed a mass occupying the anterior mediastinum. After surgical removal, a circumscribed lobulated whiteish, soft homogenous tumour measured 4.5x3x2.8cm, surrounded by a thin fibrous capsule was delivered.
Results: Histology revealed a uniform, ovoid cell population with mild nuclear atypia and minimal mitotic activity (1mitoses/mm2), arranged mostly in nests and rosettes with solid and pseudoglandular architecture. Focal infiltration of the surrounding capsule was also noticed. A few lymphocytes along with a delicate thin-walled capillary network were present. No remaining thymus tissue was evident. A differential diagnosis between paraganglioma, thymoma, and neuroendocrine tumour was suggested. Neoplastic cells showed immunoreactivity for CKAE1AE3, CK8/18 (dot-like), Chromogranin, Synaptophysin and CD56, whereas TTF1, CK20, CK5/6, PAX8, Vimentin, and p63 were negative. Ki-67 mitotic index was <2%. The diagnosis of a G1 NET was established.
Conclusion: Mediastinal neuroendocrine tumours are very rare, accounting for 2-4% of all anterior mediastinal neoplasms. The size ranges from 2-20 cm. Thymomas or thymic carcinomas can also coexist. No organ-specific histological or immunohistochemical features are seen. WHO classification is the same as their pulmonary counterparts. They can also occur as a part of multiple endocrine neoplasia type 1 (MEN1), like our presented case. Although they are slow growing tumours, regional lymph node metastases can be found at the time of diagnosis.

E-PS-22E-Poster Session Cytopathology

E-PS-22-001
Implementation of the International System for Reporting Serous Fluid Cytopathology (TIS) with cytohistological correlation and evaluation of malignancy risk

R.S. Atamanalp*, S. Erdogan-Durmus, C. Comunoglu, O. Yalcın, B. Akı
*Prof. Dr. Cemil Tascioglu City Hospital, Turkey

Background & objectives: Serous effusions offer convenient access, yielding important diagnostic information and material for further investigation. The objective of this study is to implement TIS with cytohistological correlation and to evaluate malignancy risk across each group of TIS.
Methods: We included all 515 pleural, peritoneal and pericardial effusion cases from our department over a two-year period (2022-2023) in this study. Each specimen was classified according to TIS guidelines and the risk of malignancy (ROM) was calculated for each category based on the histopathological follow-up. Our hospital's database was searched for age, gender, sample volume, and histologic diagnoses.
Results: Out of the 515 cases, 3 (0.6%) were non-diagnostic (ND) (0.6%), 355 (68.9%) were classified as negative for malignancy (NFM), 25 (4.9%) were classified as atypia of undetermined significance (AUS), 19 (3.7%) were classified as suspicious for malignancy (SFM), and 113 (21.9%) were classified as malignant (MAL). In our study, histopathologic follow-up was available of a total of 390 (75.7%) cases. Among these, 246 (63.1%) cases were diagnosed as malignant and 144 (36.9%) cases were diagnosed as benign. The malignancy risk (ROM) for the ND, NFM, AUS, SFM, MAL groups was calculated as 100%, 42.1%, 77.7%, 100%, 100%, respectively.
Conclusion: TIS system is easily applicable to effusions, with a predominance of benign diagnoses in majority of the cases (68.9%). Carcinoma metastasis emerged as the most frequent malignancy. The high ROM detected within ND category proves the importance of performing effusion sampling with adequate fluid amount. Notably, relatively high ROM observed in negative group was mostly due to peritoneal washing samples obtained during oncological surgeries. Overall, TIS stands as a valuable classification tool, offering insights that contribute to clinical therapeutic management.

E-PS-22-002
Papilloma virus humain typing at the pathology department of the Oran University Hospital Centre

B. Belbachir*

*Service de pathologie CHU Oran, Algeria

Background & objectives: Persistent human papilloma virus infection (hpv) is the necessary cause for the development of cervical cancer. by detecting the virus at an early stage, the risk of cervical cancer is decreased significantly.
Methods: At the level of the cytopathology department of the Centre University Hospital of Oran, we analysed 65 samples cervical with the digene hc2 hpv dna test and this in conjunction with a cervical smear in order to identify women with high risk of developing cervical cancer.
Results: Among the 65 cases analysed jointly by cytology and test hpv; 7 patients are positive for high-risk hpv.
Conclusion: Cervical cancer screening can certainly be improved in our country in replacing the practice of smear alone with combination with hpv testing at a faster rate safely spaced and to determine the need for colposcopy or other monitoring procedures.

E-PS-22-003
Fine needle aspiration cytology of the thyroid as diagnostic tool of secondary malignancies: Gustave Roussy Experience

N. Ben Othman*, V. Suciu, N.I. Ben Romdhane, S. Moog, L. Lamartina, R. Soufan, J. Hadoux, D. Hartl, E. Baudin, A. Al Ghuzlan, M.a. Bani
*Department of Medical Biology and Pathology, Morphological pathology laboratory, Gustave Roussy Cancer Campus, Villejuif, France

Background & objectives: Intra-thyroidal metastases (ITM) are rare. They are diagnosed following fine-needle aspiration cytology (FNAC) in 2.3 to 7.5%. The aim of this study was to describe the pathological features of ITM and to analyse the accurancy of thyroid FNAC.
Methods: This retrospective analysis included patients diagnosed with ITM between 2008 and 2023 identified in our institution. The clinical features for each patient were obtained from the medical files. For each patient, cytological, histological and immunohistochemical slides were reviewed to confirm the diagnosis and to assess cytological features.
Results: Among 9813 thyroid FNAC, a diagnosis of ITM was made in 36 cases (0.4%). Patients were aged between 33 and 85 years, with a male to female ratio of 1:1. 92% of cases were classified Bethesda VI (2023). The most frequent primary tumour was pulmonary in 28% of cases (n=10). The mean size was 26.5 mm. Metastases were predominantly located in the right lobe (46%). Histological types included pulmonary adenocarcinomas (n=6), invasive breast cancer NOS (n=7), squamous cell carcinoma of head and neck (n=9), melanomas (n=3) and clear cell carcinomas of the kidney (n=4). A confirmation by immunohistochemistry on cytoblocs was performed in 9 cases.
Conclusion: Secondary malignancies of the thyroid are rare, representing 1 to 3% of thyroid cancers. Few studies aimed to characterise these tumours on FNAC. In recent literature, the most common ITM are renal cell carcinomas mainly in autopsies, which wasn't the case in our study. Understanding the potential challenges in diagnosing thyroid

lesions through fine-needle aspiration cytology, conducting thorough clinical assessments, and employing appropriate ancillary techniques on cytoblocs can help achieve accurate diagnoses, without neccessarily the need of a histologic confirmation.

E-PS-22-004

Endoscopic lymph node sampling and oesophageal cancer surgery

B. Cheng, A. Naqvi, R. Juergens, C. Finley, M. Bonert*
*McMaster University, Canada

Background & objectives: Endoscopic lymph node sampling (EBUS/EUS) is a well-studied procedure to non-invasively stage lung cancer; however, it is not well characterized in oesophageal cancer. This analysis sought to assess endoscopic lymph node sampling (ELNS) in the context of oesophageal cancer surgery.
Methods: All EBUS/EUS and oesophageal cancer surgery (ECS) cases accessioned 2011-2020 were retrieved in a regional thoracic centre and diagnostically classified using mutually exclusive categories in a hierarchy (benign (BEN) / insufficient (INS) / suspicious (SUSP) / malignant (MAL)). EBUS/EUS cases were matched with the oesophageal cancer surgery cases with an anonymized patient identifier.
Results: In the time period 4,155 patients had ELNS for all indications and 404 patients had an ECS. Among ELNS patients, 1,562/4,155(37.6%) were classified MAL. 111 of 404 ECS patients had ELNS - 103 before surgery, 8 after surgery and 3 before and after surgery. Station 2 lymph nodes had the highest positivity rate (67%). ELNS before ECS were classified: 13/103 (12.6%) MAL, 3/103(3%) SUSP, 23/103 (22.3%) INS and 64/103 (62.1%) BEN. The majority of patients had neoadjuvant therapy (69/103) and 15/16 patients with SUSP or MAL on ELNS. The cohort by surgical nodal stage was 62/103 (60.2%) pN0, 24/103 (23.3%) pN1, 10/103 (9.7%) pN2, 3/103 (2.9%)pN3 and 4/103 (3.9%) pNX.
Conclusion: The ELNS is the context of ECS is less commonly classified as MAL than all ELNS patients (12.6% vs. 37.6%). There is a strong association between ELNS malignant/suspicious and neoadjuvant therapy. Observational data can provide insights into how a technique such as ELNS is used, how it influences management decisions and how it compares within the context of different indications.

E-PS-22-005

Weakness unmasked: a case report of primary effusion lymphoma

S. Carralas Antunes*, M. Rodrigues, D. Gomes Pinto, A.E. Teles, F. Soares Nogueira, A. Oliveira, F. Campos
*Hospital Garcia de Orta, Portugal

Background & objectives: Primary effusion lymphoma (PEL) is a rare large B-cell lymphoma universally associated with human herpes virus 8 (HHV8) and primary affecting elderly or immunocompromised individuals, particularly those infected with HIV. Diagnosis can be challenging due to its unique, effusion-based, presentation.
Methods: A 73-year-old man with a medical history of atrial fibrillation, hypertension, and type 2 diabetes, was admitted to the emergency department due to worsening weakness over the previous month. Imaging studies revealed significant pleural and pericardial effusions in risk of cardiac tamponade, and minor ascites, and the patient was submitted to pericardiocentesis and pleural drainage.
Results: Sediment samples were hypercellular, composed of large cells with immunoblastic morphology, scant cytoplasm and large pleomorphic nuclei with prominent nucleoli with coarse chromatin, disposed in a background of apoptotic debris. A cell block was created using the pericardial sample and immunohistochemistry was performed. Neoplastic cells demonstrated positivity for CD30, CD45, and HHV8, and negativity for CD3, CD5, CD20, PAX5, CD10, CD15, CD21, CD23, CD138, MUM-1, Bcl-2, Bcl-6, c-Myc, and EBER-ISH. The proliferation index, estimated by Ki-67, was 40%. These findings led to a diagnosis of PEL. HIV testing yielded negative results. The patient received 6 cycles of CHOP therapy and, one-year post-treatment, remains asymptomatic with no evidence of recurrence.
Conclusion: PEL is among the least common lymphomas associated with HIV, and it becomes even more infrequent in the absence of HIV infection, representing less than 1% of non-HIV-associated lymphomas. In elderly patients lacking immunosuppression, immunosenescence may play a role. We highlight the importance of suspecting this diagnosis in patients presenting with effusions and lacking solid masses. Effusion analysis is imperative and positivity for HHV8 immunohistochemistry serves as a pivotal diagnostic criterion for PEL.

E-PS-22-006

Pulmonary oncocytoma presenting in a 43-year old female previously diagnosed with clear cell renal cell carcinoma: a case report

A.K. Donato*, L. Cale-Subia
*Philippine Heart Center, Philippines

Background & objectives: Oncocytoma are benign tumours mostly seen in the kidney and thyroid. Occurrence in the lung is extremely rare. This case report aims to present a rare case with the immunohistochemical studies used in order to arrive with a definitive diagnosis.
Methods: The sample of the mass was taken by fine-needle aspiration biopsy and cytomorphology showed bland lesional cells with granular and eosinophilic cytoplasm. Immunohistochemical studies using Cytokeratin 7 (CK 7), Cytokeratin 20 (CK 20), RCCA Marker, Vimentin, Calretinin, c-KIT (CD117), Thyroid transcription factor-1 (TTF-1), Synaptophysin, Chromogranin, Neuron-Specific Enolase (NSE), p63, and Ki67 were employed.
Results: Immunohistochemistry revealed strong reactivity of the lesional cells with Cytokeratin 7 (CK 7). Proliferation index is low (<1%) using Ki67. All other immunohistochemical studies are non-reactive. The case was signed out as Oncocytoma.
Conclusion: Pulmonary Oncocytoma is extremely rare with fewer than 10 cases reported in literature, and none has a history of previous malignancy. They are benign and surgical excision is curative. Oncocytoma exhibit a bland cytomorphology with characteristic granular and eosinophilic cytoplasm but this may still overlap with other neoplasms. Hence, additional immunohistochemical studies should be employed to arrive with a definitive diagnosis. Despite being extremely rare, Oncocytoma should be considered in the differential diagnosis when presented with a lung mass lesion.

E-PS-22-007

Liquid-based preparations in thyroid fine needle aspiration cytology. Comparison between different series in two Italian institutions

M. Franchina*, C. Pizzimenti, V. Fiorentino, S. Cortecchia, L. Caprara, A. Ieni, G. Tuccari, M. Martini, A.M. Bonanno, M. Puccetti, G. Fadda
*Department of Human Pathology of Adult and Developmental Age "G. Barresi", University of Messina, Italy

Background & objectives: Liquid-based cytology (LBC) is a reliable diagnostic method for thyroid nodules. We compare the diagnoses made using two different LBC methods to assess the accuracy these techniques in managing patients submitted to fine needle aspiration in two Italian institutions.
Methods: We examined LBC samples processed with both ThinPrep (Hologic) and CytoFast (Hospitex) during recent periods to compare the rates of nondiagnostic, indeterminate and malignant results in two institutions (1 Messina, 2 Imola) to evaluate the efficacy of those methods in reducing the number of non-diagnostic reports without decreasing the diagnostic accuracy of the technique.
Results: We found a significant reduction in nondiagnostic reports in the cytological specimens processed using both techniques compared to the exclusive use of ThinPrep(mean 8.6 vs 4.2%). On the other side, only a slight increase in the reports of indeterminate lesions

was detected (mean 11.7 vs 10.1%) The rates of suspicious/ malignant diagnoses in the reference periods reflected the post-COVID-19 difficulty of the patients to access to diagnostic resources so they might be discussed separately.
Conclusion: Comparing LBC diagnoses using the Thin-Prep (Hologic) LBC method alone and in combination with Cyto-Fast , we assessed that the combination of ThinPrep and CytoFast decrease the inadequacy rates of thyroid cytology without reducing the diagnostic accuracy of the fine needle aspiration in correctly diagnosing the nodules of the gland.

E-PS-22-008
Guar beans in urine cytological specimen: a potential diagnostic pitfall
S. Gamba Torrez*, T. Zudaire Fuertes, S. Rubio Mediavilla, J.J. Sola Gallego
*Spain

Background & objectives: Various types of contaminants can be found in cytological specimens. In this study we describe a specific type of vegetable cells found in an ileal duct urine specimen. Our objective is to describe their origin and cytomorphology.
Methods: We describe the presence of numerous non-human structures in the urine cytological specimen of a 62-year-old woman with radical cystectomy with Bricker-type urinary diversion. After having learned to recognize them, we have occasionally found this type of cells in some urine specimens from urinary diversions of other patients, usually in smaller quantity.
Results: These structures were found either loose or in clusters, were large and ovoid, greenish with Papanicolau staining, showed thick external capsule and frequent terminal spicule. In the central zone they showed a dense, sometimes folded, wine-red material. Initially we thought that these might be Schistosoma eggs, but given the lack of epidemiological data to support the possible infection, in a later review we identified these structures as guar cells.
After ileal conduit urinary diversion, urine is collected through a bag that is adhered around the stoma by an adhesive containing hydrocolloid. One type of natural hydrocolloid used in some of these devices is guar gum derived from guar (Cyamopsis tetragonoloba).
Conclusion: Cytological specimens can be contaminated with a wide variety of materials that can sometimes, especially if they are of vegetable origin, lead to misidentification such as parasite eggs, viral cytopathic changes or dysplastic features. Guar gum is a natural hydrocolloid used in adhesives for ostomy bags and we can rarely find guar cells in ileal conduit urine specimens. Correct identification of guar cells is essential to avoid a potential diagnostic pitfall when evaluating urinary diversion specimens.

E-PS-22-009
Breast implant-associated anaplastic large cell lymphoma: cyto-histopathological correlation of an unusual entity with increasing incidence
S. García-Fuertes*, N. Franco Rubio, E. Ponce Casas, R. Vilorio, E. Mejia, C. del Agua Arias-Camisón, M.J. Cardiel García
*Hospital Clínico Universitario Lozano Blesa, Spain

Background & objectives: Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) is a rare form of ALCL, which typically develops in the fluid and capsule adjacent to the breast implant. It was formally recognized as an entity by WHO in 2016.
Methods: We present a 66-year-old woman, with history of invasive right breast carcinoma in 2015, who debuts with a size increase of her right breast, associating a periprotesic seroma. A fine needle-aspiration was performed in the lesion and given the results of cytology, she finally underwent a capsulectomy of both breast implants.
Results: Cytopathology results showed an atypical lymphoid proliferation of large pleomorphic cells with scarce cytoplasm and intermixed inflammatory cells. Immunhistochemical studies revealed that these cells were positive for CD30 and negative for ALK, EBER and CKAE1/AE3. Based on the morphology and immunophenotype, findings suggested a BIA-ALCL as first diagnostic option. We after received the capsulectomy specimen, which demonstrated the same lymphoid neoplasm infiltration, composed of large elements with atypical characteristics, infiltrating the surface of the fibrous capsule. A wide ancillary panel test was conducted, and neoplastic cells also displayed positivity for CD30, as well as for CD3 and CD4, and a negative result for ALK, confirming the diagnosis of BIA-ALCL.
Conclusion: BIA-ALCL is an infrequent entity of unknown etiology with rising incidence whose most common presentation is as an unilateral late-onset periimplant effusion or swelling around the breast implant. They are associated to textured implants, both saline and silicone, with no definite cases described in smooth surfaced implants. The mayority of cases constitute anaplastic large T-cell lymphomas, being important to exclude an ALCL with secondary breast involvement. When diagnosed, removal of the implant with the intact surrounding capsule is recommended.

E-PS-22-010
A case report of an adenoid cystic carcinoma of the breast diagnosed by fine-needle aspiration biopsy
T. Ivkovska*, L. Ivkovski, I. Prodanova, Z. Boceska
*Institute of Pathology, North Macedonia

Background & objectives: Adenoid cystic carcinoma (ACC) is a rare malignant neoplasm of the breast. It is a special subtype of a triple negative breast cancer characterized by a slow progression, low malignant potential, rare lymph node involvement and a favourable prognosis.
Methods: A 67-year-old postmenopausal woman with a palpable mass located in the left breast where mammography findings were non-specific. The physical examination of the left breast revealed a lump in the outer lower quadrant near the areola. The ultrasonography disclosed a sharply marginated, hypoechoic mass measuring 25x20 mm in the left breast. Fine-needle aspiration biopsy was performed.
Results: Cytological examination revealed numerous single and grouped small malignant cells. The epithelial cells were oriented around solid eosinophile spheres of basement membrane material - hyaline globules. From the rest of the material a cell block was prepared with the plasma-thrombin method. On the sections stained by H&E, a dual population of cells can be seen: ductal epithelial cells mixed with myoepithelial or basaloid cells arranged around eosinophilic "cylinders" comprised of basement membrane material. Immunohistochemistry showed that ductal cells were CKLMW positive. Myoepithelial cells were CKHMW and p63 positive. The solid spheres were positive for Collagen IV. The cells from ACC generally express CD117.The final diagnosis was adenoid cystic carcinoma.
Conclusion: The purpose of this case is to portray the significance of the cytologic diagnosis with the help of cell block and immunohistochemistry, in an otherwise non-conclusive radiological and ultrasonographic findings. Typically, the tumour is localized near the areola, and although the radiologic findings are non-specific for ACC, the diagnosis can be made with fine-needle aspiration biopsy (FNAB). Awareness of this type of breast tumour is important from the point of view of surgical management.

E-PS-22-011
Imprint cytology in paediatric solid tumours: a cyto-histological correlation study at a tertiary care cancer centre in South India
E. Joy*, R. P Mony, J. K, P. T
*Regional Cancer Centre, Thiruvananthapuram, India

Background & objectives: Early diagnosis and appropriate management are crucial for achieving the best outcomes in paediatric oncology.

The objective of our study was to ascertain the sensitivity of imprint cytology in the diagnosis of paediatric solid tumours.
Methods: This is a retrospective study of 28 consecutive cases of paediatric solid tumours (aged between 0-14 years) reported by touch imprint cytology from 1 st June 2022 to 31 st May 2023 (1 year) conducted in our department. Only histologically proven cases of paediatric solid tumours for which imprint cytology has been evaluated were included.
Results: Cytohistological findings were correlated, and cases were divided into 3 categories. Category 1 included concordant results in which complete cyto-histological correlation was possible. Category 2 cases included the cases in which the lesion was diagnosed without categorization. eg. Ewing sarcoma as a malignant round cell neoplasm. 3rd category included cases with discordant results. 28 cases analysed included one thymolipoma, two ganglioneuroblastoma, and 25 malignant tumours. Further analysis was done on malignant tumours. Those included neuroblastoma, osteosarcoma, ewing sarcoma, lymphoma, hepatoblastoma, rhabdomyosarcoma, and other tumours. M: F ratio was 3.1:1. 40% of the tumours occurred in the age group of 0-5 years. The sensitivity of imprint cytology was 84%.
Conclusion: Our study affirms the role of cytology in providing timely diagnosis and guiding therapeutic protocols. Imprint cytology has demonstrated good overall sensitivity even though histology is considered the gold standard. Imprint cytology can speed up the diagnosis and assess sample adequacy effectively.

E-PS-22-012
Neuroendocrine tumour of the breast showing invasive micropapillary pattern – cytological features
T. Kawasaki*, T. Tashima, Y. Hoshida, K. Taniyama, D. Taniyama, S. Ichihara, T. Kondo, A. Enomoto, Y. Nakamura, K. Kaira, H. Imai, K. Okamoto, H. Nagai, C. Muramatsu, J. Ichikawa
*Saitama Medical University, Japan

Background & objectives: Neuroendocrine neoplasms, classified into two subtypes, i.e., neuroendocrine tumour and neuroendocrine carcinoma, and invasive micropapillary carcinoma are rare malignancies with special features. Herein, for the first time, we report cytopathological features of a mixed invasive micropapillary and neuroendocrine mammary neoplasm.
Methods: The patient, a 65-year-old postmenopausal woman, had become aware of a tumour in her right breast. The cut surface of the mastectomy specimen contained a well-circumscribed, multinodular, red-brown tumour, measuring 15x15x15 cm. Macrometastases, up to 13x8 mm in size, with the same morphological features as the original tumour site, were identified in 3 of 15 dissected right axillary nodes.
Results: Fine needle aspiration of the right breast tumour cytologically showed high cellularity in a haemorrhagic background with hemosiderin-laden macrophages. Tumour cells appeared in relatively small and compact clusters, suggesting an "invasive micropapillary" architecture. However, isolated and scattered tumour cells exhibiting plasmacytoid morphologies were also observed. Fine granular, light green cytoplasm and nuclei with finely granular chromatins were characteristic of a “neuroendocrine” lesion. Immunohistochemically, tumour cells were diffusely positive for chromogranin A and estrogen receptor and focally reactive for synaptophysin and progesterone receptor. HER2 score was estimated to be 1+, and Ki67 (MIB-1) labelling index was 36.2%. MUC1 and EMA lined the stroma-facing surfaces of the cell membranes, indicating reversed polarity.
Conclusion: Our current patient, who had an invasive breast carcinoma with neuroendocrine and micropapillary features, developed multiple metastases in association with a large-diameter tumour showing a luminal B-like immunoprofile. Accordingly, these concomitant morphologies on cytological as well as histological specimens are noteworthy and should be taken into consideration both diagnostically and therapeutically. Meticulous clinical follow-up continues to be essential for this case. Future investigations based on translational research might include the application of novel molecules as therapeutic targets or prognostic markers.

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E-PS-22-013
Reliability of grading preoperative pancreatic neuroendocrine tumours (PanNET) on endoscopic ultrasound specimens (EUS)
U. Klopčič*, B. Ranković, A. Gruden, D. Siuka, M. Strojan Fležar
*Institute of Pathology, Medical Faculty, University of Ljubljana, Slovenia

Background & objectives: Grading of PanNET defined by Ki-67 index represents an important predictor of prognosis and decisional factor for clinical management of the patients. We performed retrospective analysis of concordance between grading of PanNET on EUS FNA/FNB and on excision specimens.
Methods: During 5-year period between 2019 and 2023, a total of 48 PanNET were diagnosed on EUS FNA/FNB samples. In 19 patients, cytological diagnosis of PanNET was followed by surgical resection of the same tumour. Immunocytochemistry for Ki67 on EUS samples was performed on 7 cytospins and 12 cytoblocs. The grade of PanNET was assessed according to WHO classification on PanNET.
Results: A total agreement in grade between EUS samples and resection specimens was achieved in 13 cases of grade 1 PanNET and 3 cases of grade 2 PanNET (16 out of 19 cases; 84,2%). There were two cases of undergrading (grade 1 on EUS samples, grade 2 on excision; 10,5%) and one case of overgrading (grade 2 on EUS sample, grade 1 on excision; 5,3%) on EUS samples versus surgical samples. A statistical analysis revealed a moderate agreement between grading of PanNET on EUS samples and resection specimens (kappa value = 0,56).
Conclusion: EUS FNA/FNB enabled correct grading of PanNET in the majority of the cases, revealing moderate kappa statistics between EUS grading and grading of PanNET on resection specimens. Therefore, possibilities to improve grading on EUS FNA/FNB specimens should be further explored.

E-PS-22-014
Ultrasound and cytological correlation of thyroid gland nodules using TIRADS and Bethesda classifications
T. Lakic*, T. Icin, A. Ilić, A. Lovrenski, Z. Milić, M. Panjković
*Faculty of Medicine Novi Sad, University of Novi Sad, Serbia

Background & objectives: Thyroid nodules are very common and mostly benign. The ultrasound incidence is 50-60% with female predominance, but the accuracy in differentiating between benign and malignant lesions is very low, so fine needle aspiration with cytological examination (FNAC) is necessary.
Methods: The aim of the work is to examine the correlation of clinical ultrasound and cytological findings of punctured nodules in the thyroid gland and correlation of TIRADS ultrasound classification and cytological Bethesda classification, and determining the reliability of ultrasound classification in the diagnosis of nodules in the thyroid gland.
Results: Thyroid nodules are more common in the right lobe (50,6%), average diameter of 21.5 mm, with an average age of 58, female predominance (87,8%). The Fisher test proved a significant comparison

discrepancy of the TIRADS and Bethesda within the TIRADS 4 (suspicious nodule) and TIRADS 5 (malignant nodule) groups, with the finding that 89.1% of ultrasound-suspicious lesions have benign cytology, as many as 79.8% of ultrasound malignant nodules. Benign TIRADS categories (TIRADS 1-2-3) show a high agreement degree with the Bethesda II (91.7%). Suspicious and malignant cytological categories are more often diagnosed in nodules smaller than 20 mm, while benign in nodules larger than 20 mm ($\chi 2=13,99$; p=0,001)
Conclusion: Ultrasound examination and cytological analysis of ultrasound-guided aspiration puncture of the node have a crucial role in the clinical preoperative diagnosis of thyroid nodules. However, unlike some others scoring systems, ultrasound evaluation of thyroid nodules has not yet become a routine part of the examination even in all tertiary institutions. Benign ultrasound categories (TIRADS1-2-3) in a high percentage correspond to the benign Bethesda category (Bethesda II), while TIRADS 4-5 indicate a benign process cytologically however.

E-PS-22-015
Myositis ossificans: rare paediatric case diagnosed with FNAB and confirmed by RNA genotyping of cytology sample
Ž. Ledinek*, V. Kloboves Prevodnik, M. Stefanović, M. Česen Mazić, A. Gazikalović, B. Mavčič
*Department of Pathology, University Medical Centre Maribor, Slovenia

Background & objectives: Myositis ossificans is a benign ossifying lesion most commonly affecting skeletal muscles. They usually occur in young adults but are rare in children and are attributed to muscle trauma. Typical radiographic appearance is diagnostic, however pathological correlation may be necessary.
Methods: We present a case of a 3-year-old boy with 2-week history of a painful deltoid muscle lesion that occurred after vaccination against thick-borne encephalitis. During MRI, fine needle aspiration biopsy (FNAB) and core needle biopsy (CNB) were performed. CNB was not diagnostic, additional immunocytochemistry and RNA genotyping with Archer FusionPlex Sarcoma v2 panel were performed on FNAB sample.
Results: Cytopathological evaluation revealed cellular smears with dual cell population of osteoblasts (SATB2 positive) and multinucleated osteoclast-like giant cells intertwined with fragments of skeletal muscle. Although the cytology report was signed as myositis ossificans based on cytomorphology and clinical data alone, RNA genotyping was performed to confirm the diagnosis. *COL1A1*::*USP6* fusion was detected and confirmed the diagnosis. CNB was not diagnostic, because the core needle could not penetrate the calcified outside of the lesion. The boy was referred to an orthopedic surgeon for clinical follow up with CT imaging. Since the lesion in the deltoid muscles has grown and is irritating, excision will be performed when the lesion fully matures.
Conclusion: When myositis ossificans presents with typical clinical history and a clear zonal pattern on imaging, diagnosis is relatively straightforward. However, in early lesions without typical clinical features the diagnosis may be more challenging and sometimes requires a biopsy. Our case shows that FNAB with supported by immunocytochemistry and RNA genotyping proving *COL1A1*::*USP6* fusion allows accurate diagnosis in less than 6 days and implicates the potential use of molecular methods on FNAB samples of soft tissue lesions.

E-PS-22-016
Liquid-based cytology in thyroid fine needle aspiration: a 6-year audit on 23,968 consecutive cases at a single institution
W. Lee*, H. Wang, L. Huang, M. Tseng, S. Chiang, C. Lee
*Division of Cytopathology, Department of Pathology, Chi Mei Medical Center, Taiwan

Background & objectives: In our institution, thyroid fine needle aspiration cytology (FNAC) preparation was changed from conventional smear (CS) to liquid-based cytology (LBC) in 2016. This study aimed to determine the diagnostic value of LBC with the corresponding histopathological diagnosis of thyroid lesions.
Methods: A total of 23,968 consecutive thyroid FNAC prepared by LBC SurePath were collected from July 2016 to December 2022. Cytologic diagnoses and specimen adequacy were made according to the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC). We also examined the malignant rate of the corresponding surgical pathology as the gold standard.
Results: The incidence of each TBSRTC category was: 22.3% nondiagnostic (ND), 65.4% benign, 8.4% atypia of undetermined significance or follicular lesion of undetermined significance (AUS/FLUS), 0.8% follicular neoplasm or suspicious for follicular neoplasm (FN/SFN), 1.2% suspicious for malignancy (SM), and 1.9% malignant. The surgical resection rate was 8.6% and the malignant rate was 41.5%. The malignancy rate in each category was: 20.9% ND, 15.4% benign, 37.3% AUS/FLUS, 25.0% FN/SFN, 90.6% SM, and 100% malignant. Cytological diagnosis achieved sensitivity 82.0%, specificity 97.3%, positive predictive value 96.8%, negative predictive value 84.6%, false positive rate 2.4% and false negative rate 15.4%. The diagnostic accuracy of cytological diagnosis was 89.7%.
Conclusion: Our higher nondiagnostic rate might be attributable to the routine submission of the fluid from symptomatic haemorrhagic cysts for cytologic examination in our clinical practice. The diagnostic performance of LBC SurePath in our study is similar to the reported literature. The use of SurePath in thyroid FNAC can increase the sample adequacy, increase the sensitivity and reduce the workload and avoid unnecessary surgeries with similar accuracy to CS.

E-PS-22-017
Spindle epithelial tumour with thymus-like elements (SETTLE) – a potential pitfall in the cytological diagnosis of thyroid tumours
N. Lopes*, R. Cabrera
*IPO Lisboa Francisco Gentil, Portugal

Background & objectives: Spindle epithelial tumour with thymus-like elements (SETTLE) is a rare biphasic thyroid carcinoma, predominantly occurring in the early decades of life. Its preoperative cytological diagnosis is challenging and, sometimes, final diagnosis can only be achieved through histopathological analysis.
Methods: We present a case of a 20-year-old female with a 10-month history of an anterior cervical mass, in which fine needle aspiration cytology was suggestive of medullary thyroid carcinoma, even though serum calcitonin was not elevated. Due to compressive symptoms, a total thyroidectomy was performed. Final diagnosis was achieved with the aid of immunohistochemistry and molecular studies.
Results: Cytological features of the nodule included a moderate to highly cellular aspirate of loosely cohesive spindle cells with bland oval nuclei, associated with a homogenous, metachromatic stroma, which was interpreted as amyloid, thus rendering a suspicious diagnosis for medullary carcinoma. Histopathologically, a biphasic spindle cell tumour with gland-like epithelial structures was observed, with no atypical features and abundant stromal hyalinization. The neoplasm was positive for cytokeratins and P63, and negative for TTF-1 and calcitonin. No rearrangements of SS18 gene were detected rulling out synovial sarcoma. A final diagnosis of SETTLE was made. At 6 months follow-up the patient has no evidence of disease.
Conclusion: SETTLE should be considered in the differential diagnosis of thyroid gland malignancies, in smears showing a spindle cell aspirate with metachromatic material resembling amyloid. High index of suspicion, serum calcitonin level and immunocytochemistry, when available, are crucial for a correct preoperative diagnosis. Sometimes, the diagnosis may only be reached after histopathological analysis with additional diagnostic techniques.

E-PS-22-018

Rate of malignancy in FDG positive parotid lesions in a University Hospital

N. MacAuley Srinivasan*, S. Quinn, C. Collins, D. Gibbons
*Ireland

Background & objectives: FDG positive parotid lesions may incidentally be found following a staging PET scan for malignancy. Our aim was to assess the pathology of these lesions by reviewing fine needle aspiration specimens of the parotid gland and excision specimens where available.
Methods: A list of parotid specimens over a four-year period within St Vincent's University Hospital, Dublin was generated. A total of 332 specimens were identified. 279 unique patients were included in this number. The final pathology report for each specimen was reviewed and cross referenced with those who had received a PET scan, with FDG positivity as an indication for biopsy.
Results: 16 of 279 (5.7%) unique patients received an FNA for an FDG positive parotid gland. Of these patients, 5 received a final diagnosis of malignant pathology (2 metastatic small cell carcinomas, 1 squamous cell carcinoma, 1 metastatic malignant melanoma and 1 low grade mucoepidermoid carcinoma). 6 patients were diagnosed with Warthin's tumour. 3 patients had samples inadequate for diagnosis and no subsequent surgical specimen. 1 patient was diagnosed with pleomorphic adenoma. 1 patient had normal cytology.
Conclusion: A total of 31.25% of patients who received a biopsy for an FDG positive parotid gland had a final diagnosis of malignancy, either metastatic or primary. While benign neoplasms such as Warthin's tumour and pleomorphic adenoma are associated with FDG positivity, the significant number of malignant cases indicates that all patients with an FDG positive parotid lesion should receive an FNA biopsy to exclude malignancy.

E-PS-22-019

Suitability and advantages of cytological preparations for advanced NSCLC molecular analysis

E. Maffei*, C. Ciaparone, A. D'Ardia, V. Ciliberti, P. Zeppa, A. Caputo
*Department of Pathology, University Hospital "San Giovanni di Dio e Ruggi D'Aragona", Italy

Background & objectives: For patients with advanced NSCLC, treatment strategies hinge on molecular analysis. However, diagnostic specimens are frequently limited, necessitating efficient management of these materials. This study aims to enhance the utilization of cytological samples to discern the morphological and molecular characteristics.
Methods: Molecular analyses were conducted on cytological samples obtained from patients with advanced NSCLC, employing NGS and RT-PCR methods. Sixty-five cytological samples, extracted from our database, encompass various sample types (FNA, TBNA-EBUS, and effusions) and were processed in different ways: n=23 (35%) Thin Prep, n=23 (35%) direct smears, and n=19 (29%) cell blocks.
Results: All samples have been confirmed to be suitable for molecular investigation and are poised to serve as a viable alternative to histological specimens for studying DNA mutations and RNA fusion genes.
Conclusion: Furthermore, as these samples are not subjected to formalin-based fixatives (except cell-blocks), they are faster and grant a higher nucleic acid quality compared to their histological counterparts.

E-PS-22-020

High grade serous carcinoma of the peritoneum. Case report and literature review

J.S. Marrero Afonso*, C. Febles Pérez, M. Vilar Chesa, R. López Henríquez, M.A. Krupinska, F. García Machado
*Hospital Universitario Nuestra Señora de Candelaria, Spain

Background & objectives: High grade serous carcinoma of the peritoneum is a malignant serous epithelial neoplasm with marked cytological atypia arising in the peritoneum with no gross or microscopic disease in the ovaries or fallopian tubes. Clinicopathological characteristics could justify its presentation.
Methods: We report a 66 years-old female non-smoker patient with bilateral mastectomy due to ductal breast carcinoma in 1990 and hysterectomy with double salpingectomy 20 years ago. She presented non-painful slow-growing ascites with associated dyspepsia. A CT showed abdominopelvic with findings concordant with carcinomatosis. Ascites liquid was obtained and submitted for evaluation.
Results: Microscopically, it was a clear background smear with small lymphocytes and some mesothelial cells with reactive changes. There were frequent tridimensional groups of cells with wide cytoplasm, sometimes with vacuoles and irregular hyperchromatic nuclei. Cell block revealed groups of similar cells and an immunohistochemistry panel showed positivity to BerEp4, CK7, PAX8 and negativity to CK20, GATA3 and CDX2. A peritoneal biopsy showed affectation by high grade serous carcinoma with positivity to CK7, PAX8, WT1, p16, mutate-type pattern of p53. Homologous recombination deficiency test was negative. Morpho-immunohistochemistry findings and lack of gynaecological structures lead to a probably diagnosis of high grade serous carcinoma of the peritoneum.
Conclusion: True primary high grade serous carcinoma of the peritoneum is a rare event, but its distinction from ovary origin is not critical, as both have similar behaviour and treatment.

E-PS-22-021

Warthin tumour with extensive mucinous and squamous metaplasia - a potential pitfall in fine needle aspiration evaluation

J.S. Marrero Afonso*, S. Carrión Marrero, K.M. Gallardo Rodríguez, I. González Villa, R. López Henríquez, M.A. Krupinska, C. Febles Pérez
*Hospital Universitario Nuestra Señora de Candelaria, Spain

Background & objectives: Mucinous metaplasia and squamous in Warthin tumour (WT) is a recognized phenomenon. Because of non-specific radiological findings, its wide differential diagnosis with entities in salivary gland pathology, diagnostic challenge and clinicopathological characteristics could justify its presentation.
Methods: We report a 68 years-old female non-smoker patient who presented with a non-painful slow growing left parotid gland mass. A non-guided ultrasound fine needle aspiration was performed and enough material was obtained.
Results: Microscopically, a lymphoid smear with fibrillary-mucinous matrix with histiocytes was observed. An heterogeneous epithelial cells population with wide orangeophilic cytoplasm with central nuclei and visible nucleoli, while others with dyskeratotic features and irregular nuclei and were identified. Category V Milan System diagnosis was made and a planned US-guided FNA showed a 3 cm well defined gland-dependent lesion. FNA showed a small lymphoid background with plaques of homogenous oncocytic cells, without mucinous/necrotic material, dyskeratotic bodies or mitotic figures. Due to discrepancies of findings, a category IV-B Mylan system diagnosis was made. Resection specimen was a 3x2.5x1.5 cm nodular fragment with a classical Warthin tumour morphology with extensive mucinous and squamous metaplasia.
Conclusion: In contrast to the usual type of Warthin tumour, in which the histopathologic diagnosis is usually straightforward, the presence of mucous cells and squamous cells presents a diagnostic challenge in differentiating from mucoepidermoid carcinoma in the cytological evaluation setting.

E-PS-22-022

MTAP in fine needle cytology of pancreatic carcinoma: immunohistochemical and FISH analysis

M. Montella*, S. Lucà, F. Zito Marino, E. Clery, E. Carraturo, A. Cioce, I. Cozzolino, R. Franco

*Italy

Background & objectives: Pancreatic adenocarcinomas (PDAC) diagnosis using fine-needle aspiration cytology (FNAC) is challenging. Immunohistochemical markers for PDAC have limited sensitivity. Methylthioadenosine phosphorylase (MTAP) loss often co-occurs with CDKN2A/B loss in some tumours. This study assesses MTAP IHC for PDAC diagnosis.
Methods: We retrospectively evaluate 40 cases of endoscopic ultrasound-guided fine-needle aspiration cytology (EUS-FNAC) cell-block (CB) of solid pancreatic masses suspicious for PDAC. Immunohistochemistry (IHC) was performed to study complete or partial loss of MTAP expression and S100P expression in neoplastic elements. These results were correlated with available fluorescence in-situ hybridization (FISH) that was performed on a subset of cases.
Results: In our series, benign samples (2 of 36) did showed normal MTAP expression, while 31% (11 of 36) of PDACs showed complete loss of MTAP expression. Particulalry, 72% (8 of 11) of PDACs showed MTAP- and S100P+ immunophenotype, while 18% (3 of 11) were MTAP and S100P negative. In PDACs samples with available FISH data (n=17) we found only 1 case MTAP loss, S100P negative and CDKN2A with omozygotic gene deletion, and 5 cases MTAP loss and CDKN2A wild-type. The remaining 11 cases with equivocal MTAP expression showed FISH CDKN2A wild-type.
Conclusion: In about 30% of FNC samples from PDAC cases, MTAP loss was observed at IHC analysis. CDKN2A molecular status evaluated by FISH does not correlate with MTAP IHC profile. Since MTAP expression loss isn't typical in non-neoplastic cells, MTAP IHC could be an useful tool in the PDAC diagnoses from limited neoplastic sampling. This finding highlights the potential utility of MTAP immunohistochemistry in enhancing diagnostic accuracy for PDAC.

E-PS-22-024

Our experiences in endoscopic ultrasound - guided fine-needle aspiration cytology with a focus on the interesting and rare pancreatic lesions

R. Ondruššek*
*EUC Laboratoře CGB a.s. Ostrava, Czech Republic

Background & objectives: EUS-FNA cytology is a technique that plays an important role in the diagnosis of pathological pancreatic lesions and is becoming an integral part of early diagnosis. Its accuracy is often supported by the presence of a pathologist in the room.
Methods: A retrospective search of EUC-FNAC examinations that were examined in our pathology department was performed with the aim of extracting interesting and rare pancreatic lesions. We are now reposting the cases of four patients who were examined by the Rapid On-Site Evaluation (ROSE) method. The diagnosis was based on EUS-FNA cell block with immunohistochemistry support, and using cytological smears.
Results: We discovered unusual and rare pancreatic lesions of four patients in the range of 30-80 years with the presence of lesions of both benign and malignant nature. The benign cyst of foregut - as a rare developmental residue must be considered in dif.dg. cystic lesions, extraosseous plasmacytoma - as hematological malignancy with risk of hematogenous spread, solid pseudopapillary tumour of the pancreas - as a unit typical for young women and undifferentiated carcinoma with osteoclast-like giant cells - as a highly malignant carcinoma with a very poor prognosis. The aim of the thesis is to present unique morphological features, including a typical immunotype with subsequent differential diagnosis.
Conclusion: Our work proves that EUS-FNAC of pancreatic lesions is a very effective minimally invasive and smart technique for the acquisition and diagnosis of samples available by ultrasound of the digestive tract. However, it is very important to properly set up the collaboration between the clinic and the pathologist.

E-PS-22-025

Inter-observer PD-L1 interpretation in different cytological samples (Cell block vs. Cytologic slides)

A.L. Pazmiño Arias*, I. Sánchez Güerri, A. Molina Alvarez, S. Prat Mendez, S. Calvo González, F.M. Pérez Muñóz, M.E. Patriarca, A. Quiñonero Inserte, B. Lloveras Rubio
*Department of Pathology at Hospital del Mar, Spain

Background & objectives: Programmed death-ligand 1 (PD-L1) expression, a predictor of immunotherapy response in non-small cell lung cancer (NSCLC), is often assessed using cytology samples. This study aims to evaluate interobserver variability in interpreting PD-L1 expression between cell block and cytological slides.
Methods: Twenty cytological samples from endobronchial ultrasound-guided transbronchial needle aspirations (EBUS-TBNA/TBNB) were assessed using Rapid On-Site Evaluation (ROSE). Ventana SP263 PD-L1 immunohistochemistry (IHC) was performed on both cell blocks and cytological slides in paired cases. Quality assessment required a minimum of 100 tumour cells. Agreement between observers on PD-L1 expression (negative, low, high) was evaluated by three cytopathologists and five cytotechnologists.
Results: In this study, the interobserver discrepancies in the evaluation of PD-L1 expression by IHC were assessed using twenty paired samples, comprising both cytological slides and cell blocks, with the results varying based on the chosen cut-off point. Employing a three-tiered categorization, we observed high interobserver agreement. In cytologic smears, there was substantial agreement in the high expression category, achieving 100% consensus among observers, compared to 87% in the low expression category and 62% in the negative category. In contrast, on cell blocks, the agreement among different observers was nearly perfect, with 100% agreement observed in the high expression category and 89% agreement in both the negative and low expression categories.
Conclusion: In conclusion, our study validates the feasibility and accuracy of PD-L1 IHC on cytology cell blocks and direct smears for NSCLC, showing high concordance, despite occasional discrepancies likely due to intratumoural heterogeneity. These findings underscore cytology's utility in PD-L1 assessment for NSCLC management, confirming its potential as an alternative when formalin-fixed paraffin-embedded specimens are unavailable. This supports the use of cytology samples in clinical decision-making and highlights the need for specialized training in PD-L1 interpretation.

E-PS-22-026

Meyerozyma guilliermondii: a hitherto undescribed contaminant in respiratory cytology

X. Qu*, K.L. Chew, A. Kee, N.J.H. Tan, M.E. Nga
*Department of Pathology, National University Hospital, Singapore

Background & objectives: Bronchoalveolar lavage (BAL) is useful for detecting pulmonary infections but is susceptible to contamination, which, if not recognised, can lead to unnecessary treatment. We present an unusual fungus detected in the BAL of a 54-year-old lady with pulmonary nodular densities.
Methods: The BAL was processed using a mucolytic treatment method (dithiothreitol solution) and a Papanicolaou-stained smear was made. Fungal organisms were observed, and Gomori-Grocott methenamine silver stain was performed. The morphologic features of the fungus did not match any commonly known pulmonary fungal pathogens and the patient was clinically asymptomatic and immunocompetent, hence a contaminant was suspected and an investigation launched.
Results: Smears prepared from solutions involved in different steps of specimen processing revealed that the contaminant was in the saline solution, which was kept in plastic bottles, and used in the mucolytic treatment step. On fungal culture, the organism was identified as

Meyerozyma guilliermondii using the Bruker MALDI Biotyper. Meyerozyma guilliermondii is an ascomycete fungus commonly found in the environment and as a human saprophyte. It can rarely cause invasive infections, often in immunocompromised hosts. This is the first description in literature of its presence in a respiratory fluid cytology specimen.
Conclusion: Distinguishing between contaminants and true infection in cytology samples can be challenging, and requires close attention to a combination of clinical, cytologic and microbiologic findings. The lack of clinical symptoms was an important clue in this case. Contamination of solutions and water used in laboratory processing has been well documented. Isolating the source of contamination is important to confirm the presence of contaminant and to correct operational lapses and implement preventive measures to minimise contamination in future patient samples.

E-PS-22-027
Thoracic SMARCA4 deficient undifferentiated tumour (SMARCA4-UT): first diagnosed via fine needle aspiration cytology with NGS verification (case report)
S.R. Ramazanoglu*, M.A. Aydogdu, S. Erdamar Çetin, C. Yakicier, A. Özmen
*Basaksehir Cam and Sakura City Hospital Department of Pathology, Cytopathology Division, Turkey

Background & objectives: Thoracic SMARCA4-UT with BRG1 mutations, is an aggressive malignant neoplasm with poor prognosis. Due its' morphologic diversity, the lesion poses diagnostic challenges in cytology. We present a case, first diagnosed via FNA with liquid based cytology and confirmed by NGS.
Methods: Heavy smoker, 77-year-old male patient with an anterior mediastinal mass was admitted to Basaksehir Cam and Sakura City Hospital. Under CT-guidance FNAC was performed. The sample was prepared via SurePath. Cell blocks were obtained. Immunohistocehmistry was applied to cell block sections via Ventana-Bench Mark ULTRA. Recommended NGS Panel was performed and verified at NPG Aquarius Genomix Genetic Laboratory.
Results: Immunohistocemical studies applied to cell block sections, revealed strong and diffuse tumour cell positivity with SOX2, INI1, Vimentin, and patchy reaction with Pan-CK. BRG1 loss was observed within the tumour cells. Tumour was also negative for TTF1, p40; Claudin4, WT1, CD34, SALL4, Synpatophysin, Desmin. With all the data at hand, Thoracic SMARCA4-UT diagnosis was rendered. For verification and guiding therapy decision, NGS was recommended, hence patient's cell block containing 70% tumour cells was investigated for deletion, amplification and translocations in 523 genes and 55 transcripts; SMARCA4 p.Q1004* c.3010C>T (VAF 90%), TP53 p.V157F c.469G>T, KDM6A p.G975* c.2923G>T, ZRSR2 p.S447_R448dup c.1338_1343dup6, ARID1A p.E2000* c.5998G>T mutations and TMB-H (13.3 Muts/Mb) detected.
Conclusion: FNAC is a reliable diagnostic tool even in cases with diverse and overlapping features, such as Thoracic SMARCA4-UT. Combined with liquid based cytology, a fertile cell block can be obtained even to elucidate the genetic profile of the tumour.

E-PS-22-028
Risk stratification of pancreaticobiliary lesions using the WHO reporting system for pancreaticobiliary cytopathology
M. Rao*, R. Sharma, A. G, P. Elhence, A. Nalwa, S. Khera, D. Vedant, V. Vishwajeet, D. Aggarwal, V. Verma, P. Khera, V. Varshney, C.L. Birda, A. Solanki
*Department of Pathology AIIMS, Jodhpur, India

Background & objectives: This study categorized cytology of pancreaticobiliary lesions using the World Health Organization (WHO) reporting system for pancreaticobiliary cytopathology, and calculated the risk of malignancy (ROM), positive predictive value (PPV), and negative predictive value (NPV) for each category.
Methods: A retrospective analysis of pancreaticobiliary Fine Needle Aspiration Cytology (FNAC) performed between April 2016 to September 2022 was carried out, and cases categorized according to the WHO reporting system for pancreaticobiliary cytopathology. The cytopathology results were correlated with follow up biopsies and/or imaging considered gold standard. Seventy-three cases were analysed, and ROM, PPV, and NPV were calculated for 68 cases.
Results: A total of 78 cases were collected from archives, out of which 68 had follow up biopsies and/or imaging. Among these 68 cases, 42 underwent EUS-FNA, while 26 were percutaneous USG-guided FNACs. The nondiagnostic category comprised six cases, with a ROM of 66% (4 out of 6 cases). Seven cases were categorized as benign, with follow-up. The NPV for the benign category was 100%, and ROM for benign category was 0%. ROM for atypical category was 50% (2 out of four cases). Both suspicious for malignancy category (10 cases) and malignant category (41 cases) exhibited 100% ROM and 100% PPV.
Conclusion: In conclusion, the suggested WHO reporting system for pancreaticobiliary cytology is a useful tool for the stratification of pancreaticobiliary lesions, with excellent concordance for benign, suspicious for malignancy, and malignant categories. More data on non-diagnostic, atypical, Pancreaticobiliary neoplasm, low-risk/grade (PaN-low) and Pancreaticobiliary neoplasm, high-risk/grade (PaN-high) are required for detailing the ROM, PPV and NPV of these categories, as the number of cases in these categories were very limited or did not have a single case with imaging/biopsy follow-up.

E-PS-22-029
The utility of p16/Ki67 dual staining in glandular cytological atypia
A. Repse Fokter*, A. Dovnik, S. Sramek Zatler
*Celje General Hospital, Slovenia

Background & objectives: Interpretation of glandular cytological atypia and gynaecological treatment of these patients is often difficult and time consuming. The objective of this study was to assess the performance of p16/Ki-67 dual-stained cytology in women with AGC-NOS or worse cytological results.
Methods: Ninety-six patients exhibiting AGC-NOS or more severe cytological findings on Pap smears comprised the study cohort. We conducted p16/Ki67 dual immunostaining and compared the results with histological diagnoses obtained through biopsy, large loop excision, hysteroscopy, or hysterectomy.
Results: 59 out of 96 patients (61.5%) had normal or low grade (CIN1) histology result. Among them there were 54 (91.5%) with negative p16/Ki67 dual immunostaining. Among 8 CIN3+ cervical lesions were 5 p16/Ki67 positive cases and 12 among 14 histologically detected high grade cervical glandular lesions (AIS or worse), respectively. 15 patients had histologically detected cancer elsewhere (endometrial 13, ovarian 2) and 12 of them were p16/Ki67 negative. The sensitivity for detecting high grade cervical lesions (glandular and squamous) was 77.3%, specificity 89.5.%, positive predictive value 68% and negative predictive value 93.2%, respectively.
Conclusion: Dual p16/Ki67 staining is a useful additional tool in detection of patients at risk for high grade cervical lesions in cases with atypical glandular cells on Pap smears. Besides, high predictive value of negative reaction can be helpful in avoiding overtreatment. As expected, p16/Ki67 staining cannot help in detecting cancerous cells of noncervical origin.

E-PS-22-030
Diagnostic utility of cytology in pleural effusion: a single tertiary care centre experience from South India
I. S Nair*, R. P Mony, J. K, L. A L
*Regional Cancer Centre, Thiruvananthapuram, India

Background & objectives: The principal goal of effusion cytology is to clarify presence of malignant cells, helping in disease staging. It spares patients from other invasive techniques. We assessed diagnostic yield of conventional smear, cell block and its combination in irrespective of aetiology.
Methods: Consecutive cases of pleural effusion received in our department from June 1st 2022 to May 31st 2023 (1 year) were studied retrospectively which included 200 cases. Smears, cell block sections and immunohistochemistry (IHC) slides were retrieved and reviewed.
Results: Mean age at presentation:52years. This included 105 males and 95 females.Diagnosis was classified as benign, malignant and suspicious for malignancy based on cytomorphology.Of the 200 cases,based on smear alone,43.5% were classified as benign,37% as malignant and 19.5% as suspicious for malignancy. When combined with cell block,yield increased to 44.5% in benign,49.5% in malignancy and 6 % in suspicious for malignancy. IHC done in 12 cases to assist in categorising.Commonest cause of malignant pleural effusion was ovary in females and lung in males.The sensitivity and specificity for malignancy with smear alone were 93.51% and 97.47%;cytology combined with cell block were 97.85% and 97.73%. This combination produced significantly better results (p value < 0.001).
Conclusion: Cytological smear, in combination with cell block and IHC of effusion fluids, increases the diagnostic yield and detection of malignancy at an unknown primary site.

E-PS-22-031
Use of the Milan classification in the cytological diagnosis of tumours of the salivary glands
A. Semenova*, V. Galkin, O. Tarakanova, E. Slavnova, V. Shatalov
*Moscow State Budgetary Healthcare Institution "Moscow City Hospital named after S.S. Yudin, Moscow Healthcare Department", Russia

Background & objectives: To evaluate the effectiveness of cytological examination in the differential diagnosis of benign and malignant tumours of the salivary glands and the possibility of using the Milan classification (The Milan System for Reporting Salivary Gland Cytopathology 2017,2023).
Methods: 2601 cases of cytological diagnosis of salivary gland tumours were analysed for the period 2016 to 2022. The age of the patients is 18-84 years. The ratio of men to women is 1:2. We made cyto-histological comparisons. All cytological preparations were classified according to the Milan classification. Of these, 550 patients received surgical treatment.
Results: Benign tumours - 69.82%; malignant – 24.36%; non-tumour - 5.82%. Benign tumours: pleomorphic adenoma - 66%, Warthin's tumour - 25%, basal cell adenoma - 3%, myoepithelioma - 3%, oncocytoma - 3%. Malignant tumours: adenoid cystic cancer - 20%, cancer in pleomorphic adenoma -5%, mucoepidermoid cancer -12%, acinar cell cancer - 6%, lymphomas - 4%, other carcinomas - 35%, mts -18%. Sensitivity – 89%, Specificity – 79%, Accuracy – 82%. Results according to the Milan classification: I - 5% ROM 22%, II - 4%(ROM 0%, III - 2% ROM 0%, IVA - 53% ROM 5%, IVB - 15% ROM 18%, V – 5% ROM 71%, VI – 16% ROM 90%.
Conclusion: When performing a cytological examination of the salivary glands, it is necessary to take into account clinical data (age, node size, medical history and radiation data). Cytological examination has a high accuracy of differential diagnosis of benign and malignant tumours of the salivary glands. The use of the Milan classification allows us to minimize discrepancies between cytological and histological conclusions.

E-PS-22-032
In the absence of sampling error, renal fine needle aspiration demonstrates a high concordance with histology: a prospective and controlled study
H.G. Terzioglu*, B.T. Kadow, A. Gorbonos, M.L. Quek, E.M. Wojcik, G. Akdas Barkan
*Loyola University Medical Center, USA

Background & objectives: Fine Needle Aspiration (FNA) of renal masses has emerged as a valuable technique for preoperative diagnosis and prognosis. This study aims to assess the accuracy and inter-observer variability of renal FNAs in a prospective manner, controlling for sampling error.
Methods: In a 6-month period, ex-vivo FNAs were performed on 52 renal masses immediately after surgery using 23-gauge needle. Five passes were made, each yielding one Papanicolaou and Diff-Quik stained slide. Two senior cytopathologists (SC) and a fellow independently reviewed cases, focusing on morphology to assess adequacy, cellularity, and diagnosis (category, subclassification, grading). Kappa values were calculated to assess inter-observer agreement.
Results: 52 FNAs were obtained from 21 females/31 males. Age range is 34-82 (mean 59.8) years. All FNAs were adequate, although 20 were hypocellular. 4/52 and 42/52 of cases were accurately classified as benign and malignant respectively. The most consistent diagnosis was oncocytic neoplasm of unknown malignant potential (RONUMP) (3/52 cases) with 3/3 concurrence, followed by renal cell carcinoma (RCC) and urothelial carcinoma. Benign category consisted of angiomyolipoma (2/52), inflammatory myofibroblastic tumour (1) and retroperitoneal fibrosis (1/52). Mixed epithelial stromal tumour and leiomyosarcoma were interpreted incorrectly as RCC; and one IMT case as sarcomatoid RCC. Kappa value for SCs was 0.76, and 0.91 and 0.92 for the fellow and each SC.
Conclusion: As the study used ex vivo FNA, it was able to control for the sampling error. FNA demonstrated a high concordance with histological analysis, particularly for benign/malignant categories, and great interobserver agreement even in trainee level. Subclassification remains highly accurate even without immunohistochemistry and can be enhanced with the input from cytopathologists. Ex-vivo FNAs can be performed more commonly and used as learning tool. Trainees can reliably interpret rapid on-site evaluations of renal masses when adequate samples are provided.

E-PS-23E-Poster Session Pathology in Favour of Developing Countries

E-PS-23-001
Methodologies in pathology education in the problem-based learning model
J. Carneiro Melo*, D. Nunes Oliveira, R. Osterne Lima Verde, E. Tomé de Sousa, L.S. De Carvalho Neto, M. Jales Moura, J.S. Pereira Filgueira, F.R. Oliveira Cavalcante Júnior, M.V. Pereira dos Santos, A. de Carvalho Assunção
*University of Fortaleza, Brazil

Background & objectives: Pathology is essential in integrating basic sciences with clinical practice in medical education.To report the methodologies used in pathology teaching in a medical course that employs Problem-Based Learning (PBL) as its teaching methodology.
Methods: This work consists of an experiential report, comprising a descriptive study of the methodologies used in pathology teaching at a university in Northeast Brazil.General Pathology is covered in the 3rd and 4th semesters, while specific pathology begins with some contents in the 4th semester and extends until the 7th.
Results: Case studies with surgical specimens and microscopy are used, in addition to anatomoclinical sessions. Students practice requesting, completing and discussing histopathological reports and there is a visit to the Pathology laboratory with a field research approach. Autopsy practices take place at the local death verification service, students participate in a post-mortem examination and later present it in the format of an Anatomoclinical Session. There are seminars, flipped classrooms and digital resources (digitized slides, 3D pieces, digital flashcards, mind maps, e-books, interactive handouts, autopsy website) in addition to the use of gamification. In the

field of art, there is a painting workshop and discussion of medical-themed picture
Conclusion: In the context of problem-based learning, active methodologies are used, questioning and motivating both students and teachers, making the student the subject of building their own knowledge. This approach also enhances the global perception and awareness of pathology as a specialty, similar to art, facilitating the consolidation of learning objectives and contributing to the development of skills necessary for medical training. In 2023.1, the university acquired a digital anatomy table that came to add the methodologies used

E-PS-23-002
Enhancing pathology education in low-resource settings through the OPEN-IGCS pilot program
K. Mirza*, L. Hassall, R. Gonzalez, A. Splitt, V. Parkash, K. Singh, P. Murugan
*University of Michigan, USA

Background & objectives: The Open Pathology Education Network (OPEN) and the International Gynecologic Cancer Society (IGCS) collaboration seeks to address the subspecialty workforce inadequacy in pathology within developing regions through a virtual pilot education program.
Methods: The pilot employed a structured curriculum with content from open sources, mentoring sessions, and bi-directional case sharing. The training included pre- and post-test assessments with digital slides and encouraged active participation in Gynecologic Tumour Boards. Specific engagement metrics were tracked, including progression through the gyn-onc modules by trainees.
Results: To date, 50 participants enrolled in gyn module 1, with significant completion rates: 1 mentee passed, 2 are over 50% complete, and all have attempted at least one homework question. In total, 15 participants across the network, including 10 mentees and 5 mentors, are actively involved in the Africa group, demonstrating robust engagement.The results indicated a marked improvement in diagnostic skills and confidence among trainees. Post-program assessments showed that trainees improved their diagnostic accuracy from 60% to an average of 95%. The program also facilitated the development of a supportive network across subspecialties, crucial for ongoing professional development and quality improvement in diagnostic practices.
Conclusion: The OPEN-IGCS pilot program highlights the potential of virtual international collaborations to significantly enhance the pathology workforce in resource-constrained settings. By providing accessible, high-quality educational resources and fostering an environment of continuous learning and mentorship, the program supports sustainable improvements in cancer diagnosis and treatment in developing regions. The pilot's success in engaging a diverse group of trainees through innovative educational methods offers a model for expanding pathology expertise globally, particularly in areas where traditional subspecialty training is not available.

E-PS-23-003
Synchronous pleomorphic hyalinizing angiectatic tumour and tenosynovial giant cell tumour - diffuse type in an elderly woman: a peculiar case report
G.B. Nhlonzi*, P. Meyiwa
*Ampath Laboratory Pietermaritzburg, South Africa

Background & objectives: Pleomorphic hyalinizing angiectatic tumour (PHAT) and tenosynovial giant cell tumour diffuse type are rare soft tissue tumours of uncertain malignant potential characterised by local recurrence and local aggressiveness. We report a case of synchronous presentation of these rare tumours.
Methods: A 70-year old women presented with a clinical history of a left gluteal mass and right posterior hip mass suspicious. Both masses were suspicious of a sarcoma. Computed tomography (CT) scan and magnetic resonance imaging (MRI) were undertaken. Following multidisciplinary meeting case discussion, surgical excision of both lesions was undertaken. Both samples were submitted for histopathological assessment.
Results: The right posterior hip mass was received in three, the largest piece measured 130 X 90 X 30mm. Golden brown and yellow areas areas were noted. Necrosis and fleshy areas were not seen. A tumour with a diffuse and synovial-like architecture rich in mononucleated cells, foamy histiocytes, siderophages and focal osteoclast-like giant cells was noted. Sarcomatous transformation was not seen.
Left mass measuring 110 X 100 X 60mm with a circumscribed tumour measuring 75mm X 57mm X 35mm. A firm consistency and haemorrhage were noted. A tumour composed of pleomorphic cells, large ectatic hyalinized blood vessels with organizing thrombi. Tumour cells expressed CD34. STAT6, EMA and S100 protein were negative.
Conclusion: The right hip mass was diagnosed as tenosynovial giant cell tumour - diffuse type and the left gluteal mass was diagnosed as pleomorphic hyalinizing angiectatic tumour. Both these tumours predominantly affect women and are both extremely rare. As described, our PHAT case had similar immunohistochemical profile as described in the literature; expressed CD34 and was negative for epithelial markers, STAT6, S100 protein and desmin.

Our patient despite old age, had excellent recovery post surgery with no reported tumour recurrence.

E-PS-23-004
Synchronous and metachronous primary cancers: case series of experience in a pathology laboratory
M. Samaila*, D. Suleiman, K. Sani
*Nigeria

Background & objectives: Occurrence of another primary cancer in individuals with prior cancer diagnosis is increasingly common due to improved survivor indices with modern diagnostic techniques and treatment options globally.
Methods: A clinico-pathological analysis of 9 patients with histopathological diagnosis of multiple primary cancers over a 15years period. Cases with tumours affecting contiguous structures such as urinary bladder and prostate, cervix uteri and bladder with similar tumour morphology are excluded.
Results: Nine patients with synchronous and metachronous multiple primary cancers are presented. Three, aged 57, 50 and 47years had Renal cell carcinoma in association with prostate adenocarcinoma and penile squamous cell carcinoma. Three, had colonic adenocarcinoma, eosophageal squamous cell carcinoma and anal adenosquamous carcinoma in association with vulva basaloid carcinoma, porocarcinoma and infiltrative ductal carcinoma respectively. The last three, aged 35, 72 and 62years respectively had combinations of basal cell carcinoma with infiltrative ductal carcinoma, squamous cell carcinoma with Hidradenocarcinoma and ovarian cystadenocarcinoma with uterine leiomyosarcoma. Two patients are alive after a 5year follow up, three died within 6months of second tumour diagnosis while 3 were lost to follow up.
Conclusion: The primary cancers involved the Kidney, Ovary, Uterus, Vulva, Eosophagus, Skin while the second tumours involved the colon, skin, prostate, penis and Breast. The metastatic deposits affected the chest wall, left femur and supraclavicular lymph node.

E-PS-23-005
Neglected tropical diseases: cases of ectopic S. heamatobium ova trapped in rare and curious sites
K. Adoke*, S. Zubairu
*Federal Medical Center Birnin Kebbi, Nigeria

Background & objectives: Neglected tropical diseases (NTDs) are a diverse group of chronic debilitating illnesses that affects about 2 billion people across Africa, Asia and Americas. We report ten cases of S. heamatobiun accidentally found at rare and curious sites.
Methods: This was a five-year retrospective study of cases diagnosed as NTDs in the Pathology Department of Federal Medical Centre Birnin Kebbi. Data was extracted from patient's cases notes and analysed using SPSS version 24.
Results: A total of ten cases were seen with 6 (60%) Female and 4(40%) Male. The mean age of occurrence ectopic S. heamatobium ova was 27±17.06SD. The fallopian tubes 3 (30%) was the commonest site of occurrence of ectopic S. heamatobium ova followed by the testis 2 (20%) and Uterus 2 (20%) respectively. Other sites are the conjunctiva and prostate. Associated benign lesions are ectopic gestation, leiomyoma and benign prostatic hyperplasia.
Conclusion: Ectopic S. heamatobium ova can be found in rare ectopic site and in some instances in close association with neoplastic growth in the body. Transmigration from endemic areas and the impact of COVID-19 means that the developed world will see more cases of NTDs in their communities. As WHO roll out its roadmap for 2021-2030 for NTDs and the London declaration, emphasis should be on prevention and innovative research on NTDs.

E-PS-24E-Poster Session Digestive Diseases Pathology - GI

E-PS-24-002
Study of histopathological characteristics, KIT, PDGFRA mutations and SDHB expression in gastrointestinal stromal tumours
D. Akolekar*, R. Yadav, P. Das, S. Rastogi, N.R. Dash, S. Pal
*All India Institute of Medical Sciences, New Delhi, India

Background & objectives: Gastrointestinal stromal tumours (GIST), constitute 0.1 to 3% of GI tumours. Majority of the cases are sporadic with KIT and PDGFRA being the driver mutations. We aimed to evaluate the clinicopathological, immunohistochemical and molecular profile of GISTs.
Methods: All surgically resected cases of GISTs diagnosed over a period of last 9 years at our institute, were retrieved and reviewed for various morphological parameters. A comprehensive histopathological evaluation using structured proforma was done. Immunohistochemistry for CD117, DOG1 and SDHB was performed and analysed. Next generation sequencing for KIT and PDGFRA was performed using the illumina platform.
Results: 100 cases of GIST were studied including 71 males and 29 females, ranging from 19-78 years. Tumour size varied from 0.5 to 27 cm with majority located in the stomach (40%) followed by the ileum, jejunum and duodenum. Three cases were oesophageal. Majority of the cases showed single tumour, multifocal tumours were noted in five cases. Most of the tumours showed spindle cell morphology and had high mitotic index. All were positive for CD117 and DOG1. SDHB loss was noted in one case. 67 cases revealed KIT mutation while 9 cases had PDGRFA mutation and 24 cases were classified as wild type GIST.
Conclusion: GISTs have a wide morphological and molecular spectrum. Stomach is the most common site while oesophagus is the rarest. CD117 and DOG1 expression is seen in majority of the cases and forms backbone for diagnosis. SDHB loss is uncommon and these cases present with advanced unresectable disease. KIT mutation is the most frequent and few cases show PDGFRA mutation.

E-PS-24-003
Tailgut cyst with well-differentiated neuroendocrine tumour: challenges in reporting
J. Amaral*, J. Pimentel, J.P. Maldonado, A. Alves, M.A. Cipriano
*ULS Coimbra, Portugal

Background & objectives: Tailgut cysts are rare benign lesions that present with ill-defined symptoms in a broad age range. Although benign, the risk of malignant transformation is about 26-30%, the most common being neuroendocrine tumours, followed by adenocarcinoma and squamous cell carcinoma.
Methods: We present a case of an asymptomatic 73 year old woman in which was detected a predominantly cystic retro-rectal mass with a solid area that was surgically resected.
Results: In the gross pathology evaluation we observed a complex cystic lesion with a 1.9 cm firm white parietal nodule. On histology the cysts were lined by squamous, columnar and transitional epithelia, and the nodule was composed of sheets and islands of monotonous cells with speckled cromatin, that stained with synaptofisin and chromogranin-A. The Ki67 index was 2.14% and mitotic rate was 0.2/2.37mm2. The diagnosis was a tailgut cyst with well-differentiated, G1, neuroendocrine tumour, with microscopic positive margin. Further investigation revealed synchronous multiple liver metastasis and the patient underwent systemic treatment. Despite the intervention there was evidence of disease progression with osseous involvement and the patient is awaiting palliative care admission.
Conclusion: As a retro-rectal neoplasm, it does not originate directly from a digestive organ but from an embryological development remnant. As such classification and staging is not linear. Is it a digestive system neoplasm? Which organ? Is it a soft tissue neoplasm? How to grade? How to stage? In this case we reported using the "WHO Classification of Tumours Editorial Board. Digestive system tumours" for colorectal neuroendocrine tumours and abstained from staging.

E-PS-24-004
Deciphering the immune landscape of gastro-entero-pancreatic high-grade neuroendocrine neoplasms could help in tailoring medical treatment?
V. Angerilli*, G. Sabella, M. Simbolo, V. Lagano, M. Gentili, a. mangogna, J. Coppa, G. Munari, G. Businello, C. Borga, F. Schiavi, S. Pusceddu, R. Leporati, M. Fassan, M. Milione
*Department of Medicine, Surgical Pathology Unit, University of Padua, Padua, Italy

Background & objectives: High-grade Neuroendocrine Neoplasms (HG-GEP-NENs) are a heterogeneous group of neoplasms with a dismal prognosis. Microenvironment-related immune and inflammatory markers, when combined with established Ki-67 and morphologic features, can improve prognostic stratification of HG-GEP-NENs patients and identify potential candidates for immunotherapy.
Methods: We analysed a cohort of 49 HG-GEP-NENs (21 GEP-NETs G3, 12 GEP-NECs with ki-67<55% [GEP-NECs<55] and 16 GEP-NECs with ki-67≥55% [GEP-NECs≥55]) using targeted Next-Generation Sequencing (TSO500, Illumina) and comprehensive RNA-seq. The samples were also investigated for immunohistochemical expression of PD-L1.
Results: First, we investigated the status of predictive biomarkers for immunotherapy. Overall, 18.6% HG-GEP-NENs were Tumour Mutational Burden (TMB)-high (TMB≥10 mut/Mb). GEP-NECs≥55 were enriched TMB-high tumours (42.9%, p=0.01). MSI status was detected only in a MSH2-mutated colonic GEP-NEC≥55. A pathogenetic POLE mutation was identified in a rectal GEP-NEC≥55. PD-L1 was negative in tumour and inflammatory cells in all HG-GEP-NENs. At transcriptomic analysis, a low leukocyte infiltrate was observed in all samples. Enrichment in cancer-associated fibroblast, macrophages M2-like and endothelial cells was observed in GEP-NETs G3. Differently, GEP-NECs were enriched in CD4+ and CD8+ T cells. CTLA4 gene was up-regulated in GEP-NECs, but the CTLA4 blockade signature was not overexpressed in GEP-NECs.
Conclusion: Immunotherapy has shown poor efficacy in the unselected population of HG-GEP-NENs because the immune microenvironment

landscape was scant in HG-GEP-NENs at transcriptomic analysis and PD-L1 expression was absent. Thus, there is a great need to identify subsets of HG-GEP-NENs responsive to immunotherapy approaches. The present results addressed GEP-NECs with high proliferation index as sensible candidates to immunotherapy due to the enrichment in TMB-high and MSI coupled with higher CD4+ and CD8+ T cell expression.

E-PS-24-005

Heterogeneity of predictive biomarker expression in gastric carcinoma with peritoneal dissemination

V. Angerilli*, M. Callegarin, I. Govoni, G. De Lisi, G. Spolverato, S. Lonardi, F. Bergamo, A. Vanoli, P. Parente, F. Grillo, L. Mastracci, M. Fassan
*Department of Medicine, Surgical Pathology Unit, University of Padua, Padua, Italy

Background & objectives: Temporal and spatial molecular heterogeneity is a well-established mechanism of resistance to targeted and immune therapy in gastric carcinoma (GC). This study aims to assess the differences in biomarker expression between primary gastric cancer and paired peritoneal metastasis.
Methods: A total of 74 cases of primary GCs and paired peritoneal metastases were analysed by immunohistochemistry for HER2, PD-L1, Claudin18.2 (CLDN18.2), DNA mismatch repair complex (MMR) proteins, p53 and E-cadherin and in situ hybridization for EBER were performed on both primary and metastatic tumours. Samples with HER2 score 2+ were tested by fluorescent in situ hybridization for HER2 gene status.
Results: The primary GCs of our cohort were more frequently poorly cohesive (45.9%) or mixed-type (37.8%); they showed low rates of HER2 overexpression (5.4%), MMR deficiency (4.1%), and EBER positivity (1.4%). CLDN18.2 was positive in 31.1% of cases and PD-L1 was CPS≥1 in 79.7%. The highest discordance rate between primary GC and metastasis was observed for PD-L1 CPS≥/<1 (23.0%) and CLDN18.2 (13.5%). A relatively low discordance was reported for HER2 (2.7%), E-cadherin (6.8%), p53 (1.4%). When scoring HER2 as 0/low/high, the discordance rate increased (27.0%). Overall, 11% of patients were found to be eligible for further treatment following biomarker evaluation in the metastasis.
Conclusion: Our data suggest that GCs with peritoneal metastasis have specific morphologic features and might present clinically-relevant molecular spatial heterogeneity in the setting of peritoneal dissemination. With the introduction of novel biomarkers (i.e., HER2-low and CLDN18.2) in clinical practice, the need to address heterogeneity between primary and metastasis is becoming more pressing. Multisite sampling and liquid biopsy should be explored to overcome spatial heterogeneity fueling resistance to targeted therapy.

E-PS-24-006

Expression and prognostic value of Forkhead box P3 (Foxp3) in colorectal carcinoma

R. Aouadi*, I. Helal, F. Khanchel, E. Ben Brahim, R. Jouini, A. Chadli Debbiche
*La Rabta Hospital, Tunisia

Background & objectives: Regulatory T cells expressing Foxp3 play an essential role in modulating antitumour immunity. Many studies showed an association between Foxp3 overexpression and poor cancer prognosis. Our aim was to evaluate the expression and prognostic value of Foxp3 in colorectal carcinoma.
Methods: Foxp3 expression was retrospectively assessed in 104 cases of colorectal carcinoma using immunohistochemistry and tissue microarrays. Stained cells were counted on 5 high power fields and the mean value per tumour was scored. The median number of stained cells per tumour was used as a cutoff. A survival analysis was carried out.
Results: Foxp3 staining was observed in all cases and involved only immune cells. The median value of Foxp3 expression was 15,6 stained lymphocytes / Tumour. Foxp3 was overexpressed when the number of stained cells per tumour was superior to the median value and vice-versa. The overall survival of colorectal carcinoma patients with high Foxp3 expression was higher than the overall survival of patients with low Foxp3 expression but with no significant difference. Foxp3 expression status wasn't significantly associated with survival (p=0.862). Foxp3 high expression was associated with lower tumour budding (p= 0,030). There was no significant association with the other histological or clinical prognostic factors of colorectal carcinomas.
Conclusion: Foxp3 overexpression was linked to poor prognosis in different types of cancer due to regulatory T cells' role in inhibiting antitumour immune response. Many studies suggested that it may be paradoxically associated with an improved prognosis in colorectal cancer. In our study, Foxp3 expression status didn't have a significant prognostic impact. The lack of a standardized approach of assessment may be a limitation hindering the comparison of results.

E-PS-24-007

Gastric adenocarcinoma with osteoclast-like giant cells: a case report and retrospective review of a rare disease

I. Araújo*, S. Neves, X. Wen, J.R. Vizcaíno, M. Caldas
*ULS Santo António, Portugal

Background & objectives: Tumours containing osteoclast-like giant cells are more frequently reported in the breast but are relatively rare in other sites. Gastric adenocarcinoma with osteoclast-like giant cells is an extremely rare entity, with very few cases reported in the literature.
Methods: We report the case of a 71-year-old woman who sought medical care after experiencing weight loss, stomach pain and indigestion. The patient underwent neoadjuvant chemotherapy and subsequent subtotal gastrectomy. Histological examination revealed a gastric adenocarcinoma with osteoclast-like giant cells. A 5-year retrospective review of reports was conducted to search for additional cases of the same entity in our Pathology Department.
Results: Macroscopic examination of the surgical specimen revealed a 2cm ulcerated tumour, centred in the small curvature of the pre-pyloric antrum and causing serosal retraction. Histological analysis revealed a poorly differentiated tubular adenocarcinoma containing multinucleated osteoclast-like giant cells in the stroma. Immunohistochemistry showed positivity for CAM 5.2 and negativity for synaptophysin and chromogranin. None of the 15 lymph nodes showed metastases but there were signs of response to previous treatments in one lymph node. Two hundred fifteen reports of total and subtotal gastrectomy specimens performed for malignancy were retrieved (from 01/2019 to 12/2023). No other cases of adenocarcinoma with osteoclast-like giant cells were found.
Conclusion: Gastric adenocarcinoma with osteoclast-like giant cells is a rare entity that is classified as a variant of undifferentiated carcinoma according to WHO. In this case, however, tubular morphology was still recognizable. The fact that we have retrieved no other cases in a 5-year retrospective review confirms the rarity of the entity, with a frequency of 0,47% in this study. This patient is currently being submitted to chemotherapy and maintains follow-up consultations in the Oncology Department in our hospital.

E-PS-24-008

MUC5AC expression in colorectal polyps suggests the involvement of gastric metaplasia as a trigger of the serrated pathway of carcinogenesis

I. Archilla*, M. Rodrigo, S. Lopez-Prades, V. Pablo, J. Camps, M. Cuatrecasas Freixas
*Pathology department. Hospital Clinic. University of Barcelona. Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Spain

Background & objectives: Colorectal cancer develops through different carcinogenic pathways. Recent studies suggest that serrated polyps derive from differentiated cells that undergo gastric metaplastic changes. Our objective is to evaluate MUC5AC expression by immunohistochemistry in a series of serrated polyps and conventional adenomas.
Methods: This is a prospective study of 95 colorectal serrated polyps, including hyperplastic polyps (HP), sessile serrated lesions (SSL) with and without dysplasia, and traditional serrated adenomas with low-grade dysplasia (TSALGD), as well as 30 tubular adenomas (TA). Immunohistochemistry with MUC5AC was performed in all lesions, considering as positive those polyps with MUC5AC expression in more than 5% of epithelial cells.
Results: 90% (85/95) of the serrated lesions were positive for MUC5AC, while only 13% (4/30) of the conventional adenomas were positive ($p<0.001$). The 10 serrated lesions that were negative for MUC5AC were 9 HP and 1 TSALGD, and all were located in the left colon. Of the 4 TA with MUC5AC positivity, 3 were located in the left colon and 1 in the right colon.
Conclusion: The difference in MUC5AC expression between serrated polyps and conventional adenomas suggests that the phenomenon of gastric metaplasia could play an important role in the initiation of the serrated pathway of colorectal carcinogenesis. However, serrated lesions that develop in the left colon could have a different aetiology than those developed in the right colon.

E-PS-24-009
Endometriosis presenting as acute appendicitis: a case report
A. Arnaout*, A. Moore
*St George's hospital trust London, United Kingdom

Background & objectives: Endometriosis is a common condition affecting women of childbearing age and can cause a wide number of clinical symptoms. Appendiceal endometriosis is rare, with presentations ranging from asymptomatic and incidental, to acute abdominal pain.
Methods: A 46-year-old female presented to the emergency department with a four-day history of right iliac fossa pain, nausea, and vomiting. A CT scan of the abdomen demonstrated an acutely inflamed retrocaecal appendix without perforation. The patient underwent an emergency laparoscopic appendicectomy and the specimen was sent for histopathological review.
Results: Grossly, the appendix was intact with a dusky appearance and exudate was seen on the serosal surface. On microscopy, endometrial glands and surrounding stroma were seen within the wall of the appendix and extending into adjacent fat, with an associated acute serosal reaction. The final diagnosis was that of appendiceal endometriosis with acute serositis.
Conclusion: Though rare, with a prevalence of approximately 2.7%, appendiceal endometriosis is an important differential diagnosis to consider in women of childbearing age with suspected acute appendicitis. As in our case, diagnosis often requires microscopic examination to identify the ectopic tissue. CD10 immunohistochemistry can highlight endometrial type stroma and aid in diagnosis. The pathogenesis of the ectopic tissue remains largely unknown, though ectopic transplantation via the fallopian tube has been suggested.

E-PS-24-010
Endometrioid carcinoma arising from colonic endometriosis mimicking primary colon carcinoma
G. Askan*, Ş. İlvan, C. Turker Saricoban, A. Namal, A.M. Önenerk Men, İ. Sertbudak, Ö. Gökbaşı, E. Hatipoğlu, Ş. Batur
*İstanbul University Cerrahpasa, Cerrahpasa School of Medicine, Department of Pathology, Turkey

Background & objectives: Colonic endometriosis rarely results in a visible mass and transmural endometriosis of colon with tumour-like obstruction can mimic primary colon carcinoma.
Methods: A-69-year-old female with a clinical history of mucinous borderline ovarian tumour with intraepithelial carcinoma foci in 2018, was admitted to the hospital with abdominal pain. CT revealed a mass within the sigmoid colon. The patient underwent surgery with clinical diagnosis of colon carcinoma. Macroscopically, a polypoid mass, 5,5 cm in diameter was observed. The mass was entirely submitted.
Results: Microscopically, no adenomatous change was seen within the colonic mucosa. Polypoid neoplasm was lined by single layered epithelium consists of cuboidal cells. Entire wall was involved by bland cystically dilated glands. Areas with cribriform structures that highly suspicious for malignancy/carcinoma was seen in two foci. Tumour cells and bland glands were positive for CK7, estrogen and progesteron receptors, PAX-8, while negative for CK20, CDX2, SATB2 and WT-1. Cellular stroma at the periphery of some glands were positive for CD10. Loss of PTEN expression and high Ki67 proliferation index was seen in area of carcinoma. Patients' prior hysterectomy material was re-examined and confirmed that each tumour was histologically and immunohistochemically different.
Conclusion: We reported the case as endometrioid carcinoma arising from colonic endometriosis, which is a rare tumour, difficult to diagnose preoperatively, since similar symptoms can be seen in primary colon carcinoma. Thus, a careful histologic and immunohistochemical examination is crucial for definite diagnosis and appropriate treatment method.

E-PS-24-011
Gastric calcifying fibrous tumour: pathological insights from a clinical case
G.G.M. Attanasio*, L. Memeo, C. Colarossi, L. Colarossi, G. Magro, M. Failla, E. Aiello
*Italy

Background & objectives: Calcifying Fibrous Tumour (CFT) primarily affects the gastrointestinal tract. This case report examines a gastric CFT in a young female, aiming to delineate its characteristics and emphasize its differential diagnosis in mesenchymal lesions.
Methods: A 30-year-old female with recurrent low-grade fever was assessed for an incidental gastric lesion. Endoscopy revealed an exophytic subserosal mass located in the greater curvature, well-circumscribed, unencapsulated, and lobulated. Gross examination and sectioning highlighted its firm, homogeneous, gritty, white-cut surface. Histological and immunohistochemical analyses focused on markers such as CD34, DOG-1, ALK, SMA, and CD45, confirming the diagnosis.
Results: Histological examination revealed a lesion characterized by paucicellular spindle cell proliferation within a densely hyalinized stroma, prominently featuring psammoma bodies, indicative of a calcifying fibrous tumour. Accompanying these features were significant lymphoplasmocytic infiltrates and dispersed, activated lymphoid follicles, suggesting an ongoing immune response. Immunohistochemical testing confirmed these findings, showing positive staining for CD34, a marker of mesenchymal origin and negative for DOG-1, ALK, SMA, CD45, and beta-catenin, effectively ruling out gastrointestinal stromal tumours and other mesenchymal entities. Additionally, IgG4 staining was negative, excluding associations with IgG4-related diseases. These characteristics definitively identified the mass as a gastric calcifying fibrous tumour, distinctly differentiating it from similar lesions.
Conclusion: This case emphasizes the need to consider gastric calcifying fibrous tumour (CFT) in the differential diagnosis of gastrointestinal lesions, particularly in young adult females. Other possibilities

include inflammatory myofibroblastic tumour, sclerosing mesenteritis, desmoid fibromatosis, reactive nodular fibrous pseudotumour, GIST, leiomyomas, and schwannomas. Detailed histological and immunohistochemical analyses are critical, providing the insights necessary for accurate diagnosis and guiding effective clinical management and targeted therapeutic interventions for these patients.

E-PS-24-012

Significance of KRAS and NRAS gene mutations in colorectal cancer

E. Avădănei*, L. Lozneanu, I.D. Căruntu, C. Amalinei, R.A. Balan, S.E. Giuşcă
*"Grigore T. Popa" University of Medicine and Pharmacy Iasi, Romania

Background & objectives: The aim of our study is to assess the incidence of RAS gene mutation (KRAS and NRAS) in the Romanian population diagnosed with colorectal cancer (CRC) and to correlate the presence of this mutations with the main CRC clinicopathological characteristics.
Methods: The study group included 67 patients diagnosed with CRC between 01.01.2022 and 01.06.2023. Tissue samples from patients with a diagnosis of CRC were assessed for KRAS and NRAS gene mutations using the fully automated IdyllaTM KRAS and NRAS Mutation Test sequencing system (Biocartis, Mechelen, Belgium). The MedCalc statistical package was used for all statistical analyses.
Results: In the study group, out of 67 cases that underwent genetic testing, 37 cases (55.22 %) were found to have a KRAS mutation and 30 cases (44.77 %) were found to have a wild-type. In the case of the NRAS gene, only 4 cases (5.97 %) were found to have a mutation and the remaining 63 patients (94.03 %) were found to have a wild-type. KRAS mutations were significantly associated with NOS colorectal adenocarcinoma, female gender, vascular invasion, low-grade tumours, and lymph nodes metastasis. The presence of NRAS mutations was correlated with mucinous morphology and high tumoural buds score.
Conclusion: Our date demostrate the relationship between colorectal cancers and RAS gene mutations. The analysis shows that CRC have distinct clinicopathological characteristics in relation to the presence of KRAS and NRAS mutations. This is reflected in tumour progression, prognosis and the development of resistance mechanisms to dye therapy.

E-PS-24-013

Gastric tumour in disguise: how adherence to routine workflow paves the way to the correct diagnosis

S. Aviel-Ronen*, I. Schwartz, E. Fridman, N. Balint-Lahat, A. Yosepovich, A. Lahat, J. Weidenfeld, M. Perelman, G. Schiby, I. Barshack
*Pathology department, Sheba Medical Center/ Adelson School of Medicine, Ariel University, Israel

Background & objectives: Post-irradiation angiosarcoma is a rare sequela of radiation therapy for breast cancer. Here, we describe a case of bleeding gastric ulcer due to metastatic post-irradiation angiosarcoma in a patient with breast cancer and discuss the potential pitfalls in the diagnosis.
Methods: The medical records, imaging tests, and pathological findings of a 79-year-old patient are presented. The patient was admitted due to massive hematemesis. Her medical background included lung right lower lobe segmentectomy due to squamous cell carcinoma (4 years prior) and left breast lumpectomy with irradiation due to infiltrating duct carcinoma (8 years before) with a recent recurrence.
Results: PET-CT demonstrated a mass in the gastro-oesophageal junction, and in gastroscopy, a cardiac ulcer was identified and biopsied. Histology showed extensive necrosis and gastric mucosa infiltrated by large atypical epithelioid cells with prominent nucleoli. Surprisingly, the atypical cells were negative for AE1/AE3 on immunostains. The following extended panel of stains was negative for p40, CD3, CD20, CD79a, CD10, Bcl2, Bcl6, and MUM1 but showed positive staining for CD31, c-myc, and CD34. Ki67 was positive in 80% of the atypical cells. A diagnosis of metastatic post-irradiation angiosarcoma was made. This diagnosis was supported by the revised diagnosis of her recurrent breast tumour that showed high-grade angiosarcoma.
Conclusion: This unusual case of a gastric ulcer due to metastatic post-irradiation angiosarcoma in a patient with previous breast cancer emphasizes the pivotal role of routine workflow to secure reaching the correct diagnosis. The ordered workflow includes a gradual, systematic selection of immunostains to support the postulated diagnosis and a meticulous examination of the patient's medical background. This workflow is particularly important when the diagnosis is made in a referral centre that has limited exposure to the patient medical background.

E-PS-24-014

Primary intestinal lymphoma: a clinicopathological characteristics of an uncommon tumour

R. Ayadi*, R. Yaiche, E. Braham, F. Khefacha, A. Saidani, O. Ismail, F. Chebbi, A. Ayadi
*Department of Pathology, Abderrahmen Mami Hospital, Tunisia

Background & objectives: Primary intestinal lymphoma (PIL) is very rare comprising only 0.2–1% of all intestinal malignancy. Due to the lack of characteristic symptoms, PIL is misdiagnosed until serious complications occur. This study discusses the clinocopathological characteristics of PIL.
Methods: We report 7 cases of PIL, treated in our institution from 2004 to 2023. The diagnostic was made on resected intestinal specimens. Hematoxylin and eosin stained sections were studied and IHC for CD3, CD20, CK and Ki67 were done to confirm the histopathological diagnosis. All cases were reclassified according to the World Health Organization classification of lymphoma in 2017.
Results: There were 4 male and 3 female patients, aged between 47 and 85 years with a mean of 68,5. Abdominal pain and abdominal lump were two main common presenting symptoms. There was no history of lymphoma in any of the patients.Tumour localization was small intestine in 5 patients, colon and rectum in one patient each. Histological and immunohistochemistry examination revealed peripheral T-cell lymphoma Not Otherwise Specified (NOS) (n=2), diffuse large B-cell lymphoma (n=2), mucosa-associated lymphatic tissue lymphoma (n=1),peripheral T-cell lymphoma following diffuse large B-cell lymphoma associated with coeliac disease (n=1) and mantle cell lymphoma (n=1). Histopathological and immunohistochemistry examinations led to the final diagnosis of PIL.
Conclusion: PIL is rare and differs significantly from their gastric counterpart, not only in pathology but also with regard to clinical features, management and prognosis. Initial presentation of the disease may be obstruction with or without perforation. They are difficult to diagnose and are frequently done in the setting of an urgent surgical intervention. Therefore, clinicians and surgeons should keep this entity in mind when assessing patient with intestinal obstruction.

E-PS-24-015

Simultaneous presentation of gastrointestinal stromal tumour and small bowel adenocarcinoma in a patient with neurofibromatosis type 1: exploring an uncommon convergence

A. Bdioui*, I. Hadhri, O. Belkacem, Z. Lajmi, M. Krifa, S. Mestiri, S. Hmissa
*Sousse Sahloul Hospital, Tunisia

Background & objectives: Neurofibromatosis type 1 (NF1) is a genetic disorder characterized by an increased susceptibility to

tumour formation. While NF1 patients commonly develop gastro intestinal stroma tumour (GISTs), the simultaneous occurrence of NF1, GIST, and small bowel adenocarcinoma is exceptionally rare.
Methods: Here, we present a case of NF1 with a history of treated GIST in 2018 via surgical resection and targeted therapy, now exhibiting adenocarcinoma of the small bowel. This highlights a rare simultaneous occurrence deserving attention.
Results: We present a case of NF1 in a 68-year-old woman with a history of treated GIST in 2018. She was readmitted in 2023 due to abdominal pain, leading to the discovery of a large intraperitoneal mass on imaging. A right large bowel resection was performed, revealing a circumferential tumour process infiltrating the entire 5.5cm ileal wall, with around twenty nodules protruding at the serosal level, measuring between 0.4 and 2 cm. Microscopic examination identified a low-grade NOS adenocarcinoma classified as T4aN2, with an infiltration of the serosa and 3 metastatic lymph nodes. Additionally, the subserosal nodules were confirmed as multiple GISTs strongly and diffusely positive for DOG1+ and CD117+.
Conclusion: this case underscores the rarity of concurrent occurrences of NF1, GIST, and adenocarcinoma of the small bowel. It underscores the challenges in diagnosing and managing such complex presentations, necessitating comprehensive evaluation and tailored treatment approaches. Continued investigation into the underlying pathophysiology and therapeutic interventions for these conditions is crucial to improve patient outcomes and inform clinical practice.

E-PS-24-016
HER2 expression in primary colorectal cancer
K. Ben Lazreg*, W. Majdoub, S. Mestiri, A. Bdioui, S. Hmissa, N. Missaoui
*Fattouma Bourguiba University Hospital, Monastir, Tunisia

Background & objectives: HER2 expression is a potential theranostic marker in colorectal carcinoma (CRC). Controversial rates of HER2 expression in CRC have been published. We aimed to investigate the frequency of HER2 overexpression/ amplification in primary CRC.
Methods: Over a period of two years and six months, a retrospective descriptive study included all patients diagnosed with CRC (stage I-IV) on surgical resection specimens. Immunohistochemistry was performed using the tissue microarray technique. Immunostaining was interpreted according to the gastric cancer scoring system for biopsies. Equivocal cases were tested by chromogenic in situ hybridization (CISH).
Results: A total of 144 patients were enrolled, with an average age of 61.9 years and a sex ratio of 1.18. A predilection for the left colon was noted. Distant metastases were observed in 14.6% of cases. Our patients were diagnosed on stage III in 38.9% of cases. Tumours were classified into three groups: HER2-negative status (score0/1+) in 142 cases (98.6%), equivocal HER2 status (score2+) in one case (0.7%) and HER2-overexpressing status (score3+) in one case (0.7%). CISH testing for HER2 gene amplification was negative. The rate of HER2 overexpression in metastatic CRC was 4.7%. The patient with HER2 overexpression had mutated KRAS/NRAS status and numerous metastatic relapses.
Conclusion: Our results confirm the fact that HER2 expression is a rare molecular event in CRC. The rate of HER2 overexpression and amplification found in metastatic CRC is in line with other reports. Alongside our observations, there are rare reported cases where KRAS/NRAS mutations coexist with HER2 overexpression. The overall rate in our series is lower than those reported in the literature. Larger-scale and multicentre studies are needed to confirm our findings.

E-PS-24-017
A rare case of ampullary gangliocytic paraganglioma with lymph node metastasis: histological and immunohistochemical analysis
W. Ben Makhlouf*, A. Zehani, A. Ayari, A. Khadhar, I. Chelly, H. Azouz, K. Bellil, S. Haouet
*Tunisia

Background & objectives: Gangliocytic paraganglioma(GP) is a rare tumour of the periampullary region posing a differential diagnoses with Grade-1 Neuroendocrine Tumours(NETs). However, GP typically exhibits a more favourable prognosis and infrequent lymph-node metastases(LNM). Here, we present a case of ampullary GP with LNM
Methods: We received a duodenopancreatectomy specimen from a 66-year-old man presenting with jaundice and no significant medical history.
Results: Macroscopic examination revealed a well-demarcated yellowish-white tumour measuring 55x25mm, originating from the papilla and occupying the duodenal lumen. Dissection revealed 15 lymph nodes, one of which measured 2 cm in length and exhibited metastasis. Histological examination demonstrated a triphasic tumour composed of lobules of epithelioid cells with abundant eosinophilic cytoplasm and oval, fairly monomorphic, often nucleolated nuclei. These lobules were interspersed with spindle-shaped cells resembling Schwann cells, along with a few ganglion cells. The tumour was confined to the duodenal submucosa. Immunohistochemical analysis revealed chromogranin, synaptophysin, and progesterone expression in epithelial cells, while Schwannian and lymph node cells expressed PS100, confirming the diagnosis of gangliocytic paraganglioma.
Conclusion: GP is a rare tumour of the periampullary region and the second part of the duodenum, characterized by its low metastatic potential and favourable prognosis. Reported cases of lymph node or hepatic metastases are exceedingly rare.

E-PS-24-018
Gastric microscopic findings in patients with coeliac disease
S. Ben Rejeb*, S. Sakly, M. Ayari, T. Jomni
*Pathology Department, Security Forces Hospital, Marsa, Tunisia; Research Unity of Epithelial to Mesenchyma Transition, Faculty of Medicine of Tunis, Tunis Manar University, Tunisia

Background & objectives: Coeliac disease(CD) is characterized by icreased intraepithelial lymphocytes in the duodenal mucosa associated with a villous atrophy. The aim of this study was to describe the microscopic findings in gastric biopsies from patients with CD.
Methods: This is a descriptive retrospective study focusing on CD cases diagnosed in our department over a period of 5 years (2009-2014) in whom gastric biopsy was performed concomitantly. Clinical and histological data were collected from medical records and histopathological reports. A review of gastric biopsy slides was conducted to determine the elementary lesions.
Results: 38 patients were included in our study. The mean age was 33 years (range 20-62 years) with a male-to-female ratio of 0.36. In the duodenal mucosa, total or subtotal villous atrophy associated with intraepithelial lymphocytosis was observed in all cases. In the gastric mucosa, morphological alterations were found in 100% of cases: chronic gastritis (CG) with Helicobacter pylori (HP) was found in 64% of cases, reactive gastropathy in 18% of cases, and lymphocytic gastritis in 18% of cases.
Conclusion: Numerous studies have reported gastric morphological alterations in patients with CD, presumably induced by gluten hypersensitivity. In our study, abnormalities of the gastric mucosa were found in all patients, among whom 64% had CG associated with HP. Although the etiopathogenic mechanisms involved in this association are not clearly established, the relatively high frequency of CG with HP in our study justifies the systematic performance of biopsies in these patients.

E-PS-24-019
Immunohistochemical analysis of BRAF V600E antibody in colorectal cancer
S. Ben Rejeb*, S. Sakly, R. Bahloul, F. Souai, A. Chouch
*Pathology Department, Security Forces Hospital, Marsa, Tunisia; Research Unity of Epithelial to Mesenchyma Transition, Faculty of Medicine of Tunis, Tunis Manar University, Tunisia

Background & objectives: It has been advanced that BRAFV600E antibody is a highly sensitive and specific technique for determination of BRAFV600E mutation status in colorectal cancer(CCR).In this context,we aimed to assess BRAF immunohistochemical(IHC) expression in colorectal cancer and its association to prognostic factors.
Methods: We have retrospectively collected all cases of CCR diagnosed during a period of 10years.An automated IHC analysis was performed using anti-BRAFV600E(GenomeME,IHC600) with positive and negative control tissue.We have assessed the cytoplasmic staining intensity in tumour cells comparing to the positive control and classified as follows:1-weak cytoplasmic staining,2- Moderate cytoplasmic staining and 3-Strong cytoplasmic staining.
Results: Thirty-five patients were included in the study with a mean age of 60 years and a male-to-female ratio of 2.3. The studied specimen was biopsy in 37.2% of cases and surgical resection in 62.8%. BRAF positive staining was found in 37.1% of cases with a mean percentage of positive cells of 49% (5-100%). The staining intensity was low in 5cases, moderate in 3cases and high in 5cases. No statistically significant association was found between BRAF expression and the studied clinico-pathological characteristics. All cases with KRAS mutated status were negative for BRAF(p=0.16).
Conclusion: BRAF expression was found in 37.1% of cases which is above the reported rate of BRAF mutation in CCR of 10-15%. These results suggest that BRAF labeling is not specific and must be confirmed by molecular biology. However, our findings advance that total loss of BRAF in patients with colorectal cancer is more likely to be observed in patients with KRAS mutation and could hence predict KRAS status.

E-PS-24-020
Coeliac disease (CD) and eosinophilic oesophagitis (EoO): a controversial enigma
H. Berber*, E.N. Kozan, E.K. Çagdas, E. Demir, A. Tagiyev, C.T. Kırsaçlıoğlu, Z. Kuloğlu, B. Savaş, A. Kansu Tanca, A. Ensari
*Ankara University, Medical School, Pathology Department, Turkey

Background & objectives: Despite previous reports with varying rates(2-10%) of coexistence of EoO and CD, the relationship between EoO and CD has not been fully understood. We aimed to determine the true association of oesophagitis and CD in two distinct cohorts;EoO and CD.
Methods: Two cohorts, one comprising 55 EoO, the other consisting of 22 CD with a mean age of 11,36years; 9,45years and a female/male ratio of 0,83; 1.2, respectively, were evaluated retrospectively for the coexistence of EoO and CD. The resulting three groups of pure-EoO(n=45), EoO + CD(n=11), and pure-CD(n=21) were compared for the inflammatory patterns in oeosphageal and duodenal biopsies.
Results: CD was present in 18.2% of cases in EoO cohort, while only one(4.5%) EoO was observed in CD cohort. When oesophageal inflammation was assessed in three cohorts, frequency of lymphocytic oesophagitis was higher in EoO+CD(90,9%) compared to pure-EoO(62,2%)(p=0,065) and pure-CD(14,3%)(p<0,001). Papillomatosis was more common in pure-CD(%85,7) than EoO+CD (45,5%) (p=0,016) in contrast to peripapillary inflammation which was more prominent in EoO+CD(63,6%;) compared to pure-EoO(28,9%) (p=0,037). IEL counts were higher in EoO+CD (50,18/hpf) than pure-EoO(28,47/hpf)(p=0,008) and pure-CD(9,81/hpf)(p<0,001) which was also lower than pure-EoO (p<0,001). More severe duodenal pathology(Marsh histologic type3) was found in pure-CD(76,2%) than EoO+CD(54,5%), though not significant(p=0,365). In follow-up biopsies(32 cases), 50% of EoO+CD and 38,5% of pure-EoO showed remission(p=0,470).
Conclusion: The higher prevalence of EoO detected in CD in the present study is in accordance with the literature in terms of clinicopathologic (age, symptoms, serology, histologic Marsh types)similarities between EoO+CD and isolated CD, supporting the coincidental viewpoint. Additionally, more common lymphocytic oesophagitis and higher IEL counts in EoO+CD compared to pure-EoO can be explained by the phenomenon of widespread gastrointestinal intraepithelial lymphocytosis in CD. However, the more frequent lymphocytic oesophagitis in pure-EoO than in pure-CD seems to contradict this view.

E-PS-24-022
Predictors of margin involvement in colorectal cancer
E. Ho, I. Kak, A. Naqvi, P. Major, M. Bonert*

*McMaster University, Canada
Background & objectives: Margin involvement in colorectal cancer (CRC) has been shown to be prognostic for mortality and disease recurrence. The aim of this study was to determine how common synoptic report elements relate to margin positivity (MP).
Methods: CRC cases accessioned 2012-20 and reported with a synoptic were retrieved. The parameters tumour stage, nodal stage, lymphovascular invasion (LVI), perineural invasion (PNI), y staging modifier, tumour grade, patient age and sex were extracted. MP was defined as <=0.1cm clearance. Results were tabulated using MS-Excel. Analysis was done with R using logistic regression (LR) and receiver operator characteristic (ROC) curves.
Results: The period had 2,556 CRC cases. Overall, margin positivity rate (MPR) was 8.4%. In LR, tumour stage, nodal stage, LVI, PNI, and y modifier status were all independent predictors of MP (p<0.0001); grade, sex and age were non-predictive (p>0.05). The nodal stage ROC curve area under the curve (AUC) was 0.75 and MPR was 2.9%/11.2%/27.9% in pN0/pN1/pN2 respectively. The tumour stage AUC was 0.71 and MPR was 1.6%/1.8%/7.5%/18.4%/24.5% for pT1/pT2/pT3/pT4a/pT4b respectively. AUC was 0.66, 0.63, and 0.55 for LVI, PNI, and y staging modifier. The MPRs for LVI and PNI present/absent were 4.4%/15.8% and 5.9%/18.9%.
Conclusion: Tumour stage and nodal stage were the strongest predictors of colorectal margin involvement and the highest rates were seen with the most advanced stages. Treatment effect (y modifier), lymphovascular invasion, and perineural invasion were also predictors, while tumour grade was not. Patient factors (age and sex) were not predictors; this is reassuring, as it suggests margin positivity is driven by pathologic factors alone in our environment.

E-PS-24-023
Real-life challenges in pathological diagnosis of GIST – assessment of prognosis factors
A. Bordea*, S. Zurac, L. Sticlaru, G. Micu, B. Mastalier, R. Neagu, D.M. Marinoiu, V.N. Marin, C. Popp
*Department of Pathology, Colentina University Hospital, Bucharest, Romania

Background & objectives: Assessment of pathological risk factors in GIST includes clinical, gross and microscopical parameters. Most used classifications are Miettinen and Lasota's (2006) and Fletchers' (2002). In real-life, pathologists frequently meet challenges, some of them being presented in this study.
Methods: We retrospectively examined available data in 23 cases of GIST diagnosed and immunohistochemically confirmed (with CD34, CD117 and DOG1) in our department. In all cases prognosis factors were assessed in order to formulate an oncological prognosis: localization, tumour size, necrosis, mitotic index, integrity of the capsule and of the resection, association, at the surgery moment, of a second malignancy.
Results: The examining pathologist was confronted with difficulties in assessment of risk factors in multiple cases: 7 cases were endoscopic biopsies, in two cases tumour was incompletely received for diagnosis from another department, in 4 cases the tumour was incompletely

resected, in one case the tumour was invading jejunum and transverse colon, being impossible to identify the site of origin. From the 13 cases where Ki67 stain was performed, in 4 cases there was a discordance between mitotic index (quantified on 50 HPF, hematoxylin-eosin stain) and Ki67 index. Practically, only in 10 out of 23 cases, it was possible to assess the entire panel of parameters include in the two classifications).
Conclusion: Although not a rare diagnosis, GIST is not always representing an easy job for pathologists. Better communication in the multidisciplinary team, assessment of cases in tumour boards and nominalization of the problems each specialist is having in the management of GIST are the pathways for a better care and outcome for these patients.

E-PS-24-024
Can response to neoadjuvant chemotherapy be predicted in gastric cancer?
O. Boudaouara*, W. Ben Makhlouf, W. Ghribi, C. Chaari, M. Bouhamed, T. Sellami Boudawara, M. Zghal
*Tunisia

Background & objectives: Recently, neoadjuvant-chemotherapy (NAC) became strongly recommended in locally-advanced-gastric-cancer (LAGC), and has proven its efficacy in increasing tumour-resectability and survival rates. Yet, it remains unclear which patients respond better. Herein we aim to identify factors predicting response to NAC in LAGC.
Methods: Data analysis of our LAGC database was performed in the period between January 2019 and March 2024. 42 consecutive patients underwent surgery for LAGC. 23 among them were treated with NAC, fulfilling eligibility criteria. Chi-square test was used to investigate associations between pathological response and clinico-pathological parameters. Z-score was used to compare annual incidence rates. A p-value<0.05 was statistically significant.
Results: As of 2022, the mean annual incidence rate of prescribing NAC in LAGC has significantly increased (9 cases vs 1.6 cases per year, after and before 2022 respectively, p-value=0.03). The mean age of patients was 58.2 years. Tumour size was <4.5cm in 52.2% of cases. The majority of patients were deemed stage II or III at baseline (73.9%). The tumour involved mainly distal stomach (82.6%). Conventional adenocarcinoma was the predominant histological subtype (56.5%). Perineural and lymphovascular-invasion were present in 43.4% of cases, each. A near complete after NAC (assessed as TRG-1) was rarely obtained (17.4%). The absence of lymphovascular-invasion was the only factor associated with a near complete response (p=0.023)
Conclusion: It seems difficult to obtain a complete or near complete response to NAC in LAGC unlike other solid malignancies. The results of this study demonstrated that the absence of lymphovascular invasion significantly predicts a better response to chemotherapy. However, factors influencing the quality of response remain still unclear and require further studies to be strongly established.

E-PS-24-026
Amiloidosis of the gall bladder in a patient with the presenting symptoms of acute cholesystitis
I. Buldum*, G.O. Elpek, S.B. Yolburun, D. Durna
*Akdeniz University, Turkey

Background & objectives: Amyloidosis is the extracellular accumulation of insoluble proteins in tissues, forming "amyloid." Although various organs such as the heart, kidneys, and nervous system can show it, the occurrence of accumulation in the gallbladder is extremely rare.
Methods: We analysed the specimen by employing hematoxylin and eosin staining, histochemical Congo Red staining, and immunohistochemical staining with Amyloid A and Amyloid Beta.
Results: A 46-year-old woman presented at the emergency department complaining of nausea, vomiting, and abdominal pain. After examination, she was diagnosed with acute cholecystitis and underwent a cholecystectomy. Following the surgical procedure, we thoroughly analysed the cholecystectomy specimen and identified the presence of amyloid accumulation.
Conclusion: Examining the literature indicates that amyloidosis in the gallbladder is exceptionally uncommon.The purpose of this case presentation is to emphasize the possibility of diagnosing amyloidosis of gall bladder , an uncommon condition, in a patient presenting with acute cholecystitis symptoms.

E-PS-24-027
Prognostic significance of cellular cannibalism in colorectal tumours
S. Cagaptay*, S. Sarioglu, A. Aysal Ağalar, O. Sagol, I. Gorken, T. Unek, H. Ellidokuz, F. Barlik, S. Sokmen
*Dokuz Eylul University, Turkey

Background & objectives: Cellular cannibalism (CC) is a morphological feature that can be defined as the ability of one cell to engulf another. Our research aims to examine the connection between CC and histopathological and molecular features seen in metastatic colorectal carcinomas.
Methods: Resection materials were examined between 2014 and 2019, and 128 cases with a diagnosis of colorectal cancer were assessed for the degree and presence of the CC. A statistical analysis was conducted to examine the correlation between CC and clinicopathological characteristics, as well as the molecular status of KRAS, NRAS, BRAF and microsatellite instability (MSI).
Results: CC was detected in all patients. No significant relationship was found between the CC degree and the compared parameters; pT stage (p=0.599), pN stage (p=0.993), tumour differentiation (p=0.887), tumour localization (p=0.703), perineural invasion (p=0.542), lymphovascular space invasion (p=0.561), tumour budding (p=0.561). Additionally, there is no significant relationship between CC and mutation status (p=0.173) and MSI status (p=0.235). The relationship between CC and death is not statistically significant (p=0.183).
Conclusion: There is data in the literature that CC, defined in different malignancies, may be related to the aggressiveness of the tumour. In our series, all of the cases we selected to provide data related to molecular pathological findings are metastatic cases evaluated for mutation. With these findings, it was thought that the CC grade was not related to KRAS, NRAS, BRAF mutation and MSI in metastatic cases and did not provide predictions about prognosis.

E-PS-24-028
Immune-checkpoint inhibitor-related microscopic colitis: clinical pictorial series and histopathological mini-review
A. Chang*, E. Bearblock, K. Chang, F. Chang
*King's College Hospital NHS Foundation Trust, United Kingdom

Background & objectives: Immune checkpoint inhibitors (ICIs) are effective cancer therapy, but there is growing recognition of complications caused by immune system disinhibition, including ICI-related colitis. This review provides an up-to-date summary of the clinical and histopathological features of ICI-related microscopic colitis.
Methods: We conducted a focussed literature search of Pubmed and EMBASE, for English language publications (from inception to current) specifically reporting on ICI-microscopic colitis. The evidence reviewed included case reports, case series, reviews and clinical guidelines. As part of this histopathological review, we present histological features of lymphocytic and collagenous colitides along images and observations from our own clinical practice.
Results: It is estimated that 1-3% of colitis following PD-1/PD-L1 inhibitors is histologically MC. Diagnosis is histological, with two main patterns. Lymphocytic colitis is characterised by an increased

number of intraepithelial lymphocytes (IELs) compared to normal (≥20/100). Collagenous colitis is diagnosed by a thickened subepithelial collagen band >10 μm with/without an increase in IEL predominance. The literature suggests that most ICI-related MC cases resemble lymphocytic colitis, with scanty reports of collagenous colitis-like disease. Clinical presentation is watery diarrhoea and abdominal symptoms despite largely normal endoscopy. The literature showed variability in time of symptom-onset following immunotherapy; some cases reported lymphocytic colitis presenting 4-11 months following ICI, and collagenous colitis >9 months following.
Conclusion: ICI-related MC remains a poorly-understood clinical entity. Currently, sporadic- and ICI-related MC remain almost indistinguishable histologically, and diagnosis relies on corroboration with antecedent history of immunotherapy. It is therefore difficult to distinguish whether MC following ICI is its own entity or represents pre-existing disease. Whilst the literature suggests variability in onset, a unifying feature of most case reports highlighted that ICI-related MC follows an aggressive clinical disease course, that warrants prompt histological diagnosis and treatment with steroid and immunosuppressants.

E-PS-24-029
Clinicopathologic features of anorectal melanoma: a Tunisian case series
L. Charfi*, A. Khemir, C. El Fekih, G. Sahraoui, I. Nasri, I. Abbes, N. Boujelbene, R. Doghri, K. Mrad
*Pathology department Salah Azaiez institute Tunisia / Precision Medicine and Oncology Investigation Laboratory, Tunisia

Background & objectives: Digestive tract melanomas are rare tumours developing preferentially in the anorectal region. Anorectal melanomas (AM) count for <1% of digestive tract malignancies and 1% of anorectal malignancies. In this study we'll figure out main clinicopathologic features of AM in Tunisia.
Methods: Cases diagnosed as AM in the pathology department of Salah Azaiez institute were gathered through 25 years (1999-April2024). Only patients who had surgical resections were included. Cases of AM diagnosed on biopsies were not considered.
Results: Eleven cases of AM were gathered (Six females and five males). The mean age was 67-year-old; 66-year-old in females and 70-year-old in males. On macroscopic examination the tumour mass polypoid in 2 cases. The mean size of the tumour was 60.9mm in largest diameter. The tumour was pigmented in 3 cases. Breslow depth ranged between 6 and 100mm. Deepest infiltration associated with adjacent organ invasion (2 cases) was associated with high Breslow depth (30-100mm). No lymph node metastases were identified in the last cases. In 3 cases out of 6 with lymph node metastases tumour infiltration was limited to the muscularis propria with Breslow depth ranging from 13 to 20mm.
Conclusion: According to our results, it seems to be that deepest tumour invasion is generally associated with high Breslow depth. Whereas, lymph node metastases are independent from digestive tract wall invasion and/or Breslow depth. These results should be consolidated by studies on largest series.

E-PS-24-030
Morphologic comparison of gastric poorly cohesive adenocarcinomas and corresponding peritoneal metastases
D. Chatterjee*, O. Olayinka
*The University of Texas, USA

Background & objectives: Recent studies have shown a superior survival of gastric poorly cohesive carcinomas (PCC) with >90% signet ring cell (SRC) morphology in comparison to those with a lower percentage of SRC, but the morphologic correlation to metastatic sites is lacking.
Methods: Archival H&E slides from pre-treatment gastric tumour biopsy of PCC and synchronous or metachronous peritoneal metastasis were reviewed for each case and classified into three groups, >90% SRC, 10-90% SRC, and <10% SRC. SRC was defined (as by WHO) as a tumour cell showing an optically clear, globoid droplet of cytoplasmic mucin with an eccentrically placed nucleus.
Results: 27 PCC were reviewed which had available slides from biopsies of both primary and metastatic sites (2018-current). None of the gastric biopsies with PCC that metastasized to peritoneum had >90% SRC morphology. In those where SRC component in the gastric biopsy was between 10-90% (N=15), peritoneal biopsies showed SRC morphology between 10-90% in only 7/15 cases, whereas in the remaining 8, SRC morphology was <10%. In 12 patients, SRC morphology was <10% in both gastric and peritoneal biopsies.
Conclusion: Our study demonstrated for the first time, the comparison of morphology between pre-treatment gastric biopsies for PCC, and their corresponding peritoneal biopsies. We observed that the morphology of peritoneal biopsies often demonstrate a lower proportion of SRC as compared to the gastric biopsies. Interestingly, none of the cases in our cohort had >90% SRC in the gastric biopsies. Our findings support a low risk of peritoneal metastasis with >90% SRC in PCC on diagnostic gastric biopsies.

E-PS-24-031
Paradoxical effect of maspin deficiency in poorly cohesive gastric carcinoma – increased distant spread and apparent reduced local invasion
A. Cibotariu*, L. Stanciu, M. Cioplea, B. Mastalier, L. Nichita, R. Ionescu, R. Neagu, D.M. Marinoiu, A. Bordea, C. Popp
*Department of Pathology, Colentina University Hospital, Bucharest, Romania

Background & objectives: Role of maspin (a serine) in tumours progression is still unclear in poorly cohesive gastric carcinoma (PC-GC), although there are some maspin-based treatments available. This study aims to identify correlation between maspin expression and tumour behaviour in PG-GC.
Methods: Eleven gastrectomized patients diagnosed with poorly cohesive gastric carcinoma between 2020 and 2023 were included in the study. Paraffin blocks most representative for tumour morphology and transition from normal mucosa were selected for analysis. E-cadherin and maspin were evaluated and correlated with tumour stage assessed on gross examination and preoperative MRI or CT scan (for distant metastasis).
Results: The analysed cohort included 11 patients, 10 men and 1 woman with ages between 44 and 67 (median age 59 years). All cases were locally advanced tumours (pT3-pT4b), 8 had lymph node metastasis and 3 had distant metastasis. Immunohistochemical stains showed the following patterns: E-cadherin positivity in 81.8% of cases, nuclear maspin positivity in 9.1% of cases and cytoplasmatic maspin positivity in 45.5% of cases. Among the two e-cadherin negative cases, 1 showed loss of maspin expression and the other retained cytoplasmatic positivity. Loss of maspin expression had positive significant correlation with distant and local lymph node metastases, while maspin positivity was negatively correlated with in-depth tumour invasion.
Conclusion: Results emphasize the existence of a correlation between maspin expression patterns and tumour behaviour regarding in-depth invasion, lymph node invasion and the presence of distant metastases. The present study has limitations due to sample size, but it brings valuable information about maspin involvement in local and distant spread of PC-GC: maspin deficient tumours seem to have a more aggressive behaviour.

E-PS-24-032

Mismatch repair protein deficient ampullary adenocarcinoma - an often overlooked association in a seldom diagnosed cancer

A.M. Ciongariu*, A. Dumitru, C. Alius, D. Dumitrescu, O.C. Voinea, M. Costache
*Department of Pathology, University Emergency Hospital Bucharest, Romania

Background & objectives: Ampullary adenocarcinoma is a rare gastrointestinal malignancy which may associate mismatch repair deficiency. Tumours harbouring MSI /dMMR can be caused by germline mutations or constitutional mismatch repair deficiency, such as MLH1 hypermetilation. Ampullary tumours can display intestinal or biliary phenotype.
Methods: We report the case of a 50-year-old male patient who developed an adenocarcinoma of the Vater ampulla, for which he underwent cephalic duodenopancreatectomy. Gross examination of the specimen revealed a 2 cm tumour mass centred within the ampulla, ulcerating the duodenal papilla and extending towards the duodenal wall. Invasion of the regional lymph nodes was not identified.
Results: Upon microscopic examination, we identified a malignant epithelial proliferation displaying cuboidal cells with pleomorphic nuclei, forming small glandular structures, encompassed by desmoplastic stroma. A biliary-type adenocarcinoma was suspected and ancillary studies were carried out. The neoplastic cells showed strong , diffuse MUC 1 expression and a CK7+/CK20+ immunophenotype. Expression of CDX2 and MUC5 AC was absent in the tumour proliferation. Thus, the histopathological diagnosis was confirmed. Wild-type p53 expression was also identified. Examination also disclosed mutant MLH1 and PSM2 phenotype, as expression was absent within the proliferated elements. Immunohistochemical analysis suggested a correlation between the examined lesion and Lynch syndrome and further molecular and genetic tests were recommended.
Conclusion: Ampullary adenocarcinoma with biliary phenotype is a rare malignancy with poor prognosis. Correlations between this malignancy and DNA mismatch repair genes and its incidence are incompletely studied. Researchers acknowledge that patients with MMRd carcinomas are prone to developing other colonic or extracolonic tumours throughout their lives, therefore the diagnosis should be dilligently established and complementary genetic analysis must pe performed. Although DNA mismatch associated tumours harbour complex genetic alterations, susceptibility to targeted therapy can improve the prognosis of the patients.

E-PS-24-033

Gastric duplication cyst with extensive heterotopic ossification

A.M. Colino Gallardo*, M.R. Bergillos Giménez, M. De la Torre Serrano, J. Vega González, A. García Egido, D. Hernández Martínez, M. de Hita Castillo, I. Lample Brusel, L. Ortega Medina, M.J. Fernández Aceñero
*Hospital Clinico San Carlos, Spain

Background & objectives: Gastrointestinal duplication cysts are rare congenital anomalies that can affect any segment of the digestive tract. Gastric duplication cysts account for 2%-8% of all duplications. We report a case with peculiar histopathological features.
Methods: A 34-year-old woman presented for surgical treatment of a pancreatic cyst diagnosed in the context of postpartum jaundice due to choledocholithiasis. An abdominal CT scan revealed a lobulated, homogeneous cystic lesion with peripheral calcifications measuring 7 cm in relation to the pancreatic tail. Fine needle aspiration cytology only retrieved mucinous content with no epithelium and surgical resection was decided.
Results: Surgery revealed a multinodular formation with a smooth-walled cystic cavity, yellowish gelatinous content, and a petrous cystic formation. Microscopic examination revealed a cyst wall lined by gastric mucosa from the body and antrum/pylorus, with cystic dilation of some glands and mild inflammatory infiltrate, and a well-developed muscular layer. The most peculiar finding was the presence of extensive foci of heterotopic ossification, that corresponded to the findings in the imaging techniques. Final diagnosis was gastric duplication cyst with heterotopic ossification foci.
Conclusion: Diagnosis of gastric duplications is primarily established in childhood and accurate reporting is based on the presence of connections to the stomach, outer layer of smooth muscle, and gastric lining mucosa. Differential diagnosis should include cystic lesions originating from the mesocolic compartment, liver and pancreas, as well as retroperitoneal or gastric proliferative processes.

E-PS-24-034

Exploring the role of "old" Alcian Blue as salvation stain for consistent reporting of intestinal metaplasia on gastric biopsies

A. Coman*, D. Cristea, R. Ionescu, L. Dragostin, C. Popp, L. Sticlaru, M. Cioplea, L. Nichita
*Department of Pathology, Colentina University Hospital, Bucharest, Romania

Background & objectives: Intestinal metaplasia is a precancerous lesion that appears in chronic atrophic gastritis. The aim of this study is to demonstrate that Alcian Blue at pH 2.5 can reduce interobserver differences at diagnosis, recommending this stain for routine use in gastropathology.
Methods: Two independent observers examined 113 gastric biopsies from the antral and the oxyntic region, stained with hematoxylin-eosin (HE) and Alcian Blue at pH 2.5. Intestinal metaplasia and gastric atrophy were assessed according to the OLGA/OLGIM staging system.
Results: On HE, the two observers had a concordance of 91% for cases graded with absent metaplasia, 33% for minimal metaplasia, 100% for intermediate metaplasia and 67% for severe metaplasia. The concordance obtained after analyzing the biopsies on Alcian Blue stain at pH 2.5 was 93% for absent metaplasia, 72.1% for minimal metaplasia, 75% for intermediate metaplasia and 100% for severe metaplasia. Alcian Blue proved to be a better stain when examining gastric biopsies with minimal or severe metaplasia reducing the differences between the two observers.
Conclusion: Routine use of Alcian Blue stain at pH 2.5 could have a meaningful impact on the diagnosis of intestinal metaplasia in patients with chronic gastritis and reduce interobserver confusion by decreasing the number of cases diagnosed with intermediate metaplasia and classifying them as either minimal or severe, thus raising the reliability of the diagnosis.

E-PS-24-035

Unmasking the mimic: irritable bowel syndrome vs. large bowel mastocytosis

A. Cozac-Szoke*, V. Palombo, M. Pizzi, G. Ilaria, D. Dumitrașcu, M. Rugge
*Pathology Department, Mures Clinical County Hospital; Pathophysiology Department, "George Emil Palade" University of Medicine, Pharmacy, Sciences and Technology, Targu Mures, Romania

Background & objectives: Due to its ambiguous clinical/endoscopic presentation and sometimes mild histological lesions, the diagnosis of gastrointestinal (GI) mastocytosis is challenging. Endoscopy may feature non-specific changes and detection of mast cell infiltrate relies on the extension/accuracy of biopsy sampling.
Methods: In a 42-year-old female patient, sustained diarrhea (without hematochezia) and unremarkable laboratory profile suggested the diagnosis of irritable bowel syndrome rather than microscopic colitis. Colonoscopy revealed a sessile mucosal lesion (1.2 centimeters) in

the left colon. Hematoxylin and eosin (H&E) histology of the biopsy samples showed a histiocytic-like infiltrate (1/15 samples), prompting immunohistology testing for mastocytes, followed by molecular testing.
Results: The biopsy sample (0.12 centimeters in size) microscopically included a focal mastocytic infiltrate with irregular margins, covering up to 20-25% of the biopsy specimen, restricted to the lamina propria, without architectural changes of surrounding crypts. Target cells exhibited mastocytic immunophenotype (i.e., unequivocal expression of CD117, CD25, and tryptase). Molecular testing revealed a somatic point mutation in the KIT 816V exon, establishing the conclusive diagnosis of colonic mastocytosis. The mandatory clinical and laboratory work-up to inquire about extra-intestinal mastocytosis involvement is ongoing.
Conclusion: "Primary" GI-mastocytosis may show mild endoscopy abnormalities and inconspicuous microscopic involvement. Like in microscopic colitis, reliable biopsy sampling is crucial for a histological diagnosis. Histological diagnosis relies on the expansion of the lamina propria by histiocytic-like cells, without significant architectural or inflammatory changes. Dedicated confirmatory immunohistochemistry is mandatory, along with molecular profiling. In the present case, the consistently applied biopsy protocol and the H&E-based diagnostic hypothesis were essential for the diagnosis.

E-PS-24-037
Healing process in small and large intestine occurs through MUC5AC expression and reveals gastric metaplasia differentiation
M. Cuatrecasas Freixas*, S. Lopez-Prades, M. Rodrigo, K. Saez de Gordoa, C. Fuster, L. Quing, N. De La Ossa, I. Archilla, E. Musulen
*Pathology department. Hospital Clinic. University of Barcelona. Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Spain

Background & objectives: Intestinal stem cells at the bottom of crypts sustain cell renewal of different cell types. Nevertheless, committed cells have lineage plasticity which enables efficient repair tissue damage. We aimed to assess the role of gastric metaplasia in intestinal epithelial regeneration.
Methods: We performed MUC5AC immunohistochemistry to 53 endoscopic surgical resections or biopsies from small and large bowel lesions containing mucosal regeneration of different aetiologies. We included 23 intestinal or colon ischaemic segments, some with hyperplastic-reparative epithelial regeneration, two colonic volvulus, 28 intestinal or colorectal ulcers, including granulation tissues from different causes, erosions on anastomotic stenosis or solitary rectal ulcers.
Results: MUC5AC was extensive or focally positive in 92.5% (49/53) of the ischemic lesions, ulcers, and erosions from the small bowel and colorectal mucosa. Among ulcers, two were solitary rectal ulcers, three graft-versus host disease-related, and two were infectious colitis. Surgical resections from large or small bowel ischaemia showed MUC5AC expression on the regenerative epithelium or on focal intestinal villi. Half of the polypoid granulation tissues had little epithelium left on the surface and were negative for MUC5AC. Colonic volvulus also showed expression on hyperplastic-regenerative epithelium.
Conclusion: Our results show that gastric metaplasia is present in small and large bowel epithelial healing-regeneration from multiple different aetiologies, suggesting a gut epithelial lineage plasticity of committed cells, which enables an efficient repair tissue damage. This mechanism has also been demonstrated in other settings, such as small and large bowel epithelial regeneration of inflammatory bowel disease lesions.

E-PS-24-038
Anatomical and epidemiological aspects of digestive neuroendocrine tumours - retrospective study 2012 to 2023
C. Dabaj*, O. Ouhssain, S. Benbiba, H. Rais
*University Hospital Mohammed IV, Morocco

Background & objectives: Digestive neuroendocrine tumours (NETs) represent a heterogeneous group of tumours that develop at the expense of cells of the diffuse endocrine system and have common characteristics. Objective: Evaluate the epidemiological profile and the anatomical pathological aspects of NETs.
Methods: This is a retrospective study spread from January 2012 to December 2023, including all patients with a neuroendocrine tumour of digestive location. This work focuses on 22 patients with digestive NETs diagnosed. Study parameters were collected from pathological and immunohistochemistry reports. An operating sheet has been produced to facilitate collection and analysis while respecting the anonymity of patients.
Results: The average age was 55 years. A slight female predominance was noted with a sex ratio of 0.4. The clinical presentation was dominated by non-specific digestive symptoms (abdominal pain of patients, AEG, vomiting), carcinoid syndrome was found in some patients. 81% of these tumours were well differentiated and 19% were poorly differentiated carcinomas, 52.4% were classified as grade 1, 28.6% were grade 2, and the rest were grade 3. The most common location was appendix (28.6%) and small intestine (23.8%), followed by the liver (19%).
Conclusion: Although GI-NENs have similar histological features, microscopic and immunophenotypic features need to be considered in different anatomical sites. The diagnostic accuracy of the classification system is limited by intratumoural heterogeneity, especially in biopsies. For accurate classification and pathological diagnosis, it is crucial to carefully evaluate anti-Ki-67 antibody labeling, identify areas of highest mitotic density for mitotic counting, and recognize histological features of GI-NENs. However, despite advances in investigation and treatment. The diagnosis of digestive NETs is still often delayed.

E-PS-24-039
A series of 13 cases of mesenchymal tumours of the appendix
A.S. De Oliveira Gomes*, A. Pasco Peña, H. Galindo Guzman, E. Carracedo Vega, M. García Martos, Á. Panizo Santos
*Hospital Universitar0o de Navarra, Spain

Background & objectives: The literature on appendix pathology is dominated by infectious causes and malignant neoplasms. In this review we will focus on the study of 13 cases of benign mesenchymal tumours, and some with malignant potential, comparing clinical and histopathological aspects.
Methods: Retrospective review of 13 appendectomy specimens with mesenchymal tumours from the last 26 years (1998-2024) from two university hospitals in Spain.
Results: The average patient age was 59 years with a predominance of women (69%), as findings: 5 neuromas (12%) as the most frequent tumour in our series, followed by 3 gastrointestinal tract tumours (7%), two of them as an incidental finding in right hemicolectomy specimens associated with colon adenocarcinoma, one of which was also associated with a second appendicular neoplasia: Diffuse mucinous hyperplasia. The rest of the mesenchymal tumours found incidentally in appendectomy specimens in the clinical context of acute appendicitis were: Leiomyoma, diffuse ganglioneuromatosis and granular cell tumour.
Conclusion: Mesenchymal tumours of the appendix are usually smooth muscle type, usually leiomyomas, rarely non-myogenic neoplasms occur, such as neural tumours, gastrointestinal stromal tumour, granular cell tumour, vascular tumours and other neoplasms. In our cases series, the most frequent tumour, however, was neuroma (n: 5) all of them in the context of acute appendicitis, followed by gastrointestinal stromal tumours in different contexts and associated or not with other tumours, but all as an incidental finding.

E-PS-24-040
And it was all yellow
M. De Uribe Viloria*, S. Quinones, P. Adolewska, J. Fisac Vázquez, L. G-Pastrián
*La Paz University Hospital, Spain

Background & objectives: Tangier disease is a rare autosomal recessive genetic disorder of lipid metabolism, characterized by severe deficiency of plasma HDL cholesterol and accumulation of cholesteryl ester in macrophages. Herein we describe the colonoscopic and histologic findings of such an entity.
Methods: We reviewed our files from 2014 to March 2024 and encountered a single case of Tangier disease. The diagnosis was achieved by using Hematoxylin-Eosin, histochemical and immunohistochemical studies. From the clinical history we obtained the age at diagnosis, symptomatology and endoscopy studies.
Results: A 65-year-old woman, presented with positive fecal occult blood in a screening test. Colonoscopy revealed a pale yellowish colonic mucosa and sessile lesions with similar specks. Histological analysis showed a dense infiltrate of foamy macrophages with xantomized, pale microvesicular cytoplasm within the lamina propria and submucosa in both otherwise normal colonic mucosa and also among conventional and sessile serrated adenomas. These cells were diffusely positive for CD68 while PAS- diastase and Job-fite were negative. After thorough review of clinical records, a Tangier disease diagnosis was found, 15 years earlier in a different institution. Bloodwork showed 5 mg/dL HDL-cholesterol, 55 mg/dL LDL- cholesterol, 97 mg/dL total cholesterol and 191 mg/dL triglycerides.
Conclusion: Tangier disease is an extremely rare autosomal recessive disease of cholesterol metabolism, leading to its deposit in many organs, such as tonsils, liver, gastrointestinal tract and Schwann cells. Major clinical manifestations include premature atherosclerosis, so patients are in need of close follow up of cardiovascular risk factors. Though gastrointestinal involvement is rare and easily missed, it may be the first clue for the diagnosis.

E-PS-24-041
Visceral miopathy and myopathic chronic intestinal pseudo-obstruction, an unusual gastrointestinal motility disorder
E. Del Valle Sánchez*, J.S. Castillo Malla, J. Medrano Ruiz, L. Ollero Domenche
*Hospital Universitario Miguel Servet, Spain

Background & objectives: Visceral myopathy (VM) is a rare disorder causing dysfunction by alteration of smooth muscle integrity throughout gastrointestinal tract, uterus, and urinary tract. Intestinal symptoms manifest as a clinical condition known as myopathic chronic intestinal pseudo-obstruction (mCIPO).
Methods: Ten-year-old male suffering from abdominal pain and constipation for nine months was admitted for unresponsive symptoms. CT scan revealed gastrointestinal dilation and colon caliber change. Surgery confirmed severe bowel distension without obstruction, requiring emptying. Rectal biopsies excluded Hirschsprung's disease. A month later, he presented with abdominal pain and hypotension, leading to an ileostomy. Tissue samples were sent for pathological evaluation.
Results: Microscopic examination of the ileum revealed marked vacuolar degeneration of myocytes within the muscularis propria, and to a lesser extent, within the muscularis mucosa, accompanied by myocyte loss and fibrosis of the external longitudinal layer. Rounded, pale eosinophilic intracytoplasmic inclusions were observed, staining purplish-red with Masson stain and testing negative with PAS. Weak positive immunostaining with desmin was observed, while negative immunostaining was noted with h-caldesmon and smooth muscle actin. Myenteric and submucosal plexuses were intact, and no associated inflammatory component was identified. Based on clinical, radiological, and histological findings, the diagnosis of VM was established, genetic study pending.
Conclusion: Pathogenic mechanism of VM/mCIPO remains unclear, but it is most commonly associated with mutations in contractile apparatus cytoskeletal proteins, ACTG2 being the most frequent genetic alteration. Histological study reveals intestinal myopathic changes in approximately 50% of cases. However, these histopathological findings do not impact management unless there is an inflammatory infiltrate within the muscle layer (inflammatory or immune-mediated leiomyopathy), in which case immunosuppressive therapy may be considered.

E-PS-24-042
Mesenteric inflammatory veno-occlusive disease: a case report
T.S. Driva*, F. Stavratis, S. Valsami, D. Dimitroulis, S. Sakellariou
*First Department of Pathology, Medical School, National and Kapodistrian University of Athens, Greece

Background & objectives: Mesenteric inflammatory veno-occlusive disease (MIVOD), defined as inflammation of the mesenteric veins without arterial involvement, is a rare cause of intestinal ischemia. Diagnosis is based only on histological examination after surgical resection. A histologically typical case of MIVOD is described.
Methods: A 53-year-old man with a medical history of portal and splenic vein thrombosis presented with abdominal discomfort, bloody diarrhoea and fever. Virological, immunological and thrombophilia testing was negative while CT showed pronounced thickening of the intestinal wall and luminal stenosis of the left colon and rectum. Due to suspected intestinal ischemia, a subtotal colectomy including the terminal ileum was performed.
Results: Histological examination revealed severe venous congestion and changes of ischemic necrosis along the left colon. Thickened intra- and extramural colonic and ileal veins showed obstructive alterations including myointimal hyperplasia, wall elastosis and capillarization. Large extramural veins were often occluded by thrombi in various stages of organisation. A limited number of submucosal veins exhibited inflammatory changes mostly characterised by peri- and intravascular lymphohistiocytic infiltration, disarray of the tunica media, up to complete lumen extinction and occasionally segmental necrosis and fibrin deposition. All arterial branches were intact.
Conclusion: Histological findings of intestinal ischemia require meticulous studying of the enteric vasculature. In our case, distinct lesions of the mesenteric veins combined with negative workup for thrombophilia and other hypercoagulability-related disorders support the diagnosis of MIVOD as the cause of intestinal ischemia and thrombotic occlusion of large extramural veins. Considering our patient's history of portal and splenic vein thrombosis, a more complex entity regarding the underlying pathogenetic background cannot be excluded.

E-PS-24-043
Histopathology of Meckel's diverticulum – a single centre report
M. Đuknić*, M. Backović, J. Jevtić, A. Mehmedovic, S. Sinđić Antunović, S. Radulović, M. Jovanović, S. Glumac, R. Jankovic
*University of Belgrade, Faculty of Medicine, Institute of Pathology, Serbia

Background & objectives: The Meckel's diverticulum is a remnant of the omphalomesenteric canal, mostly asymptomatic, but with potential to produce symptoms due to heterotopia. This study aims to determine the incidence and the histology of the Meckel's diverticulum in the paediatric age.
Methods: All cases of Meckel's diverticulum (136) operated at the University Children's Hospital, Belgrade in the period from January 1, 2002, to December 31, 2022. were reviewed using pathology reports from the files of the Institute of Pathology.
Results: The majority of patients was male (72%). The median age was 8 years (1 day – 17.5 years). Clinical manifestations were observed in 62.5% of patients. The most common symptoms were: abdominal pain, nausea, vomiting, and melena. Associated anomalies were found in 15.5% of patients, with hernias being the most prevalent. Heterotopic tissue was found in 50% of diverticulum, more common in males. Gastric mucosa was found alone or accompanied

with pancreatic tissue in 40.5% and 5.1%, respectively. Pancreatic heterotopia alone was diagnosed in 4.4% diverticulum. Complications occurred in 45.5% of patients, the most common in background of heterotopia. The median length of the diverticulum was 3cm (0.3-7.5 cm).
Conclusion: Pancreatic and gastric heterotopia in Meckel's diverticulum are present in half of the cases. The vast majority of complications are associated with the presence of heterotopic tissue.

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E-PS-24-044
Kissing tumours: when a metastatic ovary lesion meets an adenocarcinoma of the colon – a rare case of two malignant collision tumours
A. Dumitru*, A. Bejenariu, C. Alius, D. Dumitrescu, D. Tapoi, A.M. Ciongariu
*Department of Pathology, University Emergency Hospital Bucharest, Romania

Background & objectives: Collision tumours are entities where two independent neoplasms coexists in the same organ, each having distinctive borders and different histological and immunohistochemical characteristics. Different neoplasms could exist in the same organ, any combination of benign and malignant tumours being possible
Methods: We report a case of a 75 year-old woman who presented to our hospital with abdominal pain and bowel obstruction. CT scans revealed diffuse stenosis of the sigmoid colon with proximally distended colon, not being able to appreciate the integrity of the ovaries. Emergency Hartmann colectomy and left ovarectomy were performed, followed by histopathological and immunohistochemical assessment
Results: Microscopic examination revealed two colonic lesions consisting of malignant epithelial proliferations: the primary one showing glandular differentiation and the secondary one consisting of large cells with papillary and solid architecture with psammoma bodies. The left ovary presented a tumour mass with the same microscopic features as the secondary tumour. Thus the diagnosis of collision tumours represented by colonic adenocarcinoma and high grade serous ovarian carcinoma was established. Upon immunohistochemical analysis the tumour cells of the primary lesion showed intense diffuse positive CDX2 and CK20 and negative CK7 staining, revealing the colonic origin of the proliferation. The secondary lesion demonstrated intense positive PAX8, p16, ER and CK7, while CK20 was negative.
Conclusion: Despite the fact that colonic adenocarcinoma and high grade serous ovarian carcinoma are two of the most common malignancies of the colon and ovary, diagnosing both tumours simultaneously at the same patient is extremely rare. Collision tumours were described in many organs, but in most cases there is an association between a malignant and a benign tumour. The case we presented represents an incredibly rare association of two different malignant lesions incidentally discovered in an emergency presentation.

E-PS-24-045
Primary angiosarcoma of the small intestine in a young immunocompetent patient - a very rare tumour in an extremely rare site
A. Dumitru*, A.M. Ciongariu, D. Tapoi, D. Dumitrescu, C. Alius
*Department of Pathology, University Emergency Hospital Bucharest, Romania

Background & objectives: Primary small bowel angiosarcomas are exceedingly rare neoplasms with unspecific symptomatology which may lead to a delay in the diagnosis and consequently a worst prognosis.
Methods: We report a case of a 20-year-old woman who presented to the emergency room of our hospital with abdominal pain and bowel obstruction. CT scans revealed diffuse stenosis of the terminal ileum. Emergency segmental enterectomy was performed followed by histopathological and immunohistochemical assessment.
Results: Microscopic examination revealed a high-grade sarcomatous proliferation that invades the entire thickness of the intestinal wall. The tumour consisted of spindle cells with numerous atypical mitoses. Spindle shaped and epithelioid malignant cells with enlarged pleomorphic and hyperchromatic nuclei with speckled chromatin pattern were seen. The tumour was highly vascularized with numerous irregularly shaped blood vessels and haemorrhagic areas. Foci of tissue necrosis were present. Upon immunohistochemical analysis the tumour cells showed intense diffuse positivity for CD31 and ERG and negative staining for DOG1, CD117 and HHV8. Ki67 immunostain showed high cell proliferative activity throughout the tumour.
Conclusion: Angiosarcoma of the small bowel is an aggressive and very rare entity with poor prognosis. The occurrence of these types of tumours is extremely rare in young and immunocompetent individuals. The case we presented represents an incredibly rare tumour incidentally discovered in an emergency presentation

E-PS-24-046
Evaluating MATR3 as a prognostic marker in colorectal cancer
J. Durślewicz*, Ł. Szylberg, D. Grzanka
*Department of Clinical Pathomorphology, Faculty of Medicine, Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Torun, Bydgoszcz, Poland; Department of Tumour Pathology and Pathomorphology, Oncology Centre-Prof. Franciszek Łukaszczyk Memorial Hospital, Bydgoszcz, Poland

Background & objectives: This study investigates MATR3, a nuclear matrix protein, as a potential prognostic marker in colorectal cancer (CRC). It aims to elucidate its effects on the disease's progression, invasion, and metastasis, thereby contributing to enhanced patient management strategies.
Methods: This study analysed tissues from two CRC patient cohorts. Immunohistochemical staining used an anti-MATR3 antibody with the BenchMark® ULTRA system and quantification followed the H-score protocol. MATR3 gene expression was evaluated using data from The Cancer Genome Atlas (TCGA). Complementary studies included Western blot and quantitative PCR analyses on CRC cell lines: SW620, SW480, and CCD 841 CoN.
Results: Immunoreactivity of MATR3 was primarily localized to the nuclei in both malignant and non-malignant cells. Notably, MATR3 levels were significantly higher in CRC tissues compared to adjacent normal colon tissues across both derivation and validation cohorts. Analysis of the association between MATR3 protein expression and overall survival (OS) in CRC patients was conducted using Kaplan-Meier survival curves and log-rank tests. The results indicated a strong correlation: patients whose CRC tumours showed elevated MATR3 protein levels had significantly shorter OS compared to those with lower levels. Further examination of the TCGA cohort confirmed these findings, demonstrating a significant link between high MATR3 expression and reduced OS.
Conclusion: This study confirms MATR3 as a critical prognostic marker in CRC, with its elevated expression in CRC tissues strongly associated with decreased OS. Analysis from both patient cohorts, supported by TCGA data, indicates that high MATR3 levels correlate with a poorer prognosis. This underscores its significant role in CRC progression and highlights its potential as a target for enhancing therapeutic strategies.

E-PS-24-047
Subserosal pseudo-signet-ring cells: a diagnostic pitfall
S.K. Dursun*, H. İzol Özmen, H. Karatay
*Basaksehir Cam ve Sakura City Hospital, Department of Pathology, Turkey

Background & objectives: Signet-ring cell change is a rare pseudoneoplastic phenomenon in non-epithelial cells. We report a case involving subserosal adipocytes in the ileum, incidentally identified during resection for the ileus, expanding the spectrum of this phenomenon beyond epithelial cells.
Methods: A 54-year-old male with peritoneal catheterization and a 10-year history of chronic renal failure presented with weight loss, abdominal pain, and constipation. Computed tomography (CT) scan revealed acute intestinal obstruction, necessitating urgent surgery. Ileal torsion-related ileus was detected, prompting resection of the affected ileum. Two weeks later, severe abdominal pain necessitated subsequent surgery for suspected perforation, resulting in an ileostomy.
Results: Histomorphological evaluation revealed subserosal fibrosis and hyalinization accompanied by signet-ring cell morphology in the subserosa, mimicking signet-ring cell carcinoma invasion. However, no infiltration into other layers was observed. Cytologically, these cells appeared bland with open chromatin. Ileostomy-related skin tissue exhibited involutional changes in periadnexal and perivascular fat with small lipocytes displaying signet-ring cell morphology. Immunohistochemical analysis supported the diagnosis of atrophy-related pseudo-signet-ring cell appearance of adipocytes, indicating a non-neoplastic condition.
Observing atrophic morphology both in skin and ileum material, alongside CT scan findings of low intra-abdominal fat planes, suggests the patient may have this condition related to cachexia, localized trauma from long-term peritoneal catheterization, or an acquired generalized lipodystrophy disorder.
Conclusion: Subserosal signet-ring cell morphology can mimic carcinoma infiltration, emphasizing the importance of distinguishing them. Histomorphological patterns and immune profiles aid in differentiation, which is crucial for precise diagnosis, particularly in small biopsy specimens and frozen sections. Awareness of this entity is essential for avoiding misclassification, thereby influencing patient management and prognosis.

E-PS-24-048
Extensive lipomatosis of the small bowel revealed by intestinal infarction: a case report
N. Ellouze*, A. Bellalah, S. Mabrouk, S. Ben Hammouda, M.M. Hamzaoui, L. Njim, A. Zakhama, M. Njima
*Tunisia

Background & objectives: Lipogenic tumours of the gastrointestinal tract are uncommon. Extensive lipomatosis occurring in the small bowel is infrequent with fewer than 60 reported cases. Herein, we report a case of extensive lipomatosis of the small bowel revealed by intestinal infarction.
Methods: We describe a case of extensive lipomatosis of the small bowel in a 50-year-old woman who presented to the Emergency Department with abdominal pain, nausea and vomiting. The physical examination found an irreducible umbilical eventration and a small epigastric reducible hernia. Therefore, an emergency laparotomy was performed.
Results: The intraoperative findings showed a well-preserved 6 cm mesentery incarceration in the hernial sac. Further exploration of the abdominal cavity showed a thickened ileal portion with multiple large mesenteric nodules. This segment had a doubtful vitality. Indeed, a 132cm-long ileal resection with a double-barreled stoma was then performed. Macroscopic examination showed a dilated ileal segment. The mucosa was grey and protuberant with a fatty appearance. Histopathology showed a diffuse proliferation of mature fat cells within the submucosa and subserosa. The mucosa displayed signs of acute and chronic ischemia with focal necrosis, neutrophil infiltrate and hemorrhage extending to sub-mucosa. The diagnosis of intestinal lipomatosis was done.
Conclusion: Intestinal lipomatosis is quite rare. Most frequent complications of intestinal lipomatosis are perforation and volvulus. Acute intestinal infraction is exceptional. Infraction may be due to chronic extrinsic vascular compression by the lipomatous tumour. It should be distinguished from other relatively frequent lipomatous tumour such as liposarcoma and lipoblastoma. The treatment approach of intestinal lipomatosis should be non invasive if the patient is asymptomatic, but a follow-up is required. However, in case of complications, surgical intervention becomes necessary.

E-PS-24-049
Immunohistochemical study of microsatellite instability in colorectal adenocarcinoma: profile of 63 cases from southern Tunisia
N. Ellouze*, M. Triki, S. Makni, L. Bouzidi, R. Kallel, T. Sallemi, M. Bouhamed
*Tunisia

Background & objectives: Microsatellite system deficiency (MMR) is an important mechanism in the carcinogenesis of colorectal cancers (CRC). Microsatellite deficiency represents a carcinogenic pathway responsible for around 15% of CRC. The aim of our study is to investigate the microsatellite profile of CRC.
Methods: This is a retrospective, descriptive and analytical study that included patients with CRC collected at the department of Pathology of the Habib Bourguiba University Hospital in Sfax over a 3-year period (2019-2021). An immunohistochemical (IHC) study of MMR system proteins (MSH2, MSH6, MLH1 and PMS2) was carried out on blocks of previously selected tumours.
Results: The mean age of the patients was 59.1 years (13-83). There were 41 men (65.1%) and 22 women (34.9%), with a sex ratio of 1.86. Most cases were located in the left colon (25 cases; 39.7%), followed by the rectum (20 cases; 31.7%), then the right colon (18 cases; 28.6%). Our study showed an MMR-D status in 13 cases (20.6%) and a tumour with MMR-P status in 50 cases (79.4%). Our results were a joint loss of MLH1/PMS2 in 6 cases (46.2%), a joint loss of MSH6/MSH2 in 3 cases (23%), an isolated loss of PMS2 in 2 cases (15.4%) and an isolated loss of MSH6 in 2 cases (15.4%).
Conclusion: It seems now advisable to look for MMR protein expression in CRC. It enables us to identify less aggressive tumours and avoid sometimes toxic treatments, notably 5 Fluorouracil. It also opens the way to new therapeutic perspectives, notably immunotherapy with PDL1 inhibitors.

E-PS-24-050
Appendiceal high-grade mucinous neoplasia: a case report
V. Escobedo*, A.B. Moreno García, F.I. Aguirre Neira, D. Suárez Gómez, F. Alberto, S. Melgar Rivera
*Hospital Universitario Tauli, Spain

Background & objectives: High-grade appendiceal mucinous neoplasia (HAMN) is a rare entity, more common in women, in the sixth decade, presenting frequently as acute appendicitis and its differential diagnosis includes appendiceal mucinous neoplasms (serrated lesions, low-grade appendiceal mucinous neoplasm (LAMN) and mucinous adenocarcinoma).
Methods: A 57-year-old woman with hypertension, asthmatic bronchitis, with no previous surgical interventions, who initially presented with acute abdominal pain in the right lower flank with localized defense. The abdominal ultrasound examination showed an enlarged cecal appendix, thickened walls, with periappendicular fat involvement, and it was decided to perform a laparoscopic appendectomy.
Results: Histologically, glandular proliferation with high-grade cytologic features with nuclear stratification, enlarged pleomorphic and hyperchromatic nuclei, loss of nuclear polarity, moderate fibrosis of the submucosa, push invasion, absence of infiltration, occasional mitotic

figures, presence of apical mucin as evidenced by Mucicarmine histochemical technique and MUC 2 immunohistochemical technique, and acellular mucin dissecting periappendicular fat.
Conclusion: Few cases of HAMN, associated or not with extraappendiceal mucin, have been published. The diagnostic challenge is determined by the complexity of differentiating it from LAMN characterized histologically by low-grade cytologic atypia, and from mucinous adenocarcinoma characterized by the presence of angulated small glandular structures, wall infiltration invasion and desmoplastic stroma, not observed of HAMN and help to differentiate it from a true infiltrative component. The importance of histopathological and/or molecular classification is fundamental for a correct diagnosis and treatment.

E-PS-24-051
Mucinous adenocarcinoma arising from retrorectal cystic hamartoma - case report
T. Fadljević*, D. Fučkar Čupić, A. Dekanić, L. Kovač
*Clinical Hospital Center Rijeka, Croatia

Background & objectives: Retrorectal cystic hamartoma (RCH) or tailgut cyst is a rare developmental anomaly of the presacral space. Patients are usually asymptomatic middle-aged women. It is mostly benign, but malignant transformation is possible, usually in the form of adenocarcinoma or carcinoid.
Methods: We present a case of a 62-year-old woman referred for assessment due to recurrence of a cyst above the rectum, first diagnosed as retroperitoneal cyst in 1995. and monitored since. The cyst was resected in fragments in 1998 and pathohistologically diagnosed as pseudocyst. Due to recurrence and elevated CEA, it was resected in fragments again in 2022.
Results: We received soft tissue fragments that on cut surface had multilocular mucinous cysts. Sections identified fragments of smooth muscle and connective tissue without neural plexi, and cystic spaces focally lined by mucinous epithelium, diagnosing RCH. Disease recurred again and the cyst was resected in fragments. Gross and histological analysis was the same as in previous biopsy, except for dissecting mucinous pools containing signet ring cell and atypical glands lined by atypical mucinous epithelium, with no perineural or vascular invasion. Tumour was positive for CK20, CDX2 with Ki67 up to 80%, confirming the intestinal differentiation of mucinous adenocarcinoma with signet ring cell component originating from RCH.
Conclusion: This case represents an entity of RCH with malignant transformation to mucinous adenocarcinoma, which is described in few cases. Diagnosis of RCH is a challenge which can only be established by pathohistological examination. In our patient every surgery resulted in fragmented resection of the lesion which could explain multiple recurrences. Complete surgical resection with adequate margins is considered curative treatment which prevents malignant transformation of RCH.

E-PS-24-052
Giant cells in gastric cancer: only bystanders or main actors? Report of two cases with emphasis on phenotypical and molecular biology findings
C. Fattorini*, F. Petrelli, L. Malaspina, L. Spagnoli, M. Palmeri, A. Giusti, A. Cavazzana, M. Arganini, A. Amorosi, M.R. Ambrosio
*Pathology Unit, Azienda Usl Toscana Nord Ovest, Italy

Background & objectives: Non neoplastic multinucleated osteoclast-like giant cells (OGCs) have been described in various tumours. In gastric cancer (GC) no satisfactory knowledge about their biological and prognostic significance has been obtained. Here we report two cases of poorly differentiated GC with OGCs.
Methods: We performed a detailed phenotypical characterization of both neoplastic and OGCs components with various immunoistochemical stains including epithelial markers (Cytokeratins), mesenchymal markers (Vimentin, ZEB1), cell-to-cell adhesion markers (beta-Catenin, E-Cadherin) and macrophages associated markers (TRAP, CD163/CD68 cocktail). Moreover, next generation sequencing (NGS) analysis of both OGCs and cancer cells was obtained by using laser capture microdissection.
Results: Immunohistochemical study revealed a monocytic phenotype for OGCs in both cases, supporting a non-neoplastic origin of these cells; the CD68+/CD163+/Cytokeratins- phenotype also indicate that this population belongs to M2-like Tumour Associated Macrophages (TAM), believed to exert a protumoural role. Moreover, expression of ZEB1 and Vimentin, and loss of E-Cadherin in cancer cells was found, indicating an aberrant activation of epithelial-to-mesenchimal transition (EMT). Separate molecular analysis of neoplastic and OGCs components highlighted some shared mutations involving APC, TP53, VHL and KRAS genes. NGS also put in evidence STK11, GNA11 and HNF1A genes mutations solely belonging to OGCs and numerous oncogenes and tumour suppressor genes mutations involving cancer cells only.
Conclusion: Our immunohistochemical findings support a M2-like TAM phenotype for OGCs, exerting a protumoural effect, and an overall EMT activation in the tumoural compartment, thus partially explaining the poor prognosis associated with these neoplasia. However, some open questions remain regarding OGCs biology: molecular analysis found some shared mutations between the two compartments. Further investigations are needed to clearly define the nature and prognostic significance of OGCs and the dynamic interaction between them and neoplastic cells in GC.

E-PS-24-053
Neuroendocrine differentiation in conventional gastric adenoma: case report and molecular analysis of an underdiagnosed entity
C. Fattorini*, F. Petrelli, G. Finucci, A. Giusti, A. Cavazzana, M.R. Ambrosio
*Pathology Unit, Azienda Usl Toscana Nord Ovest, Italy

Background & objectives: Neuroendocrine differentiation is a rare phenomenon that affects both neoplastic and preneoplastic lesions of the stomach. Its molecular origin and clinical significance is not yet fully known. Here we are presenting a case of gastric intestinal-type adenoma with neuroendocrine phenotype.
Methods: We performed detailed immunoistochemical study of the lesion testing Cytokeratins, neuroendocrine markers (Chromogranin A, Synaptophysin, INSM1), mismatch repair proteins (MSH2, MSH6, MLH1, PMS2) and cell-to-cell adhesion markers (beta-Catenin and E-Cadherin). Moreover, via microdissection we were able to separate the exocrine and neuroendocrine components of the adenoma and to analyse the presence of somatic mutations with next generation sequencing (NGS) technology.
Results: Immunostains for Chromogranin A, Synaptophysin and INSM1 highlighted large adenoma areas of neuroendocrine differentiation despite having a classic intestinal-type morphology, thus resulting in an "amphicrine" phenotype. Furthermore, both exocrine and neuroendocrine components showed a strong nuclear and cytoplasmic positivity for beta-Catenin and a partial weak and incomplete membrane staining for E-Cadherin, consistent with an altered Wnt/beta-Catenin pathway. Finally, diffuse positivity for mismatch repair proteins supports a microsatellite stable profile of the lesion. Molecular characterization of the amphicrine component highlighted the presence of FGFR3 gene missense variant; the exocrine part also carried a FGFR3 gene mutation together with RET and ERBB2 genes alterations.
Conclusion: The presence of an altered Wnt/beta-Catenin pathway and of mutations involving FGFR3 gene in both components together with the lack of specific mutations carried by neuroendocrine cells seems to suggest that cells with neuroendocrine phenotype and exocrine cells

are genetically related, thus having a monoclonal origin. Further studies are needed to fully elucidate the origin of these rare lesions and to evaluate the influence of the neuroendocrine phenotype on the clinical behaviour of gastric adenomas.

E-PS-24-054

Sarcina ventriculi: the importance of morphology in absence of distinct symptoms

N. Franco*, S. García-Fuertes, D. González-Suárez, J. Ros-Giménez, N. Sanz-Pérez, E. Ponce Casas, R. Vilorio
*Hospital Ernest Lluch, Spain

Background & objectives: Sarcina ventriculi, an uncommon gram-positive coccus rarely seen in the upper gastrointestinal tract, can be easily identified by its characteristic morphological features. Recognition is prior because it is associated with severe complications such as emphysematous gastritis and gastric perforation.
Methods: We present the case of a 26-year-old man with no relevant history, who starts with vomiting and epigastric pain associated with constitutional symptoms and significant weight loss in the last six months. A CT performed showed duodenal thickening, confirmed by endoscopic examination, as well as serpinginous ulcers located at cardia, gastric antrum and duodenum. Multiple biopsies were taken.
Results: Histological examination of all biopsies received, revealed marked acute inflammation with ulcer bed formation and the presence of cuboid shape structures, with tetrad arrangement and basophilic staining. They showed red blood cell-size and flattened cell walls, and were concordant with a type of microorganism, in particular Sarcina ventriculi. Based on these findings, easily identified on routine hematoxylin and eosin stain with no other ancillary studies needed, and given the clinical symptoms and imaging studies, we could establish the diagnosis.
Conclusion: Although the pathogenicity of Sarcina is unclear, histopathologic examination of classic morphological features is the key to accurate diagnosis. Given that there are no consistently associated histologic characteristics in gastrointestinal mucosa, a high level of suspicion is necessary, particularly when examining gastric biopsies from patients with a history of gastrointestinal surgery or delayed gastric emptying. Treatment in symptomatic patients may prevent severe complications such as ulcers and peritonitis, among others.

E-PS-24-055

Cadherin-17 expression in colorectal adenoma and adenocarcinoma

I. Franin*, N. Baršić, B. Krušlin, K. Barišić, N. Ljubičić, A. Demirović
*Department of Pathology and Cytology, Sestre Milosrdnice University Hospital Center, Zagreb, Croatia

Background & objectives: Expression of Cadherin-17 (CDH17) is known in colorectal adenocarcinomas and epithelium. Sparse data are available on CDH17 expression in colorectal adenomas. Identifying CDH17 with blood immunoassays is described as possibility for adenoma detection. We investigated imunohistochemical CDH17 expression in adenomas.
Methods: We evaluated immunohistochemical expression of CDH17 on a paraffin embedded tissue blocks of colorectal adenoma and colorectal adenocarcinoma in a cohort of 93 patient using primary monoclonal antibody (Invitrogen, clone 7D10E1, 1:400, pH9). Staining was scored as follows: 0 (no staining); 1+ (< 25% positive cells); 2+ (25–50% positive cells); 3+ (>50-75% positive cells); and 4+ (>75% positive cells).
Results: The study included 93 patients, 35 with colorectal adenoma and 58 with colorectal adenocarcinoma. The average age was 76.5 years, ranging from 42 to 92 years. Among the 35 colorectal adenomas, there were 5 tubular adenomas with low-grade dysplasia, 14 tubular adenomas with high-grade dysplasia, 1 tubulovillous adenoma with low-grade dysplasia, 13 tubulovillous adenomas with high-grade dysplasia, 1 traditional serrated adenoma, and 1 mixed type adenoma. All cases of adenomas were positive for CDH17 with more than 75% positive cells. Also, all cases of colorectal adenocarcinoma showed positive reaction for CDH17 with more than 75% positive cells.
Conclusion: Our study revealed positive immunohistochemical reaction for CDH17 in all cases of adenomas, that was not previously described in literature. Additionally, positive reaction in adenocarcinoma cohort confirmed previously published data. A positive finding of CDH17 in adenomas and better understanding of CDH17 expression in colorectal adenomas could possibly improve the surveillance and detection of high-risk individuals. Further multidisciplinary studies are needed to clarify these possible benefits, for example comparing immunohistochemical analysis with results of detecting CDH17 from blood with immunoassay.

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E-PS-24-056

Peutz-Jeghers Syndrome - case report and a literature review

M. Gabeshia*, M. Jikurashvili
*CSD-Georgia, Georgia

Background & objectives: Peutz-Jeghers syndrome presents with characteristic gastrointestinal polyps and mucocutaneous pigmentation. It's inherited in an autosomal dominant manner and is caused by a mutation in the STK11 gene. Individuals with PJS are at increased risk for a wide variety of malignancies.
Methods: We report a case of a young male in his second decade with multiple gastrointestinal polyps necessitating emergency surgery due to intestinal obstruction. Histopathological analysis of the excised specimen from both small and large intestine fragments revealed numerous polyps obstructing the lumen. We actively sought clinical information, including medical and family history, to facilitate accurate diagnosis.
Results: Histopathological examination (H&E sections) revealed polyps with a distinctive papillary villous architecture. These polyps were characterized by a tree-like arborization of compact smooth muscle bundles, accompanied by relatively normal overlying epithelium showing glandular dilation and distortion. No secondary ulceration or erosion was observed. Notably, one of the polyps located in the small intestine exhibited pseudoinvasion in the submucosal layer. Consistent with the patient's medical history, mucocutaneous dark blue to dark brown macules were observed around the mouth and eyes, alongside hyperpigmentation noted on the fingers.
Conclusion: Peutz-Jeghers syndrome remains a rare yet significant disorder characterized by hamartomatous polyps, mucocutaneous pigmentation, and an increased risk of gastrointestinal and extraintestinal malignancies. Early recognition and multidisciplinary management are essential for optimizing patient outcomes and minimizing associated morbidity and mortality. By fostering collaboration among clinicians, pathologists, geneticists, we can continue to enhance our knowledge of this complex syndrome and improve patient care.

E-PS-24-057

Intestinal lipomatosis: a case series of an underdiagnosed entity

H. Galindo Guzman*, B.B. Ardaya Lopez, M. García Martos
*Hospital General Universitario Gregorio Marañón, Spain

Background & objectives: Intestinal lipomatosis is a rare entity that affects the intestinal submucosa. When diagnosed, this is usually a finding accompanying other pathologies. Due to their infrequency,

we present a series of 10 cases diagnosed in our service between 2020 and 2024.
Methods: A retrospective, descriptive study was carried out based on a clinical review of all patients undergoing gastrointestinal surgery and diagnosed by pathological anatomy as lipomatosis between the periods 2020 to 2024. 10 cases were detected that met the inclusion criteria. These were re-evaluated to confirm the histopathological criteria of said entity, being confirmatory in all the cases found.
Results: 10 patients with a diagnosis of intestinal lipomatosis were detected, ranging in age from 25 to 78 years and with a male:female ratio of 1:1. Nine of them presented gastrointestinal symptoms which were attributed to other conditions. Imaging techniques were not conclusive in the diagnosis of this entity. Eight patients underwent colectomy: three of them for primary colon neoplasia, three for stenosing Chron's disease, one for chronic post-colectomy dehiscence and one for abdominal pain. One patient underwent mucosectomies and a clinical autopsy was performed in the last patient. In all cases, the diagnosis of lipomatosis was made by histopathology and was not suspected by imaging or clinical symptoms.
Conclusion: Intestinal lipomatosis is a rare clinicopathological condition which in some cases can present asymptomatically, in others it can rarely be a cause of intestinal obstruction and occasionally, as in our review, accompanying other entities in which the symptoms can be superimposed and make the clinical and imaging diagnosis of this entity, more difficult. Histopathology may be important to reach the diagnosis in this type of cases in order to make a better clinical-pathological correlation.

E-PS-24-058
Review of the percentage of gastric cancer cases with positivity for HER2 or dMMR in the era of immunotherapy
A. García Cosculluela*, P. Santiago Díaz, M.E. Patriarca, S. Medina, E. Hinchado, A. Molina Alvarez, M. Larrubia Loring, A.L. Pazmiño Arias, P.Y. Rauseo Aristigueta, P. Tornero Piñero, D. Naranjo-Hans, M. Iglesias
*Hospital del Mar, Spain

Background & objectives: HER2 and MSI/dMMR determinations are useful nowadays to decide if immunotherapy should be used in metastatic gastric (GC) and gastro-oesophageal junction (GEJ) cancers. The present work analyses if the percentage of each biomarker determination is within the expected ranges.
Methods: We conducted a retrospective review of cases of GC/GEJ diagnosed at a non-university community hospital between 2019 and 2024. Data on patient demographics, tumour characteristics, as well as results of HER2 (HercepTest™, Agilent®) and dMMR (Agilent®) testing were collected from the study cohort. The percentages of each biomarker was calculated, and their associations with other variables were analysed.
Results: Our cohort included 102 cases (64% male, 36% female); 71% were GC and 30,29% GEJ cancers. Of these, 94 patients had both determinations, while 98 only had dMMR and another 98 only HER2. Global HER2 positivity was 13,4% (13/98), while dMMR was 11,22% (11/98). There were no cases with overlap of both alterations. HER2 positivity was 13,30% (4/30) in GEJ cancers and 12,50% (9/72) in GC. No differences were observed between both localizations, being mostly detected in the tubular adenocarcinoma pattern. dMMR alterations were more frequent in women (8/11, 73%), found in 15,2% (11/72) of GC and none of the GEJ cancers. This was mostly observed in the tubular pattern.

E-PS-24-061
How can we better diagnose metaplasia in Crohn's disease? A tale of two stains
E. Gedik*, S. Sevim, B.P. Kővári, B. Savaş, A. Ensari
*Ankara University, Pathology, Turkey

Background & objectives: Recognizing pyloric metaplasia(PM) and foveolar metaplasia(FM), indicators of chronic damage in Crohn's disease(CD) can be challenging in early lesions for the inexperienced. We aimed to evaluate our detection skills for metaplasia and to propose a novel approach for improvement.
Methods: Terminal ileum biopsies (62 initial,63 follow-up) from 125 CD patients were evaluated for PM, FM and inflammatory parameters of terminal ileitis (erosion/ulcer, villous changes, cryptitis, crypt distortion, lamina propria inflammation…) independently by two pathologists; experienced(EXP) and inexperienced(INEXP). Subsequently, the real status of metaplasias was investigated using MUC5AC and MUC6 immunohistochemistry and compared with H&E diagnosis of the two pathologists.
Results: MUC6 demonstrated PM in 45.6% and MUC5AC found FM in 51.2%. Detection rates of PM and FM were 56%, 37.6% by EXP and 47.2%, 21.6% by INEXP. Sensitivities, specificities and accuracies were 87%,70%,78% and 66%,69%,68% for PM with a correlation rate of R=0.585, R=0.357($p<0.0005$) between H&E and MUC6 for EXP and INEXP, respectively. Sensitivities, specificities and accuracies were 57%,83%,70% and 34%,91%,62% for FM with a correlation rate of R=0.427, R=0.318($p<0.0005$) between H&E and MUC5AC for EXP and INEXP, respectively. Between EXP and INEXP, kappa was 0.527 for PM, 0.292 for FM. MUC6 and MUC5AC improved the diagnosis by 47.1%, 60.2% for the INEXP and only 27.5%, 42.0% for the EXP.
Conclusion: Our results clearly showed that PM, and particularly, FM, which are suggestive features of chronic ileitis in the setting of CD, can easily be overlooked in H&E sections not only by the inexperienced but also by the experienced pathologist. Our dual MUC5AC and MUC6 staining approach seems to improve the recognition of both metaplasias significantly and could be employed as an ancillary technique in the diagnostic workup of terminal ileal biopsies aiding in accurate diagnosis and better patient outcome.

E-PS-24-062
Immunohistochemical and molecular insights into colon adenocarcinoma from a single institution in Romania
A. Georgescu*, T. Georgescu, A. Tecuceanu, M.V. Olinca
*University of Medicine and Pharmacy "Carol Davila" of Bucharest, Romania

Background & objectives: According to the scientific literature, MMRd adenocarcinoma represents 13% of colon adenocarcinomas while p53 and RAS mutations are encountered in 60% and 55% of cases. In this study we analyse the molecular profile of a short series of colon adenocarcinomas.
Methods: Thirty-five cases of colon adenocarcinoma have been analysed from an immunohistochemical and molecular perspective. Besides the TNM stage and histological subtype, the following parameters have been immunohistochemically analysed: MSH2, PMS2, MLH2, MSH6, p53, panTRK. Additionally, PCR tests that allow the identification of KRAS, NRAS and BRAFV600E mutations have been used.
Results: From a clinical and pathological point of view, 60% of the analysed cases were evaluated as pT3, 34% were mucinous adenocarcinomas and one case had already developed pathologically documented metastasis in the uterine cervix (pM1). Immunohistochemical assessment of MMR proteins has revealed instability (MMR deficiency) in 20% of cases and p53 (block or null) mutations in 71% of cases. Pan-TRK reactivity has been observed in only one case. From a molecular point of view, 57% showed KRAS mutations in exon 2 (90%) or in exon 4 (10%); 8,5% featured NRAS mutations (exons 2 and 4) and 5.7% featured BRAF mutation. Among mucinous adenocarcinomas, 25% of cases were MMR deficient.
Conclusion: Although colon adenocarcinoma has been widely investigated worldwide, only a few studies with emphasis on the molecular

aspects of these tumours have been conducted in the Romanina population. However, the present study shows a concordance between published scientific literature and our findings, confirming the relatively high incidence of KRAS mutations in colon adenocarcinoma. MMRd colon adenocarcinomas represent only a minority of cases that pose clinical challenges in respect to both the clinical follow-up and the genetic counseling.

E-PS-24-063

Diffuse gastric cancer associated with herpesvirus infection

Z. Gioeva*, L. Mikhaleva, A. Biryukov, K. Midiber, N. Shakhpazyan, V. Pechnikova, K. Maslenkina, R. Vandysheva
*Petrovsky National Research Centre of Surgery, Russia

Background & objectives: Understanding the role of viruses in the development of gastric cancer is a promising direction in science and medicine. The aim of this study was to identify herpesviruses in diffuse gastric cancer.
Methods: We studied material from 52 patients with diffuse gastric cancer. We performed a series of research methods: histological, histochemical, immunohistochemical (IHC) and molecular biological (real-time polymerase chain reaction (PCR) using fluorescent oligonucleotide probes to detect DNA amplification products of Epstein-Barr virus (EBV), cytomegalovirus (CMV) and herpes virus type 6 (HHV6)). PCR data were processed using CFX Manager v.3.1 software.
Results: In our work, identification of EBV by IHC did not result in any positive observations, but using real-time PCR in the same patients, a positive result was recorded in 46.15% of cases. CMV was detected in 15.38% of observations and HHV6 in 9.61%. The combination EBV/CMV was detected in 11.53% of patients, EBV/HHV6 in 5.76% and CMV/HHV6 in 3.84%. The seemingly contradictory data obtained by IHC and PCR in the detection of the EBV virus is due to the higher specificity of the real-time PCR method, which detects DNA particles remaining in human memory cells after EBV infection, which is often latent.
Conclusion: We have found that in diffuse gastric cancer a significant proportion of tumours contain viral agents. To date, the role of previously transferred or latent herpesvirus infection in carcinogenesis has not been studied, and the possible mechanisms of CMV and HHV6 influence on the development or progression of gastric malignancies are unclear. This study has demonstrated the need for further detailed investigation of this issue using modern genetic methods.

E-PS-24-064

Immunophenotyping of amyloid deposits in gastric biopsy and autopsy samples

Z. Gioeva*, A. Tebenkova, M. Mnikhovich, T. Bezuglova, V. Mkhitarov, L. Mikhaleva
*Petrovsky National Research Centre of Surgery, Russia

Background & objectives: The gastrointestinal tract often becomes involved in patients with systemic amyloidosis. This retrospective study was focused on the pathomorphological and demographic characteristics of the most common types of gastric amyloidosis.
Methods: Biopsy and autopsy samples were fixed with 10% neutral buffered formalin solution and paraffin embedded. Then, Congo red-stained sections were examined with light and polarized light microscopy. Immunohistochemical amyloid typing was performed with an antibody panel to different amyloid proteins using Leica BOND-Max immunostainer.
Results: The study included 27 patients (18 males and 9 females) with gastric amyloidosis (15 autopsies, 12 biopsies). There were 11 (41%) cases of AL-λ amyloidosis (5 biopsies and 6 autopsies). Intravascular amyloid deposition was found in 2 cases and both interstitial and intravascular deposition – in 9. AL-κ amyloid was identified in 26% of patients (4 biopsies and 3 autopsies), presenting an apparent interstitial and intravascular amyloid pattern. Amyloid typing revealed ATTR in 4 (15%) samples, focal amyloid deposits were mainly interstitial. AA amyloid was detected in 1 biopsy and 4 autopsies (18%).Intravascular amyloid deposits were found in two cases and both interstitial and intravascular – in four.
Conclusion: In our study, AL amyloidosis of lambda type was the most common form of the disease diagnosed in 41% of patients (mean age 72 years). The most extensive amyloid deposits were determined in cases of AL amyloidosis of kappa type suggesting that such patients may have a more rapid progression of the disease.

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E-PS-24-065

Fistula-associated anal canal adenocarcinoma - report of a case

C. Glava*, I. Nikolopoulos, D. Riga, A. Paraskeva, S. Ritsatou, G. Theodoropoulos, G. Kafiri
*Department of Pathology, Hippocratio General Hospital of Athens, Greece

Background & objectives: Fistula-associated mucinous adenocarcinoma (FAMAC) is a rare type of anal adenocarcinoma, accounting for approximately 2% of anal cancers. This slow growing, locally aggressive neoplasm clinically manifests late in the disease course.
Methods: We present a case of a 51-year-old man with a history of surgical debridement and follow-up of perianal fistulae (PF). The patient did not appear for regular follow-up for 2 years and he presented with a rectal mass.
Results: Biopsies obtained showed infiltration by mucinous adenocarcinoma, intestinal type, moderately differentiated, and adjacent presence of dysplasia. Immunohistochemistry showed strong and diffuse expression of CK20, CDX2 and MUC-2 and focal moderate-to-intense expression of CK7. These histopathologic features, considering the history of PF, and upon exclusion of rectal carcinoma, were reported as FAMAC. Abdominoperineal resection was performed. The specimen included part of the perianal gluteal skin with multiple fistulas. During opening, the fistulas' walls were hard, with areas of mucous appearance. The colonic mucosa along the entire length of the specimen appeared normal. The biopsy diagnosis was confirmed in the surgical specimen and the stage was pT3N0MxR0.
Conclusion: FAMAC is extremely rare and is described as a sub-entity of anal adenocarcinomas in the latest WHO edition. A long history of PF (fistula usually precedes carcinoma about 10 years) and exclusion of adenocarcinoma elsewhere in the colon allow the diagnosis of FAMAC. Chronic mucosal regeneration seems to play a key role in pathogenesis. Both surgeons and pathologists should be aware of this entity, as this neoplasm is locally aggressive and surgical R0 excision is difficult to achieve.

E-PS-24-066

Adult idiopathic hypertrophic pyloric stenosis - an underreported diagnostic dilemma in adults

T. Gul*, W. Butt, C. Muldoon, N. Ravi
*Histopathology Department, Ireland

Background & objectives: The aim of writing this case report is to remind clinicians that Adult Idiopathic Hypertrophic Pyloric Stenosis (AIHPS) is a rare but established entity in adults which should always be kept in mind in patients presenting with gastric outlet obstruction.
Methods: A 74-year-old lady presented with symptoms and signs of gastric outlet obstruction (GOO). Endoscopy showed complete gastric

outlet obstruction secondary to a cicatrizing process in the distal stomach. Although the appearances were suspicious for malignancy, repeated biopsies were benign. She was maintained on a total parenteral nutrition (TPN), and subsequently underwent a D2 distal gastrectomy with Roux-en-Y reconstruction.
Results: Gross inspection of the specimen revealed a 17mm focus of mural thickening with rugal flattening and overlying serosal puckering. This was very suspicious and was dealt as being a malignant lesion. However, microscopic examination showed dramatic muscular hypertrophy and mural fibrosis with scattered lymphoid aggregates and subserosal vascular congestion. The mucosa showed patchy inflammation but no frank ulceration. Intestinal metaplasia was noted at the proximal resection margin. Fifty-two lymph nodes retrieved from the specimen were benign. There was no evidence of a malignant process despite mucin and cytokeratin stains as well as additional sampling. Features were of an adult idiopathic hypertrophic pyloric stenosis (AIHPS).
Conclusion: Though AIHPS is a well-documented entity, the rarity of this disease in adults and its clinical resemblance to other neoplastic and non-neoplastic processes makes it a diagnostic dilemma. In this case the clinical team were very suspicious of this being a malignant neoplasm which led to multiple biopsies in this patient. Even on surgical resection though no well- defined lesion was identified, exhaustive sampling and staining was performed on multiple sections to exclude a poorly differentiated neoplasm.

E-PS-24-067
Efficacy of fine needle aspiration biopsy findings in diagnosis and risk assessment of gastrointestinal stromal tumours
B. Günay Gülen*, D. Nart, N. Oruç, E. Güler, M. Sezak, A. Veral, B. Doğanavşargil
*Ege University Faculty of Medicine, Department of Pathology, Turkey

Background & objectives: Gastrointestinal stromal tumours are histologically diverse, consisting of spindle cells, epitheloid cells or a combination. Endoscopic fine-needle aspiration biopsies are useful for diagnosis but not for predicting risk assessment. Risk depends on localization, size, mitotic index per Miettinen-Lasota-AFIP criteria.
Methods: We retrospectively reviewed endoscopic fine-needle aspiration biopsies and cell block sections of 9 tumours (6 stomach, one duodenum, pancreatico-gastric region, lower-mediastinum) diagnosed between 2015 and 2022. Cytological features such as cellularity, cell type, stromal features, mitosis, Ki67 proliferation index, presence of atypia and necrosis were reassessed blinded to the original pathology report and clinicopathological findings.
Results: The mean age was 65.7±13,09 (40-81). The mean tumour size was 6,9 ± 3,4 cm (1.5-13). Two cases were labeled "high risk for recurrence" based on tumour location, radiological size. Smear preparations were hypocellular but cell blocks contained 2-18 high power fields with tumour fragments, sufficient for further immunohistochemistry. Cell type was epitheloid in two cases, increased sellularity was observed in 6 cases with presence of mitosis in 4 cases (1-5/5 mm2), Ki-67 proliferation index was less than 1% in 4 cases, 5% in 4 cases (including two cases with metastatic disease) and 17% in a 9 cm-stomach lesion. Necrosis and atypia was observed only in two “high risk” cases.
Conclusion: EUS-FNAB, although not routinely practiced in our centre is a safe and effective method for providing early histological diagnosis and enabling prompt neoadjuvant treatment for clinically high-risk cases. Cell blocks provide sufficient tissue for immunohistochemistry and differential diagnosis of leiomyosarcoma, schwannoma, lipoma, pancreatic rests. In cell blocks presence of atypia, and necrosis were the most valuable features for the estimation of high-risk cases diverging from the criteria of resection specimens, an observation that needs to be confirmed by larger series.

E-PS-24-068
A case report of high-grade appendiceal mucinous neoplasm: histological characteristics and clinical course with a two-year follow-up
M. Gündüz*
*Bingol State Hospital, Turkey

Background & objectives: Appendiceal mucinous neoplasm, classified as low (LAMN) and high (HAMN) grade in the current WHO classification, is a mucinous epithelial proliferation with extracellular mucin and a pushing tumour margin. HAMNs are only rarely encountered.
Methods: A 61-year-old female with abdominal pain, who had no history of surgery or background disease, underwent right hemicolectomy due to imaging suggesting complicated appendicitis or a tumour. Macroscopic examination revealed a 7x5x5 cm cystic area in the appendix region containing mucin and necrotic debris in the lumen. Microscopically, the appendiceal mucosa was completely effaced, replaced by a neoplastic lesion
Results: with the surface epithelium mostly sloughed off. The epithelium of the neoplastic lesion consisted of mostly monolayered, partially pseudostratified cells with an enlarged, hyperchromatic nucleus, scant cytoplasm and high-grade cytologic morphologic features, forming mostly flattened, in some areas cribriform glandular, occasionally micropapillary structures. Mitotic figures, including atypical mitoses, were frequent. Extracellular mucin was present between epithelial cells and in the appendix lumen; however, there was no evidence of mucin dissecting through the appendix structures. The submucosal tissue was completely fibrotic with scattered calcifications; no lymphoid aggregates were present. The tumour was extending into subserosa, exhibiting a rounded, pushing pattern of invasion, without an infiltrative invasion pattern or desmoplasia.
Conclusion: No metastases were found in the dissected lymph nodes. Laparoscopic examination revealed no implants. Without chemotherapy or additional treatment, during 2-year follow-up, computed tomography and positron emission tomography scans showed no recurrence or metastasis. LAMN can be confused with serrated neoplasms or reactive epithelial changes seen in diverticular disease of the appendix, whereas the differential diagnosis of HAMN includes mucinous adenocarcinoma. Adequate macroscopic and microscopic examinations and knowledge of morphological features of these entities are crucial for accurate diagnosis.

E-PS-24-069
EoEHSS and EoEHRS in pathomorphological evaluation of eosinophilic oesophagitis
M. Gushchin*, L. Mikhaleva, K. Maslenkina, E. Motylev, N. Shakhpazyan, E. Zentsova
*A.P. Avtsyn Research Institute of Human Morphology Petrovsky National Research Center of Surgery, Russia

Background & objectives: Histological evaluation of biopsy specimens in eosinophilic oesophagitis (EoE) includes count of eosinophils in oesophageal mucosa and application of EoE histology scoring system (EoEHSS). The aim of our study was to analyse histological features of EoE using EoEHSS.
Methods: Biopsy was performed in 50 patients with EoE before (234 biopsies: 88 distal, 78 proximal and 68 – not specified) and in 10 patients after treatment (63 biopsies: 32 distal and 31 proximal). Biopsy specimens were fixed in 10%-neutral buffered formalin and stained with haematoxylin and eosin and Mallory for assessment of fibrosis. EoEHSS was applied for histological evaluation.
Results: Among 60 patients with EoE 41 were men (68%) with median age 29.5 (22; 39.25). In untreated patients, peak eosinophil count (PEC)

ranged from 17 to 220 (Me 47 eos/hpf). Basal zone hyperplasia varied from 20 to 80%. Eosinophilic abscesses were noticed in 46%, surface layering – in 14%, dilated intercellular spaces – in 97.7% of patients. Surface epithelial alteration was present in 60% and dyskeratotic epithelial cells – in 5% of cases. Lamina propria of mucosa was present in 76.7% of biopsy specimens, and various degree of fibrosis was observed in all but one cases. EoEHSS median grade and median stage scores comprised 12 (8;14.5) and 10 (8;12), respectively.
Conclusion: EoEHSS is a tool to evaluate features of EoE in biopsy specimens that is useful in diagnosis of EoE especially in cases with comparatively low number of eosinophils in hpf. The most common features of EoE include PEC> 15 eos/hpf, basal zone hyperplasia, dilated intercellular spaces and lamina propria fibrosis. EoEHRS (EoE histology remission score) derived from EoEHSS is suitable to assess biopsy specimens obtained after treatment and is associated with clinical remission.

E-PS-24-070
Immunohistochemical characterization of oesophageal cancer
M. Gushchin*, L. Mikhaleva, K. Maslenkina, M. Naumenko, N. Shakhpazyan, E. Zentsova
*A.P. Avtsyn Research Institute of Human Morphology Petrovsky National Research Center of Surgery, Russia

Background & objectives: Oesophageal cancer (EC) includes 2 main histological types – squamous cell cancer (ESCC) and adenocarcinoma (EAC). The aim of our morphological study was to assess histological type, grade and immunohistochemical profile of oesophageal cancer.
Methods: Biopsy was performed in 25 patients with oesophageal tumours localized in the upper third (2 patients), middle third (8 patients) and lower third and distal oesophagus (15 patients). Biopsy specimens were fixed in 10%-neutral buffered formalin and stained with haematoxylin and eosin and combined PAS/Alcian blue. Immunohistochemical evaluation was performed using p53 (D0-7), p16 (SP49), Ki67 (MIB-1) and EGFR (3C6).
Results: Most of patients were men (19 patients, 76%) with median age 70 (65-77). ESCC was diagnosed in 12 patients (G1 – 2 patients, G2 – 7 patients, G3 – 3 patients). Low-grade EAC was observed in 10 patients and high-grade EAC – in 3 patients. Positive p53 expression presented in 5 patients with ESCC (41.67%) and in 7 patients with EAC (53.85%), $p>0.05$. Expression of p16 was negative in all ESCC and positive in 7 patients with EAC (53.85%). Ki67 level was higher in EAC (90% (85-95%)) compared with ESCC (median 70% (52.5-80%)), $p<0.01$. EGFR was positive in 7 patients with ESCC (58.33%) and in 6 patients with EAC (46.15%),$p>0.05$.
Conclusion: Approximately half of patients with ESCC and EAC displayed positive expression of p53 pointing essential role of TP53 in oesophageal carcinogenesis. Positive expression of p16 was noticed in EAC only while positive expression of EGFR was observed with equal frequency in both histological types of EC. Despite equal distribution of poor differentiated cancers, Ki67 level was higher in EAC. Further research is needed to reveal immunohistochemical profile of EC histological types in aspect of their genetic landscape diversity and prognosis.

E-PS-24-074
Identification of a monophasic epitheioid gastroblastoma with a novel EWSR1:CTBP1 fusion
M. Hanks*, S. MacMahon, A. Arthur, S. Ibrahim, I. Hennig, T. McCulloch
*Department of Cellular Pathology, Nottingham University Hospitals NHS Trust, United Kingdom

Background & objectives: Gastroblastoma is an exceptionally rare gastric epithelial-mesenchymal tumour with fewer than 20 reported cases in the literature. The majority of cases have been reported in children or young adults. These lesions usually have a MALAT1-GLI1fusion.
Methods: We report the case of an 18-year-old male found to have multiple masses in the abdomen on CT imaging. A biopsy of one of the mesenteric lesions was performed and sequentially analysed using immunohistochemistry, fluorescence in situ hybridisation and RNA next generation sequencing to formulate a diagnosis and further classify the complex nature of the lesion.
Results: Biopsy showed solid sheets of small cuboidal epithelioid cells with distinct cell membranes and centrally placed small round nuclei. No rosettes, necrosis or mitotic activity were seen. There was no spindle cell component. Immunohistochemistry was positive for AE1/3, Beta-Catenin (cytoplasmic), CD56, focal EMA and CK5/6 and negative for Desmin, S100, SMA, SOX10, Melan-A, HMB45, Myogenin, CD99, WT-1, BCOR, OCT 3/4, Glypican-3, CD117, DOG1, CD34, CK7, CK20, TTF-1, CDX-2, PAX-8, GATA-3, Chromogranin, Hepatocyte marker, Synaptophysin, AFP, CEA, MUM1, LCA and Glutamine Synthase. Fluorescence in situ hybridisation (FISH) showed EWSR1 rearrangement; next generation sequencing (NGS) confirmed EWSR1:CTBP1 fusion. The combination of immunohistochemistry, FISH and NGS lead to a diagnosis of gastroblastoma.
Conclusion: Our case adds to the limited literature available and is the second reported case of gastroblastoma (or any tumour) with EWSR:CTBP1 fusion. This lesion was added to the World Health Organisation Classification of Digestive System Tumours in 2019 and usually demonstrates MALAT1::GLI1 fusion and biphasic morphology. Whether our case represents a novel variant or separate entity requires further research. We highlight the importance of a multi-disciplinary approach and essential role of multi-dimensional nature of pathology to ensure optimal patient management.

E-PS-24-075
The combined tumour budding-stromal score for risk stratification in mismatch repair-proficient localized colon cancer patients
B. Heras Morán*, B. Palomar, N. Tarazona, M. Huerta, D. Moro, S. Roselló, D. Roda, V. Pla, A. Cervantes, C. Martinez-Ciarpaglini

*Department of Pathology. Hospital Clínico Universitario of Valencia. Biomedical Research Institute INCLIVA, University of Valencia, Spain
Background & objectives: Histological biomarkers are pivotal for the management of localized microsatellite-stable colon cancer (MSS-CC) patients. This study evaluates two features associated with mesenchymal differentiation, tumour budding (TB) and tumour-associated stroma (TS), to create a combined risk-stratification score for localized MSS-CC patients.
Methods: We retrospectively analysed 254 colectomy specimens from stage I-III MSS-CC patients. TB and TS were evaluated in two different areas: the hotspot field (limited) and the complete tumour area (extended). We built a combined three-tiered tumour budding-stroma (TBS) score based on both assessment protocols (TBS-limited and TBS-extended). Clinical and follow-up information was obtained from medical records.
Results: TB and TS exhibited significant correlation with depth of tumour invasion, lymph node invasion, lymphovascular invasion, and perineural invasion. However, in the univariate survival analysis, only TB grade was statistically associated with risk of relapse, while TS demonstrated no prognostic value. The TBS-extended score was independently associated with disease-free survival (DFS) probability (low-TBS: HR 0.12, 95% CI 0.04–0.33, p=0.000, intermediate TBS: HR 0.26, 95% CI 0.10– 0.65, p=0.003). The prognostic value of TBS-extended score was statistically superior to the one obtained by studying TB and TS individually and the TBS-limited score.
Conclusion: The assessment of TB and TS across the complete tumour area instead of the hotspot field provides a more realistic panorama of

tumour heterogeneity. TBS-extended score obtained by combining TB and TS is independently correlated with DFS probability and improves the prognostic value of each parameter studied individually. Pending further validation, we believe the three-tiered TBS score is promising for its application in routine analysis as a useful prognosis biomarker for MSS localized CC patients.

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E-PS-24-076

Prognostic impact of mutational status in gastrointestinal stromal tumours: a retrospective cohort study

H. Ismaili*, S. El Bardai, M. Zaryouhi, S. Arifi, L. Tahiri Elousrouti, N. Hammas, L. Chbani
*Hassan II University Hospital, Morocco

Background & objectives: Gastrointestinal stromal tumours are characterized by a variable molecular profiles. Understanding the prognostic implications of mutational status is essential to optimize patient management. Our study aims to investigate the prognostic impact of the mutational status of gastrointestinal stromal tumours.
Methods: A retrospective cohort study was conducted to collect the clinicopathological , mutational status and follow-up data of 100 patients with gastrointestinal stromal tumour , covering the period from 2014 to February 2024.
Results: The mean age was 57years, with 1,3 male(s)/female. 75% of cases were high risk according to Miettinen's classification. Mutations in exon11(KIT) were present in 89% of cases, and exon9 mutations in 8%. Mutations in exon18(PDGFRA) were observed in 3% of cases. 75% of cases with exon11 deletion (KIT) had an overall survival of up to 108 months, while 25% showed disease progression or recurrence, usually involving codons 557 and/or 558 of KIT. A deletion/insertion or point mutation in exon11(KIT) had a similar overall survival as deletion. Cases with duplication in exon11 had a survival of up to 72 months. Mutations in exon9 (KIT) and exon18 (PDGFRA) had also favourable prognosis.
Conclusion: Mutational status in gastrointestinal stromal tumours influences tumour behaviour, response to treatment, and overall patient outcomes. Understanding its prognostic implications is essential for tailoring personalized therapeutic strategies and optimizing patient management.

E-PS-24-078

Synchronous liver metastases from colonic and lung adenocarcinoma: diagnosis supported with molecular characterization

M. Jimeno*, R. López-Martos, A. Hernández, C. Sanz, A. Muñoz, L. Arnaldo, C. Perello-Fabregat, M. Saigí, J.L. Manzano, A. Urbizu
*Hospital Universitari Germans Trias i Pujol, Spain

Background & objectives: Multiple liver tumours can be a challenging scenario for both clinicians and pathologists. Special attention must be paid to the patient's history and the histological morphology, with emphasis on the molecular study for an accurate characterization of these neoplasms.
Methods: A 60-year-old male presented with synchronous lung and colonic adenocarcinoma at cT1N0M0 and cT4N2M0 clinical stage, respectively. After diagnosis with fine needle aspiration and endoscopic biopsy, lung adenocarcinoma was treated with stereotactic body radiation therapy, and neoadjuvant chemotherapy was initiated for colon adenocarcinoma with subsequent surgical intervention. During treatment multiple liver nodules appeared on magnetic resonance study.
Results: A liver core needle biopsy (CNB) showed an adenocarcinoma immunoreactive to CK7 and CDX2 (isolated nuclei) and negative for CK20, TTF1 and Napsin A. Due to the inconclusive results PCR study was performed, showing a RAS, BRAF, EGFR, ALK, ROS1 and MET wild type profile. Colonic surgical specimen was then characterized, finding mutations in KRAS (exon 2: c.35G>C:p.) and TP53 (exon 8:c.857_858insG:p.). A second liver CNB was taken from a different lesion, which highlighted an adenocarcinoma immunoreactive to CK20, CDX2, MUC2 and negative for CK7, TTF1, Napsin A. Next generation sequencing was performed on this sample, detecting the same mutations in KRAS and TP53 genes as in the colonic specimen.
Conclusion: Finding synchronous liver metastases of different neoplasias is an unusual scenario that can be a diagnosis challenge, not only due to the exceptional situation but also to unknown primary tumour, to unexpected tumour progression, sample deficit or heterogeneity in immunohistochemical cell expression. In this exceptional situation, molecular study is essential to achieve an accurate diagnosis and characterization of tumours, which leads to state prognosis and to adequate treatment schemes, providing information even on possible therapeutic targets.

E-PS-24-079

Clinicopathological profile of low-grade appendiceal mucinous neoplasms (LAMN): a single-centre experience of 38 cases

E. Joy*, R. S, T. Somanathan, I. S Nair, R. S, C. K, J.K. K M
*Regional Cancer Centre, Thiruvananthapuram, India

Background & objectives: Low-grade appendiceal mucinous neoplasm (LAMN) is a perplexing tumour that lacks the capacity for classic invasion but can dissect through the appendiceal wall, causing pseudomyxoma peritonei (PMP). Timely workup and management are essential to prevent progression to PMP and metastasis.
Methods: In this retrospective study, we aimed to investigate the clinicopathological features and follow-up of Low-grade appendiceal mucinous neoplasms. All cases reported as LAMN in 8 years (from 1st January 2016 to 31st December 2023) were included. Clinical and demographic data were obtained from medical records. H&E slides were reviewed, and histopathological features were analysed.
Results: Total cases - 38. Males-16, females-22, M:F- 1:1.3. Age range- 32 to 78 years, mean age- 48 years. 24 cases (63%) presented with abdominal pain. Histopathological findings: Epithelial denudation -32 cases (84%), flattened epithelium -16 cases (42%), villiform or undulating epithelium- 22 cases (58%), loss of muscularis mucosae- 38 cases (100%), submucosal fibrosis- 31 cases (81.5%), luminal/mural calcification- 5 cases (13%), pushing invasion-16 cases (42%). Rupture of the appendix was observed in 4 cases (10.5%). Pathological staging: pTis-n=24 (63.15%), pT3-n=2(5.26%), pT4-n=12 (31.57%). Eight cases showed PMP. One case of LAMN was seen as a collision tumour with neuroendocrine tumour grade 2. Metastasis to the ovary was noted in three cases.
Conclusion: LAMNs are unique in histological appearance and form of dissemination. It does not metastasize lymphatically or hematogenously, but if granted access to the peritoneum by perforation it can cause pseudomyxoma peritonei. Meticulous histopathological analysis and immunohistochemical profiling are essential for achieving accurate diagnosis. Multidisciplinary collaboration among clinicians, radiologists, and pathologists is imperative to navigate diagnostic complexities and formulate tailored therapeutic interventions.

E-PS-24-080

Incidental detection of Crohn's disease-associated small bowel adenocarcinoma in clinically traumatic perforation: a case report

H. Jung*, Y. Lee
*CHA Ilsan Medical Center, Republic of Korea

Background & objectives: Crohn's disease (CD) can be diagnosed by combination of relapsing heterogeneous clinical symptoms, endoscopic evaluation, radiologic findings, and/or pathologic confirmation.

Chronic bowel damage by CD can lead a variety of complications, even malignancy. Of them, small bowel cancer is rare.
Methods: Herein, we report a case of 44-year-old male patient who had not been diagnosed as CD before, presented with acute abdominal pain after amateur boxing game. As traumatic perforation was suggested by initial physical examination and radiologic findings, the patient underwent an exploration surgery and small bowel resection was conducted.
Results: Gross examination of resected small bowel specimen in pathology department showed multiple perforation sites and background inflammatory mucosal changes with longitudinal ulcer formation. There was no specific mass-forming area. Microscopic examination revealed diffuse chronic active inflammation with transmural inflammation and neural hypertrophy. Histologic findings suggested that small bowel perforation coincidentally occurred from thinned bowel wall due to underlying Crohn's disease. And separately, multiple atypical glands invading to proper muscle were also identified near the perforation sites. The final pathologic diagnosis was small bowel adenocarcinoma and perforation associated with Crohn's disease.
Conclusion: After the diagnosis of CD, computed tomography and magnetic resonance imaging work-up revealed multifocal abnormal wall thickening in the remnant small bowel and ileocecal valve with prominent reactive lymphadenopathy. Small bowel endoscopy disclosed large deep ulcer and narrowing. Medical treatment with Azathioprine was administered and clinician planned follow up surveillance study. In this case, we describe the clinicopathologic features of small bowel adenocarcinoma discovered incidentally in the background of CD in the specimen originally thought to be a traumatic perforation.

E-PS-24-082
Age matters! Defining the diversity in upper gastrointestinal involvement in inflammatory bowel disease
H.K. Kahraman*, H. Berber, J. Jevtić, A.T. Bol, J.N.R. Davaji, S. Özdemir, C.T. Kırsaçlıoğlu, Z. Kuloğlu, B. Savaş, A. Kansu Tanca, M. Törüner, A. Ensari
*Ankara University, Medical School, Pathology Department, Turkey

Background & objectives: Despite being a well-known feature of paediatric inflammatory bowel disease(IBD) upper gastrointestinal involvement(UGI),though at a lower rate, can also be seen in adults. We aimed to investigate clinicopathological diversity of UGI between adult and paediatric IBDs in a detailed manner.
Methods: Study cohort comprised 47 ulcerative colitis(UC), 33 Crohn's disease(CD), and 5 unclassified IBD patients(47 paediatric, 38 adults) with UGI. Oesophageal, gastric, and duodenal biopsies were evaluated for inflammation patterns including focally active gastritis(FAG), focally enhanced gastritis(FEG), IELosis, granuloma and extent of involvement across multiple sites. Age groups were compared for site and pattern of UGI in association with ileocolonic disease.
Results: Paediatric cases consisted of 23 males(11 UC, 12 CD), 24 females(16 UC, 7 CD, 1 unclassified IBD) with a mean age of 11,7years while adult cases comprised 17 males(4 UC, 12 CD, 1 unclassified-IBD), 21 females(10 UC, 8 CD, 3 unclassified IBD) with a mean age of 44,9years. Majority of oesophageal involvement(20.5%) presented as lymphocytic oesophagitis(87.5%) while FAG(58.9%) was common in gastric involvement(80%), FAD(44.4%) was observed in duodenal disease(49.4%). FAG was more frequent in paediatric group than adults(p=0.002). While FEG was more common in corpus.(p=0.007), FAG was more frequent in the antrum (p=0.009) in adults. Oesophageal involvement (p=0.04) and multiple site UGI (p=0.006) were more frequent in CD than UC.
Conclusion: Based on comparative analysis of 85 IBD cases with UGI, distinctive patterns seem to exist in paediatric and adult IBD. Although our results are in line with existing literature, we have shown more common oesophageal involvement and FAG in corpus in paediatric CD. These findings emphasize the importance of age-specific considerations in understanding the histopathological spectrum of IBD. Also, by identifying these variations, diagnostic and therapeutic strategies specific to paediatric and adult populations can be refined to optimize patient care.

E-PS-24-083
Value of the combination of intraepithelial tumour-infiltrating lymphocyte density and the heterogeneity of density as prognostic marker in stage III colorectal cancers
H. Jin, L. Jin, N. Cho, J. Bae, J.H. Kim, H.S. Lee, G. Kang*
*Seoul Natl Univ College of Medicine, Republic of Korea

Background & objectives: Tumour-infiltrating lymphocyte (TIL) density is both a prognostic and a predictive factor in colorectal cancer (CRC). Whether the heterogeneity of TIL density across the tumour plays an important role in the clinical outcome of CRC is not well known.
Methods: Adjuvant chemotherapy-treated patients with stage III CRC or high-risk stage II CRC were analysed for survival according to TIL density and density heterogeneity, which were determined on CD8-immunostained slides using a machine learning method and by calculating the Simpson evenness index, respectively.
Results: High heterogeneity of the intraepithelial TIL density was found to be an independent prognostic factor, with a hazard ratio of 2.176 (1.391-3.403) in the multivariate analysis of recurrence-free survival. High heterogeneity was closely associated with high T category, venous invasion, perineural invasion, and KRAS mutation. The combination of both intraepithelial TIL density and density heterogeneity was significantly associated with the prognosis of patients: low TIL density/high TIL heterogeneity showed hazard ratios of 3.284 (1.639-6.578) and 4.176 (1.713-10.178) in the discovery and validation cohorts, respectively.
Conclusion: Our findings suggest that the heterogeneity status of intraepithelial TIL density might help delineate patients with better vs. worse survival when combined with intraepithelial TIL density.

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E-PS-24-085
Superficial early colon cancer revealing only distant metastases – a potential origin in cases with an unknown primary tumour
T. Kawasaki*, T. Tashima, T. Muramatsu, R. Jinushi, S. Ryozawa, M. Hirasaki, M. Yamato, Y. Sonoda, Y. Horita, T. Hamaguchi, R. Kawamura, M. Suzuki, S. Takemi, M. Saitoh, J. Ichikawa
*Saitama Medical University, Japan

Background & objectives: Colorectal carcinoma metastasizes to regional lymph nodes, and distant metastases commonly occur hematogenously in the liver and lungs. We describe an exceptionally rare case with superficial bowel cancer detected by distant metastasis to the "Virchow" lymph node.
Methods: The patient was a 62-year-old postmenopausal Japanese woman who visited our hospital with a chief complaint of decreased appetite. CT revealed left supraclavicular and abdominal aortic lymphadenopathy. A biopsy of the Virchow node was performed, yielding a diagnosis of adenocarcinoma of unknown origin.
Results: Lower gastrointestinal endoscopy revealed two polyps (pedunculated type measuring 19x17 mm and sessile type measuring 7x4 mm), treated with polypectomy and EMR, respectively. The diagnosis of the former lesion was adenocarcinoma in situ (pTis), well differentiated, with focal neuroendocrine differentiation, in

adenoma. The latter was adenocarcinoma NOS, moderately differentiated, with adenoma component, submucosal invasion (950 μm, pT1) and venous infiltration. The supraclavicular nodal lesion corresponded to moderately to poorly differentiated adenocarcinoma, composed of highly atypical cells similar to the colon cancer. Immunohistochemically, these lesions showed similar expression profiles: cytokeratin 7 (-)/20 (+), CDX2 (+), SATB2 (+), CD10 (+), p53 (+, mutant pattern), TTF-1 (-), estrogen receptor (-), and PAX8 (-).
Conclusion: In addition, an intramucosal tubular adenocarcinoma, well-differentiated, of the stomach and a non-ampullary, intestinal-type adenoma were also identified during upper gastrointestinal examination. Although she subsequently underwent systemic chemotherapy for colonic carcinoma, she died 17 months after the onset, after developing multiple pulmonary metastases and carcinomatous pleuritis. It is noteworthy that, although extremely rare, early colorectal cancer can lead to distant metastases as well as being a potential candidate disease in patients with a primary tumour of unknown origin.

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E-PS-24-086
Histological features of the invasion front are predictive of lymph node metastasis in oesophageal squamous cell carcinoma and adenocarcinoma
É. Kocsmár*, Á. Jakab, L. Zarándy, T. Várkonyi, I. Kenessey, I. Kocsmár, A. Szijártó, T. Vass, A. Kiss, G. Lotz
*Department of Pathology, Forensic and Insurance Medicine, Semmelweis University, Hungary

Background & objectives: Our objective was to investigate the prognostic significance of histologic phenomena at the invasion front, such as Tumour Budding (TB), Poorly Differentiated Cluster (PDC) and Stroma Areactive Invasion Front Areas (SARIFA) in oesophageal squamous cell carcinoma (ESQCC) and adenocarcinoma (EAC).
Methods: H&E-slides from 100 patients (43 EAC and 57 ESQCC) were investigated. TB was defined as isolated tumour cell or cell cluster of up to four cells, while PDC was defined as a tumour cell cluster of five or more cells. The presence of SARIFA (Tumour-associated fat cells without desmoplastic stroma reaction; -/+) in the invasive front area was also determined.
Results: SARIFA+-status was significantly more frequent in EAC than in ESQCC (p=0.004). No correlation was found among TB/PDC/SARIFA factors in ESQCC, but SARIFA+-status was significantly more frequent in EAC patients with a high number of small cell clusters (TB and low cell count PDC), compared to tumour cases with a low number of cell clusters of few cells (p<0.001). A high TB/SARIFA+-statuses were more frequent in higher T-stage EAC cases (p=0.01; p=0.001). In multivariate analysis by backward selection, independent prognostic factors of lymph node metastasis were found to be the high TB-status in ESQCC (p<0.001) and the SARIFA+-status in EAC (p=0.01).
Conclusion: Although the prognosis of oesophageal cancer is known to be generally poor, few tissue markers of prognostic significance are identified. Our results show that the invasion fronts of ESQCC and EAC show histologically different infiltrative patterns. Occurence of lymph node metastasis is associated with a high TB-status in ESQCC, and presence of the recently described SARIFA in EAC.

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E-PS-24-087
Analysis of Helicobacter pylori infection status and clarithromycin-resistant strains in gastric mucosa-associated lymphoid tissue lymphoma patients using RT-PCR: a single-centre study in Korea
J.Y. Koo*, K. Lee, S.B. Cho, Y. Choi, N. Kim, S.S. Kim, J.Y. Lee
*Republic of Korea

Background & objectives: Helicobacter pylori is a well-known risk factor for gastric MALT lymphoma. However, the information regarding the rates of clarithromycin-resistant H. pylori strains in patients with gastric MALT lymphoma is largely unknown compared to their rates in the general population.
Methods: From January 2021 to February 2024, the H. pylori test was performed on samples from 4686 patients who underwent gastric biopsy, including 89 patients diagnosed with gastric MALT lymphoma at Chonnam National University Hospital and Chonnam National University Hwasun Hospital. The presence of H. pylori infection and resistant strains (A2142G and A2143G) was investigated using real-time PCR-based diagnostic kits.
Results: H. pylori was detected in 1964 out of 4597 cases in the non-MALT lymphoma group (42.7%), while H. pylori infection was present in 51 out of 89 cases (57.3%) in the gastric MALT lymphoma group (p = 0.006). The frequency of clarithromycin-resistant strains was 39.2% (20 out of 51 cases) in the gastric MALT lymphoma group, which was significantly higher than 26.8% (527 out of 1964 cases) in the non-MALT lymphoma patient group (p = 0.05). The ratio of the resistant strain A2142G was higher in the gastric MALT lymphoma group (20.0%, 4/20) than in the non-MALT lymphoma patient group (13.0%, 58/527) with marginal statistical significance (p = 0.071).
Conclusion: The results of this study are consistent with the trend of a gradual decline in the rate of H. pylori infection in gastric MALT lymphoma but were the lowest among recently published studies. The high infection rate of clarithromycin-resistant H. pylori in the gastric MALT lymphoma group suggests that there is a high possibility that tumour regression may not be successful with first-line eradication therapy containing clarithromycin.

E-PS-24-088
Amoebic caecal ulcer masquerading as a malignant caecal mass - a clinicopathological case report
F. Kubba*, A. Qasim, T. Almeida, G. Wallis, T. Agarwal, C. Caroff, S. Shariq
*Ealing Hospital, London North West University Healthcare NHS Trust, United Kingdom

Background & objectives: A 60 year-old Asian man with recent travel to India presented with right sided lower abdominal pain and blood in stools. He tests showed anaemia and FIT test was positive. He had no bowel obstruction symptoms or family hsitoryof cancer.
Methods: Colonoscopy revealed a 15mm caecal ulcer in the submucosa opposite the ileocaecal valve and another smaller lesion near the appendiceal orifice. The lesions were thought to be malignant. The rest of the colon appeared normal. Biopsies were taken which showed nongranulomatous moderate active chronic colitis with cryptitis and ulceration. On review by another pathologist PAS stain revealed Entamoeba trophozoites.
Results: Direct stool examination and stool cultures as well as special stains of Periodic Schiff and trichrome stains have good diagnostic yield in detecting amoebic trophozoites. As Entamoeba histolytica is

not a commonly seen infection in the UK, applying special stains for solitary/multiple caecal ulcers which have benign features is helpful in increasing the diagnostic yield, especially if the clinical history of recent travel to tropical or subtropical countries have not been mentioned in the request form. The interpretation of endoscopy was also challenging as the benign findings may masquerade as cancer. The patient was treated with oral tinidazole which was followed by paromomycin tablets and did not have further complications.
Conclusion: We present a case of a classical amoebic caecal ulcer clinically a d endoscocpically thought to have been a malignant caecal tumour. Amoebic dysentery is still thrive in many tropical and subtropical countries however in countries where they are not present, it may represent a diagnostic challenge. Combining a PAS stain in solitary caecal ulcers may help in better identification of Entamoeba histolytica trophozoites in the undermined flask-shaped caecal ulcers in patients with history of recent subtropical and tropical travel.

E-PS-24-089
Encapsulating peritoneal sclerosis in a young man, a rare case report with review of literature
F. Kubba*, N. Pore, M. Jagniani
*Ealing Hospital, London North West University Healthcare NHS Trust, United Kingdom

Background & objectives: A 29-year-old Asian male presented with intermittent abdominal fullness of six months duration. He reported a 6-7kg weight loss over a six-month period associated with nausea and sensation of incomplete bowel evacuation. He underwent appendicectomy at 8 years of age.
Methods: On examination he looked well and haemodynamically stable. Abdominal examination showed fullness in the right paraumbilical region with tenderness but the abdomen was soft. CT scan findings were in keeping with encapsulating peritoneal sclerosis(EPS)/ abdominal cocoon as there was encasement of the small bowel within a thick fibrocollagenous membrane. He had an emergency open resection of the bowel due to obstruction.
Results: Histopathology of the small bowel showed thickened peritoneum of up to 1.5mm encasing loops of adherent bowel macroscopically. Microscopically the peritoneum was collagenised. Elastic van Gieson and trichrome stains confirmed the collagenised peritoneum. WT1 and CK5 immunohistochemical stains confirmed the loss of the mesothelial cell layer. D240 showed vascularised areas within the peritoneum. A few rare cases of EPS are reported in patients undergoing peritoneal dialysis. In a recent review, other causes of EPS include autoimmune disease, sarcoidosis, malignancies, chronic ascites, intraperitoneal chemotherapy, intraperitoneal exposure to particulate matter/disinfectants, previous abdominal surgery, endometriosis, intraperitoneal infections (tuberculosis) and beta blocker administration. Treatment is needed when the adhesions/encasement result in bowel obstruction.
Conclusion: We have presented a case of encapsulating peritoneal sclerosis in a young male, 21 years following open appendicectomy. Macroscopic and microscopic findings are distinct showing collagenising peritoneum encasing adherent bowel loops. Similar cases were reported in patients undergoing peritoneal dialysis. The cause found was his previous open appendicectomy. The pathophysiology is likely to be related to local intraperitoneal factors such as low grade infections and mechanical factors such as intraabdominal trauma resulting in adhesions. Treatment is by open surgical resection.

E-PS-24-090
Immunohistochemical PD-L1 expression and patient survival tendencies in gastric carcinoma excised before hyperthermic intraperitoneal chemotherapy (HIPEC) procedure
M. Kupryte*, P. Gedminas, R. Kupčinskaitė-Noreikienė, D. Mačiulienė, Ž. Dambrauskas, L. Poškienė
*Lithuanian university of health sciences, Lithuania

Background & objectives: PD-L1 is tested as predictive marker optimizing immunotherapy strategy in advanced oncologic cases. PD-L1 combined positive scoring (CPS) in correlation with gastric carcinoma patient survival remains unclear. Aim is to optimize PD-L1 CPS application in stomach carcinoma excised before HIPEC.
Methods: Immunohistochemical reactions against PD-L1 (clone 22C3) were performed for 15 selected gastric carcinoma cases excised before HIPEC, scanning them with „Pannoramic Viewer (3D Histech)". CPS was calculated from digital morphometric data (five annotated 304 558 μm2 microscopic fields per sample) in digital microimaging software. Disease free, overall, and long-term survival were evaluated. Mann-Whitney, Kruskal-Wallis's tests, Kaplan-Meier method were applied ($p<0.05$).
Results: PD-L1 CPS median of 3.05 (interquartile range-12.40) was calculated in gastric carcinoma excised before HIPEC procedure. PD-L1 CPS was significantly lower in gastric carcinoma of diffuse type vs mixed/intestinal type according to Lauren classification (median-1.09, interquartile range-4.60 vs median-12.40, interquartile range-17.17, correspondingly; $U=44.00$, $p=0.019$). Medians of PD-L1 CPS were similar among different clinical stages of gastric carcinoma ($H=3.63$, $p=0.163$). Patients with higher than median CPS score and higher then median number of PD-L1+ immune cells had a longer disease free (10 vs 22 months, $p<0.05$) and overall survival (17 vs 26 months, $p<0.05$). There was no difference in number of long survivors (>3 years) in different PD-L1 expression groups ($p>0.05$).
Conclusion: A significant lower PD-L1 CPS in gastric carcinoma of diffuse type according to Lauren classification identified during study may contribute to revealing yet unknown PD-L1 role in microenvironmental processes of diffuse gastric carcinoma. Also, patients with high PD-L1 CPS score and high number of PD-L1 positive immune cells demonstrate significantly longer disease free and overall survival suggesting that these parameters can be applied as an additional diagnostic marker for selecting patients to undergo prophylactic and/or curative HIPEC in gastric carcinoma.

E-PS-24-091
Microsatellite instablity can predict pathologic response to neoadjuvant therapy in rectal cancer: a single institution study from Croatia
N. Kurtovic*, L. Klobučarić, Z. Radicevic, A. Kovačević, I. Zagorac, M. Bakula, R. Alaghehbandan, J. Rajc
*Department of Pathology and Forensic medicine, Osijek University Hospital, Osijek, Croatia

Background & objectives: The variability of pathologic response to neoadjuvant therapy in rectal cancer persists, prompting numerous studies on potential predictive biomarkers like microsatellite instability, which have yielded conflicting results. This study explores microsatellite instability and other pertinent factors in predicting therapy response.
Methods: We retrospectively analysed 125 cases of locally advanced rectal cancer treated with neoadjuvant therapy at University Hospital Osijek from 2018-2023. Clinicopathological data were collected. Mismatch Repair (MMR) status was determined immunohistochemically and compared to tumour response using the Ryan regression score (good: score 0-1; poor: score 2-3). Chi-square test and logistic regression analysis were used to examine potential correlations.
Results: The mean age and tumour size were 66.6 years and 6.4 cm, respectively. Among 125 patients, 33 (24.6%) had a good response

(Ryan regression score 0 or 1), and deficient MMR (dMMR) was detected in 12 patients (9.6%). The dMMR rate was higher among tumours with a good response compared to the poor response cohort (p = 0.016). Using the logistic regression model, we found that the odds of having a good response (Ryan score 0 or 1) were 4.9 times higher in tumours with dMMR. Furthermore, the combination of dMMR status and larger tumour size was 6.6 times more predictive of a good pathologic response to neoadjuvant therapy.
Conclusion: Our findings show that MMR status (i.e., dMMR) can reliably be used as a predictive factor in pathologic response to neoadjuvant therapy. Tumour size, in combination with MMR status, can also be used as a predictive value for tumour response to therapy. These results emphasize the importance of accurately and routinely determining the MMR status of the tumour, along with precise measurements of tumour size, prior to neoadjuvant therapy.

E-PS-24-093
The role of diabetes mellitus in epigenetic alterations in patients with colorectal cancer
E. Lampri*, S. Papadatos, C. Bali, I. Parthymos, M. Katsipaneli, A. Klaroudas, A. Betzou, A. Varouktsi, A. Mitselou, V. Galani
*Department of Pathology, Faculty of Medicine, School of Health Sciences, University of Ioannina, Greece

Background & objectives: Epigenetics influence the expression of genes without structural gene rearrangements. Epigenetic mechanisms include DNA methylation, histone modifications and non-coding RNAs. They all are thoroughly studied in serious diseases such as colorectal cancer (CRC) and Type 2 Diabetes Mellitus (T2DM).
Methods: Malignant colon tumours from 46 patients were retrieved from the archived material of the Department of Pathology of University Hospital of Ioannina. Immunohistochemical expression of TET2 and GST3 proteins were classified as none, weak, moderate and strong expression and correlated with the comorbidity of T2DM.
Results: All tumours showed GST3 expression in different intensities (weak, moderate, strong) and approximately 2/3 of tumours weak/moderate expression of TET2. Patients without T2DM had a statistically significant higher percentage of weak/no expression of TET2 (p=0.038). T2DM patients had a higher percentage of strong/moderate expression of GST3, approximately seven times more likely to have moderate (rather than weak/none) TET2 expression and a 2.7-fold higher relative likelihood of showing strong (rather than moderate/weak) GST3 expression than tumours derived from non-diabetic patients. The association between T2DM and the group of maximum observed TET2 expression remains statistically significant as well the results for GST3 were close to statistical significance.
Conclusion: TET2 and GST3 are highly expressed in malignant colon tumours. History of T2DM in CRC patients was associated with the highest observed GST3 expression and the absence of T2DM was associated with the lowest observed TET2 expression in the studied tumours. T2DM increases the probability of observing GST3 and especially TET2 expression, independent of specific tumour microscopic features and patient demographics.

E-PS-24-094
Exploring associations in vascular invasions of colorectal adenocarcinoma: morphological patterns, vessel type and pTNM
M. Larrubia Loring*, A. Tramuns-Fresnadillo, D. Álvarez-Villanueva, J. Riera-Suso, J. Gimeno Beltrán, L. Espinosa, M. Iglesias
*Hospital del Mar Research Institute, Spain

Background & objectives: The classification of vascular invasion morphology in colorectal cancer is not included in diagnostic guidelines and may be related to prognosis and metastatic potential. Our aim is to characterise the morphology of tumour migration through different vessels in these patients.
Methods: We performed an observational analytical study based on simple random sampling from our hospital's electronic database. Vascular tumour invasions (178) in H&E samples were evaluated, defining their morphology (glandular, cribriform, solid and cluster) and the type of infiltrated vessel (small or venous), analysing their association with pTNM. Categorical variables were analysed using the chi-squared test and Fisher's exact test.
Results: We classified vascular invasions according to the patterns of the tumoural infiltrate: cluster (23%), glandular (36%), cribriform (9.6%), solid (7.3%) and their combinations (24.2%). Fisher's test showed no relationship between vascular invasion pattern and pTNM. However, the Chi-square test revealed a significant association between the type of invasion pattern with infiltration of small vessels (clusters) or large vessels (glandular or glandular plus cribiform in the same vessel) (chi-sq 2.555E-9). We also found a non-significant correlation (p=0.087) between cluster infiltration of large vessels and higher N staging.
Conclusion: Different morphological patterns of vascular invasion can be established in colorectal adenocarcinomas.
No statistically significant association was observed between vascular invasion pattern and pTNM. However, a significant association is observed between the type of vessel invaded and the pattern of invasion. For future work, it would be advisable to increase the sample size, as well as to review the clinical evolution of the patients (relapses and survival).

E-PS-24-095
Intestinal spirochetosis: presentation of two cases
A.I. Lavado Fernández*, C. Gimena Latapie, A. Escalona García, A. Gutiérrez Salas, L. Santos Aranda, J.M. Mellado Soria
*Analizalab. Hospital Universitario El Ángel (Málaga). Research Laboratory of Biomedical Research Institute of Malaga (IBIMA). University Hospital of Malaga (Virgen de la Victoria)), Spain

Background & objectives: Human Intestinal Spirochetosis (HIE), described in 1967 by Harland and Lee, is defined as colonization of the colon and rectum by bacteria of the phylum Spirochaetes. Its prevalence is very high in developing countries, although notably lower in developed countries.
Methods: We present two patients: a 30-year-old female who consulted for abdominal pain, vomiting, and diarrhea, and a 50-year-old male who consulted for heartburn and reflux. Endoscopies were performed without relevant findings. Biopsies were taken, yielding multiple irregular fragments of whitish tissue between 0.2-0.3 cm. Histological sections were stained with hematoxylin-eosin.
Results: Microscopically, a basophilic band was observed in the colonic surface epithelium, composed of multiple helical filamentous structures. To confirm the presence of the bacteria, we used immunohistochemistry for T. pallidum. Immunofluorescence (which is positive due to cross-reactivity with the genus Brachyspira) or the histochemical technique of Warthin-Starry (the most specific for this type of bacteria) can also be used.
Conclusion: HIE is a rare cause of chronic diarrhea, most commonly observed in patients such as homosexual men, patients with multiorgan failure, or HIV+ patients. Therefore, these cases are extraordinarily rare because they do not belong to these subgroups. Hence, it must be considered as a differential diagnosis. In humans, Brachyspira aalborgi and Brachyspira pilosicoli species are the most frequent. In colonoscopies, mucosal alterations are not usually found; therefore, the gold standard for diagnosis is histological examination.

E-PS-24-096
Ganglioneuromatosis with an atypical presentation mimicking Crohn´s disease: a case report and literature review
C. Leal*, A. Marques, I. Gullo
*Unidade Local de Saúde de São João, Portugal

Background & objectives: Diffuse intestinal ganglioneuromatosis is a rare form of neoplastic disease of the enteric nervous system characterized by a benign proliferation of ganglion cells, Schwann cells, and nerve fibers in the bowel wall.
Methods: Here we present the case of a 77-year-old woman with unexplained anemia. Hematological causes of anemia were excluded. Upper and lower conventional endoscopy showed no lesions. Capsule enteroscopy showed multiple small ulcers associated with stenosis in the jejunum, however, the biopsies taken during balloon- assisted enteroscopy were non-diagnostic. The suspected clinical diagnosis was Chron's disease involving the jejunum.
Results: The patient underwent laparoscopic segmental enterectomy for symptomatic relief. Macroscopic examination showed a stenotic area with 19cm in lenght, associated with multiple foci of ulceration, which was totally sampled. Histopathological examination revealed multiple, ill-defined areas of expansion of the submucosal nerve plexus, showing a proliferation of Schwann-type spindle cells and ganglion cells, isolated or in small aggregates. The mucosa lining these areas showed necrobiotic changes and erosion/ulceration. By immunohistochemistry the lesional cells showed expression of S100, SOX-10, calretinin, and synaptophysin, confirming their neuronal origin. The remaining mucosa and intestinal wall showed no other significant pathological changes, excluding other causes of mucosal ulceration and stenosis, such as Crohn's disease.
Conclusion: The findings were consistent with diffuse intestinal ganglioneuromatosis. This is a rare form of ganglioneuromatosis which occurs more commonly in children but has also been described in adults like. It has been described in both sporadic and syndromatic context (NF1, MEN2 II, and Cowden's syndrome). Genetic testing is currently on-going. This case illustrates an atypical presentation of a rare disease and emphasizes the importance of histopathological examination for accurate diagnosis.

E-PS-24-097
Rare cause of dysphagia in middle aged patient - giant fibrovascular polyp of the oesophagus / GFE
M. Lenarcik*, W. Januszewicz, M. Polkowski, A. Mróz
*Department of Gastroenterology, Hepatology and Clinical Oncology,Centre of Postgraduate Medical Education, Warsaw, Poland; Department of Cancer Pathology, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland, Poland

Background & objectives: 52 years old patient with symptoms of dysphagia and weight loss since 3 months. On clinical history the patients was operated on laryngeal cysts and appendicitis. He also suffered from gastro oesophageal reflux disease. The patient was qualified to diagnostic workup.
Methods: On endoscopic examination 12x1x2,5cm submucosal lesion was revealed which was attached proximally to oesophageal wall with 2-2,5cm long stalk. Endosonographically the lesion was hyperechoic covered with normal mucosa. On Doppler mode there were some vessels in superficial part of the lesion with no signal enforcement after contrast application. No biopsy was taken and the patient was admitted for EMR resection.
Results: Macroscopically the lesion was slingshot shaped with the stalk of 4x1,5cm and the arms of 6,5 and 5,5cm. It was covered with unchanged, shining mucosa reach in superficial visible vessels. On cut section it was solid, glistening, mostly yellowish with areas of haemorrhages and no necrosis. Microscopically the combination of mature adipose, connective tissues and vessels was revealed. No features of atypia nor malignancy were present. The lesion was covered with reactive multilayered oesophageal epithelium. Based on these hamartomatic benign pedunculated subepithelial lesion was diagnosed – giant fibrovascular polyp of the oesophagus.

E-PS-24-098
The role of carbonic anhydrase IX on extramural venous invasion in oesophageal squamous cell carcinoma patients
Z. Lin*, J. Plukker, S. Chen, M. Su, G. Kats-Ugurlu
*University Medical Center Groningen, The Netherlands

Background & objectives: Extramural venous invasion (EMVI) has an independent adverse effect on survival in oesophageal squamous cell carcinoma (ESCC) patients. Carbonic anhydrase IX (CAIX) is involved in hypoxia and anoikis. Here we examined its role in promoting dissemination in ESCC.
Methods: CAIX expression was investigated immunohistochemically in tumour and EMVI tissues from 53 patients with locally advanced ESCC and EMVI-positive after surgery only (period 2009-2013). Photomicrographs were evaluated with Aperio ImageScope. H-score was used as a mathematical product of proportion score (% positive cells) and intensity score (estimated fraction-stained tumour cells), resulting in a low/high level according to the median H-score.
Results: Of the 23 EMVI tissue (23/53, 43%), 12 showed high CAIX expression. CAIX expression in ESCC and its EMVI tissues was insignificant for gender, age, lesion location, pT stage, pN stage, differentiation grade, lymph-vascular invasion and perineural invasion. CAIX expression level in ESCC seemed to influence CAIX expression in EMVI (Logistic regression, $P = 0.002$), but not its level. The univariate Cox regression analyses showed high CAIX in primary tumour and EMVI correlated with worse overall survival ($P = 0.04$) although this was insignificant when CAIX expression in primary tumour or its EMVI tissues was correlated with prognosis. In multivariate analyses, lymph node metastasis was the only independent adverse factor.
Conclusion: High CAIX expression in primary tumour and EMVI tissues is associated with worse survival in ESCC patients. Inhibition of CAIX might reduce the potential of tumour cells to establish disseminated disease.

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E-PS-24-099
Evaluation of TCD4+ TCD8+ immune cell infiltrationin lefs and right-sided colorectal cancer: a comparative study
B. Loucif Latreche*, T. Rouxane, N. Benyehiya, I. Soufli, N. Sididris, A. Slimani
*University of Algiers and Beni Messous Medical Center, Department of Pathology, Algeria

Background & objectives: This study evaluates the differences in immune cell density and the production of immune mediators between right-sided and left-sided colorectal cancer
Methods: Tumour samples from patients were used to quantify the density of cells TCD3+, TCD4+,TCD8+,CD56+ , NK cells, and CD68+ macrophages. Histological and immunohistochemical (n=33) studies were conducted on these samples. Additionally, the measurement of nitric oxide (NO) in plasma using the modified Griess method and transforming growth factor-beta (TGF-β) in serum using ELISA techniques was performed.
Results: Differences in immune cell density and immune mediator levels between the two locations were observed. A significant correlation was noted between the density of CD68+ macrophages and systemic levels of TGF-β and NO.
Conclusion: These findings highlight potential differences in the immune landscape and suggest important clinical implications for the treatment of colorectal cancer. Further research is needed to deepen our understanding of the underlying mechanisms.

E-PS-24-100

Association of extra-capsular extension of metastatic lymph nodes in gastric carcinoma and other prognostic factors

F. Loued*, D. Bacha, M. Hajri, I. Mallek, l. Gharbi, A. Lahmer, H. Mestiri, S. Ben Slama
*Department of Pathology, Monji Slim Hospital, 2070, Tunis, Tunisia

Background & objectives: Gastric carcinoma is the fourth most common cancer worldwide. Therapeutic management takes into account, among prognostic factors, the lymph node status. Our aim was to investigate the association between extra-capsular extension (EEC) and other prognostic markers in gastric adenocarcinoma (GA).
Methods: A retrospective study was conducted between January 2008 and December 2017 in the pathology and surgery departments of M. Slim hospital. We included patients with GA and lymph node metastases. EEC was defined by the protrusion of carcinoma cells beyond the capsule of the metastatic lymph node to reach peri-nodal adipose tissue, outside the afferent lymphatic vessels.
Results: There were 29 men and 13 women. The mean age was 60.36. Univariate analysis showed that EEC was correlated with tumour size greater than 58mm (p=0,006), presence of vascular invasion (p= 0,037), peri-neural invasion (p= 0, 02), poorly differentiated tumours (p=0,014), pT4 and pN3 stages (p<0,001), synchronous metastases (p=0,017), stages III or IV (p= 0,024), lymph node ratio greater than 35% (p<0,001), and metastatic recurrence (p=0,007). EEC was not correlated with age, gender or local recurrence. In a multivariate study, the presence of EEC was correlated with pN3 stage (OR=3.84; p=0.006), advanced tumour stage (OR=2.35; p= 0.016) and a lymph node ratio greater than 35% (OR=2.29; p=0.002).
Conclusion: EEC of metastatic lymph nodes is in fact a prognostic marker, which should be validated in standardized GA reports.

E-PS-24-101

Oesophageal adenocarcinoma post Roux-en-Y gastric bypass with gastrogastric fistula

B. Luu*, N. Lao, D. Hurlbut, A. Giles, C. Orr
*Queen's University, Canada

Background & objectives: We present a case of oesophageal adenocarcinoma post Roux-en-Y gastric bypass with gastrogastric fistula to illustrate the hypothesis that this fistula complication predisposes to gastro-oesophageal acid reflux, and therefore may raise the risk of distal oesophagus cancer.
Methods: A 64-year-old female received a Roux-en-Y gastric bypass for the treatment of obesity. Seven years later, she presented with unintentional weight loss and worsening dysphagia. Endoscopy confirmed an adenocarcinoma at the oesophagogastric junction. During subsequent oesophagectomy, a plane of separation could not be established between the gastric pouch and gastric remnant, raising suspicion of a gastrogastric fistula.
Results: Macroscopic examination of the resected specimens revealed a ligated, widely patent gastrogastric fistula previously connecting the gastric pouch to the gastric remnant. Microscopic examination of the oesophageal tumour showed a poorly differentiated oesophageal adenocarcinoma invading into the adventitia. The adenocarcinoma involved the proximal (gastric pouch) and distal (gastric remnant) ends of the fistula, which suggests the adenocarcinoma originating from the oesophagus invaded into the gastric remnant from the gastric pouch via the connecting fistula. To our knowledge, this is the first report of an oesophageal adenocarcinoma that developed following Roux-en-Y gastric bypass surgery complicated by a gastrogastric fistula.
Conclusion: Bariatric surgery is an effective treatment for long-term weight loss that is associated with lower all-cause cancer mortality, however, its impact on the incidence of oesophageal adenocarcinoma remains inconclusive. Gastrogastric fistulae are associated with reflux disease as they facilitate acid flow from the gastric remnant into the gastric pouch and upwards into the oesophagus. We postulate that this fistula complication is a risk factor for oesophageal adenocarcinoma development via gastro-oesophageal acid reflux.

E-PS-24-102

Concurrent gastric granular cell tumour (GCT) and gastrointestinal stomal tumour (GIST): a very rare synchronous presentation

M. Hussain, S. Amer, A. Lazim, D. Doan, A. Seth, D. M Proca*
*Temple University, USA

Background & objectives: GISTs account for 0.1-3% of all GI neoplasms. With an estimated annual incidence ranging from 11 - 15 cases/ million people, the synchronous occurrence of GISTs with other primary GI tumour, such as GCT, is exceedingly rare.
Methods: In our retrospective analysis spanning a decade (2010-2020), we identified 80 GIST, out of which three were synchronous with adenocarcinoma and one was a unique case of synchronous GIST and GCT, both originating in the stomach. To our knowledge, fewer than 10 such instances have been documented in the available literature.
Results: We describe a very rare case of synchronous GCT and GIST, both occurring in the stomach in a 56 yo female with no past medical history. A GIST was diagnosed on biopsy after an abdominal CT showed a large gastric mass involving the greater curvature of the stomach and extending into the spleen. The patient underwent partial gastrectomy, splenectomy and wedge resection of the liver and the pathological exam showed: 9.5 cm GIST with extensive necrosis and active mitotic rate (11 mitoses/ 5mm2). A 1.7 cm separate nodule was identified in the gastric wall, away from the GIST; and was diagnosed GCT, positive with S100, negative with desmin, c-kit, DOG-1.
Conclusion: Although GCTs are rare, constituting less than 1% of mesenchymal tumours, they can manifest within the gastrointestinal (GI) tract in 10% of cases. Meanwhile GISTs predominantly occur in the stomach (50-60%). The simultaneous presence of GISTs and GCT in the stomach is highly uncommon. To elucidate any potential genetic connections between these concurrent tumours, next-generation sequencing (NGS) is currently underway. This investigation aims to unveil any underlying genetic anomalies that may link these distinct, rare neoplasms.

E-PS-24-104

Association of tumour budding in gastric carcinoma and other prognostic factors

I. Mallek*, D. Bacha, M. Hajri, F. Loued, B. Troudi, M. Zaafouri, l. Gharbi, H. Mestiri, S. Ben Slama, A. Lahmer
*Department of Pathology, Abderrahmen Mami Hospital, 2083, Ariana, Tunisia

Background & objectives: Tumour budding (TB) represents small clusters of less than five carcinoma cells at the tumour's front. In gastric adenocarcinoma (ADK), TB's prognostic impact is debated. We aimed to determine TB's prognostic value by studying its association to other prognostic factors.
Methods: A retrospective study was carried in the pathology department of Mongi-Slim Hospital. We included patients with gastric ADK from January 2008 to December 2017. TB was graded as 1 (0-4 buds), 2 (5-9 buds), and 3 (≥10 buds), with additional low-grade (<10 buds) and high-grade (≥10 buds) classifications. We considered the WHO digestive system 2019 and the 2017 pTNM system.
Results: We included 68 patients.Sex ratio (M/F) was 2.57 with a mean age of 61.34 years. Tubular type ADK occurred in 40% of cases. TB grades were 1 in 51%, 2 in 18%, and 3 in 31% of cases, with low-grade TB in 69% and high-grade in 31%. Significant correlations were found between TB and poorly differentiated ADK (p=0.035), vascular invasion (p=0.006), perinervous invasion (p=0.038), parietal

infiltration (p=0.003), lymph node involvement (p=0.005), metastases (p=0.015), advanced tumour stages (p=0.014), and metastatic recurrence (p=0.033). High-grade TB predicted poor 5-year overall survival (p=0.007) and recurrence-free survival (p=0.02).
Conclusion: Since there is a significant association between TB and other histo-prognostic factors in gastric ADK, it may be considered as a prognostic marker, which should be validated in standardized reports. This marker would provide additional information for prognostic stratification and therapeutic decision-making more effectively.

E-PS-24-105
Histological response of gastric adenocarcinomas after chemotherapy: comparison of two scoring systems
I. Mallek*, D. Bacha, F. Loued, M. Hajri, M. Zaafouri, l. Gharbi, H. Mestiri, A. Lahmer, S. Ben Slama
*Department of Pathology, Abderrahmen Mami Hospital, 2083, Ariana, Tunisia

Background & objectives: Gastric cancer (GC) is fifth most common globally and in Tunisia. Tumour regression grade (TRG) after neoadjuvant treatment is crucial for prognosis, but lacks a consensus scoring system. This study compares Mandard and Becker scoring systems for GC TRG evaluation.
Methods: Patients with non-metastatic gastric adenocarcinomas, treated with neoadjuvant chemotherapy followed by surgery, were collected from the pathology department of Mongi Slim Hospital, over a period of 15 years. The study assessed the performance of these scores by analyzing their homogeneity ($\chi 2$), monotony, and discriminative ability, evaluated by the area under the ROC curve (AUC).
Results: Forty patients with an average age of 61.95 years and sex ratio of 2.64 were studied. With Mandard system, average survival for TRG1 was 49.2 months and 39.2 months for TRG5. With the Becker system, TRG1 had an average survival of 50.3 months, contrasting with 42.2 months for TRG3 (p=0.496). Positive predictive values (PPV) for Mandard and Becker were 1.116 and 0.418 at one year, and 5.719 and 1.820 at five years respectively. Linearity values were 0.6 and 0.3 at one year, and 2.5 and 2.2 at five years, respectively. AUC values at one year were 0.568 (Mandard) and 0.545 (Becker), and both were 0.606 after five years.
Conclusion: The TRG emerged as an independent predictive factor for survival. No significant difference was observed between the Mandard and Becker systems. Using the TRG system in combination with ypTNM staging could significantly enhance the prediction of survival in patients with GC.

E-PS-24-106
Mucosal healing in Crohn's disease – when pathology does not agree with endoscopy
V.N. Marin*, L. Stanciu, A. Bordea, A. Cibotariu, R. Neagu, D.M. Marinoiu, R. Ionescu, E. Grămadă, B. Mateescu, M. State, L. Nichita, C. Popp
*Department of Pathology, Colentina University Hospital, Bucharest, Romania

Background & objectives: Mucosal healing (MH) is a desirable therapeutical target in Crohn's disease (CD) since its achievement is associated with a reduced risk of severe complications. This study aims to identify histologic features that correlate with endoscopic MH in CD.
Methods: We retrospectively selected 15 patients that achieved endoscopic MH and compared various features between the biopsies taken during MH and the ones taken during a previous or further period of endoscopic activity: architectural distortion, inflammatory infiltrate (amount and nodularity), presence of macrophages, eosinophils and neutrophils in lamina propria, presence of intraepithelial neutrophils.
Results: None of the biopsies with endoscopic MH had histologic MH, but most cases (14/15) had mild inflammatory infiltrate and 12 cases had no intraepithelial neutrophils (inactive disease). Architectural distortion was significantly more severe during activity periods (t test p=0.0060). Numbers of lamina propria neutrophils and eosinophils were also significantly increased during activity (t test p=0.0001, respectively p=0.0080). Conversely, the number of macrophages was similar in both moments (MH and active disease). Another observation was the fact that in biopsies from endoscopic MH period, we identified, in lamina propria an increased number of eosinophils, even in ones without any neutrophils).
Conclusion: As in ulcerative colitis, endoscopic MH is not always accompanied by histologic MH, which seems much harder to obtain. Probably, this quiescent histologic inflammation is the reason for relapses in CD. New therapy targets should not only address histologic MH, but also try to control the number of eosinophils that seem to normalize later.

E-PS-24-107
AA amyloid deposition in ileocecal valve as a cause of pseudo-obstruction -case report and literature review
J.S. Marrero Afonso*, C. Febles Pérez, R. López Henríquez, M.A. Krupinska
*Hospital Universitario Nuestra Señora de Candelaria, Spain

Background & objectives: Amyloid deposition in the gastrointestinal tract is associated with bleeding, malabsorption, protein-losing enteropathy and motility disorders presenting as gastroparesis, nausea, diarrhea, bacterial overgrowth, constipation, or chronic intestinal pseudo-obstruction. Because of nonspecific radiological findings and clinicopathological characteristics could justify its presentation.
Methods: We report a 87 years-old female patient with complete response IV-A mantle cell lymphoma, diabetes mellitus, long term microcrystalline arthritis and atypical pneumonia. She developed dyspepsia, loss of appetite and weight and diarrheic syndrome. A colonoscopy was scheduled, a diffuse erythematous edematous colonic mucosa with circumferential stenotic ileocecal valve were noted and multiple biopsies were taken and submitted to evaluation.
Results: Gross examination revealed multiple red-whitish tissue fragments with moderate consistency. Microscopically, it was a colonic mucosa with conserved architectural pattern with some erosive foci and expansion of lamina propria with mixed inflammatory infiltrate, mostly lymphocytes and plasmatics cells. Next to the erosion zone, some small vessels showed thickening walls with deposition of amorphous eosinophilic material with Congo Red staining and apple green birefringence in polarized light, whose positivity was intact after potassium permanganate addition. AA amyloid immunohistochemistry supported it. AA amyloidosis deposition was concordant with her clinical picture and the patient next developed protein-losing enteropathy, acute renal failure, urinary tract infection and she died 2 weeks after diagnosis.
Conclusion: Generally, AA amyloidosis is secondary to an underlying condition while AL amyloidosis is associated with hematological disorders, even though both may coexist. The gold standard to diagnose GI amyloidosis remains to be endoscopic biopsy and histopathological examination.

E-PS-24-108
Gastroduodenal mantle cell lymphoma - case report and literature review
J.S. Marrero Afonso*, C. Febles Pérez, S. Carrión Marrero, R. López Henríquez, M.A. Krupinska
*Hospital Universitario Nuestra Señora de Candelaria, Spain

Background & objectives: Gastroduodenal mantle cell lymphoma is an infrequent way of presentation of disease. Because of nonspecific

radiological findings, its wide differential diagnosis with entities in gastrointestinal area, rarity and clinicopathological characteristics could justify its presentation.
Methods: We report a 71 years-old male patient with Fournier's gangrene. A CT showed diffuse mucosal enhancement with associated lymphadenopathy in gastroduodenal area and 19 cm splenomegaly, while analytics revealed lymphocytosis and anemia. In gastroscopy, loss of distensibility, diffuse tendency to nodularity, friability and duodenal lymphangiectasia were noted. Therefore, multiple biopsies were submitted and morphologic description with immunohistochemistry tests were made.
Results: Gross examination revealed multiple red-whitish tissue fragments with moderate consistency. Microscopically, it was formed by gastroduodenal mucosa with striking loss of glandular component and expansion of lamina propia in relationship with a lymphoid proliferation of small lymphocytes with tendency to nodularity. Lymphoepithelial lesions were inconspicuous. A panel of immunohistochemistry revealed diffuse positivity to CD20, CD5, BCL2 and cyclin-D1, and negativity to CD3, CD10, CD23, CD43, CD138 and BCL6, without monotypic expression of light chains, wild-type pattern of p53 expression p53 and a 30-40% proliferative index. A final diagnosis of gastroduodenal affectation by mantle cell lymphoma was made and systemic treatment were planned.
Conclusion: The digestive tract has been identified as one of the most common extranodal locations for mantle cell lymphoma, with the colon being the organ that is usually affected by this condition. It should be taken into account in differential diagnosis to exclude other lymphomas with more predilection to this anatomic zone.

E-PS-24-109
Colorectal cancer - a quick overview of the impact of the COVID-19 Pandemic on its diagnosis in Romania
R. Matei*, S. Pittau, C. Lazureanu, M. Cornianu, A. Dema, A. Muresan, S. Costi, M. Lacob, D. Anderco, C. Suciu, R. Cornea, D. Herman, D. Szilagyi, S. Taban, A. Vaduva
*Pathology Department, "Pius Brinzeu" Emergency County Clinical Hospital Timisoara, Romania

Background & objectives: The COVID-19 pandemic brought with its periods of lockdown that restricted movement and decreased the addressability of healthcare centres for other pathologies. We aimed to determine the pandemic's impact on colon cancer diagnosis in a county hospital in western Romania.
Methods: We performed a retrospective analysis of colon resection cases reviewed in our department between March 2018 an March 2022, representing two years of pre-pandemic and two years of COVID-19 restrictions. The patient's demographic and pathology report data were collected. Based on inclusion and exclusion criteria, 873 cases of colon resection were identified.
Results: Of all cases, 446 (51.1%) were pre-pandemic, while 427 (48.9%) were pandemic. We noticed a decrease in cases originating from our county, with a slight increase from neighboring ones, with significant differences in geographical distribution groups (p=0.0031). The incidence of adenocarcinomas based on tumour location showed a rise of 8.7% in left side of the colon in pandemic period (66.7% vs 58%, p=0.0095). There was a 7.8% increase in cases of lymphovascular invasion, while the perineural invasion showed a 10% increase rate during the pandemic period. Regarding the response to neoadjuvant therapy, there was a 23.3% increase in tumour regression group 3 (TGR3) during the pandemic.
Conclusion: Colorectal cancer is a significant and potentially life-threatening condition that requires early detection through effective nationwide screening programs. During the COVID-19 pandemic, healthcare systems worldwide experienced increased pressure due to the high number of daily hospitalizations resulting from the high contagiousness of the SarsCov2 virus. Considering all the results, diagnosed cases tend to be more severe during the pandemic, leading to a worse prognosis.

E-PS-24-110
Analyzing the correlation of lesion size and macroscopic features in colorectal endoscopic mucosal resection specimens and their association with histopathological diagnoses
M. Mexia*, G. Carrola, D. Sá, A.P. Rodrigues, J.R. Vizcaíno, N.J. Lamas, R. Marcos Pinto, R. Küttner Magalhães, X. Wen
*Anatomic Pathology Service, Pathology Department, Unidade Local de Saúde de Santo António, Portugal

Background & objectives: Adenocarcinomas comprise 96-98% of colorectal malignancies, with well-established precursor lesions. Endoscopic mucosal resection (EMR) removes superficial lesions impossible to excise through standard polypectomy. The aim is to investigate correlations between the macroscopic features with histopathological diagnoses.
Methods: A retrospective analysis was conducted on 129 colon EMR specimens collected between November 2021 and February 2024. Lesions were classified as four types by macroscopic features: superficial lesions, superficial-sessile lesions, sessile lesions and pediculated lesions, and three categories by size: <10mm, 10 to 20mm and ≥20mm. The correlations between the macroscopic features with histopathological diagnoses were evaluated.
Results: The sizes of the lesions varied from 4 mm to 104 mm, with a median of 28mm. Among low-grade lesions, 6% measured <10 mm, 18% were 10 to 20 mm, and 76% were ≥20 mm. High-grade lesions were only present with lesions ≥10 mm, with nearly 88.1% being ≥20 mm. Regarding carcinoma, none were <10 mm; 78.6% were ≥20 mm. High-grade lesions exhibited various macroscopic features: 30.5% sessile polyps, 5.1% pediculated polyps, 33.9% superficial-sessile, and 30.5% superficial forms. Carcinoma lesions comprised 35.7% serrated polyps, 42.9% superficial-sessile, and 21.4% superficial forms.
Conclusion: Our data shows that the majority of the studied lesions were ≥20 mm. High-grade lesions and carcinoma predominantly exhibit larger sizes and diverse macroscopic features, but less frequently in pediculated lesions. Our pilot study highlights the myriad of pre-neoplastic and neoplastic colon lesions normally identified in colon EMR specimens in our reference centre.

E-PS-24-111
Exploring the relationship between lesion characteristics in gastric endoscopic mucosal resection specimens and histopathological diagnosis
M. Mexia*, S. Neves, D. Sá, A.P. Rodrigues, M. Caldas, N.J. Lamas, R. Marcos Pinto, R. Küttner Magalhães, X. Wen
*Anatomic Pathology Service, Pathology Department, Unidade Local de Saúde de Santo António, Portugal

Background & objectives: Endoscopic Mucosal Resection (EMR) is a minimally invasive procedure that plays a crucial role in the management of early-stage gastric cancer and precancerous lesions. The aim is to investigate correlations between the macroscopic features with histopathological diagnoses.
Methods: A retrospective analysis was conducted on 128 stomach EMR specimens collected between October 2021 and March 2024. Lesions were classified as three types by macroscopic features: superficial lesions, superficial-sessile lesions and sessile lesions, and three categories by size: <10mm, 10 to 20mm and ≥20mm. The correlations between the macroscopic features with histopathological diagnoses were evaluated.
Results: Lesions spanned from 5 mm to 110 mm in size, with a median of 21mm. Macroscopically, majority were superficial lesions (76.7%),

followed by superficial-sessile lesions (12.4%) and sessile lesions (10.9%). 67.5% of high-grade dysplasia lesions, 67.6% of intramucosal carcinoma and 60% of pT1b adenocarcinoma were identified in ≥ 20mm lesions. Only 24.4% of low grade dysplasia were found in this category. No pT1b adenocarcinoma was found in < 10 mm lesions. Most of lesions (80.5% of low grade, 72.5% of high grade, 78.4% of intramucosal carcinoma and 80% of pT1b adenocarcinoma) presented as superficial form. No pT1b adenocarcinoma were identified in sessile lesions.
Conclusion: High-grade dysplasia and adenocarcinomas were more frequent in larger lesions, namely, lesions ≥ 20 mm in size. Majority of EMR lesions presented as superficial form. pT1b adenocarcinoma seemed less frequent in sessile lesions. Our pilot study showcases the range of pre-neoplastic and neoplastic stomach lesions commonly found in stomach EMR specimens at our reference centre.

E-PS-24-112
Appendiceal mucinous neoplasms: an overview
W. Mokni*, D. Chiba, S. Bentekaya, I. Bahri, N. Ouini, A. Benabdelkader, B. Sriha, M. Mokni
*Department of Pathology, Farhat Hached University Hospital, Sousse, Tunisia

Background & objectives: Appendiceal mucinous neoplasms (AMNs) are a rare heterogeneous group with varying malignant potential. Their classification has evolved over time.Treatment is based on stagea nd histological features. We aim to study the epidemiology, classification, histopathology and management of this group.
Methods: A retrospective case-series study was conducted, which included 18 histologically confirmed AMNs, diagnosed at our pathology department during the period between 2017and 2024.
Results: Patients was aged between 26 and 69 years-old, with a mean age of 50 years-old. The sex ratio F/M was 17/1. Appendiceal syndrome was the most prevalent presentation, followed by abdominal mass. We found 17 low-grade AMN cases, with only one case of high-grade AMN associated with a primary non mucinous adenocarcinoma. Other associated lesions have been described such as colorectal adenocarcinoma, mucinous ovarian tumour and appendiceal diverticulitis. 9 cases were classified as pTis, 6 as pT4a and the remaining three as pT3 according to the 8th edition of AJCC.
Conclusion: AMNs account for 0.5% of all gastrointestinal neoplasms. They tend to occur in the sixth decade with female predilection. They include Low-grade AMNs, High-grade AMNs, and mucinous adenocarcinomas with/without signet-cell component.Appendiceal mucocele is associated with colonic and ovarian tumours in 11-20% of cases, requiring thorough explorations of the peritoneal cavity. Pseudomyxoma peritonei can occur with all entities, regardless of their grade. This renders the treatment challenging, with controversies regarding the extent of surgery and the role of chemotherapy.

E-PS-24-113
Oesophageal lichen planus: a rare location of a common cutaneous disease
A. Molina Alvarez*, N. Manzanares, J.E. Naves, A. Herrera Galera, R. Fernandez, S. Segura, M. Iglesias
*Department of Pathology at Hospital del Mar, Spain

Background & objectives: Oesophageal lichen planus (ELP) is a rarely reported and underdiagnosed manifestation of lichen planus (LP) in an extra-cutaneous location, with documented high morbidity and risk of malignization. This is a revision of clinical manifestations and current pathological diagnostic criteria.
Methods: Retrospective collection of clinical data, follow up, endoscopic and pathological findings, of eight patients with EPL during the period of 2005-2024 at Hospital del Mar. Detailed slide evaluation by two pathologists of every oesophageal biopsy taken from each patient, before and after the ELP diagnosis. Redefinition of the diagnosis of the previous biopsy according to current literature criteria for ELP.
Results: Eight patients were included (1 male, 7 females) with a mean age of 77,5 +/- 8,1 years. The most common symptom was dysphagia (8/8). All eight presented LP in other locations: 8/8 oral, 1/8 cutaneous, 2/8 genital and 1/8 pilaris. Endoscopy found 8/8 presented lesions in the proximal third of the oesophagus in the form of fibrotic rings, stenosis or mucosal denudation. Histologically, 7/8 presented lichenoid-like changes in at least one biopsy (apoptotic keratinocytes, epithelial detachment, lymphocytic infiltrate and/or dyskeratosis), while 1/8 presented nonspecific changes. There was a delay in diagnosis of ELP of 4,7 +/- 2,4 years. 6/8 presented improvement with treatment. None evolved into esophageal squamous cell carcinoma.
Conclusion: ELP is most common in middle-aged women, with dysphagia being the most referred symptom. Patients associate LP in other locations, predominantly oral mucosa. Diagnostic delay occurs mostly because of lack of clinical suspicion, paired with unspecific endoscopic findings and subtle histologic changes. All three of these must be taken into consideration for an accurate and swift diagnosis of this disease. It is important to suspect ELP in patients with mucosal LP and oesophageal symptoms because of its malignization potential.

E-PS-24-114
A rare case of symptomatic Brunner gland hamartoma in a 24-year-old patient
F. Muresan*, R. Gandabescu, A. Iliesiu
*Bucharest University Emergency Hospital, Romania

Background & objectives: Brunner gland hamartoma (BGH), a rare benign duodenal tumour, is typically an incidental finding observed in middle-aged individuals. Various etiological factors have been proposed, including dysembryoplasia, hyperchlorhydria, Helicobacter pylori infection, and chronic pancreatitis. The literature lacks a clear etiopathogenic model.
Methods: This paper presents a notable case of BGH occurring in an unusually young patient who presented with severe upper gastrointestinal bleeding requiring surgical intervention. Special stainings (Giemsa) and immunohistochemical markers (MUC2, MUC5AC, MUC6, CDX2, Villin, KI-67, p53) were used to manage the case and establish the histopathological diagnosis. The aim of the study is to provide a pathogenical model.
Results: A 23 y.o. male presented with hematemesis and melena, as well as a low hemoglobin level of 8.2 g/dL, which required surgical resection of the antrum and proximal duodenum. No risk factors for gastrointestinal malignancies were identified. The pathological examination revealed an ulcerated tumour in the proximal duodenum, characterized by an encapsulated, lobulated proliferation of mature Brunner glands (BG) draining into large ducts. Based on histological and immunophenotypical aspects, we propose a pathogenic model consisting of a complex, multi-step epithelial transition. A chronic injurious stimulus directed against the duodenal mucosa determines ductal and BG proliferation. Foveolar metaplasia appears to contribute to the proliferative process.
Conclusion: Symptomatic BGH is exceptionally rare among young patients and can easily be mistaken for malignancies. To date, only 7 cases of symptomatic tumours in patients under 24 years of age have been documented in the scientific literature. Our study attempted to elucidate the pathogenic cascade of BGH and raise some important questions regarding the role that foveolar metaplasia, a common ancillary finding, may have in this process.

E-PS-24-115
Colorectal carcinoma in young individuals: an emerging challenge
V. N Gowda*, A. Nalwa, M. Rao, S. Khera, D. Vedant, V. Vishwajeet, D. Aggarwal, V. Verma, P. Elhence
*Department of Pathology, AIIMS, Jodhpur, India

Background & objectives: Studying colorectal cancer (CRC) in individuals under 40, known for its poor prognosis and lower survival rate, aims to uncover distinct histopathological and clinicopathological features, shedding light on its unique characteristics in this age group.
Methods: Cases of CRC received in the Department of Pathology at AIIMS Jodhpur from January 2022 to March 2024 were evaluated, and patients falling in the age group below 40 years were included in the study. Demographic data and clinical data, along with the presence of any precursor lesions, colonoscopy findings, histopathological examination and immunohistochemistry findings, were noted and evaluated.
Results: We examined 42 cases of CRC in individuals aged 14-40 years (mean age:30) with male predominance. Clinical presentation included bleeding per-rectum and abdominal pain. Colonoscopy revealed ulcero-proliferative growth in majority of cases. Two cases exhibited polyps: hyperplastic polyp and tubulovillous adenoma. Location included rectum, followed by sigmoid colon, transverse colon and caecum. Adenocarcinoma-NOS was the predominant morphological type, followed by mucin-secreting adenocarcinoma with signet ring cell morphology. Metastatic disease was observed in 22 cases. One case was associated with a neuroendocrine tumour, and another was a known case of ulcerative colitis. Therapy and follow-up data evaluated, revealed poor chemo-response score and metastasis in patients who had received adjuvant chemotherapy post-surgery.
Conclusion: CRC in young individuals, though rare, displays a more aggressive cancer biology compared to adult cases. Understanding its epidemiology, etiology, and clinical characteristics is vital for early detection and tailored treatment. Further research is needed to uncover the mechanisms behind its rising incidence and develop targeted interventions. Our study underscores the need for heightened awareness and prompt evaluation in young patients presenting with symptoms suggestive of colorectal malignancy to improve outcomes.

E-PS-24-117
Case report of a peritoneal mesothelioma in differential diagnosis with an extrinsic tumour infiltration of the intestinal wall. Which are the odds?
A. Neamţu*, N. Zurbău-Anghel, B.D. Totolici, O.S. Cotoi
*Victor Babes University of Medicine and Pharmacy, Romania

Background & objectives: Mesotheliomas represent malignant tumours that arise from the serosal lining the pleura, peritoneum, pericardium, and tunica vaginalis. The most common localization is the pleura, followed by the peritoneum (rare, more frequent in women, carcinogenesis notably linked to asbestos exposure).
Methods: A 70-year-old female was admitted by the Surgery Department due to a strangulated umbilical hernia. Imaging and intraoperative appearance revealed peritoneal carcinomatosis and the course of treatment was cytoreductive surgery, without prior cytologic analysis of the peritoneal fluid or needle biopsy. For a diagnosis of certainty, the probes were assessed by the Pathology Department,intially histopathologically and then immunohistochemically.
Results: Grossly, the fragment of intestine assessed presented at serosal level multiple white nodules with increased consistency and diameters around 10 mm. Microscopically, a tumoural proliferation was observed in the serosa and muscularis propria. It was presenting a papillary pattern, constituted from cells of medium size, round/oval in shape, with scant eosinophil cytoplasm, oval nuclei, and distinguishable nucleoli. Rare psammomatous bodies were present. Immunohistochemical assessment revealed in the tumour arrangements the following: CK7 multifocal positive reaction, with strong cytoplasmic staining; CK20 negative; Calretinin uniformly positive with both cytoplasmic and nuclear staining; WT1 uniformly positive nuclear staining; CA125 multifocal positive; ER negative; p53 negative. All markers had the appropriate controls.
Conclusion: Clinical presentation and histological appearance pleaded for an extrinsic tumour infiltration of the intestinal wall, most likely due to a low grade serous ovarian carcinoma, without the possibility to exclude a peritoneal mesothelioma. Nevertheless the tumour architecture correlated with the results of the immunohistochemical assessment pleaded for a peritoneal (malign) mesothelioma of the tubulo-papillary type.

Due to the rarity and aggressiveness of peritoneal mesotheliomas, alongside the lack of a specific immunohistochemical marker, awareness should be raised among pathologists.

E-PS-24-118
Clinical-pathological characteristics of gastric crawling-type adenocarcinoma in a Portuguese single centre: a case series on an emerging entity
S. Neves*, M. Mexia, A.P. Rodrigues, C. Peixoto, M. Caldas, N. Jorge Lamas, J.R. Vizcaíno, X. Wen
*Unidade Local de Saúde de Santo António (ULSSA), Portugal

Background & objectives: The gastric crawling-type adenocarcinoma is an adenocarcinoma characterized by its particular histological pattern with predominantly horizontal expansion and a "WHYX" pattern displaying tortuous and anastomosing glands, frequently mixed with poorly cohesive component.
Methods: We report the five cases of gastric crawling-type adenocarcinoma that have been diagnosed at our institution between 2021 and March 2024. The following data were evaluated: age and gender of patients, location, macroscopic appearance, tumour size, histological subtype, erosion, tumour extent, vascular/lymphatic involvement and changes of non-neoplastic mucosa.
Results: The patients had ages between 47 and 82 and two were women. Three cases occurred in the gastric body and two in the antrum. Three of the lesions were flat and two were slightly depressed, which showed erosion. The largest dimensions of the lesions were between 23mm and 43mm. According to WHO classification, two of the lesions were tubular adenocarcinoma while the others were mixed-type with tubular and poorly cohesive components comprising some signet-ring cells. All of the lesions were intramucosal carcinoma, with involvement of muscularis mucosae in three of them. No vascular/lymphatic invasion was observed. There was chronic gastritis and intestinal metaplasia in the non-neoplastic mucosa in all cases.
Conclusion: Gastric crawling-type adenocarcinoma is an increasingly encountered diagnosis, with specific clinical-pathological characteristics. In this study, we reported 5 cases. Four patients are currently under surveillance, without disease recurrence. The other patient, after multidisciplinary team discussion, was recently submitted to subtotal distal gastrectomy given the size of the lesion, as well as its mixed histology with signet-ring cells. The histological examination of the surgical specimen showed no residual neoplasia.

E-PS-24-119
De novo dedifferentiated gastrointestinal stromal tumour (GIST): a case report on an unusual and diagnostically challenging neoplasia
S. Neves*, A.P. Rodrigues, I. Araújo, N. Jorge Lamas
*Unidade Local de Saúde de Santo António (ULSSA), Portugal

Background & objectives: Gastrointestinal stromal tumours (GISTs) are well-described gastrointestinal tract mesenchymal tumours. A small minority undergo a process of dedifferentiation that usually occurs after prolonged therapy. De novo dedifferentiated GISTs have scarcely been reported and their biological behaviour is largely unknown.
Methods: We report the case of a male 85-year old patient with a common iliac artery aneurism. The patient did not have any history of

chemotherapy, nor immunotherapy. During the pre-operative exams, an abdominopelvic CT scan revealed a gastric wall mass. The patient underwent an atypical gastrectomy.
Results: The surgical specimen comprised a 5x3,5x1,5 cm whitish vaguely multinodular lesion. The histopathological analysis showed a biphasic neoplasm composed by monomorphic solid areas of epithelioid cells with rounded nuclei, evident nucleoli and eosinophilic cytoplasm with ill-defined borders; and areas of edematous stroma, containing cells with a high nuclear-cytoplasmic ratio, irregular contour, hyperchromatic nuclei with evident nucleoli and eosinophilic cytoplasm. Pleomorphism was light to marked. Aberrant morphological aspects were evident. Necrotic foci were absent and the mitotic index was low (<1 mitosis/5 mm2). CD117 positivity was present in the epithelioid component, while DOG1 and CD34 (focally) were positive in both components. The NGS study revealed a PDGFRA p.I843_D846del pathogenic variant.
Conclusion: This case highlights the unusual and exceptional morphological aspects that dedifferentiated GISTs can harbor, namely marked pleomorphism with morphologically aberrant neoplastic cells in the presence of an extremely low mitotic index. In addition, this neoplasia developed in a patient without previous history of cancer-related therapies, adding further to the uniqueness of the case. Nearly 16 months have elapsed since surgery and the patient remains under a strict surveillance protocol, without evidence of disease recurrence or metastases onset.

E-PS-24-120
A rare case of mucinous cystic neoplasm arising from gastric heterotopic pancreas
L. Njim*, S. Ben Hammouda, D. Beltaifa, A. Ben Mabrouk, M.A. Chaouch, A. Zakhama, M. Njima
*Fattouma Bourguiba University Hospital, Monastir, Tunisia

Background & objectives: Heterotopic pancreas (HP) is a congenital anomaly that is susceptible to developing the same complications that can affect the orthotopic pancreas, such as neoplasms. Herein, we report a rare case of mucinous cystic neoplasm (MCN) arising from gastric HP.
Methods: A 30-year-old male presented to the gastroenterology department with a history of chronic epigastric abdominal pain. Computed tomography was performed and revealed a 7.5 cm multicystic mass within the stomach. The patient underwent a gastric tumourectomy and the specimen was sent for pathological examination.
Results: Gross examination of the specimen identified a 7.5 × 5.5 cm multicystic mass filled with clear liquid. Microscopic examination revealed a well-limited tumour made by cysts of varying size and developing in the different gastric parietal layers from the submucosa to the subserosa. These cysts were lined by regular gastric foveolar type epithelium, which was surrounded by characteristic ovarian-type stroma with some smooth muscle cells. There were numerous ectopic exocrine pancreatic lobules surrounding tumour cysts. Immunohistochemistry findings showed positive labeling of cells of ovarian-type stroma surrounding cysts with Estrogen receptor (ER), Progesterone receptor (PR) and CD10. Based on the above features, we concluded to MCN arising from gastric HP.
Conclusion: The most affected patients of HP are asymptomatic and it is thought to occur almost exclusively in women. The emergence of MCN from a HP is uncommon and especially in male patients. Its prognosis depends on the severity of epithelial lesions like dysplasia and the presence of an invasive component, which makes it less favourable. Its preoperative diagnosis is difficult. Thus, it should be considered as differential diagnosis and surgical resection must not be delayed.

E-PS-24-123
Gastrointestinal leiomyomas do not show fumarate hydratase (FH) expression loss
G. Karpathiou, J. Pascal*, T. Amaamri Seebach, M. Peoch, M. Mobarki
*CHU of Saint-Etienne, France

Background & objectives: Uterine et cutaneous leiomyomas can show expression loss of fumarate hydratase (FH), somatic or germline, like in the context of the hereditary leiomyomatosis and renal cell carcinoma (HLRCC) syndrome.
We sought to determine whether gastrointestinal leiomyomas (GI-LM) express FH.
Methods: In contrast to the cutaneous and uterine leiomyomas of the HLRCC syndrome, leiomyomas of other sites have been rarely studied. A total of 47 whole slide GI-LMs were studied for the immunohistochemical expression of FH. We also compared them with 27 GISTs, the most common mesenchymal tumours of the gastrointestinal tract.
Results: All 47 leiomyomas studied expressed the FH diffusely. Of these, 17 had moderate or strong staining (36%). Similarly, all 27 GISTs were FH diffusely positive, 52% in a moderate/strong manner.
Conclusion: Our results show for the first time that gastrointestinal leiomyomas are FH proficient tumours, and probably not associated with the HLRCC syndrome. To the best of our knowledge, the expression of FH has been never studied before.

E-PS-24-124
A case of malakoplakia in the setting of Crohn's disease and CMV co-infection
A. Pergaris*, T.S. Driva, M. Tampaki, A. Koutsoumpas, S. Sakellariou
*First Department of Pathology, Medical School, National and Kapodistrian University of Athens, Greece

Background & objectives: Malakoplakia is related to inability of macrophages to properly digest phagocytosed gram-negative bacteria, resulting in accumulation of microorganism-laden histiocytes in hosts' tissues, clinically stimulating neoplasia. We present a case of malakoplakia in the setting of Crohn's disease and CMV co-infection.
Methods: A 51-year-old male with a history of Crohn's disease under treatment with prednisolone and Ustekinumab and of multiple hospitalizations due to Salmonella and Campylobacter infections, presented in our institution with severe diarrhea. Endoscopy of the lower gastrointestinal tract revealed raised white plaques and polypoid structures. Multiple biopsies from different colon compartments were obtained for histological examination.
Results: On histology, inflammatory changes consistent with Crohn's disease were present in the terminal ileum, cecum, left colon and the rectum. In the right and transverse colon, lamina propria was expanded by sheets of PGM1-positive and CD1a-negative epithelioid macrophages engulfing round and targetoid laminated bodies. Their characterization as Michaelis–Gutmann bodies was confirmed by positive staining with PAS, Alcian Blue and von Kossa stains and negative for acid fast stains, thus rendering the diagnosis of malakoplakia. CMV co-infection was additionally diagnosed and proven immunohistochemically by the detection of multiple CMV-positive histiocytes and endothelial cells (7 CMV-positive cells/high-power field).
Conclusion: The rarity of the presented case relies on the co-existence of malakoplakia and CMV infection on the background of Crohn's disease as an expression of severe derangement of immunity in the context of immunosuppressive medication. The awareness of such rare complications is mandatory in patients under immunosuppression and the usage of new biologic agents.

E-PS-24-125

EBV-positive gastric carcinoma displays varied morphological spectrum, and Cytokeratin 7 can be utilized for screening of this important neoplasm subtype - evaluation of a large consecutive case series

P. Pires*, M. Alessandra Pereira, U. Ribeiro Júnior, E. Sobroza de Mello
*HCFMUSP, Brazil

Background & objectives: Gastric cancer (GC) infected with Epstein-Barr virus (EBV) are a distinct molecular group, exhibiting unique clinicopathological characteristics, with benefits from immunotherapy. This study aimed to explore screening methods for identifying EBV-positive GC, considering morphology and cytokeratin 7 expression.
Methods: All patients with GC who underwent surgery between 2009 and 2017 at our institution were included. Tissue microarray blocks were fabricated with three representative tumour areas, and immunohistochemistry for cytokeratin 7 (CK7) and chromogenic in situ hybridization for EBV were performed. All EBV-positive cases were reviewed for evaluation of morphological patterns, tumour-infiltrating inflammatory (TII) cells, and morphological subtype.
Results: In the study, 347 patients were included (60% male, 40% female, mean age 63.2 years), 67 were CK7 negative, and 42 were EBV positive. A strong statistical association ($P < 0.00001$) was found between EBV positivity and CK7 negativity. CK7 negativity as a diagnostic test for EBV-positive GC, showed a sensitivity of 88.1%, specificity of 90.2%, and negative predictive value (NPV) of 98.2%. For EBV-positive GC cases, morphological review revealed that 21 cases (50.0%) were medullary carcinomas with lymphoid stroma, 15 cases (35.7%) tubular adenocarcinomas, and 6 cases other subtypes. Moreover, 31 (73.8%) cases exhibited moderate to intense or intense TII.
Conclusion: This study highlights the strong association between the absence of CK7 expression and the molecular subtype of EBV-positive GC, with a high NPV indicating CK7-positive cases are EBV-negative. CK7 negativity suggests further EBV investigation by CISH, making CK7 a great cost-effective screening tool.

However, morphological review revealed only half of cases had a medullary morphology, and three-quarters had moderate to intense or intense TII. Thus, neither morphology nor TII are effective screening methods.

E-PS-24-126

Xanthogranulomatous oophoritis missdiagnosed as diverticulitis: a case report

C. Plesa*, D. Marton, E. Horvath, S. Gurzu
*Romania

Background & objectives: Xanthogranulomatous oophoritis is a rare type of chronic inflammation that, under microscope, can mimick a lymphoma. The aim of this paper is to present a case in which surgery was done for suspicion of diverticulitis.
Methods: A 64-year-old female, with Hartman procedure done for a previously perforated sigmoid diverticulitis, was hospitalized with acute abdomen. Emergency surgery was necessary. During the reversal of Hartmann procedure, on intraoperative examination, the presence of a mass located between sigmoid colon and ovary raised the suspicion of possible malignancy. Colectomy and left ovarectomy was done.
Results: Pathologic examination showed diverticula, without perforation, and extensive adhesions between the sigmoid colon and ovary forming a wel-defined mass measuring 70x100 mm. Pale-yellow lobulated cut surface and large areas of necrosis were emphasized. Histologically, the ovarian stroma proved to be infiltrated by extensive proliferation of foamy macrophages, CD138-positive plasma cells, CD20-positive B cells, and CD15-positive neutrophils, along with CD68-positive foreign body giant cells. The Ki67 index was below 10%. Extensive diverticular disease of the colon was also noted, without diverticulitis. The immunohistochemical assessment was performed to exclude a lymphoma.
Conclusion: Xanthogranulomatous oophoritis is a challenging diagnosis for surgeons and pathologists. The exact etiology remains undetermined but diverticulitis can trigger its evolution. Transdisciplinary team assessment and correlation of clinically, radiologically, and histopathological examination, along with immunohistochemistry is required for an accurate diagnosis.

E-PS-24-127

Comparison of assessment methods for tumour budding in gastric cancer

T. Polushkina*, T. Sotnikova, N. Danilova
*Lomonosov Moscow State University, Russia

Background & objectives: Tumour budding (TB, single cancer cells or clusters of up to 4 cancer cells) - a promising biomarker in gastric cancer (GC), predicting disease progression and unfavourable survival. However, today there is no uniform assessment method of TB for GC.
Methods: Three methods for assessment TB were compared on 173 surgical specimens of GC. Method by H.Ueno: one field of view with maximal TB (hot spot) on H&E slides (lens magn.x20). Method by L.Wang: five fields of view (5 hot spots) on H&E slides (lens magn. x20). Method by E. Karamitopolou: 10 fields of view on ICH slides (Pancytokeratin, AE1/AE3, lens magn.x40).
Results: After counting GC were divided into two groups - high grade of TB (10 or more foci in the field of view) and low grade (less than 10 foci in the field of view. Multivariate analysis of factors affecting overall survival was performed using Cox proportional hazard model. Risk ratio (RR) TB counted by H.Ueno method was 1,77 (CI: 1,07-2,93, p=0,03). When using E. Karamitopolou method RR=2,12 (CI: 1,26–3,56, p=0,02). By using L.Wang method RR=1,81 (CI: 1,10–3,01, p=0,01). All assessment methods revealed significant differences in patient survival between groups with low grade TB and high grade TB (Log Rank Mantel-Cox p=0,000).
Conclusion: Today there is a need to compare different assessment methods. In our study we showed TB is a strong negative prognostic factor in gastric cancer using any scoring method. Although E. Karamitopolou method has the greatest negative predictive value (RR=2,12), we consider that the H.Ueno method should be used because it is the least labor intensive.

E-PS-24-128

Correlation of tumour budding with MSI and PD-L1-status in gastric cancer

T. Polushkina*, T. Sotnikova, D. Kalinin, N. Danilova
*Lomonosov Moscow State University, Russian Federation

Background & objectives: Tumour budding (TB) – promising prognostic biomarker in gastric cancer (GC), associated with unfavourable prognosis. There are conflicting data on the relationship between TB, PD-L1 and MSI status in GC.
Methods: Identification of MSI and PD-L1-status was performed by immunohistochemical staining on markers MSH2 (clone FE-11), MSH6 (clone EP49), MLH1 (clone ES05), PMS2 (clone EP51), PD-L1 (clones SP142 and SP263, Ventana). Tumours were classified as MSI-positive if there was no expression of at least one of the markers (MLH1, MSH2, MSH6 and PMS2). Positive PD-L1-status was considered positive with CPS >1.
Results: We used three methods for assessment TB in GC: method by H. Ueno (H&E, 1 hot spot, lens.magn.x20), E. Karamitopolou (PCK, lens.magn.x40) and L.Wang (H&E, 5 hot spots, lens.magn.x20). GC were divided into two groups - high grade/low grade of TB. Using the

H.Ueno method a predominance of low grade TB was found in the group of MSI-positive carcinomas (90,5% of MSI-positive cases were LG TB, p=0,035). The L.Wang method revealed 85,7% of MSI-positive cases were LG TB, p=0,028. With the E. Karamitopolou method 76,2% of MSI-positive cases were LG TB, p=0,106. When analyzing the relationship between TB and PD-L1 expression, no statistically significant differences were found (p>0,05).
Conclusion: Assessing TB in surgical specimens can provide information about the response to treatments, such as immunotherapy, which have been introduced into the treatment of GC in recent years. In this study, we demonstrated the relationship between TB, PD-L1 and MSI status in GC: Low grade TB, assessed by methods H.Ueno and L.Wang, correlates with MSI-positive status, but not with PD-L1-status of GC.

E-PS-24-129
Expression of PD-L1 in gastric cancer
T. Polushkina*, T. Sotnikova, D. Kalinin, N. Danilova
*Lomonosov Moscow State University, Russia

Background & objectives: Tumours have the ability to express PD-1 ligands on their surface, which ensures that they escape from the anti-tumour immune defense mechanism of the body. The possible association of PD-L1 expression with variants of gastric carcinomas is being actively studied.
Methods: Samples from 131 patients diagnosed with stomach cancer were used. Reactions with PD-L1 (clones SP263 and SP142) were performed using the Ventana BenchMark Ultra device (Roche Ventana, USA) according to the standard protocol and stained by in situ hybridization using primers to small viral RNAs of the Epstein—Barr virus (INFORM EBER, Roche Ventana, USA).
Results: The positive PD-L1 status detected by clones SP263 and SP142 is significantly associated with the macroscopic form according to the R. Bormann classification (p=0.003/p=0.003), morphological type according to the WHO 5th edition classification, 2019 (p=0.001/p=0.018) and the presence/absence of signet ring cells (p=0.001/p=0.010). Among EBER-positive cases, a positive PD-L1 status (SP263) was observed in 15 (100%) out of 15, and the number of cases with a positive PD-L1 status (SP142) was 10 (76.9%) out of 13. The overall five-year survival rate of patients in the PD-L1-negative tumour group was significantly lower than in patients in the PD-L1-positive tumour group, which was 50.0% and 40.0% also for both clones (p=0.027).
Conclusion: The macroscopic form according to R. Borman, the morphological type according to the classification of WHO 5th edition, 2019, and the presence/absence of signet ring cells are statistically significant parameters, where there is a significant relationship with PD-L1 expression. Positive PD-L1 status is significantly more often detected in HBV-associated gastric carcinomas. An increase in the expression level of PD-L1 clones SP263 and SP142 are significant prognostic signs that reduce the likelihood of death in patients.

E-PS-24-130
Glomus tumour of the stomach: a potential diagnostic pitfall
A. Praf*, V. Enache, M. Hortopan, M. Ciocirlan
*Department of Pathology, University Emergency Hospital, Bucharest, Romania

Background & objectives: Glomus tumours are mesenchymal tumours that arise from modified smooth muscle cells of the glomus body and usually occur in the distal extremities. However, rare cases have been reported in the gastrointestinal tract, most often in the gastric antrum.
Methods: A 46-year-old female presented with upper epigastric pain and early satiety for several months. Upper endoscopy and CT scan revealed a distal antral mass, suggesting a gastrointestinal stromal tumour (GIST). Endoscopic ultrasound (EUS) with simultaneous fine needle biopsy (FNB) was conducted and revealed a 22-mm-sized hypoechoic, well-circumscribed lesion, located on the fourth layer of the stomac wall.
Results: The biopsy specimen showed features suggestive of gastric glomus tumour. After that, partial gastrectomy was performed. Macroscopically, a well-defined intramural mass with soft, brown cut surface, measuring 25/20/25 mm was identified. Histopathologically the tumour consisted of sheets and nests of uniform round cells with monotonous nuclei and pale to clear cytoplasm, arranged around a conspicuous vasculature. Mitoses were rare (1/50 HPF) and necrosis was not observed. Immunohistochemical stains were strongly positive for SMA and focally positive for calponin. In contrast, tumour cells were negative for AE1/AE3, S100, HMB45, synaptophysin, CD 34, CD117 and DOG1. The Ki-67 proliferation index was 2%. Morphological features and further IHC studies confirmed the initial diagnosis.
Conclusion: Preoperative diagnosis of gastric glomus tumours is challenging due to the generally deep location of the tumours and the lack of unique clinical, endoscopic and CT features. Therefore, the diagnosis depends primarily on pathological and immunohistochemical findings. Although rare, glomus tumour should always be included in the differential diagnosis among other gastric tumours, such as epithelioid GIST, leiomyoma, schwannoma, solitary fibrous tumour and neuroendocrine tumour.

E-PS-24-131
Is there a difference in the number of malignant diseases of the appendix in the pre-COVID and post-COVID period?
M. Radošević*, D. Matić, I. Čapo, M. Živojinov, S. Trivunić Dajko, M. Djolai
*General Hospital "Djordje Joanović" Zrenjanin, Serbia

Background & objectives: Appendiceal malignancies are exceedingly rare diseases with uclear etiology. Therefore, the objective of this epidemiological study was to determine whether there is an impact of COVID-19 infection on the increase in the number of such neoplasms.
Methods: Epidemiological analysis utilized data of all operated appendices from the Center for Pathology and Histology, UKCV Novi Sad, for April 1, 2018-April 1, 2020 (pre-COVID 19-first group) and April 1, 2022- April 1, 2024 (post-COVID 19-second group). All neoplastic specimens were categorized by histological type and grade and prevalence by age and gender.
Results: All patients required surgery due to acute inflammation. Sume of operated pacient in first group was 1407 and in the second 1345. The incidence of malignant neoplasms increased from 11 in the first group to 29 in the second. A significant increase in prevalence among women (from 55% to 72%) and decrease among men (from 45% to 28%) were noted. The average age of patients was increased from 40 years pre-COVID to 47,4 years post-COVID. Additionally, an increase in the number of LAMN and Goblet cell tumours was observed in the second group, compared to HAMN, NOS adenocarcinoma and neuroendocrine tumour.
Conclusion: Based on the conducted epidemiological analysis, an increase in malignant neoplasms of the appendix in the period after COVID-19 infection was determined.

E-PS-24-132
Diagnostic value of nuclear β-catenin expression and precancerous lesions of the colon
G. Raskin*, N. Ogurchenok, I. Bryukhovetskiy
*Dr. Berezin Medical Institute, Russia

Background & objectives: β-catenin, in collaboration with the PI3K/Akt/mTOR signaling pathway, plays an important diagnostic role as a marker for the transformation of precancerous lesions into CRC, which may be a solution to emerging disputes in pathomorphological diagnosis.

Methods: We studied 257 samples from patients, aged 13 to 78 years, with various precancerous lesions of the colon: hyperplastic polyps, serrated adenomas, tubular adenomas, intraepithelial neoplasia in inflammatory bowel diseases, intraepithelial and intramucosal adenocarcinomas (early cancers). Using immunohistochemistry, the relationship between cell stemness (CD44) during epithelial-mesenchymal transition, cell proliferation (Ki67), and translocation of nuclear β-catenin, p53 protein status, was analysed.
Results: Nuclear translocation of β-catenin was most strongly expressed in intraepithelial and intramucosal cancers, in combination with p53 overexpression, especially in early signs of epithelial-mesenchymal transition, as well as in high-grade intraepithelial neoplasia, predominantly in tubular adenomas and in patients with recurrent precancerous lesions colon. Also, β-catenin was nuclearly expressed in IBD patients newly diagnosed with IBD and was cytoplasmically expressed in treated IBD patients.
Conclusion: Immunohistochemical assessment of nuclear β-catenin overexpression in premalignant colonic lesions is a practical method for differentiating early-stage cancer from dysplasia, and may also improve the assessment of treatment efficacy for IBD itself and IBD-associated lesions.

E-PS-24-133
Tumour budding and poorly differentiated clusters are independent prognostic factors in Brazilian patients with stage II colorectal cancer
M. Reis*, M. Matsushita, W. Santos, V. Teodoro, M. Reis, D. Guimarães, R. Manuel Reis
*Barretos Cancer Hospital, Brazil

Background & objectives: TB and PDC are risk factors for recurrence in CRC and may indicate adjuvant treatment. This work aims to evaluate the prognostic value of TB and PDC in stage II patients and their association with clinical, histopathological, and molecular features.
Methods: Two hundred fifty-seven patients treated with upfront surgery in a cancer hospital between 2008 and 2016 were analysed. TB and PDC were evaluated according to ITBCC - 2016 in hematoxylin-eosin (H&E) sections. Mismatch repair proteins (MMR), microsatellite instability (MSI), BRAF mutation, and Fusobacterium nucleatum (Fn) were also evaluated. Statistical analyses were performed using the IBM SPSS Statistics program; p= 5%.
Results: High and intermediate TB and PDC were associated with high-grade tumours and perineural invasion. High and intermediate PDC were associated with MSI-H tumours, deficient MMR, BRAF mutation, and high Fn quantification. Higher disease-specific survival (DSS) and disease-free survival (DFS) at 5 and 10 years were observed in patients with low TB and PDC compared to high TB and PDC. Multivariate Cox regression: Patients with high PDC have a higher risk of death from cancer, and patients with high TB have a higher risk of recurrence/metastasis. In stage II patients who did not receive adjuvant treatment (n=150), DSS and DFS were lower than those observed in the general group (n=257).
Conclusion: High and intermediate TB and PDC were associated with clinicopathological features of greater tumour aggressiveness and molecular features with predictive potential. TB and PDC are independent prognostic factors for the Brazilian population with stage II CRC.

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E-PS-24-135
PD-L1 expression in DNA mismatch repair deficient and proficient colorectal cancer (CRC): correlation with clinicopathological features
S. Zargarzadeh, S.U.R. Khan, J. Linares, B. Ganeshan, D. Allen, M. Jansen, M. Rodriguez-Justo*
*University College London and University College London Hospitals NHS Foundation Trust, United Kingdom

Background & objectives: CRC is a heterogeneous disease, with the deficient subtype exhibiting distinct immune responses and favourable outcomes with immunotherapy. We aim to explore PD-L1 expression in dMMR and pMMR, to elucidate potential therapeutic targets and underlying mechanisms driving its expression.
Methods: 100 CRC cases (53 MMR-deficient, 47 MMR-proficient) were stained with PD-L1 and CD8 for T-cells. PCR for MSI was used to validate MMR deficient phenotype. PD-L1 expression (CPS: 0, ≥ 1 or ≥ 10) was scored in tumour and immune cells and digital image analysis was used to quantify CD8 populations. Results were correlated with pathological and clinical variables.
Results: The PD-L1 positivity rate in MMR-deficient tumours was 41.51%, which is higher compared to that in MMR-proficient tumours. Positive correlations was observed between CD8 and PD-L1 expression levels, suggesting a potential linkage or co-regulation between CD8 T cell presence and PD-L1 expression. Additionally, PD-L1 expression correlated with Tumour stage in MMR-deficient tumours. Comparative analysis revealed a significant difference in PD-L1 expression between MMR-deficient and MMR-proficient groups. The PCR results for microsatellite instability-high (MSI-H) demonstrate complete concordance across all MMR-deficient cases, confirming that each MMR-deficient case exhibits MSI-High status. Interestingly a subgroup (23%) of pMMR had high PD-L1 expression suggesting a potential role for immune-checkpoint inhibitors in this subgroup.
Conclusion: This study demonstrates a higher prevalence of PD-L1 expression in MMR-deficient CRC, suggesting a potential immunogenic phenotype in view of the high CD8 expression. Its association with advanced TNM stages highlights PD-L1's importance in tumour progression, providing insights into its heterogeneous expression and therapeutic use in MMR-deficient CRC. A subset of MMR-proficient (MMR-p) CRC also exhibited high PD-L1 expression, suggesting that a subgroup of pMMR CRC may benefit from immune checkpoint inhibitors.

E-PS-24-136
Utilising a γδ T-lymphocyte immunohistochemical marker to quantify γδReceptor T lymphocytes in Coeliac disease, refractory Coeliac Disease and enteropathy associated T cell lymphoma
W. Jervis, S.U.R. Khan, B. Ganeshan, M. Rodriguez-Justo*
*University College London and University College London Hospitals NHS Foundation Trust, United Kingdom

Background & objectives: Coeliac-disease is a condition that is treated with gluten-free -diet, those non-responsive are diagnosed as refractory CD, associated with increased risk of developing lymphoma (EATL). We aim to evaluate correlation between the γδ T-lymphocytes in healthy and pathological duodenal biopsies
Methods: We used immunohistochemistry (antibody H-41) to analyse γδ T lymphocytes in 95 FFPE duodenal biopsies: normal (20), lymphocytosis (20), CD (21), RCD (20), EATL (14) . H-41 has been demonstrated to stain and quantify intraepithelial γδ T-lymphocytes with high specificity and sensitivity for coeliac disease in formalin-fixed paraffin-embedded (FFPE) duodenal biopsies. Digital image analysis was used to quantify intraepithelial lymphocytes.
Results: Compared to normal controls (n=20) γδ T lymphocytes counts were significantly increased in coeliac disease patients (n=21, $p<0.001$). γδ T lymphocytes counts in EATL (Enteropathy-associated T-cell lymphoma) patients (n=16) were significantly lower in comparison to coeliac disease patients (n=21, $p<0.001$). Coeliac disease (n=21) and refractory coeliac disease patients (n=17) did not show statistically significant changes in γδ T lymphocytes counts ($p>0.05$).

Conclusion: Immunohistochemistry stained and quantified raised intraepithelial γδ T-lymphocytes in FFPE duodenal biopsies of patients in coeliac disease in comparison to normal controls and other duodenal lymphocytosis, emphasising how γδ T-lymphocyte immunohistochemistry can assist in the diagnosis of coeliac disease. No significant relationship was demonstrated between γδ T-lymphocytes counts in coeliac, refractory coeliac disease and EATL patients indicating that the γδ receptor does not play a significant role in the progression of coeliac disease/refractory coeliac disease towards EATL.

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E-PS-24-138

Malignant melanoma of the gastrointestinal tract: a retrospective study spanning a decade from a tertiary care centre

I. S Nair*, R. S, T. Somanathan, E. Joy, C. K, R. S
*Regional Cancer Centre, Thiruvananthapuram, India

Background & objectives: Mucosal melanoma is a rare and aggressive subtype of malignant melanoma,accounting for 1.3% of melanomas.Compared to Caucasians, Asians show a higher prevalence of melanoma involving the gastrointestinal tract, specifically the anorectum. Early accurate diagnosis is crucial for initiating prompt treatment.
Methods: In this retrospective study of 10 years, all cases of melanoma involving gastrointestinal tract reported from January 2014 to December 2023 were analysed. Hematoxylin and eosin slides, along with immunohistochemistry slides were retrieved and reviewed. Clinical and demographic details were analysed from the medical records.
Results: Total number of cases:57. Included Females-29,Males-28, M:F-1:1.03. Age range-29 to 76 years.Sites; anorectum (n=47,82.5%), oesophagus (n=7,12.3%), stomach (n=2,3.5%) and gall bladder (n=1,1.75%). All the 47 cases in anorectum and 7 cases in oesophagus were primary lesions.One case of gastric melanoma was metastasis from primary of toe.Gall bladder melanoma was metastasis from cutaneous melanoma of thigh.
Histopathological features : Epithelioid appearance-18 cases (31.6%), spindle cells-14 cases (24.6%), pleomorphic cells-6 cases (10.5%) and plasmacytoid morphology-5 cases (8.7%).There were 10 cases of amelanotic melanoma(17.5%).
Immunopositivity for S100 in 95.8% (46/48), HMB45 in 97.9% (46/47) and Melan A in 95.6% (22/23) cases.
Three cases showed distant metastasis involving liver, pleura and breast.
Conclusion: Unlike cutaneous melanoma, lesions on mucosal surfaces are less likely to be detected early in their development leading to its aggressive clinical course and poorer prognosis. Awareness of the varied morphological spectrum of mucosal melanoma is crucial for early accurate diagnosis and prompt treatment thereby improving patient outcome.

E-PS-24-139

Ordinary colorectal cancers expressing synaptophysin: myth or reality?

G. Sabella*, G. Centonze, F. Belli, S. Pusceddu, A. Mangogna, V. Angerilli, M. Fassan, G. Pruneri, S. La Rosa, C. Capella, F. Sessa, M. Milione
*Switzerland

Background & objectives: The significance of variable neuroendocrine differentiation in conventional colorectal cancer (CRC) without a suggestive morphology, is of clinical relevance. Although the occurence of this uncommon evidence has been extensively investigated, established criteria for its classification have yet to be established
Methods: We tested 663 ordinary CRCs with a non-neuroendocrine morphology for synaptophysin expression (Syn) and correlated the results with clinicopathological characteristics and molecular profile, as well as patient survival, and compared the survival characteristics of syn expression group to those of ordinary CRCs and additionally to those of pure 14 mixed adeno-neuroendocrine carcinomas (MANECs)
Results: Syn expression >30% CRC patients group, compared to ordinary CRCs, correlated with BRAF mutation (p=0.04) and variables, significantly associated with poor overall survival (OS) and disease-free survival (DFS), were 10-years increase (p= 0.001), stage IV-III (p= 0.001) and amphicrine status, understood as co-expression of neuroendocrine and non-neuroendocrine phenotype in the same neoplastic cells (p= 0.001). Therefore, in terms of both OS and DFS, Syn expression in >30% of gland forming tumour cells, proved to be an independent negative prognostic factor. On the other hand, patients with MANECs, showed a significantly shorter DFS than all conventional adenocarcinomas with or without SYN expression in univariate analyses (p<0,001)
Conclusion: Our investigation focused on examining the clinicopathological and molecular characteristics of an unexplored category of CRC displaying variable degrees of neuroendocrine differentiation. We established a strong association between prognosis, the morphological and immunohistochemical phenotype observed. Additionally, we are currently conducting further molecular analyses to better dissect the biological behaviour and to facilitate personalized treatment strategies for patients

E-PS-24-140

A rare case of appendiceal goblet cell adenocarcinoma: a case report

S.M. Sabo*, A. Evsei, M. Gheorghe, A. Birceanu, C. Costras, R. Ardeleanu, T. Turcu, R.G. Grigore
*Colentina Clinical Hospital, Romania

Background & objectives: Goblet cell adenocarcinoma (GCA) is a rare appendiceal tumour with amphicrine differentiation that has distinct morphologic and clinical features compared to carcinomas seen elsewhere in the gastrointestinal tract. We report a case of a 54-year-old woman with disseminated asymptomatic disease.
Methods: Female patient presents with painless, but palpable right flank abdominal mass. Endoscopic examination of the right colon highlights invagination of the appendix into the cecum with infiltrative erosion of the appendicular base. Open surgery revealed appendicular mucinous tumour with cecal and ileal wall invasion and multiple peritoneal and greater omentum metastases. Right hemicolectomy, bilateral adnexectomy and epiploic removal was performed.
Results: Frozen section and paraffin histological examination revealed complex tubular structures, clusters, sheets and individual mucin-filled cells infiltrating the entire appendiceal wall with cecal submucosal and greater omentum involvement, and regional lymph nodes metastases. Tumour showed areas with extensive extracellular mucin and areas of necrosis. There was no adnexal involvement. Immunohistochemistry highlighted synaptophysin and chromogranin A positive neuroendocrine cells scattered through the goblet-like mucinous cells, showing the amphicrine differentiation. Staining for mismatch repair proteins showed no loss of expression. A diagnosis of GCA of the appendix, pT4b pN1b pM1b, with high-grade histological features, was made.
Conclusion: Goblet cell adenocarcinoma is a very rare tumour occurring almost exclusively in the appendix. GCA arises from pluripotent, intestinal crypt base stem cells that are able to differentiate into both mucinous and neuroendocrine cells. Clinical features can be variable, from appendicitis-like symptoms to asymptomatic, as in our patient. Early diagnosis is very important, as prognosis is highly dependent on stage and tumour grade. GCA must be differentiated from metastatic signet-ring cell adenocarcinoma, other neuroendocrine tumours or mixed neuroendocrine-adenocarcinoma neoplasms.

E-PS-24-141

Somatic mutations in colorectal carcinomas: comparison of mutations in carcinomas with and without micropapillary features

Z. Sagnak Yilmaz*, S. Aydin Mungan, S. Sarioglu
*Dokuz Eylül University Institute of Health Sciences, Department of Molecular Pathology, Izmir, Turkey

Background & objectives: Micropapillary carcinoma (MPC) has been identified in many organs and is also associated with lymph node metastasis and poor prognosis. Our aim is to identify somatic mutations that may be related to MPC morphology in colorectal carcinoma cases.
Methods: 159 colorectal adenocarcinomas whose DNA mutations were examined with the next-generation sequencing (NGS) method were retrospectively examined. The cases were examined on various NGS panels that included a different number of genes. We statistically compared somatic mutations in cases with and without the MPC component using the chi-square test. Also, demographic and clinicopathological features were compared.
Results: MPC areas were detected in 10 cases (6.3%). The KRAS mutation frequency in non-MPCs is slightly higher (non-MPC: 44.3%; MPC: 40%). All MPCs were TP53 mutant (100%). 64.9% of those without an MPC had the TP53 mutation. We detected the PIK3CA mutation in 20% of MPCs and 21.5% of other cases. In MPCs, somatic mutations were detected in 1 case in the ERBB2, MAP2K1, and BRCA2 genes. Despite obtaining similar results in terms of age, gender, and location between MPC and non-MPCs, we determined that MPCs exhibited more advanced pathological T and N stages, as well as a higher prevalence of lymphovascular invasion, perineural invasion, and tumour deposits.
Conclusion: TP53, KRAS, and PIK3CA mutations were most frequently observed in both MPCs and cases without MPC components. We detected no statistically significant difference about clinicopathologic features and somatic mutations between two groups ($p > 0.05$). There is limited data in the literature about somatic mutations in MPCs. The results of this and previous studies suggest that the effect of epigenetic changes may be more important than somatic mutations in MPCs.

E-PS-24-142

BRAF gene mutational profile in locally advanced and metastatic colorectalcarcinoma: experience of a tertiary health care Tunisian's institution

G. Sahraoui*, M. Ben Thayer, H. Douik, A. Khemir, D. Ben Ghezala, L. Charfi, R. Doghri, K. Mrad
*Pathology department Salah Azaiez institute Tunisia / Precision Medicine and Oncology Investigation Laboratory, Tunisia

Background & objectives: The detection of BRAF mutation in advanced and metastatic colorectal carcinomas (CRC) has become increasingly valuable for prognostic risk stratification.We aimed to study the mutational profile of the BRAF gene in locally advanced and metastatic CRC in a Tunisian population.
Methods: We retrospectively included the cases of locally advanced or metastatic colorectal adenocarcinomas referred to our department for molecular testing of BRAF gene. The study period extended from the first of April 2021 to 31 December 2022. Paraffin blocks of tumour samples were used.The molecular testing of the BRAFgene mutations' was performed by an integrated and automated multiplex real-time PCR platform.
Results: Our sample consisted of 496 cases. The average age of patients was 59 years.Vascular emboli and perineural involvement were noted in 13.7% and 10.3% of cases respectively.The TNM stage was classified as II, III and IV in 25.4%, 32.8% and 41.8% of cases respectively. BRAF mutation was detected in 21 cases (4%) and consisted in V600E/D mutation in all cases.The presence of BRAF mutation was statistically correlated with the tumour location in the right colon (p=0.002) and tumoural depth of invasion (pT4)(p=0.046). No correlation between BRAF mutation and histological grade, perineural involvement, vascular emboli, TNM stage, distant metastasis, and MMR status was found.
Conclusion: Our results were in line with the literature date. The prevalence of BRAF mutation inour study was consistent with those detected in Tunisian and worldwide series. The V600E/Dwas the most common mutation. BRAF mutant CRCsr epresent an extremelycomplex subtype of CRC, with poor prognosis.Current treatment options in these patients have insufficient clinical efficacy.The advent of therapies targeting these molecular alterations could improve the prognosis of these patients.

E-PS-24-143

RAS gene mutational profile in locally advanced and metastatic colorectal carcinoma: a Tunisian tertiary health care institution's experience

G. Sahraoui*, M. Ben Thayer, H. Douik, A. Khemir, Z. Abdelkafi, R. Doghri, B. Hedhli, L. Charfi, K. Mrad
*Pathology department Salah Azaiez institute Tunisia / Precision Medicine and Oncology Investigation Laboratory, Tunisia

Background & objectives: The detection of RAS mutations in patients with advanced colorectal carcinoma (CCR), has significant clinical and therapeutic implications.We aimed to study the mutational profile of the KRAS and NRAS genes in locally advanced and metastatic CCR in a Tunisian population.
Methods: We retrospectively included the cases of locally advanced or metastatic colorectal adenocarcinomas referred to our department for molecular testing of KRAS and NRAS genes. The study period extended from the first of April 2021 to 31 December 2022. The molecular testing of the RAS genes mutations' was performed by an integrated and automated multiplex real-time PCR platform.
Results: Our sample consisted of 496 cases. The average age of patients was 59 years Mutations in KRAS gene and in NRAS gene were detected respectively in 243 cases (49%) and 21 cases (4%). In the KRAS gene, 13 point mutations were detected.The 5 most frequently observed ones were G12D (28.4%), G12V (20.2%), G13D(16.5%), G12C(9.9%) and 146P/T/V in (9.9%).Exons 2, 3 and 4 were the site of the mutation in 83.1%, 5.8% and 11.1% of cases respectively. In the NRAS gene, 7 point mutations were detected: Q61K (38.1%), G12D (19.1%), Q61L (9.5%), Q61H (9.5%), G13D (4.8%) G13R/V (4.8%). Exon 3 was the mutational site in (57.1%) and exon 2 in the remaining cases.
Conclusion: Our findings were in line with the literature data. The prevalence of KRAS and NRAS gene mutations in our study was consistent with those reported in Tunisian and worldwide series.However, higher frequency of KRAS mutations in exons3 and 4 were found in our study. Nearly 10% of KRAS mutations wouldn't be detected if the testing method doesn't include the screening of exon 3 and 4.A broad molecular platform, ensuring the testing of exons other than exon 2 is therefore required.

E-PS-24-144

Colonic tubular adenoma with clear cell change – case report with whole exome sequencing

A. Sejben*, Á.K. Ferenczi, L. Kuthi, I. Sejben
*University of Szeged, Hungary

Background & objectives: Colorectal tubular adenomas displaying clear cell change are rare entities, with unknown clinical relevance, prognosis, immunohistochemical, and molecular features.
Methods: Hereby we report a case of a 43-year-old female patient with a rectosigmoid polyp.

Results: Histologically, conventional dysplasia was visible with scattered areas displaying clear cell change. Whole exome sequencing (WES) was carried out and revealed high tumour mutation burden, and 7 pathogenic mutations, including TP53, APC, FGFR4, EHBP1, IL4R, TYR, and ACTN3.
Conclusion: Clear cell change may only be present in less than 0,1% of adenomas. Aetiology is not well understood, additionally, few authors suggest autolysis or fixation problems. Our WES resulted in newly found pathogenic mutations, and high mutation burden, proving the lesion's neoplastic origin. Hitherto, neither special stainings, nor immunohistochemical markers proved to be useful in the diagnostic process. From a differential diagnostic perspective, enteroblastic differentiation, primary and secondary clear cell adenocarcinoma has to be excluded.

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E-PS-24-145
Examination of non-conventional dysplasias besides colorectal adenocarcinoma in patients with inflammatory bowel disease – pilot study
A. Sejben*, S. Almási, B. Baráth, D.M. Janotka, Z.K. Török, P. Szaszák, T. Lantos, B.P. Kővári
*University of Szeged, Hungary

Background & objectives: Knowledge on the development, morphology, and clinical significance of neoplasms associated with inflammatory bowel disease (IBD) is currently limited. In the last few years, several new morphological variants of IBD-associated dysplasias have been described.
Methods: The aim of our study was to re-evaluate some of our IBD-associated carcinoma cases, and to retrospectively identify non-conventional dysplasias. We re-evaluated a total of 28 cases, diagnosed between 2010 and 2022. We recorded the patients' gender, age at diagnosis of IBD and neoplasia, type of IBD, type of specimen, histological type, grade, localization, stage, and overall survival.
Results: The mean age at carcinoma diagnosis was 47 years in the conventional, and 50 years in the non-conventional dysplastic group. The male:female ratio was 13:2 in the conventional group, and 10:3 in the non-conventional group. Conventional dysplasia was observed in 15, and non-conventional dysplasia in 13 patients. They were detected combined in 9 patients. Altogether, 25 non-conventional dysplasia foci were identified, that were identified as: hypermucinous (n=9), goblet cell deficient (n=6), serrated NOS (n=6), and traditional serrated adenoma-like dysplasia (n=4). The majority of non-conventional dysplasias were associated with ulcerative colitis (n=12).
Conclusion: IBD-associated non-conventional dysplasias show unique clinicopathologic features. They are more frequently endoscopically flat, harbor aneuploidy, and are associated with high-risk carcinomas. Our findings prove that these recently described dysplasia subtypes are not uncommon (75%) in a Central European population. Their recognition may become clinically significant as these patients may benefit from closer follow-up and random biopsy sampling.

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E-PS-24-146
Features of Desmin expression in colorectal cancer
I. Sertakov*, E. Priputnevich, A. Filin, E. Chupandina, J. Starykh, A. Sokolova
*Voronezh State Medical University, Russia

Background & objectives: Desmin is a protein produced both by muscle cells and cells that began to look and behave like muscle cells. The role of Desmin in the morphogenesis of colorectal cancer is not fully studied and controversial.
Methods: Histological examination of surgical material was carried out. Desmin was detected by immunohistochemical method on paraffin sections using monoclonal mouse antibodies. Desmin was assessed both qualitatively and quantitatively. The relationship between the Desmin distribution and tumour differentiation degree, life expectancy, Mast Cells distribution, metastases to regional lymph nodes and other clinical and morphological indicators was studied.
Results: Desmin expression was represented almost in all cases. Desmin was found in stroma and in tumour itself, but its distribution was different: there were cases with Desmin expression only in stroma and cases with Desmin expression only in tumour. But mostly Desmin expression was performed both in tumour and in stroma.
The relationship between Desmin distribution and tumour differentiation degree was found. Moreover, the relationship was found between life expectancy and Desmin localization in tumour. Correlations between the Mast Cells distribution and the Desmin distribution were studied. Correlations between the distribution of Desmin and metastases to regional lymph nodes, tumour size and other indicators were not revealed.
Conclusion: The results suggest that there is a relationship between Desmin expression and some clinical and morphological indicators. The most valuable was the establishment of correlations between the presence of Desmin in tumour and life expectancy.

Desmin is a relatively new, but very perspective object of research in oncopathology, but it is still necessary to continue to investigate its role in the morphogenesis of colorectal cancer, especially taking into account the interaction with other cellular elements.

E-PS-24-147
An overlooked pathology of appendix: appendiceal diverticule
G. Sivrikaya*, M. Sezak, E. Güler, Y.A. Altunci, T. Gümüş, B. Doğanavşargil
*Ege University Faculty of Medicine, Department of Pathology, Turkey

Background & objectives: Appendix diverticule is a relatively rare pathological finding. Appendiceal diverticulosis is usually incidental and clinically asymptomatic. Symptomatic cases are usually complicated by diverticulitis, with/without acute appendicitis. Appendiceal diverticulitis differs from acute appendicitis in several clinical and pathological aspects.
Methods: We reviewed clinicopathological features of 81 appendicial diverticulosis biopsies evaluated between 2007 and 2023 years in a single centre. The demographic details and clinical data including radiological characteristics, gross findings and histopathological features were analysed by nonparametric tests.
Results: With median age of 39±16,3 years-old(11-88), 54% of cases were male(n=30).The most common accompanying findings were phlegmonous appendicitis(n=69, 85.2%),localised peritonitis(n=56, 69.2%),perforation(n=16, 19.8%),and diverticulitis(n=21, 25.9%). Leiomyoma, neural hyperplasia, and serrated polyp were exhibited once. Sole diverticula formation without inflammation was observed in 10 incidental appendectomies(12.3%) while sole diverticulitis without mural inflammation was noted in only twice(2.4%).Notably,

a consultation case previously reported as appendiceal mucinous neoplasia with subserosal invasion was re-diagnosed as a diverticula. Preoperative radiological findings were consistent with acute appendicitis, perforation, abscess, and plastron formation.Twice exhibited suspicious malignancy, but no diverticula were officially reported.Presence of diverticulitis was not correlated with age or gender. None of the patients exhibited diverticular disease(colon,bladder,etc).
Conclusion: Appendiceal diverticula is an overlooked pathology both radiologically and histologically. This may be due to the extensive phlegmonous inflammation and accompanying perforation and peritonitis. However, it is important to be aware of the entity for distinguishing malignancies.

E-PS-24-148
A case of invasive aspergillosis of the colon
E. Spiteri*, E. Gioti, A. Georgiou, A. Bairamis, S. Avgousti, C. Vourlakou
*Department of Pathology, Evangelismos General Hospital, Athens, Greece

Background & objectives: Invasive aspergillosis (IA) is a fungal infection with high mortality rate. Although the most commonly affected site is the lung, involvement of the gastrointestinal tract has been reported. We present a case of Intestinal Aspergillosis in an immunocompromised 30-year-old male.
Methods: We received two specimens, a right colectomy and a gallbladder. The colectomy consisted of distal ileum 3 cm and cecum / ascending colon 17 cm in length, while the gallbladder was 11.5 cm. The specimens were dissected and prepared into slides. The slides were stained with hematoxylin / eosin. Periodic acid-Schiff (PAS) and Grocott-Gomori methenamine silver (GMS) stains were conducted.
Results: Macroscopically the colon was sectioned to reveal a tan brown ulcerative lesion measuring 3.5x2 cm. No remarkable gross lesions were found in the gallbladder. Histologic examination revealed surface ulceration of the colon mucosa accompanied by severe transmural acute inflammation and vasodilation. In the submucosa and muscularis propria both diffusely and inside some vessels multiple fungal hyphae were detected. The hyphae appeared angular with < 45-degree-angle branching and septated, a morphology most compatible with Aspergillus species. Identical fungal hyphae were observed inside vessels of the gallbladder wall. PAS and GMS stains were assessed and the hyphae proved to be positive for both stains, thus confirming the diagnosis.
Conclusion: Invasive aspergillosis is associated with a 50 to 60% mortality rate. The gastrointestinal tract is the second most common site and it commonly presents with fungal invasion of the mesenteric arteries, intravascular thrombosis and subsequent tissue ischemia. It may lead to infarction and even perforation of the intestine. Consequently, in the setting of an immunocompromised patient with necrotic ulcers on endoscopic examination, Intestinal Aspergillosis should be included in the differential diagnosis.

E-PS-24-149
Caspase-1 and Caspase-9 in poorly cohesive gastric carcinoma – new players modulating local and distant spread
L. Stanciu*, A. Cibotariu, G. Micu, L. Nichita, C. Botezatu, A. Bordea, R. Ionescu, D.M. Marinoiu, V. Marin, R. Neagu, C. Popp
*Department of Pathology, Colentina University Hospital, Bucharest, Romania

Background & objectives: Poorly cohesive gastric carcinoma is a rapid progressive, highly aggressive and therapy-resistant neoplasm, affecting an increasing number of younger patients. Investigation of various immunohistochemical markers, including caspases, can open new pathways of treatment.
Methods: We designed a retrospective study including 11 patients who underwent gastrectomy for poorly cohesive gastric carcinoma (2020-2024). Immunohistochemical staining for E-cadherin, caspase-1 and caspase-9 was performed on the most representative blocks, then evaluated using a four-grades scale, and data were correlated with tumour invasion and metastasis. Stage of local and systemic extent was assessed using gross data and preoperative investigations.
Results: The pathological extent of the tumour was pT3 in one case, pT4a in eight cases and pT4b in two cases. Eight patients had multiple lymph nodes metastasis. 3 out of 11 patients (all with positive lymph nodes) had distant metastasis. 81.8% were positive for E-cadherin, 55.6% had negative caspase-1 expression and 66.7% were negative for caspase-9. Additionally, the two patients with negative E-cadherin were also negative for caspase-9, and one was negative for caspase-1. The findings indicated a negative correlation between caspase-1 and -9 expression and tumour invasion extent (pT stage), along with a positive correlation with lymph node (pN stage) and distant metastases (evaluated on MRI or CT scans).
Conclusion: Caspase-1 and -9 positive advanced tumours seem to have a higher propensity of lymph node and distant metastasis. Despite the limited size of the studied cohort, these results form the base for further studies exploring involvement of caspase expression in tumour progression in naive and mutant E-cadherin poorly cohesive gastric carcinomas, since various available treatments have caspase inhibitor or activator role.

E-PS-24-150
Prevalence of neuroendocrine cell hyperplasia in high and low adenocarcinoma risk cohorts of patients with autoimmune gastritis
M. Stepanchenko*, A. Gubanova, M. Livzan, S. Mozgovoi, I. Ostroglyadova
*Omsk State Medical University, Russia

Background & objectives: The aim of the study was to determine the prevalence of neuroendocrine cell hyperplasia among patients with autoimmune chronic gastritis in terms of assessing correlation with stratified risk assessment of gastric cancer.
Methods: A total of 54 cases of chronic autoimmune gastritis were investigated. Biopsies were taken according to the OLGA system. Chromogranin A staining was performed in gastric body mucosal specimens to detect neuroendocrine cell hyperplasia. The stage of gastritis was assessed and scored; absence of current Helicobacter pylori infection was reconfirmed. Type and extent of neuroendocrine cell hyperplasia were evaluated.
Results: 23 cases were classified as low-risk group (Stage I and II) based on the combined atrophy score, and 21 cases were classified as high-risk group (Stage III and IV). Neuroendocrine cell hyperplasia was registered in 46 cases, the remaining 8 cases showed no pathological changes in number of neuroendocrine cells. The distribution of hyperplasia types: simple hyperplasia 38 cases (70.37%), linear hyperplasia 25 cases (46.29%), nodular hyperplasia 17 cases (31.48%), adenomatous hyperplasia 1 case (1.85%). A combination of linear and nodular hyperplasia was the main changes in the high-risk group in comparison with the low-risk group - a combination of simple and linear patterns
Conclusion: The presence of pseudopyloric metaplasia (Se=90%, Sp=78%) as well as neuroendocrine cell hyperplasia (Se=95%, Sp=98%) were found to be the most reliable markers of autoimmune gastritis.The relatively higher prevalence of neuroendocrine cell hyperplasia in the high-risk group for adenocarcinoma development compared to the low-risk group may indirectly indicate the risk of gastric adenocarcinoma development. These results are of interest for further investigation into the relationship between this phenomenon and gastric adenocarcinoma.

E-PS-24-151

Use of modality in pathology reports on gastric dysplasia: can cognitive distortions be avoided?

M. Stepanchenko*, A. Kononov, S. Mozgovoi, A. Shimanskaya, J. Fedotova, E. Abrosimova
*Omsk State Medical University, Russian Federation

Background & objectives: The pathology report based on the results of biopsy investigation is a complex communicative phenomenon that combines the tendency for standardisation, objectivity, accuracy, and the need to reflect the personal point of view of the specialist.
Methods: A list of 12 most frequently used words and modifying phrases was formulated after analisis of 500 biopsy pathology reports: not reliably determined/not revealed; doubtful/doubtful signs; suggestive of ...; similar to ...; can't be excluded; suspicious in ...; similar to …; typical picture; probable; the most probable; most consistent; reliably determined.
Results: A simple questionnaire was used to assess the degree of physicians' confidence (15 pathologists and 20 general practitioners and gastroenterologists) with a simple 10-point ranked scale: from 0 - absence, to 10 - 100% - obligatory presence of the sign/disease. The study revealed a high level of variability in the confidence/validity score for each of the presented phrases, reflected in terms of descriptive statistics in the form of a relatively wide interquartile range with the following score: from 3 for the phrase "reliably determined" to 6 (!) for the phrase "similar to...". It is obvious that chaotic, unsystematic use of heterogeneous modal elements means introduces significant interference in professional communication.
Conclusion: We see possible solutions to the problem as follows: 1) strictly limiting the usage of these words and expressions in a separate section of the report ("additional remarks"), 2) proposing a list of modal (modifying phrases), 3) introduction of an algorithmic interpretation, 4) regulated transition from the narrative-descriptive format to the model of formalised synopsis and template, in which no variations are allowed, 5) introduction of quantitative evidentiary parameters in the conclusion that reflect the level of certainty.

E-PS-24-152

Inflammatory fibroid polyp of the oesophagus: a case report

A. Stofas*, A. Patereli, K. Palamaris, P. Papadakis, K. Belogiannis, H. Gakiopoulou, P. Korkolopoulou
*1st Department of Pathology, School of Medicine, National and Kapodistrian University of Athens, Greece

Background & objectives: Inflammatory fibroid polyp, a rare benign lesion of the digestive tract, occurs more commonly in the stomach, followed by small and large intestine. Rarely (1%) it can involve the oesophagus, most often located in the distal part.
Methods: A 43-year-old male presented with dyspeptic symptoms. CT scan revealed an oesophageal mass. A partial oesophagogastrectomy performed showed a submucosal pedunculated polypoidal lesion arising from the oesophagus, just above the gastro-oesophageal junction, measuring 5,7 mm. The lesion was whitish, with soft and fleshy consistency.
Results: H&E sections showed a benign submucosal myofibroblastic lesion, with areas of collagenized stroma, and infiltration of inflammatory cells, rich in eosinophils and lymphocytes, in the background of a myxomatous stroma. Nuclear pleomorphism and mitoses were absent. Immunostaining showed positivity for vimentin, and CD34 (with focally whorled pattern) and focal reactivity for SMA, whereas Desmin, S100, CD31, ERG, Caldesmon, C-KIT, DOG-1, EMA, SOX10, ALK, STAT6 and Pankeratin were negative. The Ki67 index was estimated between 5-10%. Cyclin D expression was evaluated as low.
Conclusion: Studies recently have revealed activating mutations in the platelet-derived growth factor receptor alpha (PDGFRA) gene, supporting the theory of a neoplastic origin. PDGFRA gene is also involved in the pathogenesis of gastrointestinal stromal tumours (GIST). The differential diagnosis is made with GIST, desmoid fibromatosis, inflammatory myofibroblastic tumour, leiomyoma and schwannoma. Inflammatory fibroid polyp is treated in principle by local surgical resection with excellent prognosis.

E-PS-24-153

Succinate dehydrogenase deficient gastrointestinal stromal tumour: a case report

A. Stofas*, A. Patereli, A. Papachristou, P. Korkolopoulou, H. Gakiopoulou
*1st Department of Pathology, School of Medicine, National and Kapodistrian University of Athens, Greece

Background & objectives: The majority of gastrointestinal stromal tumours (GISTs) are caused by KIT and PDGFRA mutations. Approximately 15% of GISTs lack these two and BRAF mutations and are classified as «wildtype». Succinate dehydrogenase (SDH)-deficient GISTs, constitute the largest group of them.
Methods: We report a case of a 72-year-old male previously diagnosed with gastric GIST on biopsy. The patient underwent total gastrectomy. On gross examination a tumour measured up to 5.2 cm in diameter was found.
Results: Microscopically the tumour had a multinodular appearance, composed of mixed spindled/epithelioid cells, arranged in a fascicular pattern. Hyalinization of the stroma and necrosis were also present. The mitotic index was 50 mitosis/5 mm2 and the Ki-67 labeling index was approximately 25%. Tumour cells were positive for CD117, DOG1 and CD34 and negative for Desmin, S100, Pankeratin and SDHB. Mutational analysis showed no BRAF mutations in the exons examined (11 and 15) and no mutations in all other targets [CKIT, PDGFRA, BRAF, FGFR1, FGFR2, FGFR3, ALK, RET, ROS1, NTRK1-3 & FGRF1-3 (NGS analysis)]. Therefore, the diagnosis of a triple-negative ("wildtype") SDH-deficient GIST was established. The tumour was classified as pT3N0(0/23), R0.
Conclusion: Although the majority of GISTs appear to be sporadic, they can be syndromic in around 5-10% of cases. Most of the latter are SDH-deficient and appear mainly in young girls/women on the contrary to our case which is an old male. SDH-deficient GISTs have varying biologic behaviour and are non-responsive to the conventional tyrosine kinase inhibitor therapy.

E-PS-24-154

CLDN18.2 expression in gastric cancer for adoption in clinical practice

C. Taffon*, S. Vantaggi, B. Canalis, F.M. Di Matteo, D. Caputo, G. Perrone
*Italy

Background & objectives: Claudin-18, a tight junction protein expressed in various cancer types including gastric (GC) and gastro-oesophageal junction cancer (EGJA) represents a promising target for novel experimental drugs. We investigated CLDN18.2 expression in GC for adoption in clinical practice.
Methods: 62 samples from 48 patients with GC were retrospectively valuated for CLDN18 expression. IHC staining for CLDN18 was evaluated by two pathologists, and a consensus session for discordantly scored samples defined an agreement score for each case. Clinicopathological parameters considered were: sex, age at diagnosis, histotype, grade, TNM, HER2, MSI and PDL-1 (CPS).
Results: Inter-rater reliability showed a concordance rate of 82,8%. (41/62;66.1%) of tested samples showed high CLDN18 expression

(intensity of 2+/3+ in >75% of tumour cells), with 58.3% exhibiting a positive correlation between bioptic and surgical specimens. Staining inhomogeneity was noted, reflecting internal heterogeneity of most tumours, particularly in intestinal histotypes with a diffuse component. Among cases with HER2 gene amplification, (8/23;75%) showed high CLDN18 expression, while 86.6% of HER2- cases showed positive CLDN18 staining. 75% of cases with MSI instability showed high CLDN18 expression, and 83.3% without MSI instability showed high expression. Additionally, in cases with PD-L1 CPS >5, 76.9% showed high expression, compared to 100% of cases with CPS <5.
Conclusion: We studied the immunohistochemical staining pattern of CLDN18.2, the agreement between pathologists and between biopsy and surgical specimens and its correlation with histopathological features. The suggested CLDN18.2 scoring criteria are reproducible among pathologists with substantial interobserver agreement rates. Our findings significantly strengthen the foundation for introducing CLDN18.2 stain in clinical practice, notably with a focus on PD-L1 negative and HER2-non-amplified tumours and the possibility to attempt a personalized target therapy improving medical options for selected patients.

E-PS-24-155
Gastrointestinal stromal tumour (GIST) and it's rare mimickers - plexiform fibromyxoma and neurofibroma: report of three cases
M. Tanasă*, D. Franciug, A. Vasilescu, L. Lozneanu, D. Iosep, V. Gramă, S. Tanasă, D. Ciobanu-Apostol
*"Grigore T. Popa" University of Medicine and Pharmacy of Iasi, Romania, County Clinical Emergency Hospital of Iasi "Sf. Spiridon", Romania

Background & objectives: Gastric mesenchymal tumours encompass several rare entities with challenging diagnosis. We aim to showcase morphological and immunohistochemical features of gastric plexiform fibromyxoma and neurofibroma, and their differences compared to GIST, based on three cases with certain clinical and imaging similarities.
Methods: We present a series of three female patients – 40, 48 and 39 years old respectively, who underwent partial gastrectomy for a gastric wall mass. Gross examination, in all cases, revealed the presence of an intramural, nodular, circumscribed fleshy lesion, close to 5 cm in diameter. The specimens were processed by classic histopathological methods with additional immunohistochemical tests.
Results: In all 3 cases histopathological examination showed similar well circumscribed spindle cell proliferations within the gastric wall, with fascicular, storiform or plexiform growth patterns, composed of cells with round to oval or elongated nuclei, with little to no atypia, and low mitotic activity - suggestive of a gastric GIST. Several immunohistochemical tests were performed. CD117, DOG1 and CD34 positivity was observed only in the first case, thus establishing the diagnosis of GIST. The second case showed S100, NSE and SOX10 positivity, confirming a gastric neurofibroma. The third case had prominent plexiform growth pattern with myxoid areas, and stained positive for SMA and desmin markers, corresponding to a gastric plexiform fibromyxoma.
Conclusion: As most pathologists would agree, a spindle cell gastric proliferation readily requires CD117 and DOG1 immunostains to establish a GIST diagnosis, which is by far the most common. However, a negative staining profile may sometimes result in a long journey of shuffling through different markers, overloading the immunohistochemistry department and delaying the diagnosis. Despite immediate risk of local complications (ulceration, bleeding, perforation) the tumours that we presented have good prognosis and all the patients had a favourable postoperative outcome.

E-PS-24-156
Hepatoid adenocarcinoma mimicking hepatic tissue in the stomach: a case report
A.E. Taskale*, A. Koyuncuer, T. Canbak, A. Acar
*Department of Pathology,Umraniye Training and Resarch Hospital, Universty of Healty Sciences, İstanbul, Turkey

Background & objectives: Hepatoid adenocarcinoma of the stomach , also known as alpha-fetoprotein producing gastric adenocarcinoma,represents an uncommon and malignant type of tumour ,charactered by the presence of neoplastic cells similar to the hepatocytes.
Methods: A 46-year-old female patient was admitted to our hospital with dyspeptic complaints. Endoscopy performed revealed a 5 cm diameter ulcer extending from the antrum to the incisura.Abdominal CT-scan examinations revealed many lymphadenopathy around the stomach. Total gastrectomy was planned for the patient, who was found to have elevated serum alpha-fetoprotein, and was sent to us for histopathological diagnosis
Results: In our microscopic examination, we observed hepatocyte-like polygonal cells with eosinophilic cytoplasm organized in a solid and trabecular pattern. These cells had large nuclei and hyperchromatic nucleoli, and we observed luminal secretion in some places. Necrosis, hyperemia, and a reaction due to chronic inflammation were noteworthy in the background. In immunohistochemical studies, tumour cells were SALL4, AFP, Glypican3 (30%) positive and WT1, Napsin A, pax8 were negative.
Conclusion: The differential diagnosis of AFP-producing gastric adenocarcinoma includes the diagnoses of undifferentiated adenocarcinoma and metastatic hepatocellular carcinoma. Different treatment options for these tumours emphasize the importance of diagnosis. Serum AFP level, radiological findings and IHC panel help in correct diagnosis.

E-PS-24-157
A rare case of metastatic lobular carcinoma of the breast presented as small bowel obstruction
Z. Tatsiou*, K. Chatzidimitriadis, I. Triantaffylidis, M. Apostolidou, A. Orfanidou, G. Zarrou, R. Avgerinos
*Greece

Background & objectives: Small bowel metastatic disease has atypical symptoms that mimic many other diseases; as a result, signs and symptoms may be overlooked. The most common primary focus of metastatic tumour of the small intestine is lung cancer and breast cancer.
Methods: Our case concerns a 59-year-old woman who was admitted with clinical symptoms of bowel obstruction. The imaging test showed presence of adhesions in the small intestine. An emergent small bowel enterectomy was performed.
Results: The microscopic examination of multiple sections of the small bowel showed a focal fibroblastic reaction of the serosa and symphysis with diffuse infiltration by a low-differentiated, low-cohesive carcinoma. Immunohistochemical examination was positive for cytokeratin 7, GATA-3, ER/PR-receptors (about 40%) and CerbB2 (2+), while it was negative for E-cadherin, calretinin, mesothelin, cytokeratins 5/6 and WT -1. The mucosa showed no specific microscopic alterations. Accordingly, a diagnosis of metastatic lobular carcinoma of the breast to small bowel was made. The patient died a few days after the operation.
Conclusion: In conclusion, we present a rare case of metastatic lobular carcinoma of the breast presented as small bowel obstruction.

Histopathological examination along with an immunohistochemical panel are valuable in differential diagnosis from other primary or secondary tumours of the small intestine and set the correct diagnosis.

E-PS-24-158

Primary perianal extramammary Paget's disease: a rare tumour

Z. Tatsiou*, K. Chatzidimitriadis, M. Apo'stolidou, S. Gianjaklidis, A. Orfanidou, G. Zarrou, R. Avgerinos
*Greece

Background & objectives: Perianal Extramammary Paget's disease (EMPD) is a rare malignancy and is frequently associated with underlying adenocarcinoma. Primary EMPD is a diagnosis of exclusion, and only a few cases have been reported in the English literature.
Methods: Our case concerns a 69-year-old man who presented due to skin lesion in the perianal area. Physical examination showed whitish perianal plaques with erosions and a skin excision was performed.
Results: Microscopic examination of the skin section showed intraepithelial growth of neoplastic cells with foci of infiltration of the underlying dermis. Immunohistochemical examination was positive for cytokeratin 7, EMA and CEA, while it was negative for cytokeratins 20,5/6 and 34βE12, p63 protein, SOX10, HMB45, CDX2, PSA, PSAP, S100 protein, Synaptophysin and Chromogranin. Accordingly, the diagnosis of EMPD was made. Staging imaging examinations with CT and PET-scan were negative for underlying neoplastic disease. The patient received adjuvant radiotherapy and six months later is on regular follow-up.
Conclusion: In conclusion, we present a very rare case of primary perianal EMPD. Histopathological examination along with an immunohistochemical panel are valuable in differential diagnosis from other primary or secondary tumours of the anal skin and set the correct diagnosis.

E-PS-24-159

Malignant gastrointestinal neuroectodermal tumour with history of melanoma: a case report

M.F. Tekin*, I.T. Ceran, S. Coşkun, Ç. Çelikel
*Marmara University, Turkey

Background & objectives: Malignant gastrointestinal neuroectodermal tumour (GNET) is a rare mesenchymal tumour, morphologically similar to clear cell sarcoma (CCS) but distinguished by its molecular and immunohistochemical characteristics. The presentation of our rare case aims to be a scientific contribution to the literature.
Methods: An 83-year-old male with a history of right below-knee amputation due to malignant melanoma (15 years ago) presented to our emergency department with abdominal pain and constipation for 2 days duration. Physical examination revealed acute abdominal signs. Abdominal CT disclosed ileal segment invagination. Diagnostic surgery revealed a 2x2 cm mass obstructing the passage in small bowel, necessitating segmental resection.
Results: Resection material showed 2.7x2.2x2 cm cream-colored mass causing a serosal indentation. Microscopically, the neoplasia showed epithelioid and spindle cells, the majority with clear cytoplasm, each intermingling and forming tumour cell islands; however, there were also areas where neoplastic cells had pale eosinophilic cytoplasm. The nuclei were vesicular, round-oval, with high mitotic activity and there was no evidence of lymphovascular and perineural invasion. Immunohistochemistry indicated positivity for S100, SOX10, CD56, while being negative for melan-A, HMB45, CD117, CD34, DOG1, desmin, SMA, inhibin. Molecular analysis revealed EWSR1 gene rearrangement, supporting the diagnosis of GNET. The patient was opted for surveillance without any treatment and showed no recurrence or metastasis within 4-months follow-up.
Conclusion: In conclusion; this case report delineates clinical, histopathological, immunohistochemical and molecular characteristics of a GNET in small intestine. Among the reported cases in which the age ranges from 10 to 81, our case is the oldest. Despite melanoma history in our case, negative melanocytic markers ruled out melanoma metastasis and CSS. To the best of our knowledge, our case is the second reported case of GNET with a history of melanoma. Therefore, this association must be clarified in the future.

E-PS-24-160

Evaluation of gastrointestinal system biopsies with 2-slide-serial sections: analysis of findings in 1715 consecutive cases focused on clinical impact

N. Tezcan*, R. Esmer, G. Canbaloglu, G. Baysoy, P. Korkmaz, M. Senturk, B. Saka
*Koç University, School of Medicine, Department of Pathology, Turkey

Background & objectives: Small biopsies (tru-cut, punch, bronchoscopic) are vulnerable to technical details. There is currently no standardized approach for handling gastrointestinal (GI) biopsies. This study was designed to determine the utility of 2-slide serial sections in the daily routine for endoscopic&colonoscopic biopsies.
Methods: A total of 1715 consecutive GI biopsies were prospectively reviewed using 2-slide serial sections, with 8 sections on each, by a single observer. Diagnoses were categorized as: no lesion, non-neoplastic lesion, and neoplastic lesion. Discrepancies between the initial and second slides was investigated. If there is a difference, its clinical significance, and any identifiable reason for it were analysed.
Results: Comparison of 1st and 2nd slide assessment revealed discrepancy in 38 (2.2%) cases ($p< 0.001$). Out of 799 cases initially diagnosed with no lesion on the first slide, lesions appeared in 31 (4%) of them on the second slide. Among the 916 cases with a lesion detected on the first slide, it disappeared in 7 (0.8%) of them on the second slide. Clinically significant difference was detected in 17 (<1.0%) cases, with gastric intestinal metaplasia (54%) being the most common. Most frequent difference (28/38) was noted in the antrum. No impact of age, gender, size of biopsy and number of fragments were noted on diagnostic difference or its clinical significance.
Conclusion: Cases in which diagnostic differences affecting clinical management were detected by the 2-slide serial section method were less than 1%, with no malignancies found among them. Lesions appeared in 4% of biopsies initially diagnosed as non-lesional, while 1% of lesions disappeared. Antrum localization emerged as a factor influencing diagnostic changes ($p<0.05$).

E-PS-24-161

Large cell neuroendocrine carcinoma (LCNEC) of the colon arising from a tubulovillous adenoma - an extraordinary case report

H. Trihia*, E. Souka, E. Tsironi
*Metaxas Cancer Hospital, Greece

Background & objectives: Composite intestinal adenoma-neuroendocrine tumour (CIAN) is a rare intestinal lesion. It is found incidentally during the pathologic examination of adenomatous polyps, usually in the cecum. We describe a case of a large cell neuroendocrine carcinoma in adenoma of the cecum.
Methods: A 68-year-old woman has been diagnosed with a 5cm polyp of the cecum. The polyp was resected endoscopically in piecemeal fashion and sent for pathological examination.
Results: Multiple polypoid fragments were received of maximum diameter of 0,5cm-2,2cm. Histologically, there were fragments of a tubulovillous adenoma with areas of low and high grade dysplasia. In one of them, there was an incidental finding in the lamina propria and

muscularis mucosa of a 2,2mm neoplasm with solid-trabecular pattern of growth, of small-medium sized cells, with prominent nucleoli and high mitotic activity (21mitoses/2mm2). The cells were cytokeratin (CK) 8/18+, CK20+, chromogranin A+, synaptophysin+, p53+ (>95%), CDX2+ (mild) and MIB1 proliferative index 70% and therefore with morphologic and immunophenotypic characteristics of a large cell neuroendocrine carcinoma (NEC).
Conclusion: Mixed benign adenoma-NEC is a rare neoplasm coexistence with uncertain histogenesis and biological behaviour. Pathologists must be aware of this coexistence, which has been rarely described and which may go under-recognized, given its rarity and occasional morphologic subtlety. The presence of NEC causes concern even if it is restricted in the mucosa of an adenoma, since NEC has a highly aggressive behaviour. Prognosis remains elusive, due to small number of similar cases.

E-PS-24-162
Neuroendocrine carcinoma of the oesophagus: a case report and literature review
O. Tzaida*, G. Galanopoulos, P. Bafaloukos, E. Souka, N. Novkovic, P. Markopoulos
*Metaxa Cancer Hospital, Piraeus, Greece

Background & objectives: Neuroendocrine carcinoma (NEC) of the oesophagus is a very rare malignancy. The incidence rate varies between 0.4% and 2% of all oesophageal malignant neoplasms and accounts for 0.4% of all NECs. The incidence is higher in males than in females.
Methods: A 71-year-old male patient was admitted for dysphagia, pain and progressive weight loss investigation. Gastroscopy showed an ulcerative lesion located in the lower segment of the oesophagus. The rest clinical and imaging examination revealed no other tumour focus. An oesophageal biopsy was performed. The biopsy specimens consisted of multiple whiteish tissue samples measured from 0.1 to 0.4 cm.
Results: On histology, oesophageal mucosa, lined with stratified squamous epithelium preserved in small areas, was extensively infiltrated by a poorly differentiated carcinoma. The tumour had solid architecture composed of large cells with basophilic cytoplasm, large ovoid nuclei and severe nuclear atypia. Mitotic activity was brisk. Squamous differentiation was focally identified. Inflammatory cells, mostly lymphocytes, were also present. Alcian blue stain was negative for mucin. Immunohistochemistry showed immunoreactivity for CKAE1AE3, CK7 and p63 (focal staining). The neuroendocrine markers: Chromogranin, Synaptophysin and CD56 were extensively expressed. Ki-67 mitotic index was extremely high; >95%. A high-grade large cell carcinoma with neuroendocrine differentiation was suggested.
Conclusion: NEC of the oesophagus is an aggressive malignancy with poor prognosis. It is mostly found in the middle and lower segment of the oesophagus. Although the origin of oesophageal NEC remains unknown, it probably originates from neuroendocrine cells in the submucosal glands or in Barrett mucosa. Large cell NEC is the predominant type. Co-existence of squamous cell carcinoma or adenocarcinoma can also be found. Given the rarity of oesophageal NEC, there is no unique TNM staging system for this cell-type.

E-PS-24-163
Unveiling rarity: a case report on gastrointestinal clear cell sarcoma/malignant gastrointestinal neuroectodermal tumour
M. Urgancı*, B. Öğüt, Ö. Ekinci
*Gazi University, Department of Pathology, Turkey

Background & objectives: Gastrointestinal clear cell sarcoma (CCS)/ malignant gastrointestinal neuroectodermal tumour (GNET) is a very rare primary malignant mesenchymal tumour of gastrointestinal (GI) tract that shows neuroectodermal differentiation and EWSR1 gene translocations.
Methods: Our case was 57 years old female patient with admitting endophytic polypoid anorectal mass. Firstly diagnostic colonoscopic biopsy and after that excisional abdominoperineal resection was performed.
Results: In macroscopic examination, a well-circumscribed gray tumour with endophytic growth, 3.5 cm in diameter, located in the dentate line of the anorectal canal, was observed. Histologically, tumour was consisted of epitheolid morphology that have eosinophilic cytoplasm and round nuclei with vesicular chromatin and prominent nucleoli. The tumour mostly showed nested pattern. The neoplastic cells were diffusely positive for Vimentin and SOX10, focally positive for S-100 and negative for CK7, CK20, CK5/6, CK8/18, CDX2, HMB45, Melan-A/MART1, Synaptophysin, Chromogranin, CD117, CD34, Desmin, SMA, MDM-2, CDK-4. Molecular genetic testing was performed using the fluorescence in situ hybridization method with the ZytoLight SPEC EWSR1 dual-color break apart probe, and EWSR1 gene rearrengement was detected.
Conclusion: CCS/GNET is an extremely rare malignant tumour of GI tract and can be mistaken for other mesenchymal tumours or malignant melanomas that ocur in GI tract. A tumour with epitheloid morphology and diffusely positive for SOX10 should prompt a pathologist to consider CCS/GNET in the differential diagnosis and and demonstration of EWSR1 gene translocations should be attempted.

E-PS-24-164
Gastrointestinal Kaposi sarcoma, eight cases with eight different presentations
H.K. Uzkuç*, B. Doğanavşargil, B. Sarıkaya, M. Buyruk, B. Yaman, M. Sezak, T. Akalın
*Turkey

Background & objectives: Kaposi sarcoma is a vascular tumour caused by Human Herpes Virus 8 (HHV8) and it is usually seen in immunocompromised (particularly HIV-infected) hosts, gastrointestinal Kaposi sarcoma (GI-KS) is not an uncommon diagnosis but it is rarer than its skin counterpart.
Methods: We reviewed clinical (age, gender, tumour localization, history of HIV infection, immunosuppression, endoscopic findings, previous diagnosis, previous biopsies, recurrence, survival) and pathological features (mucosal infiltration pattern, accompanying lesions, type of inflammation) of eight cases diagnosed between 2000-2023 years.
Results: The female/male ratio was 2/6, median age was 40±15.94 years old. The tumour localization was stomach (n=4), duodenum(n=1), colon (n=2, multipl in one case) and both colon-stomach in one case. Five cases had prior skin diagnosis, while one case developed afterward. GI symptoms were faint in all cases. Two cases were HIV(+); one of which also had "Primary effusion lymphoma" and died of the disease; two cases had a history of renal transplantation. The tumour was easily identifiable in two biopsies, but was inconspicuous in one case where only HHV8 immunohistochemistry aided in the diagnoses. The mucosa was eroded in one case and harbored intratumoural eosinophils in four cases (Range:4-25 eosinophils/HPF)
Conclusion: The diagnosis of GI-KS is challenging as the patients are often asymptomatic and can easily be interpreted as granulation tissue in biopsies if the pathologist is unaware of the clinical history. The clinicopathological features of GI-KS should also be reevaluated according to the newly proposed taxonomic classifications defined as "classic, endemic, epidemic/HIV associated and iatrogenic KS, and KS in men who have sex with men" by larger series.

E-PS-24-165
Gastric glomus tumour: a case report
A. Üzümcü*, M. Buyuk, N. Berker, M. Gulluoglu
*Istanbul University, Istanbul Faculty of Medicine, Turkey

Background & objectives: Visceral involvement of the glomus tumour (GT) which usually originates in extremities is extremely rare. Herein, we present a case of gastric glomus tumour mimicking other gastrointestinal mesenchymal neoplasia clinically and histologically.
Methods: A 38-year-old male patient presented with abdominal pain and gastroscopy revealed a submucosal mass lesion in the prepyloric antrum disrupting the pyloric function. Endoscopic ultrasonography (US) confirmed a hyperechoic tumour originating from the muscularis propria measuring 38 mm, with a hypoechoic halo. Computed tomography revealed a 45x30 mm, well-circumscribed lesion compatible with gastrointestinal stromal tumour (GIST).
Results: Evaluation of the US-guided fine needle biopsy revealed mesenchymal cells with epiteloid features. With the preliminary diagnosis of GIST, a distal subtotal gastrectomy was performed. Macroscopic examination revealed a well-circumscribed submucosal mass measuring 35x30x20 mm. The tumour was composed of solid areas and ectatic vascular spaces, which dissected muscle fibers with infiltrative borders. Round-oval shaped tumour cells with scanty cytoplasm and well-defined borders had uniform round nuclei with inconspicuous nucleoli, lacking nuclear pleomorphism and mitosis. The differential diagnosis included GT, GIST, leiomyoma, and neuroendocrine tumour. The immunohistochemical (SMA, caldesmon, calponin, vimentin positivity and keratin, CD117, DOG-1, desmin, CD34, S-100, chromogranin, synaptophysin negativity) and histomorphologic findings were compatible with a GT.
Conclusion: Being a mesenchymal tumour usually arising from the superficial soft tissues of the extremities, GT is rarely located in the stomach, and achieving a preoperative diagnosis can be challenging. Cytological or histologic findings may be confusing due to the resemblance to more commonly seen mesenchymal tumours such as GIST, leiomyoma or neuroendocrine tumour. Our aim in presenting this case is to raise awareness among pathologists regarding this rare location.

E-PS-24-166
A case of combined oesophageal small cell-squamous cell carcinoma: composite or collision?
S. Vese*, A. Orosz, A.C. Pop, M. Muresan, A. Vigdorovits, A. Camarasan, A. Pașcalău, O. Pop

*Emergency Clinical County Hospital Oradea, Bihor, Romania
Background & objectives: Mixed tumours of the oesophagus are classified as composite or collision. They can present with mixed morphologies and variable immunohistochemical patterns, creating diagnostic challenges. We present the case of a 53 year-old man with a mixed malignancy of the oesophagus.
Methods: The patient was admitted with complaints of complete dysphagia for liquids and solid food, dysphonia and supraclavicular adenopathies.Initial evaluation of the patient included history, physical examination as well as endoscopy and CT scan. Morphologic as well as immunohistochemical analysis for CK5, CD56, TTF1 and Synaptophysin were performed.
Results: Endoscopic examination revealed an infiltrative, circumferential, haemorrhagic, tumour. In the cervical segment of the esophaential, CT scan revealed a circumferential parietal thickening, with signs of infiltration and stenosis. The biopsy revealed a mixture of squamous and small cell carcinoma morphologies. The squamous component was positive for CK5 and negative for CD56, TTF1 and Synaptophysin. The small cell component was negative for CK5 and positive for TTF1, CD56. The patient underwent decompressive external radiotherapy at the level of the oesophagus and mediastinal adenopathies.
Conclusion: The current case report gives a brief perspective over the challenges associated with the diagnosis and management of mixed neuroendocrine non-neuroendocrine neoplasms, particularly in the oesophagus. Due to the rare occurrence of these lesions, more research is needed in order to provide patients with better diagnosis and treatment.

E-PS-24-167
Primary malignant melanoma arising from digestive system: a review of diagnosed cases in a third level hospital
S. Vicente Arregui*, N. Marínez Arnau, L. Ollero Domenche, J.L. Delgado, J. Martínez Castillón, E. Del Valle Sánchez, C. Hörndler, M.A. Trigo
*Spain

Background & objectives: Primary malignant melanoma arising from digestive system is a very uncommon entitiy. The most common location of the digestive system is the anus. They have variable clinical presentation and they are more aggressive than cutaneous melanomas.
Methods: Following a recently diagnosed case, a retrospective review was carried out, using the PAT-Win database of all the GI tract biopsies coded with the SNOMED "melanoma", excluding metastatic cases, during the period from 2014 to 2024 at the Miguel Servet University Hospital. The epidiomiological, histopathological and molecular characterisctics of the cases were analysed and compared with the literature.
Results: 5 cases with primary melanoma in the GI tract were obtained: 3 in anus, 1 in stomach and 1 in gastro-oesophagic junction. 4 of the patients were males with ages between 62 and 81 years. Only 1 case occured in a 76 years old female. Histologically, an undifferentiated neoplastic proliferation with intermediate size cells with large atypical nucleous was seen in all cases. Furthermore, in 2 of the cases an in situ component was observed. Immunohistochemically, diffuse and intense expression of SOX10 and HMB45 was observed. BRAF mutation was detectd in one of the cases. In all cases, the presence of a primary cutaneous or ocular melanoma was ruled out.
Conclusion: Melanomas arising in gastrointestinal tract are very uncommon (an average rate of 0.45 per million people according to bibliography). Given its discovery, it is mandatory to rule out a metastatic origin. A fundamental clue for the diagnosis of primary melanoma is to observe an in situ component. Our results showed the same characteristics as those found in literature, except that our cases were most frequent in males than in females.

E-PS-24-168
Comprehensive review of inflammatory fibroid polyps: clinical, morphological, and molecular insights
P.I. Voinescu*, S. Quinones, V. Hincapié, L. G-Pastrián
*La Paz University Hospital, Spain

Background & objectives: Inflammatory fibroid polyps (IFPs) are rare benign lesions that can arise throughout the gastrointestinal tract. As their clinical, morphologic, immunohistochemical and molecular features are so varied, we aimed to review these parameters focusing on differential diagnoses and their pitfalls.
Methods: We searched our files from 2014 to March 2024 for IFPs diagnoses. Epidemiological data, symptoms, morphology, location, size, immunohistochemistry, molecular analysis based on Next Generation Sequency (NGS) and follow-up were recorded and analysed.
Results: Our study included 29 patients (24 female (82.8%), 5 male (17.2%); median age 64). Gastric antrum was the most frequent location (51.7%), followed by ileum (10.3%). The average size was 1.64 cm (0.3-6.5 cm). Most frequent histological feature was a bland spindle cells proliferation with prominent vasculature (“onion-skinning”) and eosinophils. Occasionally, epithelioid morphology was found. Inmunohistochemical studies are useful to make differential diagnoses with other mesenchymal tumours, being CD34 positive in most cases. Molecular analysis was preliminary performed finding platelet-derived growth factor receptor alpha (PDGFRA) mutations.Although the majority were incidentally discovered, 13.8 % of patients presented with obstructive symptoms. None of the patients experienced recurrence during the follow-up.

Conclusion: Our retrospective study is a comprehensive analysis of the clinical, morphological and molecular features of IFPs throughout the gastrointestinal tract and enriches our knowledge of an elusive lesion than can lead to wrong diagnoses, including malignant tumours.

E-PS-24-170

Correlation between CD24 and PD-L1 expression and clinicopathological features of sporadic colorectal cancer

Q. Xia*, Y. Wang
*China

Background & objectives: Many Colorectal cancer (CRC) patients couldn't benefit from immunotherapy. Therefore, it is of great significance to explore potential immunotherapy combination strategy to guide Micro Satellite stability (MSS) and Micro-satellite High Instability (MSI-H) CRC immunotherapy.
Methods: CRC patients with stage IIB-IIIC were selected, including 180 cases of MSS and 52 cases of MSI-H. Immunohistochemical were used to detect the expressions of CD24 and PD-L1. Multivariate analysis of progression-free survival (PFS) was conducted by Cox analysis. We also established mice models to analyse and compare the CD24 and PD-1 monoclonal antibody administration effects on MSI-H CRC.
Results: The results showed that CD24 was correlated with tumour stage and lymph node invasion. And PD-L1 was correlated with the maximum tumour diameter. The results showed that PFS in CD24 high expression group of MSS CRC and MSI-H CRC patients were significantly lower CD24 low expression group. Multivariate Cox proportional hazard regression analysis showed that CD24, tumour stage, lymph node invasion, and nerve invasion were related to PFS in MSS CRC patients. The experimental results of administration model showed that compared with the control group, and the most significantly reduced group is CD24 monoclonal antibody + PD-1 monoclonal antibody combined administration group.
Conclusion: CD24 expression in MSS CRC patients are correlated with tumour stage and lymph node invasion; CD24 may be an independent influencing factor for PFS in MSS and MSI-H CRC; MSI-H CRC patients with PD-L1 CPS≥1 had the worse prognosis when accompanied with CD24 high expression; Combined application of CD24 + PD-1 monoclonal antibody has the most significant effect on MSI-H CRC, it provides a theoretical basis for combined immunotherapy of CD24 and PD-1 monoclonal antibody for MSI-H CRC.

E-PS-24-171

Clinicopathologic spectrum of malignant gastrointestinal neuroectodermal tumour: a study of 25 cases from a single tertiary-care oncology centre in India

S. Yadav*, S. Satav, N. Seshadri, G. Deshpande, R. Kaushal, K. Deodhar, B. Rekhi, M. Ramadwar, M. Bal
*Tata Memorial Hospital, India

Background & objectives: Malignant gastrointestinal neuroectodermal tumour (GNET) is a primary gastrointestinal mesenchymal tumour with high risk of local recurrence and metastasis. The hallmark of GNET is Ewing sarcoma breakpoint-region-1 (*EWSR1*) gene rearrangement. Our study aims to review the clinicopathological features of GNET.
Methods: We retrieved all cases reported as GNET or clear cell sarcoma of the gastrointestinal tract between 2012 and 2023. Cases were reviewed and the diagnosis was confirmed. Immunohistochemical results were evaluated. *EWSR1* gene rearrangement results were incorporated in the study wherever available (n=10). A total of twenty-five cases diagnosed on morphology were included in the study.
Results: The median age of patient was 45 years with male-to-female ratio of 1.27:1. The commonest presentation was pain in abdomen (32%,n=8) and abdominal mass (16%,n=4). The most common location was small intestine (56%,n=14) followed by colo-rectum (28%,n=7). Liver metastasis was seen in 36% (n=9). On histology, the tumour growth pattern were sheets (48%,n=12), nests (36%,n=8) and fascicles (24%,n=6). The tumour cell morphology was round-to-oval (32%,n=8), epithelioid (24%,n=6), and spindled (20%,n=5). By immunohistochemistry, S100p/SOX10 were positive in all cases (100%) while other melanocytic markers (HMB45 and Melan-A) were negative. *EWSR1*-gene rearrangement study showed 100% concordance in cases performed (n=10). Follow-up information was available in 13 patients (range: 2 months-83 months).
Conclusion: GNET is a rare gastrointestinal mesenchymal tumour with poor prognosis occurring in young to middle-aged adults. Therefore, GNET should be suspected in all gastrointestinal tumours with epithelioid to spindle cell morphology showing positivity for S100p/SOX10 and are negative for other melanocytic markers as also seen in our study. Detecting and diagnosing GNET and distinguishing it from other malignant neoplasm thus requires a high level of suspicion, substantial resources (immunohistochemistry and molecular tests) and considerable expertise.

E-PS-24-172

The prognostic value of tumour - infiltrating lymphocytes in MSS/MSI adenocarcinomas of colon, stage II-IV

L. Zakhartseva*, B. Shkurupii
*Bogomolets National Medical University, Ukraine

Background & objectives: Tumour-infiltrating lymphocytes (TILs) are one of the key players in the tumour microenvironment that have been shown influence on overall survival in patients with colon adenocarcinoma. Methodology of TILs calculation vary.
Methods: 73 patients with colon adenocarcinoma. TILs have been calculated on H&E slides according to International Guidelines on TIL assessment in Breast Cancer. The average observation period was 34 months. Kaplan — Meier method with a log-rank test was used to analyse survival data. TILs correlation with MSS/MSI status was calculated by Pearson`s correlation coefficient.
Results: According to TILs intensity samples have been divided into Group A (TILs 0-9%) (n=23); Group B (TILs 10-39%) (n=28); Group C (TILs >40%) (n=22). In 86% (n=63) of cases were MSI-stable (MSS); 4% (n=3) – MSI-low; 10% (n=7) – MSI-high accordingly. Overall survival differs statistically significant between ABC Groups (p=0.042). Due to univariant Cox's proportional hazard regression model survival rates in a Group C (TILs >40%) had significantly higher overall survival rates (HR 0.19, 95% CI 0.04-0.88, p=0.035) compared to the Groups A and B. There was statistically significant correlation between TILs and MSS/MSI status (p=0.039); TILs and Stage (p <0.001). No statistically significant relationships between MSS/MSI status and Stage.
Conclusion: Our data confirm that high TILs can be considered as a prognostic marker. There is an association between TILs and MSS/MSI status that can be considered as factors influence on immunotherapy success and overall survival rates for patients with colon adenocarcinoma. These factors require a further studies for understanding a potential of this factors for treatment decision making.

E-PS-24-173

Immunoscore assessment in rectal cancer: about 54 cases

M. Zaryouhi*, I. Hasnae, L. Tahiri, N. Hammas, l. Chbani
*Department of Pathology, Hassan II hospital University, Morocco

Background & objectives: Many factors may impact the response to neoadjuvant treatment in locally advanced rectal cancer. The immunoscore evaluates the immune infiltrate within tumours. This study investigates the impact of immunoscore on therapeutic response, survival, and prognosis in 54 rectal cancer patients.

Methods: A retrospective study involving 54 cases of rectal cancer (2011 -2020). Different samples were diagnosed on histology with the help of immunohistochemistry (CD3, CD8). Clinical data, therapeutic protocols, and specimens' response were collected and analysed. Immunoscore was determined based on cytotoxic T lymphocyte density. Results were correlated with therapeutic response, disease progression, and survival outcomes.
Results: 54 cases were included. The mean age was 55,25 years. Sex ratio was 0,68 M/F. the classification of densities according to the threshold determined has enabled us to distinguish 5 immunoscore classes: I0 in 9,3% of the tumours, I1 in 18,5%, I2 in 22,2%, I3 in 18,5% and I4 in 31,5% of the tumours. The analysis revealed diverse Immunoscore distributions among patients, correlating with survival rates and therapeutic responses. Patients with higher immunoscores exhibited improved overall survival and better responses to neoadjuvant treatment.
Conclusion: The findings underscore the prognostic significance of Immunoscore in rectal cancer, highlighting its potential utility in guiding treatment decisions and predicting patient outcomes. Therefore, it is necessary to incorporate immunoscore detection into pathology reports and integrate immunoscore assessment into clinical practice.

E-PS-24-174
Perioperative chemotherapy in gastric cancer: pathological response and correlation with age
M. Zaryouhi*, I. Hasnae, L. Tahiri, N. Hammas, l. Chbani
*Department of Pathology, Hassan II hospital University, Morocco

Background & objectives: Perioperative chemotherapy is the preferred treatment options for gastric carcinoma. Response to perioperative chemotherapy is an important predictor of overall survival. This study assesses pathological response in gastric carcinoma based on age after perioperative chemotherapy (POC).
Methods: We performed a retrospective study from 2018 to 2024 in the Department of Pathology of the Hassan II University Hospital of Fez. The patients included are those with gastric carcinoma who underwent POC. The pathological response was evaluated on patient with perioperative chemotherapy. Pathological response was correlated with age.
Results: 70 cases were included with a sex ratio 1,6 (M/F). The mean age was 59,74 years. Adenocarcinoma was found in 76,67%, adenocarcinoma with signet cells component in 13,33%, and SCC in 10%. Therapeutic responses varied among adenocarcinomas with signet cells and pure adenocarcinomas. Responses were characterized by fibrosis (66.66%), inflammation (53.33%), mucinous modifications (20%), and necrosis (33.33%). The analysis found that the proportion of patients who responded positively to treatment generally increased with age.
Conclusion: Our results confirm that perioperative chemotherapy for gastric carcinoma can be safely administered in clinical practice, achieving an improvement in pathological response. Furthermore, we observed a correlation between age and pathological response, suggesting that age may influence the effectiveness of chemotherapy in this context.

E-PS-24-175
Sporadic plexiform neurofibroma of the vagus nerve of the stomach: an exceptional case report
M. Zghal*, O. Belhadj, L. Bouzidi, S. Kanoun, L. Ayadi, T. Sellami Boudawara, M. Mellouli
*Department of Pathology, Habib Bourguiba University Hospital, Sfax, Tunisia

Background & objectives: Plexiform neurofibroma (PN) is a rare benign peripheral nerve tumour mainly associated with neurofibromatosis type 1 (NF1). Sporadic PN is extremely rare; its location in vagus nerve is even rarer. We aimed to investigate the clinicopathological aspects of this entity.
Methods: A 72-year-old woman was admitted to the surgery department for the management of gastric carcinoma. She underwent a total gastrectomy. A nodule at the right paracardial lymph node site was incidentally disjointed during the intraoperative procedure and was resected. Pathological examination of the gastric tumour concluded mixed adenocarcinoma (90% poorly differentiated adenocarcinoma; 10% poorly cohesive carcinoma) with lymph node metastases.
Results: Macroscopic examination of the paracardial tumour showed a well circumscribed nodule with myxoid-like white tan cut surface. The nodule measured 1.2cm of greater size. Histological examination revealed a multinodular and plexiform bundles of bland spindle cells. These cells exhibit a wavy serpentine nuclei and moderate eosinophilic cytoplasm, without atypia or mitosis. The stroma was fibrous with myxoid area. The tumour was intimately adjacent to a nerve bundle. Immunohistochemically, the tumour cells were positive for S-100 and Sox10, and negative for c-kit and Dog1. These findings were consisting with a PN. Due to the absence of other signs of NF1, the diagnosis was a sporadic PN of the stomach vagus nerve.
Conclusion: PN is a rare benign tumour of the peripheral nervous system, that rarely occurs as a solitary lesion without features of generalized neurofibromatosis. The location of PN in the stomach vagus nerve is exceptional; to our knowledge this is the second case of sporadic PN of stomach vagus nerve reported in the literature. The lesion was discovered incidentally, and the diagnosis was established by histological features. Gastrointestinal stromal tumour should be excluded. Complete resection is recommended due to degeneration risk.

E-PS-24-176
Incidence of conventional and non-conventional dysplasia in randomized biopsies during dysplasia surveillance for inflammatory bowel disease: a retrospective analysis of 150 biopsies
Z. Calixto Alvarez, A. Hidalgo Romero, J.T. Zúñiga Gaitán, S. Ramón y Cajal, S. Landolfi, A. Zucchiatti*
*Vall d'Hebron University Hospital, Spain

Background & objectives: Conventional dysplasia (CD) is a well-recognized feature of inflammatory bowel disease (IBD). However, non-conventional dysplasia (NCD) patterns have been identified but not yet routinely reported. This study investigates the incidence of CD/NCD in dysplasia screening biopsies from IBD patients.
Methods: An initial screening of 150 randomized colonic biopsies from IBD patients obtained between 2021-2023 was performed by a GI pathologist. Immunohistochemical (IHC) staining for p53 (DO-7) and SATB2 (EP281) were analysed on biopsies with histological uncertainty of dysplasia (CD or NCD). Dysplastic cases were reviewed by a blinded consensus panel.
Results: Two out of 150 randomized colonic biopsies (1,3%) showed dysplasia. The first case, a 60-year-old male smoker with a 12-year history of ulcerative colitis, was diagnosed with CD, low-grade intestinal type. The second case, a 63-year-old non-smoking woman with a 14-year history of ulcerative colitis, was initially diagnosed as negative for dysplasia but was reclassified as goblet cell-deficient dysplasia (NCD subtype) with a mutant/null p53 pattern and normal SATB2 expression. Neither case showed primary sclerosing cholangitis association. Additionally, other morphological changes were observed, including crypt-associated anomalies (CAA) (6.6%) and hyperplastic changes (4%).
Conclusion: The usefulness of randomized biopsies in IBD is highlighted by the detection of CD and NCD through histological evaluation. Morphological changes in IBD colonic tissue can be subtle and are not limited to dysplasia alone, but also to hyperplastic changes and abnormalities associated with cryptogenesis. Even if uncommon, it is important for pathologists to be able to identify NCD. More research is needed to understand the real significance of NCD, hyperplastic changes and CCA in these patients.

E-PS-25E-Poster Session Infectious Diseases Pathology
E-PS-25-001
Primary mesenteric hydatid cyst
D. Almeida*, O.M. Da Rocha Moreira Pedro, M. Nunes, R. Machado-Neves, M. Honavar, T. Rama, T. Amaro
*Portugal

Background & objectives: Hydatidosis is a zoonotic disease most common in rural areas. Hydatid cysts are caused by a parasite (Echinococcosis granulosus) and often seen in liver, which may disseminate leading to intraperitoneal cysts. Very rarely (2%) there are primary mesenteric cysts.
Methods: We present a case of a primary mesenteric hydatid cyst in a 76-year-old male with a palpable abdominal mass of 60 mm. He had close contact during his childhood with non-vaccinated and non-dewormed animals. History of brachytherapy for a prostatic cancer.
Results: Emergency room visit in April of 2023 due to a painless, palpable abdominal mass. CT scan and MRI showed a well circumscribed, lobulated and partially calcified mesenteric lesion. Serum IgG Anti-Echinococcus was positive, making hydatid cyst the most probable diagnosis. Surgical specimen of greater omentum with a multilobulated cystic lesion of 60x60x50 mm with a thick wall and a whitish, laminated and mucinous content. Microscopically there was a cyst wall with three structural components: acellular laminated membrane, a germinal membrane and the presence of birefringent ovoid structures with hooklets - protoscolices. There was no evidence of cysts elsewhere, and a diagnosis of a primary mesenteric hydatid cyst was made.
Conclusion: Hydatid cysts are usually seen in liver, lungs, bone or central nervous system. Our patient had a primary mesenteric hydatid cyst which is a very rare form of presentation of this parasitic infection.

E-PS-25-002
Unusual presentation of necrotizing fasciitis due to fungal infection by fusarium species in a transplanted patient
J. Alvarez*, M. Rolon, L. Chacon Zambrano
*Fundación Santa Fe de Bogotá, Colombia

Background & objectives: In transplant patients, immunosuppressive therapy significantly escalates the susceptibility to severe opportunistic infections. Herein, delineate a case of necrotizing fasciitis precipitated by a polymicrobial infection, encompassing both bacterial and fungal pathogens as Fusarium, in an individual with a renal allograft.
Methods: A retrospective analysis was conducted on the clinical records and biopsy specimens of a 78-year-old patient with a history of chronic kidney disease due to benign prostatic hyperplasia, who underwent transplantation 10 years ago, followed by acute humoral graft rejection BANFF 2A. Conventional histopathological techniques and special stains (Gram, PAS, and Gomori) were employed to identify pathogens.
Results: The patient presented with persistent edema in the right lower extremity, complicated by venous thrombosis, which required management with anticoagulants. Treatment included intravenous immunoglobulin due to previous acute humoral rejection, further complicating the clinical outcome. Biopsy findings revealed extensive necrosis and severe acute inflammation with the presence of neutrophil microabscesses and neovascularization affecting the subcutaneous tissue and fascia. Special stains (PAS, Gomori, and Gram) identified thick, hyaline, septate hyphae characteristic of Fusarium, along with bacterial colonies. These findings led to the diagnosis of a rare presentation of necrotizing fungal and bacterial fasciitis in the context of post-transplant immunosuppression.
Conclusion: This case underscores the critical importance of timely recognition and interdisciplinary management of opportunistic infections in immunocompromised patients. Necrotizing fasciitis, caused by unusual pathogens, particularly Fusarium in this instance, can result in devastating outcomes if not appropriately managed. Collaboration among dermatopathology, infectious disease specialists, and surgical teams is vital for effective treatment. This report adds to the existing literature by emphasizing the need to consider fungal etiologies in the differential diagnosis of severe cutaneous lesions in transplant recipients

E-PS-25-003
Hydatid cysts of the central nervous system in children: about 6 cases
R. Aouadi*, A. Zehani, A. Ayari, A. Khadhar, I. Chelly, H. Azouz, K. Bellil, S. Haouet
*La Rabta Hospital, Tunisia

Background & objectives: Hydatid cyst, typically caused by Echinococcus granulosus larva, is a parasitic disease commonly affecting children in liver and lungs. The central nervous system is an uncommon location. Our aim was to study the characteristics of this entity in paediatric patients.
Methods: We retrospectively collected 6 cases of hydatid cyst of the CNS occurring in paediatric age group, diagnosed in our department over an 8-year period spanning from 2016 to 2024. Patients had no pertinent past medical history.
Results: The patients were 5 boys and one girl aged 3 to 18 years old. The mean age was 11 years. All patients were from rural backgrounds. Five cases involved the brain hemispheres, and one case involved the brainstem. The clinical presentation was dominated by intracranial hypertension associated with focal neurological deficit. One patient suffered from reduced visual acuity for about a year. In this case the cyst was voluminous involving frontal, parietal and occipital lobes. Radiologic exams showed cystic lesions strongly suggestive of hydatid cyst in all cases. All patients underwent surgery. Histological examination identified acellular laminated eosinophilic hydatid membranes and daughter cysts with protoscolices, confirming the diagnosis.
Conclusion: Hydatid cyst rarely involves the central nervous system, but this site of occurrence seems to be more common in younger patients. Early diagnosis is essential to avoid serious complications, including major neurological deficit and even anaphylactic shock.

E-PS-25-005
Tuberculosis infection in an unusual sites: a challenging diagnosis
R. Ayadi*, E. Braham, R. Yaiche, F. Khefacha, A. Saidani, O. Ismail, F. Chebbi, A. Ayadi
*Department of Pathology, Abderrahmen Mami Hospital, Tunisia

Background & objectives: Pulmonary location is the most common site of tuberculosis. Extrapulmonary tuberculosis (EPTB) with the rarest and most unexpected sites remains an important public health problem. The aim of this study is to present clinocopathological characteristics of rare EPTB cases.
Methods: The study included rare EPTB patients diagnosed at our department of pathology between 2004 and 2023. Cases with pleural TB and lymph node TB were excluded from the study. The diagnosis of EPTB was made by histopathological findings.
Results: Eighty-one patients were included (female/male=53/28) aged between 14 and 84 years with a mean of 45,57. The most frequently involved organ were peritoneum (n=25), skin (n=25) followed by gastro-intestinal (n=11) and hepatic (n=6) site. The other localizations female genital and breast were noted in two cases each. There was multi-organ involvement in 18 cases. Co-existence of EPTB with PTB was determined in 2 cases (2,46%). The major complaints were abdominal pain, weight loss, night sweats, fever, and cough. The diagnostic was confirmed by a tissue samples. In microscopic examination, granulomatous reaction was composed of epithelioid cells and multinucleated giant cells with variable number of lymphocytes and centred by caseous necrosis.

Conclusion: Diagnosis of EPTB is challenging due to its nonspecific clinical presentation, the limitation of laboratory testing, and the similarities of radiographic to other diseases. Microscopic findings are variable and sometimes uncertain, especially with non caseating necrosis. The histopatological examination must be completed with bacteriological studies, mainly when the clinic presentation suggest the diagnosis.

E-PS-25-006

Schistosomiasis appendicitis: report of a rare entity and review of the literature

O. Belhadj*, S. Makni, S. Graja, M. Bouhamed, R. Kallel, C. Chaari, T. Sellami Boudawara, M. Triki
*Department of Pathology, Habib Bourguiba University Hospital, Sfax, Tunisia

Background & objectives: Schistosomiasis is a tropical parasitic infection caused by Schistosoma haematobium, mansoni or japonica. Schistosomiasis appendicitis (SA) is rarely reported and accounts for between 0, 02% and 6,3%. We herein present a case of SA and include clinical and histological features.
Methods: A 67-year-old man was presented to the Department of General and Digestive Surgery following 4 days of increasing right iliac fossa pain and fever. The patient reported neither previous pathological history nor recent travel.
Results: Physical examination revealed tenderness at Mc Burney's point and a positive Rovsing's sign. The biological assessment showed leukocytosis (13×109/l). Based on these findings, the diagnosis of acute appendicitis was made. A laparoscopic appendectomy was performed. On macroscopic examination, the appendix measured 4.5×1.5 cm, and presented circumferential thickening and millimetric nodules in the subserosa suggesting a mucinous tumour. Histopathological examination revealed acute focal appendicitis with eosinophilic and neutrophilic inflammatory infiltrate in the mucosa. Parasitic eggs measuring approximately 119µm with lateral spines were present in the subserosa surrounded by sclerotic and calcified fibrosis. The final diagnosis of SA was made. Parasitological examination of stool and urine was indicated to identify schistosoma eggs.
Conclusion: Schistosomiasis is frequent in tropical and subtropical countries. Parasitic transmission is caused by contact with contaminated water sources. SA is an uncommon. Positive diagnosis is based on microscopic detection of eggs in stool or urine. Additionally, to surgical treatment, anti-shistosoma drugs such as praziquantel are recommended. It has been established that schistosomiasis infection can have many multisystem effects. Clinicians and pathologists should be aware of this infection especially when dealing with patients presenting from endemic countries.

E-PS-25-007

Cutaneous fungal infection in a renal transplant recipient: is it cryptococcosis?

O. Boudaouara*, M. Mellouli, M. Triki, N. Gouiaa, C. Kammoun, T. Sellami Boudawara, O. Belhadj
*Tunisia

Background & objectives: Cryptococcus is an opportunistic fungus, infecting mainly immunocompromised hosts including HIV/AIDS-patients and solid-organ-transplant-recipients. We report a case of a primary-cutaneous-cryptococcosis in order to underline the pathologist's role in suggesting the right diagnosis based on distinctive morphological features of cryptococcus yeasts.
Methods: We describe a case of a primary cutaneous cryptococcosis diagnosed in our pathology department and treated in infectious diseases department of Sfax Hospital.
Results: A 28-year-woman, having a history of renal transplantation 7 years ago, presented with an inflammatory-plaque of the left thigh suggesting an acute-cellulitis. A skin biopsy was performed. Histological findings revealed a dense-dermal-histiocytic-infiltrate with necrotic and suppurative changes. Several encapsulated budding-yeasts measuring 5 to 10 µm were evidenced within the inflammatory infiltrate. Yeasts-forms stained with PAS and methenamine-silver stains, remaining widely separated by a thick-unstained-capsule. The latter was highlighted by Alcian-Blue-stain suggesting cryptococcosis. Cryptococcus neoformans was also isolated in the skin lesion. Imaging findings revealed no fungal-systemic-spread. The diagnosis of a primary-cutaneous-cryptococcosis was made. Fluconazole therapy was maintained during 6 months inducing lesion healing. Eighteen months later, a histologically-proven-recurrence occurred.
Conclusion: Cryptococcosis is a serious invasive fungal infection with frequent skin involvement presenting a wide range of skin manifestations. Thus, unexplained skin lesions, occurring in immunosuppressed patients, are not only suspicious for malignant neoplasms but also for opportunistic infections and particularly cryptococcosis. Skin biopsy constitutes a valuable tool to guide clinician in patient's management.

E-PS-25-012

An integrated approach to the diagnosis of meningococcemia in a 47-year-old patient with alcohol-related illness

O. Sudareva*, S. Lezhenina, E. Ignatieva, A. Grigorieva, E. Guryanova
*I.N.Ulianov Chuvash StateUniversity, Russia

Background & objectives: In this article, we for the first time identified a case of meningococcemia in a patient suffering from chronic alcohol intoxication, and showed a multi-stage approach to making a pathological diagnosis is demonstrated.
Methods: Bacteriological blood tests, autopsy and microscopic examinations were used in the analysis of the fatal case. Immunohistochemical stains with analysis of CD4, 21, 57 and 68 for typing the nature of the immune status. Biochemical examination of cadaveric blood samples was carried out using a column-free ion exchange method for glycosylated hemoglobin and glucose; Acetone was determined by chromatography.
Results: The corpse was found to have: a "star-shaped" rash of a confluent nature on the skin and serous membranes; necrotizing vasculitis in the leptomeningeal membrane, myocardium, lungs; in the heart – subendocardial necrosis of the myocardium; in the adrenal glands there was hypoplasia of all layers, haemorrhages characteristic of Waterhouse-Friderichsen syndrome. In the spleen and lymph nodes, there was delymphatization of the lymphoid follicles (decrease in CD4, 21, 57 populations, increased expression of CD 68), focal sclerosis and hemosiderosis in the pulp. Bacteriological culture of the blood showed moderate growth of Neisseria meningitidis. He also had comorbidity: alcoholic cirrhosis of the liver; secondary cardiomyopathy with manifestations of congestive heart failure.
Conclusion: Taking into account the medical history and autopsy, the patient was found to have an atypical course of meningococcal infection, which was offset by severe comorbid pathology in the form of alcoholic illness with multiple organ failure, metabolic disorders in the form of hypoglycemia that cannot be corrected, and decompensated ketoacidosis. The role of immunodeficiency in the patient in the form of adrenal hypoplasia and delamphatization of lymphoid organs should not be underestimated.

E-PS-25-013

Isolated laryngeal leishmaniasis: an uncommon and overlooked cause of persisting voice hoarseness

M. Sassi, I. Nitsios, N. Tepelenis*, A. Kostopoulou, A. Tsagkovits, A. Spyrou, T. Choreftaki
*Department of Pathology, General Hospital of Athens "Georgios Gennimatas", Athens, Greece

Background & objectives: Leishmaniasis is caused by parasitic protozoa of the Leishmania species, transmitted by infected sandflies. Three main forms exist: cutaneous, mucocutaneous, and visceral. Rare cases of primary mucosal leishmaniasis, linked to L.infantum subspecies, have been reported in Europe.
Methods: We describe a case of a 68-year-old male who presented with a month history of voice hoarseness. He had a medical history of depression under treatment. He had not travelled outside Greece. Microlaryngoscopy was performed, which demonstrated bilateral oedema of the false vocal cords and of the left laryngeal ventricle. Biopsies were taken for pathological evaluation.
Results: Histology revealed dense chronic and granulomatous inflammation along with small, round, uniform intracytoplasmic formations consistent with Leishman bodies. Serum leishmania antibodies were positive, followed by PCR analysis, which came back conclusive for the diagnosis of L.infantum. Additional tests excluded evidence of visceral or cutaneous leishmaniasis or presence of HIV antibodies. The patient received intravenously liposomal amphotericin 3mg/kg/day for 20 consecutive days which resulted in significant improvement on follow-up one month later.
Conclusion: Despite the rarity of mucosal leishmaniasis in the Mediterranean region, the endemic Leishmania species in Europe should not be disregarded. Isolated laryngeal lesions mimic other inflammatory and neoplastic conditions. This results in the delay of the correct diagnosis and treatment. It is of utmost importance to consider this parasitic disease as a possible cause of mucosal lesions, especially in travelers to and from endemic regions as well as among residents, in order to avoid mistreatment of a potentially fatal disease.

E-PS-25-014
Herpesvirus 6 as a risk for HIV immunosuppressed patient's neuro commitment: case report
E. Tomé de Sousa, L. Vasconcelos Cavalcante*, J.P. Feitosa Cajuaz Castro, L. Teles Moreira Lopes, L. Creston Aldigueri Arruda, L. Costa Gurgel, T. Teixeira Monteiro, D. Nunes Oliveira
*University of Fortaleza, Brazil

Background & objectives: CNS infections are an important cause of mortality in HIV-positive patients. Human herpesvirus 6, which usually affects children, can be reactivated in adults due to immunosuppression. We report a case of herpetic meningoencephalitis in an HIV-positive patient.
Methods: Case report of a 38-year-old woman who presented with bleeding, abdominal pain, diarrhea and headache. She was admitted to a hospital with hyporesponsiveness, hypoglycemia and vomiting. She tested positive for HIV and herpesvirus 6 was detected in the patient's cerebrospinal fluid. The patient progressively worsened and died.
Results: Histopathological study of the brain showed perivascular lymphocytic infiltrate, congestion of capillaries and edema in the meninges. The kidney presented vascular congestion and acute tubular necrosis. Heart and lungs with lymphomonocytic infiltrate accompanied by interstitial edema in both tissues, suggestive of myocarditis and pneumonitis respectively, conditions already widely described in the reviewed literature as a consequence of the etiological agent herpesvirus 6 in patients immunosuppressed by bone marrow and liver transplantation.
Conclusion: Cases of acute herpesvirus 6 infection in adults are rare and with mild symptoms. Despite this, in immunosuppressed adult patients, HHV-6 infection presents a high risk of systemic involvement, which can lead to death, as demonstrated in the reported case. Furthermore, Herpesvirus 6 is an agent of high morbidity and mortality in patients with HIV and should be considered as a differential diagnosis.

E-PS-25-015
Peritoneal anisakiasis in a patient with a history of relapsed Hodgkin's lymphoma: a case report
M.N. Villca Huayta*, A. van der Biezen, C. Vieru, M.L. Abascal Camacho, F.J. Díaz Crespo
*Hospital General Universitario Gregorio Marañón, Spain

Background & objectives: The incidence of anisakiasis is increasing in Europe, mainly affecting the gastric and intestinal mucosa. However, peritoneal and mesenteric involvement is rare and may mimic neoplasia on CT scans. We describe a case with a view to improving knowledge.
Methods: A reported case of peritoneal anisakiasis in a patient with a history of relapsed Hodgkin´s lymphoma. Female patient with severe abdominal pain and bilious vomiting. An emergency PET-CT scan was performed which showed an intestinal obstruction and multiple peritoneal nodules, the largest measuring 3x2 cm. Tumour dissemination was considered due to progression of the lymphoproliferative process. Blood eosinophilia was absent.
Results: Resection of the peritoneal nodules was performed. Macroscopy showed solid white nodular formations, the largest being 2.5 cm. Histologically, they consisted of fibrous tissue, mixed inflammatory infiltrate, gigantocellular reaction, foci of necrosis and within these there were tubular structures with digestive apparatus, cuticle-like membrane with peripheral spicule suggesting parasitic elements consistent with Anisakis. There were no findings consistent with malignancy. Microbiology was consulted and confirms the etiology with specific serology and treatment with amebendazole + praziquantel was started. The control CT scan after treatment showed a decrease in unresected peritoneal nodules.
Conclusion: Extragastrointestinal anisakiasis is a rare form of presentation in < 1% of cases and its uptake has been described in PET-CT scan, as in our patient, mimicking a primary or metastatic neoplasm. As we can see, imaging tests are non-specific and represent a diagnostic challenge for clinicians; therefore, in most cases the histological diagnosis is made after resection of the lesions. It is important to take this entity into account in the differential diagnosis to avoid unnecessary surgery and chemotherapy.

E-PS-25-016
Cryptococcal inflammatory pseudotumour of the lung - a diagnostic pitfall
M. Zacharias*, A. Thüringer, L. Brcic, G. Gorkiewicz
*Medical University of Graz, Austria

Background & objectives: A 34-year old woman with known myasthenia gravis presented with a progressively growing 3 cm large pulmonary nodule within the left lower lobe, suspicious for malignancy. Consequently, the nodule was surgically removed by a wedge resection.
Methods: Next to histomorphological and immunohistochemical analyses, the Archer Fusion Plex Pan Solid Tumour v2 panel as well as 16S rRNA and internal transcribed spacer (ITS) sequencing were performed.
Results: Histomorphologically, the nodule consisted of a spindle cell proliferation with intermixed inflammatory cells, including lymphocytes, plasma cells, eosinophils, and neutrophils. Furthermore, some of the spindle cells showed nuclear atypia and few multinucleated giant cells were detectable. Multifocally, there were also necrotic areas within the nodular proliferation. Immunohistochemically, the spindle cells were positive only for SMA but negative for Keratin, TTF1, p40, TdT, CD117, ALK, Desmin, CD34, STAT6, SOX10, S100, MyoD1, MyoFD5 and Caldesmon. With the Archer panel, no fusions could be detected. While the 16S rRNA analysis was also negative, ITS

sequencing revealed the presence of Cryptococcus neoformans DNA. This finding was then confirmed with special stains (Grocott, PAS, Mucicarmine).
Conclusion: Based on histopathological and molecular results, the diagnosis of cryptococcal inflammatory pseudotumour was made. Only a few cases of cryptococcal inflammatory pseudotumours have been reported in the literature, mainly in HIV-positive patients. Our patient was not HIV-positive but ten months before the wedge resection, she had a type B2 thymoma treated with induction chemotherapy and consecutive resection (R1) as well as adjuvant chemotherapy. Due to the patients history, we suspect that immunosuppression and/or immune dysregulation promoted the pseudotumour formation.

E-PS-26E-Poster Session Ophthalmic Pathology

E-PS-26-001
Case report: Primary cutaneous mucinous carcinoma of the lower eyelid
R. Agrawal*, S. Marquez, S. Karim, C. Roberts
*United Kingdom

Background & objectives: Primary cutaneous mucinous carcinoma (PCMC) is a very rare tumour typically presenting as an insidiously growing and asymptomatic solitary papule or cyst in the periorbital area. We present a case of PCMC in an 88-year-old male.
Methods: Our patient initially presented to his general practitioner with a 2-week history of a slowly enlarging cystic swelling under his right eye.
Incisional biopsy showed dermal clusters and nests of monomorphic epithelial cells with peripherally orientated nuclei floating in pools of extracellular mucin and separated by thin fibrous septae. There was no in-situ component seen.
Results: Immunohistochemistry showed the epithelial cells were positive for Cam5.2, EMA, CEA, CK7, GATA3, oestrogen receptor and progesterone receptor. They were negative for CK20, CDX2, TTF1 and neuroendocrine markers (chromograninA, synaptophysin and CD56). Subsequent full body CT scan did not identify any other masses to suggest another primary source, therefore confirming the diagnosis of PCMC rather than metastatic mucinous carcinoma.
Conclusion: We present a very rare case of PCMC within the lower eyelid. This case highlights how immunohistochemistry often cannot distinguish between PCMC and metastatic mucinous carcinoma from another source, particularly metastatic mucinous breast carcinoma due to the co-expression of CK7, GATA3, oestrogen receptor and progesterone receptor by PCMC. A multidisciplinary approach with appropriate work-up is essential to determine the source and therefore the correct management.

E-PS-26-002
Ocular Cicatricial Pemphigoid (OCP) in a 49-year old man: a case report on a rare mucocutaneous entity
I. Araújo*, G. Carrola, D. Sá, N. Jorge Lamas
*ULS Santo António, Portugal

Background & objectives: Ocular Cicatricial Pemphigoid is a potentially blinding disease. It might constitute a manifestation of a systemic and autoimmune disorder called mucous membrane pemphigoid, which normally afflicts the mouth, oropharynx, skin, among other regions. Timely treatment is fundamental to prevent sequelae.
Methods: Here we report the case of a 49-year old man who came to the ophthalmology emergency services with redness and mucopurulent secretion in both eyes. In the previous month the patient sought private medical care after noticing macules and vesicular lesions in the dorsum, as well as ulcers in the oral mucosa. Conjunctival biopsies were performed.
Results: We received two whitish conjunctival fragments of 3 mm and 4 mm. The histological analysis showed an epithelium with decreased number of goblet cells, areas with squamous metaplasia and infiltration by neutrophils. Furthermore, an incipient blister-like lesion was identified at the epithelial-subepithelial connective tissue interface, predominantly filled with neutrophils. The direct immunofluorescence study revealed linear deposits of C3, IgA and IgG at the basement membrane, with absence of deposits of IgM and C4. The histochemistry study using Gram and Periodic Acid Schiff (PAS) after diastase stains did not reveal the presence of microorganisms. The diagnosis of Ocular Cicatricial Pemphigoid (OCP) was suggested.
Conclusion: This case highlights the main features of OCP, which has potential devastating impact on the quality of life of the patients and their sight capabilities. Despite optimized immunomodulatory treatment, the patient experienced bilateral corneal ulceration and perforation with endophthalmitis in the right eye, which resolved upon antibiotic treatment. Overall, his condition has progressively worsened. Currently, his vision is significantly impaired in both eyes and he maintains multiple follow-up appointments in different medical specialities.

E-PS-26-003
Case of an ocular melanocytosis with aspects of a blue cellular nevus: between "Scilla and Cariddi"
C. Cacchi*, M. Lammert, D. Jonigk
*Institute for Pathology, Germany

Background & objectives: Ocular melanocytosis is an infrequent congenital disorder. It is usually characterised by an indolent course. The aim of the presentation is to describe a case associated with a clinical/radiological progression and to discuss the diagnostic approach.
Methods: A 64-year-old patient, with a previous history of melanocytosis, presented to the clinic for the progression of an infiltrative orbital lesion affecting the extrinsic musculature of the eye and the periocular adipose tissue: postoperative diagnostic material was obtained, immunohistochemistry and molecular analysis were conducted on the submitted tissue.
Results: We observed fragmented fat and muscle tissue with diffuse cord-like, at least 1.5 cm large formations of a highly pigmented melanocytic lesion with partially, proliferating, hypopigmented areas. The lesion showed increased ki67-positive cells (focally up to 20 %) and at least 1 mitosis per 2 mm². Moreover, we noted repeated necrosis in some areas and tumour-involvement of surrounding striated muscle. The tumour-prolferation had a molecular pathological evidence of a GNAQ mutation (Q209P). The other molecular pathological analysis of a GNA11, BRAF or NRAS mutation are negative. We did not find molecular cytogenetic evidence of a monosomy 3.
Conclusion: We concluded with the diagnosis of ocular/orbital melanocytosis with aspects of blue nevus and focal areas suspicious for transformation into malignant melanoma. The second opinion requested for this case confirmed the diagnosis specifying that a malignant melanoma cannot be excluded. The rarity of the lesion makes the diagnosis of melanoma in these cases particularly complicated. An integrated approach of histopathology, clinical aspects and molecular biology is essential.

E-PS-26-004
A retrospective analysis of Orbital Lymphoma at a Portuguese University Hospital from 2018 until 2024
G. Carrola*, I. Araújo, J.R. Vizcaíno, X. Wen, F. Emanuel Costa, N. Jorge Lamas
*Anatomic Pathology Service, Pathology Department, Unidade Local de Saúde de Santo António, Portugal

Background & objectives: Ocular adnexal lymphomas (OAL) comprise 1-2% of all lymphomas, are normally unilateral and more

frequently afflict the eyelid, conjunctiva and lacrimal gland. Extraocular muscle involvement is rarely reported. The majority of the cases are extranodal marginal zone lymphomas (EMZL).
Methods: We identified four orbital lymphoma cases diagnosed at our institution from 2018 to 2024. Patients, aged 54 to 69, included three males and one female. Two cases were centred in the conjunctiva, one affected the eyelid and the other the inferior rectus muscle. Three of the cases were restricted to the orbit, while one also had pulmonary involvement.
Results: In three cases we observed the proliferation of small lymphocytes with nodular or diffuse architecture, scant cytoplasm, lumpy chromatin, and small nucleoli. Immunohistochemistry showed reactivity for CD20 and BCL2 and lack of CD10, BCL6, CD23, Cyclin D1, CD3, and CD5 in the neoplastic cells. These cases were diagnosed as EMZL. In the only female patient case there was a lesion centred at the left inferior rectus muscle composed by mononucleated lymphoid cells with clear cytoplasm, hyperchromatic nuclei, and irregular contours. Immunohistochemistry demonstrated CD3, CD43, CD5, CD2, and CD8 positivity, and absence of CD7, CD10, CD20, CD4, CD56, and TdT immunoreactivity. The diagnosis of Ocular Adnexal T-cell Lymphoma (OATCL) was suggested.
Conclusion: In line with the literature, EMZL was the predominant orbital lymphoma type in our series. The overall prognosis is normally good with adequate treatment. The OACTL has normally an inferior prognosis, yet in our case, there is no evidence of disease recurrence. All our patients are currently well and without disease relapse. Accurate and prompt diagnosis of orbital lymphoma is instrumental to start the appropriate treatment and prevent a bad outcome upon the diagnosis of these rare lymphoproliferative diseases.

E-PS-26-005
Bilateral multiple retinal white lesions with diffuse large B-cell lymphoma
S. Cati*, N. Özdemir
*Kartal dr lütfi kırdar, Turkey

Background & objectives: Aim
We report a case of intraocular involvement in diffuse large B-cell lymphoma.
Methods: A 70-year-old man presented with low vision in right eye and retinal white lesions
Results: Ophthalmological examination revealed bilateral intense corneal endothelial capillarization on the right, mild corneal endothelial capillarization on the left, bilateral peripheral retinal white lesions, and bilateral irregular subretinal deposits. However, considering the general symptoms, a biopsy was taken from the right eye retina and choroid with the preliminary diagnosis of lymphoma. On systemic examination, the patient was diagnosed with retinal involvement in diffuse large B-cell lymphoma. Bilateral visual acuity improved after systemic chemotherapy. The patient continues to receive chemotherapy.
Conclusion: In cases with prominent symptoms, comprehensive systemic evaluation should be performed to rule out severe systemic conditions, such as malignancies

E-PS-26-006
Conjunctival CD5 negative mantle cell lymphoma (cMCL): an interesting case report
D. Chiba*, I. Bahri, Y. Sarra, A. Benabdelkader, S. Ben Tekaya, W. Mokni, H. Yoni, M. Mokni
*Department of Pathology, Tunisia

Background & objectives: Orbital and ocular-adnexal lymphoma are rare,representing around1%to2% of all lymphomas.Mantle cell lymphoma(MCL) represents4%to9%of all non-Hodgkin lymphomas.Only about 5%of MCL lack CD5-expression and is poorly characterized.This work aims to report a case of cMCL and analyse its epidemiological and pathological characteristics.
Methods: A 70-year-old woman presented an eyelid unilateral mass that has been increasing in size over the 9 months to his presentation, adherent to the deep tissues without cervical lymphadenopathy. The patient underwent lesion excision with pathological examination of the specimen.
Results: The histological examination showed a proliferation of monomorphic, small-to-medium-sized lymphoid cells with irregular nuclear contours. These cells proliferated in a diffuse-to-vaguely nodular pattern. Hyalinized vessels were commonly present as well. An immunohistochemical study showed That the neoplastic cells expressed CD20, cyclin D1, and CD23. They were negative for CD3 and CD5. Ki67 was estimated at 30%.
Conclusion: Primary non-Hodgkin's lymphomas of the conjunctiva are uncommon. They are almost exclusively extra-nodal marginal zone B-cell lymphomas. A few cases of MCL have been reported in the literature. It affects frequently adults in the sixth decade with male predominance. Most patients present a high proportion of systemic involvement. The prognosis is poor marked by multiple relapses and short survival time.

E-PS-26-007
Adult-Onset Xanthogranuloma of the periorbital area: a case report on an unusual periorbital lesion
N. Chiote*, G. Carrola, D. Sá, J.R. Vizcaíno, N. Jorge Lamas
*Portugal

Background & objectives: Adult Xanthogranulomatous diseases infrequently involve the periocular tissues and its pathogenesis is poorly understood. There are four main entities within this disorder, which portend a diverse clinical approach, follow-up and prognosis.
Methods: We report the case of a 67-year-old man presenting with a slight swelling of the medial aspect of the inner corner of the right eye, without affecting the lacrimal system. The lesion was surgically excised and a 6x6x3 mm skin fragment exhibiting a whitish papule with 6x5 mm was received, which was fully submitted for microscopic observation.
Results: Upon histological analysis, the epidermis had an area of slight erosion/ulceration. In the underlying papillary dermis and the superficial half of the reticular dermis, there was an intense histiocyte-rich infiltrate, often containing a foamy cytoplasm. The infiltrate also included frequent lymphocytes, occasional Touton-type multinucleated giant cells, as well as occasional plasma cells and rare neutrophils. The infiltrate had well-defined limits. Cytological atypia, mitotic activity, images of emperipolesis and vasculitis lesions were not evident. Immunohistochemistry showed diffuse positivity for CD68, rare positivity for S100, in the absence of immunorreactivity for CAM5.2, CD1a and BRAFV600E. The diagnosis of Adult-Onset Xanthogranuloma (AOX) of the orbit was suggested.
Conclusion: This case highlights the main features of AOX, which is the least common entity among the four types of Adult Xanthogranulomatous diseases afflicting the orbit. Unlike its counterparts, AOX is a localized event without systemic involvement and, thus, aggressive treatment is likely not required as the disease is often self-limited. Ruling out other Adult Orbital Xanthogranulomatous diseases, such as Adult-Onset Asthma and Periocular Xanthogranuloma (AAPOX) is fundamental.

E-PS-26-008
Conjunctival lymphangioma: a case report of a rare entity
S. Kanoun*, M. Bouhamed, M. Rekik, A. Elarem, C. Chaari, C. Kammoun, T. Sellami Boudawara, M. Triki
*Department of Pathology, Habib Bourguiba University Hospital, Sfax, Tunisia

Background & objectives: Conjunctival lymphangioma (CL) is a rare ocular benign neoplasm, typically seen in children. It is regarded as hamartomatous in origin. The aim of this study is to report an observation about a CL and discuss its differential diagnoses.
Methods: A 66-year-old man presented with a history of gradually progressing, painless conjunctival swelling in his left eye over the course of one year. His medical and family history was unremarkable. A slit-lamp examination of the right eye was unremarkable, while in the left eye, it revealed a well-circumscribed, red conjunctival mass measuring 1.3 x 0.5 cm.
Results: The lesion was clinically diagnosed as a conjunctival tumour with superficial keratinization, and it was completely excised. Histopathological examination revealed an unencapsulated mass of endothelial-lined channels of various sizes. Some channels contained clear eosinophilic fluid, and others were filled with blood. The overlying conjunctival epithelium was slightly thickened, with focal metaplasia towards keratinizing epithelium. The diagnosis of Conjunctival lymphangioma was confirmed. After 2 months, the patient remained healthy, with no recurrence of the conjunctival lesion.
Conclusion: Lymphangiomas are benign, hamartomatous, vascular tumours usually diagnosed in early childhood, with approximately 20% found in the orbit. Lymphangiomas constitute 1%-3% of orbital masses and may involve the conjunctiva, eyelids, and orbit. Clinically, conjunctival lymphangioma (CL) appears as a diffuse or circumscribed, red, painless conjunctival lesion with focal or diffuse hemorrhage. Histologically, it is characterized by the presence of dilated lymphatic channels. The differential diagnosis of CL includes cavernous hemangioma, conjunctival lymphangiectasia, and cystic compound melanocytic nevus.

E-PS-26-009
The added value of comprehensive genomic profiling to understand metastatic uveal melanoma: insights from a case report
N.J. Lamas*, C. Vilasboas, T. Santos, F.E. Costa
*Centro Hospitalar Universitário de Santo António (CHUdSA), Portugal

Background & objectives: Uveal melanoma (UM) is the most common tumour developing inside the adult eyes. Metastases eventually develop in nearly 50% of the patients, preferentially to the liver, signaling a poor prognosis since therapeutic options for the metastatic disease are frequently ineffective.
Methods: We present the case of a 64-year old man submitted to right eye enucleation in 2014 due to UM. A spindle cell predominant UM was identified, without signs of lymphovascular invasion. Surgical margins were free of neoplastic. Recently, the patient developed liver, brain and abdominal metastases. A Next-Generation Sequencing (NGS) study was requested on the archived enucleation paraffin-embedded material.
Results: Rigorous morphological control of the case was performed. BAP-1 immunohistochemistry was ordered, demonstrating BAP-1 preservation in the melanoma cells. To conduct the NGS study, macrodissection of the area with UM was then performed. The NGS study was initially conducted for both DNA and RNA using the Oncomine Precision Assay (OPA) assay in the Genexus (Thermo-Fisher Scientific) platform, demonstrating the presence of a GNA11 p.Q209L UM initiating mutation. Later, using the same material, the NGS study was repeated using the Oncomine Comprehensive Assay (OCA) v3 assay in the same platform, confirming the presence of the previsouly identified GNA11 p.Q209L mutation and additionally revealing the presence of a pathogenic SF3B1 p.R625H mutation.
Conclusion: We were able to successfully conduct NGS studies in paraffin-embedded material archived for 10 years using both middle-sized (OPA) and large (OCA v3) NGS panels. The identified S3FB1 mutation helps to explain the onset of metastases, even though the patient had spindle cell predominant UM with BAP-1 preservation, which are normally associated with decreased metastases risk. Our case highlights the value of using large NGS panels to unravel the molecular landscape of UM and further understand this unique eye cancer.

E-PS-26-010
A rare case of ocular metastatic endometrial adenocarcinoma
M. Murkovic*, M. Mrak, T. Čaljkušić-Mance, S. Eminović, A. Dekanić
*Clinical Hospital Centre Rijeka, Clinical Department of Pathology and Cytology, Rijeka, Croatia

Background & objectives: To report a rare case of a patient with uveal metastasis from endometrial adenocarcinoma and describe the diagnostic pathway.
Methods: A 45-year-old female presented with a loss of right eyesight and ocular pain that started 3 weeks prior. Magnetic resonance showed intraocular lesion 13x9 mm. Right eye was surgically removed, and silicone eye was implanted. The biopsy of the eye showed tumour comprised of atypical glandular formations with areas of necrosis and bleeding.
Results: The tumour was panCK, vimentin, NSE, CK7, CK18 and PAX8 positive, and negative for ER, PR, CK20, CD56 and MelanA. Patients' prior medical history was considered, and biopsy was concluded as metastatic endometrial adenocarcinoma. Four years earlier the patient was diagnosed with endometrial carcinoma of the cervix and underwent hysterectomy and bilateral salpingo-oophorectomy with partial colectomy. Endometrial carcinoma was found in the uterus and locally spread to colon; lymph nodes were without metastasis. She underwent chemoradiotherapy. A year prior to intraocular metastasis CT scan showed multiple pulmonary metastasis. Molecular analysis found PIK3CA gene mutation.
Conclusion: Uveal metastasis is the most common intraocular tumour, most cases arise from breast cancers, and from lung cancers, and only in 2 % of cases from uterine cancers. While extremely rare, metastatic disease to the eye should not be overlooked in a patient with a history of endometrial cancer and new onset vision changes.

E-PS-26-011
Conjunctival malignant melanoma in both eyes from primary acquired melanosis
J. Osuna Soto*, A. Sanz Zorrilla, A. Sanz Zorrilla, M.J. Gálvez-Medina, M. Pérez Cordobés
*Hospital Universitario Reina Sofía, Pathology Unit, Spain

Background & objectives: Primary acquired melanosis (PAM) is a premalignant conjunctival lesion. When associated atypia, frequently leads to the development of conjunctival melanoma. Differentiating between melanoma in situ and PAM with atypia could be difficult. Approximately 53-74% of conjunctival melanomas develop from PAM.
Methods: We conducted a retrospective review of the most recent cases diagnosed with conjunctival melanosis, highlighting the description, histology, and immunohistochemical expression in those melanomas developed from PAM, presenting a case of very poor prognosis.
Results: The most severe case involves a patient with binocular PAM with development of infiltrating conjunctival melanoma (T3) in his right eye with microsatellites in the eyelid on the same side. The left eye (amblyopic) also presented PAM and a focus of infiltrating melanoma (T1).
Conclusion: As the presence of contralateral infiltrating melanoma was unknown before surgery; sentinel lymph node biopsy was performed on the right side of the patient with negative result. These results support that melanomas derived from PAMs have a lower frequency of metastasis than those that originate from nevi or de novo.

E-PS-26-012
Primary adnexal tumours of the eyelid: a single centre ten-year review analysis
T. Stojanović*, M. Bosić, D. M. Rašić
*Department of Pathology, Pathohistology and Medical Cytology, University Clinical Centre of Serbia, Belgrade, Serbia

Background & objectives: Primary adnexal eyelid tumours (PAET) are rare neoplasms with heterogeneous histology and specific behaviour related to unique characteristics of this anatomic site. This retrospective study aimed to describe characteristic features of PAET diagnosed at university centre for ophthalmic pathology.
Methods: We screened the hospital records of patients treated at Clinic for Ophthalmology, University Clinical Centre of Serbia during the period 2014-2023 and found 271 patients diagnosed with 284 PAET. The tumours were reclassified based on the 5th WHO Classification of eye and orbit tumours. Demographic, clinical and histopathological features were analysed.
Results: PAET represented 3.2% of all excised tumours and around 15% of all eyelid tumours. They were more common in women (56%) and in patients older than 50 years (75%), but occurred rarely in childhood (3%). Most common benign PAET were pilomatricomas (73% of patients <20 years old) and eccrine ductal hidrocystoma (52% of adults). Malignant tumours were rare (15%) and mostly occurred in older patients (>60 years old) (82%), on upper eyelid (58%), and as sebaceous carcinoma (88%). A third of patients with sebaceous carcinoma presented in pT3/pT4 stage, all but three with perineural invasion; recurrences occurred after one (one patient) or seven years (two patients) in eyelids or orbit.
Conclusion: Primary adnexal tumours, especially carcinomas, are rare neoplasms of the eyelid, even at the university hospital setting. As such, their diagnosis and treatment should be performed only in specialized centres. Carcinomas never occur in childhood. Higher-stage sebaceous carcinomas should be carefully examined for the presence of perineural invasion. The age-dependent distribution of subtypes of benign tumours suggests different aetiology which could be a subject of future research.

E-PS-27E-Poster Session Uropathology

E-PS-27-001
Nectin-4 immunohistochemical expression and HPV infection evaluation in penile squamous cell carcinoma (pSCC)

L. Aguirrezabal Marcotegui*, A. Azueta Etxebarria, E. Elvira Uriarte, I. Lopez de Gamboa, I. Fernandez de la Prieta, R.I. Alvarado Cuenca, M.T. Abad Villar, A. Ugalde Olano, M. Zufiaurre Echavarri, M.C. Etxezarraga Zuluaga, A. Cortina Ormaetxea, D. Gonzalo Aparicio
*Basurto University Hospital, Bilbao, Spain

Background & objectives: Metastatic pSCC remains a global health challenge due to its poor prognosis and limited therapies. Enfortumab vedotin, an antibody-drug conjugate targeting Nectin-4 protein, was approved for urothelial carcinoma. We evaluated if pSCC expresses Nectin-4 and if it is HPV infection-related.
Methods: Nectin-4 protein expression was evaluated with standard immunohistochemical method (Abcam clone EPR15613-68) and HPV detection and genotyping was carried out by PCR. Ten patients from our hospital, diagnosed with metastatic pSCC between 2013 and 2023 were assessed. Tissues from primary tumour and their matched metastatic carcinoma samples were studied.
Results: The 30% of pSCC showed focal and intense expression of Nectin-4, and the 66% of these maintained the positivity in metastatic lymph nodes. High-risk HPV infection (genotype 16) was detected in 30% of the cases, being the 10% of them positive of Nectin-4.
Conclusion: This study demostrates that Nectin-4 expression is maintained in more than half of the metastatic samples. Furthermore, it shows that it might be independent of HPV status. To our knowledge, a recent study described significant expression of Nectin-4 in pSCC, also a case report provided evidence of response to Enfortumab vedotin in metastatic pSCC. These findings may warrant additional research.

E-PS-27-004
Biphasic squamoid papillary renal cell carcinoma: clinicopathological features of nine cases

A.E. Akın*, G. Güner, K. Kösemehmetoğlu
*Hacettepe University, Department of Pathology, Turkey

Background & objectives: Biphasic squamoid papillary renal cell carcinoma is a rare morphologic pattern of papillary renal cell carcinoma (PRCC) that is not included in the current WHO classification. This study aimed to analyse the clinicopathological features of this unique variant.
Methods: We reviewed 9 cases (8 males, 1 female) in terms of dominant morphological pattern, presence of emperipolesis, psammoma bodies, necrosis, intratumoural lymphocytic infiltration, foamy histiocytes, and mitotic count as well as KRT7, AMACR, and CyclinD1 expressions.
Results: The median age was 58,6 years (40-71). Median tumour size was 5,8 cm(2,5-8,6). Seven patients were smokers with an average of 45 pack-years. Seven tumours(%78) were found in the left kidney. The dominant pattern was papillary and alveolar in 5 and 4 cases, respectively. All cases had emperipolesis, foamy histiocytes, and intratumoural lymphocytes. Psammoma bodies were found in eight cases. Necrosis was present in six cases(%5-30). Sarcomatoid differentiation was observed in one case. KRT7, AMACR, and CyclinD1(especially in larger cells) were positive in all cases. Lymph node metastases were present in 3 patients and two of them died of disease within a year, whereas seven patients were alive (2-117 months).
Conclusion: Generally, the patients were elder men who were heavy smokers. Presence of alveolar and solid patterns, emperipolesis, psammoma bodies, intratumoural lymphocytes, and CyclinD1 positivity in larger cells could be helpful to diagnosis. The mortality rate appears to be higher than a regular PRCC.

E-PS-27-005
Epithelioid angiomyolipoma of the kidney: a diagnostic challenge. A case report

A. Alpeza*, M. Mrcela
*University Hospital Center Osijek, Croatia

Background & objectives: Epithelioid angiomyolipoma is a rare variant of angiomyolipoma. About a third of all cases are associated with malignant behaviour. Unlike angiomyolipoma, epithelioid angiomyolipoma is characterized by scarce fatty tissue and an abundance of atypical epithelioid cells.
Methods: We present the case of a 54-year-old female patient who was scheduled for laparoscopic nephrectomy after a CT scan revealed a lesion measuring 5.3x4x3.1 cm in the upper third of the left kidney, with a dorsally located component measuring 1.5 cm. The material was sent to the Clinical Department of Pathology and Forensic Medicine at the University Hospital Center Osijek.
Results: Grossly, we observed a brownish-gray nodule with a diameter of 1.6 cm in the fatty tissue above the kidney. Histologically, the tumour tissue consisted of polymorphic and spindle-shaped cells with large nuclei and eosinophilic nucleoli. The cytoplasm of the tumour cells exhibited focal richness in Fontana-positive pigment. Additionally, a significant number of multinucleated giant cells (CD68 positive) were present. The tumour tissue exhibited two mitoses per ten high-power fields (HPF), along with the presence of pathological mitoses. Immunohistochemically, Melan A, HMB45, Vimentin, Actin-SMA, and, focally, GATA3 and CD1a were positive. Conversely, CK7, CK20, pancytokeratin, RCC, S100, CD117, PAX8, and EMA were negative. The Ki-67 proliferation index was 10%.
Conclusion: The differential diagnosis excluded variants of renal cell carcinoma and melanoma metastasis. We classified the described

tumour in the group of tumours with potentially aggressive clinical behaviour because it meets three out of four given morphological criteria, necessitating further monitoring of the patient. We suggest that epithelioid angiomyolipomas with a large number of intratumoural CD68 positive multinucleated giant cells should be classified as a special subgroup.

E-PS-27-006
Clear cell urothelial carcinoma - a rare subtype
A. Alves*, R. Almeida, M.A. Cipriano
*Unidade Local de Saúde de Coimbra, Portugal

Background & objectives: Clear cell urothelial carcinoma is a rare subtype of urothelial carcinoma sharing a similar immunohistochemical profile with its conventional counterpart, that can be difficult to diagnose in biopsy specimens or without immunohistochemistry technics.
Methods: We present a case of a female patient in her 80's with a long history of dysuria, increased urinary frequency and episodes of hematuria, presenting with a nodular, focally ulcerated bladder mass on imaging studies. Initially she underwent transurethral resection of the lesion, followed by radical cystectomy with hysterectomy and bilateral salpingo-oophorectomy.
Results: The transurethral resection specimen revealed an infiltrative tumour displaying trabecular and small nested patterns, comprising cells with well-defined borders, abundant clear cytoplasm and irregular, pleomorphic nuclei. Immunohistochemistry showed positivity to CK7, GATA3 and P63, while PAX8 and napsinA were negative. PAS stain was positive but no stain was identified on PAS-diastase. Gross evaluation of the cystectomy specimen showed a 5cm ulcerative white mass on the bladder wall, with histological features akin to the biopsy specimen but with a minor component of conventional urothelial carcinoma. A diagnosis of clear cell urothelial carcinoma diagnosis was made. The patient underwent adjuvant chemotherapy and remains under surveillance one year post-surgery.
Conclusion: Identifying urothelial carcinoma with a major clear cell component can be diagnostically challenging and other clear cell malignancies should be considered, such as clear cell adenocarcinoma of the urinary tract or metastatic lesions like clear cell renal cell carcinoma or carcinomas with mullerian origin. Due to limited literature reports on this subtype, evaluating clear cell urothelial carcinoma remains challenging but immunohistochemistry can be of great value.

E-PS-27-007
Anastomosing hemangioma of the kidney: a case report
M. Alzamora*, I. Carneiro, A.R. Coelho, R. Henrique
*Department of Pathology, Portuguese Oncology Institute of Porto (IPO-Porto), Portugal

Background & objectives: Anastomosing hemangioma (AH) is an unusual variant of capillary hemangioma primarily affecting the genitourinary system, especially the kidney. They may pose diagnostic challenges due to their resemblance to primary renal angiosarcomas. Herein, we report a case affecting the right kidney.
Methods: A 83-year-old man with a background of advanced urothelial carcinoma, having previously undergone cystectomy and penectomy, was submitted to right radical nephroureterectomy following suspicion of recurrence.
Results: Upon gross examination, an exophytic neoplasm centred and limited to the renal pelvis and a porous intravascular mass, occupying renal vein lumen, were identified and sampled. Microscopically, the intravenous tumour measured 1.2cm and was well-demarcated, consisting of anastomosing sinusoidal capillary-sized vessels lined by cytologically bland endothelial cells. No endothelial cell multilayering, papillary tufting, necrosis, or mitotic activity was apparent. Immunohistochemistry revealed diffuse positivity for CD31/CD34, confirming the diagnosis of AH. High-grade non-invasive papillary urothelial carcinoma and in situ urothelial carcinoma were diagnosed in the renal pelvis. One year post-surgery, the patient remains in good health with no signs of recurrence of either neoplasm.
Conclusion: Renal hemangiomas encompass various subtypes, including cavernous, capillary, and anastomosing, with AH being the most prevalent. Their etiology remains unclear, some cases having been linked to end-stage renal disease. Recurrent GNAQ and GNA14 mutations have been described. The prognosis is excellent. Awareness of this rare entity is vital to avoid misdiagnosis, especially with angiosarcoma, distinguished by specific features: spindled or epithelioid cells, variable degrees of vasoformation, cytologic atypia, prominent mitotic figures, endothelial cell multilayering, papillary tufting, and necrosis.

E-PS-27-008
Molecular and clinicopathologic features of mucinous tubular and spindle cell carcinoma: institutional experience of three cases
S. Amer*, S. Wei, M. Mollaee
*Pathology department - Temple University Hospital, USA

Background & objectives: BACKGROUND: Mucinous tubular and spindle cell carcinoma (MTSCC) is a rare, low-grade renal neoplasm, accounting for 1% of all renal cell carcinomas included in 2022 WHO classification. It is characterized by its heterogeneous composition of cuboidal cells forming tubules and
Methods: cords, along with spindle cell foci and a myxoid stroma. Despite similarities in immunohistochemical and morphologic features with papillary renal cell carcinoma (PRCC), MTSCC is genetically distinct. CASE PRESENTATION: We present three cases of MTSCC diagnosed in our institution with patient's mean age of 52 years (41-69 years), all observed in females who underwent nephrectomy, 2 partial and one radical.
Results: On gross examination, well-circumscribed mass was identified in two cases. The third one showed a partially exophytic mass, all confined to the kidney. The mean size of the tumours was 5 cm. Histologically tumour cells were arranged in tubular and papillary patterns with foci of spindle cells and mucinous stroma. No areas of high-grade morphology, necrosis, and invasion were identified. Tumour cells were positive for CK7, AMCAR, and PAX8. Final pathology staging was pT1aNx in one and pT1bNx in the other 2 cases with margins being negative. The differential diagnosis included MTSCC versus PRCC based on morphology and immunohistochemical stains. Therefore, cytogenetic microarray assay was performed for further characterization. All
Conclusion: 3 cases revealed loss of chromosomes 1, 4, 6, 8, 9, 13, 14, 15, 22, and X supporting the diagnosis of MTSCC. DISCUSSION: MTSCC is a rare, low-grade malignant renal tumour predominantly seen in females. It has imaging and pathological features that overlap with PRCC making this distinction challenging. MTSCC has a specific genomic signature which distinguishes it from PRCC. Most cases show an indolent clinical course after resection. Therefore pathologic distinction and recognition of this tumour is very important.

E-PS-27-009
Plasma cell granuloma of the kidney: report of a case in this rare location
M. Arias Duart*, P.J. Armijos González, J. Huerta Aragonés, F.J. Díaz Crespo
*Hospital General Universitario Gregorio Marañón, Spain

Background & objectives: Plasma cell granuloma is a rare tumour of unknown cause. It is considered a reactive inflammatory lesion with a good prognosis. The aim of this abstract is to describe the microscopic and immunohistochemical features on the kidney.

Methods: We present a 6-year-old patient previously diagnosed with a poorly differentiated high-risk abdominal neuroblastoma involving the mediastinum. The subject completed his treatment in September and during the follow-up, a renal mass located on the lower pole of the left kidney was detected. Said mass was hypointense after contrast administration. A partial nephrectomy was performed.
Results: The renal cortex was preserved. In the medulla a well delimited non-encapsulated lesion was found. The lesion was composed by an inflammatory infiltrate consisting mainly of mature plasma cells without atypia. This infiltrate separated the interstitium and was accompanied by an edematous estoma and histiocytic aggregates without evidence of permeation in the tubular epithelium. Said epithelium did not present dysplastic changes. The surgical resection border was negative. No acute inflammatory infiltrates, histiocytic granulomas, microbiological elements or histological signs of malignancy were observed. Plasma cells stained MUM1/CD138+ and polytypic, Kappa+/Lambda+, predominantly IgG, with no alterations in the IgG4/IgG ratio (<10%). ALK, CKAE1/AE3 and SV-40 were negative.
Conclusion: Plasma cell granuloma is a soft tissue neoplasm characterized by a proliferation of myofibroblastic and inflammatory cells. It is most frequently located in the biliary tract (32%), lungs (27%) and gastrointestinal tract. In the genitourinary tract is commonly observed in the bladder but extremely unusual in the kidney. Abundant spindle cells and lymphocytes with an immunohistochemical profile of LCA (+), VIM (+), CD68 (+), Ki-67 (10%), SMA (-), ALK (-), IgG4 (5-10%) are identified in hematoxylin staining.

E-PS-27-010
Expression of Fibroblast Growth Factor Receptor 3 (FGFR3) & Vascular Endothelial Growth Factor (VEGF) in malignant tumours of the urothelial tract
A. Arora*, A. Nalwa, M. Rao, P. Elhence, G.R. Choudhary
*Department of Pathology, AIIMS, Jodhpur, India

Background & objectives: We assessed the expression of Fibroblast Growth Factor Receptor 3 (FGFR3) & Vascular Endothelial Growth Factor (VEGF) in malignant tumours of the urothelial tract received in the Department of Pathology by immunohistochemistry & correlated its expression with various clinicopathological parameters.
Methods: The antibodies for FGFR3 & VEGF were applied manually in all 79 cases of urothelial carcinomas and the interpretation of the immunohistochemistry was done by semi-quantitative (Q score) scoring system.
Results: Among 79 cases of urothelial carcinoma, 86.5% of non-muscle invasive urothelial carcinomas &13.5% of muscle invasive urothelial carcinomas were immunopositive for FGFR3. Positive expression of VEGF was observed in 85.9% of non-muscle invasive urothelial carcinomas & 14.1% of muscle invasive urothelial carcinomas. Mean age for development of urothelial carcinoma was 61 years with a male to female ratio of 4:1. Both FGFR3 & VEGF were highly expressed in non-muscle invasive urothelial carcinomas as compared to muscle invasive urothelial carcinomas
Conclusion: In the current era of personalised cancer treatment and targeted therapy, role of bio markers like FGFR3 & VEGF is becoming more relevant in cancer management. The present study showed strong expression of FGFR3 & VEGF in non- muscle-invasive urothelial carcinomas. Immunotherapy is gradually revolutionising the bladder cancer management, hence, the present study underscores the need for more clinical trials to shed light on the role of FGFR3 & VEGF in bladder cancer.

E-PS-27-011
Clinicopathological comparative study of squamous cell carcinoma versus urothelial carcinoma with squamous differentiation of urinary bladder
S. Bansal*, A. Arora, M. Pal, P. Maitre, G. Prakash, A. Joshi, V. Murthy, S. Menon
*Tata Memorial Hospital, India

Background & objectives: Pure squamous cell carcinoma (SCC) of urinary bladder and urothelial carcinoma with squamous differentiation (UCSD) are rare bladder cancers. In this study, we compared the clinicopathological parameters of squamous cell carcinoma and urothelial carcinoma with squamous differentiation of urinary bladder.
Methods: A detailed retrospective clinicopathologic analysis was done for SCC and UCSD from 2012 to 2018. Association and correlation of categorical variables between two groups were assessed using chi-square test. Log-rank and Kaplan-Meier analysis were used to determine univariate factors associated with overall survival, recurrence-free survival in available cases, and comparison of survival outcomes for each group was assessed
Results: 101 cases were reviewed. 47 cases were SCC (29 TURBTs; 18 cystectomies) 54 cases were UCSD (42 TURBTs; 12 Cystectomies). Mean age of presentation was 56.8 years(SCC) and 62 years (UCSD). Male: female ratio for SCC group was 2.5:1, while 3.6:1 for the UCSD group. SCC(83%) patients presented at higher clinical stage than UCSD(50%) which was statistically significant (pvalue=0.04). Median follow up for SCC was 12.2 months and for UCSD was 13.5 months. 2 years survival estimate was 80.8% for SCC and 64.2% for UCSD with comparable outcomes in two cohorts (p value=0.99). Mean duration for recurrences in SCC was 8.8 months, UCSD was 9 months (pvalue=1); no significant difference.
Conclusion: Pure squamous cell carcinoma and urothelial carcinoma with squamous differentiation clinically and pathologically present as a high-stage disease. Other histological parameters, clinical, and survival analyses of both groups (SCC and UCSD) showed comparable results.

E-PS-27-013
Female urethral hemangioma: an unusual cause of hematuria. Review of the literature and presentation of a case
C. Barrera*, M. Plata Salazar, M. Palau Lazaro
*Fundación Santa Fe de Bogotá, Colombia

Background & objectives: Hemangioma is a benign vascular tumour. Its location in the genitourinary tract is very rare, and recurrence is uncommon. We present the case of a woman with spontaneous, painless urethral bleeding associated with voiding symptoms, diagnosed as recurrent cavernous hemangioma.
Methods: A 65-year-old woman presented with urethral bleeding, a sensation of mass, and voiding disorders for 1 year. A 2 cm solid periurethral lesion was identified. Pathological analysis showed a cavernous vascular lesion, with vessels lined by a single layer of endothelial cells without cytological atypia and recent thrombi, consistent with a cavernous hemangioma. After a month, the hemangioma recurs.
Results: Urethral masses and bleeding are the most common findings in women; in men, they occur after an erection or ejaculation. The differential diagnosis includes: urethral caruncle, urethral prolapse, urethral polyp, urethelial carcinoma, sarcoma, and melanoma. Cystourethroscopy and MRI may be useful to better determine lesions, especially in women, if their nature or extent is uncertain. Endoscopic management and laser ablation are recommended for small lesions. In the case of more extensive lesions or recurrence, open exploration followed by adequate urethral reconstruction is indicated.
Conclusion: Urethral cavernous hemangioma in women is indeed a rare condition within the urinary system, and its diagnosis can be challenging due to its rarity and the lack of specific symptoms. Physical examination of the genital area is crucial to detect any urethral lesions, and considering hemangioma as a potential differential diagnosis for patients presenting with symptoms like hematuria or bloody urethral discharge is essential for timely and accurate management.

E-PS-27-014
Rare metastases a common disease: prostate adenocarcinoma
C. Barrera*, C. Medina, P. Rodríguez, F. Arías Amézquita, M. Palau Lazaro
*Fundación Santa Fe de Bogotá, Colombia

Background & objectives: We presents two cases of prostatic adenocarcinoma metastasizing to uncommon sites like the testicles and peritoneum, post prostatectomy and radiotherapy. It highlights the varied pathways of cancer dissemination and emphasizes the importance of histological assessment in guiding treatment decisions.
Methods: Men in their sixth decade of life, with high histological grade prostate adenocarcinomas, undergoing Robot-assisted Laparoscopic Radical Prostatectomy (RALRP), followed by salvage radiotherapy due to biochemical recurrence, presented with a testicular mass and peritoneal lesions, respectively, along with increased PSA levels. Histopathological analysis revealed involvement of metastatic adenocarcinoma of prostatic origin.
Results: Histology of the testicular mass showed solid sheets of tumour cells with round nuclei, prominent nucleoli, and scant cytoplasm, mimicking primary germ cell tumours, except for intertubular growth and lymphovascular invasion, characteristics that favour metastasis. Immunohistochemistry was reactive with PSA and AMACR, and negative with SALL4. In the fragments of the peritoneum, small tumour cells were observed, with scant cytoplasm and hyperchromatic nuclei, exhibiting an infiltrative pattern. Immunohistochemistry with PSA and EMA was useful in the diagnosis. PSA levels responded adequately. Patients were initiated on triplet therapy, consisting of an ARAT, docetaxel, and ADT.
Conclusion: Testicular metastasis from prostate adenocarcinoma is a rare phenomenon and occurs in 0.5% of cases. It has been suggested that retrograde lymphatic dissemination or direct invasion of prostate cancer through the duct deferens to the testis could be causes of these metastases. Peritoneal dissemination without involvement of any other organ is very rare. There are only 13 cases published in the English literature of iatrogenic diffusion. Hematogenous/lymphatic spread may occur in some aggressive prostate cancers.

E-PS-27-015
An interobserver reproducibility study on PD-L1 (SP263) in urothelial carcinoma
N.B. Barut*, O. Hurdogan, I. Kilicaslan, Y. Ozluk
*Istanbul Faculty of Medicine, Turkey

Background & objectives:
PD-L1 is a useful predictive biomarker for immunotherapy. Various antibodies, clones, and scoring systems exist. The complexity of scoring methodologies challenges interobserver agreement. In our single-centre study including three observers, we primarily aimed to evaluate its reproducibility.
Methods: Archive records showed 41 cases, which underwent PD-L1 testing, using SP263 assay on Ventana-Benchmark platform. Tumour proportion score(TPS), combined positive score(CPS), immune cell score(IC) were re-evaluated by researchers (one of whom was third-year resident) with varying levels of experience, who were blinded to the original scores. Interobserver reproducibility was tested using intraclass correlation coefficient (ICC) and Fleiss kappa statistics.
Results: Thirty-three(80.5%) patients were male (median:65, 53-91). Thirty-one(75.6%) samples were from primary and 10(24.4%) from metastatic foci. Twelve(29.3%) underwent transurethral resection(TUR), 9(21.9%) cystectomy, 8(19.5%) nephrectomy. Twelve(29.2%) tumours were with squamous, 3(7.3%) glandular and 1(2.4%) neuroendocrine differentiation. Histologic subtypes included sarcomatoid(7.3%), micropapillary(7.3%) and plasmacytoid(2.4%). Most tumours were ≥pT2 (17)(pT available in 20). ICC kappa scores for TPS, CPS, and IC as continuous values were 0.967, 0.974, and 0.695, respectively. Kappa scores ranged from a minimum of 0.399 (0.394-0.405) for IC (cut-offs 1%, 5%, 10%, 25%) to a maximum of 0.733 (0.728-0.739) for TPS (cut-offs 1%, 25%, 50%). Kappa scores for CPS were 0.628 and 0.689 for cut-off values 1 and 10, respectively.
Conclusion: Albeit PD-L1 scoring is challenging, it provided at least moderate interobserver agreement in our study. TPS demonstrated the highest, while IC exhibited the lowest concordance. As threshold values changed, the interobserver agreement varied. The limitations of our study were the retrospective design, and that it is conducted by pathologists working in collaboration within the same centre. Its potential strength could be providing an exercise for scoring and an insight into assessment practices. Evaluation standardization and training may improve interobserver agreement.

E-PS-27-016
Undifferentiated pleomorphic sarcoma: an unusual histological type of bladder tumour
A. Bdioui*, Z. Lajmi, A. Mahmoudi, O. Belkacem, S. Mestiri, N. Missaoui
*Sousse Sahloul Hospital, Tunisia

Background & objectives: Undifferentiated pleomorphic sarcoma is a rare tumour of soft tissue, its location in the bladder wall is exceptional and diagnosis challenging. Due to its low incidence and heterogeneous morphology little is known about its behaviour, treatment and prognosis.
Methods: A 56 year old male, with no medical history, complaining from hematuria and dysuria of 3 month lasting. Cystoscopy revealed a right bladder horn solid tumour; a resection was performed.
Results: Microscopic examination showed highly cellular neoplasm, cells were large globular and non cohesive, or more rarely elongated, these cells are frankly atypical with eosinophilic cytoplasm and an irregular nucleus with preeminent eosinophilic nucleoli; haemorrhagic and necrotic foci were also seen. The immunohistochemical study was carried, showing: Cytokeratin, P63, GATA3, HMB45, Chromogranin and Synaptophysin , MDM2, SMA, were all negative, excluding sarcomatoid carcinoma, poorly neuro endocrine carcinoma, melanoma and pointing that there was no line of differentiation. Only Vimentine was positive. After multidisiplinary concertation and expert consultation, the diagnosis of primary undifferentiated pleomorphic sarcoma was made and the patient was scheduled for surgery.
Conclusion: Primary undifferentiated pleomorphic sarcoma of the urinary bladder is an extremely rare and aggressive tumour, which does not show line of differentiation and obvious morphological features on histopathology. Complete workup is recommended to exclude sarcomatoïd carcinoma and other sarcoma.

E-PS-27-017
Recurrent paratesticular well-differentiated liposarcoma: a case report
O. Belkacem*, W. Blaiech, M. Alaya, M. Krifa, A. Bdioui, Z. Lajmi, S. Mestiri
*University hospital Sahloul, Tunisia

Background & objectives: Paratesticular sarcomas are tumours of mesenchymal origin that may arise from the spermatic cord or testicular tunic. Herein, we present a controlateral recurrence of a treated paratesticular liposarcoma. To our knowledge, there are few cases reported with recurrent paratesticular liposarcoma.
Methods: We report the case of a 62-year-old man who presented with a rapidly growing painless right scrotal swelling. Clinical and radiographic evidence suggested the presence of two paratesticular tumours. The patient underwent a radical orchidectomy with resection of the two tumours.
Results: The macroscopic examination of the surgical specimen revealed two tumours of similar appearance and finely encapsulated. Both measured 6x5x2cm and were connected to the spermatic cord. On the cut surface, they were yellowish containing white septal

bands. On histopathological examination, the two masses consisted of a tumour proliferation made up of lobules of mature adipocytes associated with multivacuolated lipoblast separated through thick sclera-hyaline fibrous septa. This proliferation also included focal areas of cartilaginous differentiation. There were focal capsular tumour effractions. The diagnosis of sclerosing well-differentiated liposarcoma with focal areas of cartilaginous differentiation was made. A follow-up of 12 months showed a recurrence of the contralateral scrotum revealed by an FDG-PET/scan.
Conclusion: Paratesticular liposarcoma is often misdiagnosed preoperatively. it is typically managed through radical orchidectomy, which includes wide excision and high ligation to ensure free surgical margins and avoid recurrence. The role of adjuvant therapy remains debatable. Despite a generally favourable prognosis, long-term follow-up is crucial because of the elevated risk of recurrence.

E-PS-27-018
Prognostic significance of E-Cadherin and B-Catenin in non-muscle invasive bladder cancer
S. Ben Rejeb*, S. Sakly, R. Boulma, K. Bellil, H. Khouni
*Pathology department , Security Forces Hospital, Marsa, Tunisia; Research unity of epithelial to mesenchyma transition, Faculty of medicine of Tunis, Tunis Manar University, Tunisia

Background & objectives: Non muscle invasive bladder cancer(NMIBC) has unpredictable outcomes raising the need for identify new prognostic factors. The aim of our study was to assess the prognostic value of the immunohistochemical (IHC) markers E-Cadherin and B-Catenin in NMIBC.
Methods: We have retrospectively collected all cases of NMIBC(pTa/pT1) diagnosed during a period of 5years.An IHC analysis was performed using E-CD(Leica, 36B5) and B-CT(Leica, 17C2).Reduced or loss of E-CD membranous staining was assessed abnormal.B-CTstaining was deemed normal when it exhibited intense distribution along the cell membrane.Conversely, staining was considered abnormal when it appeared cytoplasmic, nuclear,or weak along the cell membrane.
Results: 40patients have been included in the study with a mean age of 58years old and a male to female ratio of 19.Abnormal E-CD expression was found in 52.5% of cases and aberrant B-CT phenotype(either protein loss or aberrant distribution) was seen in 70%.A correlation was found between abnormal E-CD expression and stage(p=0,001),grade(p=0,0 000000),recurrence(p=0,0000000),progression (p=0,01),recurrence free survival(p=0,00000001) and progression free survival(p=0,01).A statistically significant association was found between B- Catenin and stage(p=0, 05),grade (p=0, 02) and recurrence (p=0, 02). Recurrence free survival and progression free survival were not associated to B-CT (p=0, 09 and p=0, 17). No statistically significant association was found between E-CD or B-CT and the other studied clino-pathological factors.
Conclusion: Abnormal E-CD and B-CT expression can predict aggressiveness, recurrence and progression in NMIBC. The lack of expression of these markers could help to identify a high-risk subgroup of NMIBC that might benefit from either more accurate follow-up or more aggressive primary treatment. Further multicentre studies are necessary to definitively assess the benefit of E-Cadherin and B-Catenin in NMIBC and provide convincing results to include these biomarkers to the prognostic factors in EORTC guidelines.

E-PS-27-019
Predicting metastatic potential in pheochromocytoma: report of 11 cases
Y. Ben Romdhane*, Z. Lajmi, A. Mahmoudi, A. Bdioui, S. Hmissa
*University Hospital Sahloul, Tunisia

Background & objectives: Pheochromocytomas are rare catecholamine-secreting tumours. Most pheochromocytomas are benign. Approximately 10% are malignant. The Pheochromocytoma of the Adrenal Gland Scaled Score (PASS) is a scoring system to predict metastatic potential in pheochromocytoma.
Methods: A retrospective study of 11 cases of pheochromocytomas with a minimal Pass score of 4 (high risk behaviour) treated at Sahloul university hospital's urology department, from November 2019 until March 2024. Clinical and pathological data were reviewed.
Results: Our series comprised 10 females and one male. The mean age was 46.81 years. 7 cases presented with Menard's triad and 4 cases were incidentally discovered through imagery. 8 patients underwent adrenalectomy and 3 patients underwent tumourectomy. The tumour was right-sided in 8 cases and left-sided in 3 cases. PASS scores were 4 in 5 cases, 5 in 2 cases, 9 in 2 cases, 8 in one case and 11 in one case. 2 female patients develop liver metastasis, with PASS scores of 11 and 9. One patient deceased of cardiac arrest. 5 patients are under surveillance until now without metastasis. The other 3 patients are lost to follow-up.
Conclusion: Our study underscores the prognostic value of the PASS score in predicting outcomes of high-risk behaviour PCCs. The association between higher PASS scores and metastatic spread, particularly in female patients, highlights the importance of early detection and tailored management strategies for improved patient outcomes. Further research is warranted to validate these findings and refine risk stratification in PCC management

E-PS-27-020
Prognostic value of tumour infiltrating neutrophiles in muscle invasive urothelial bladder carcinoma
Y. Ben Romdhane*, Z. Lajmi, A. Bdioui, I. El Hadhri, O. Belkacem, S. Mestiri, S. Hmissa
*University Hospital Sahloul, Tunisia

Background & objectives: Tumour-infiltrating neutrophils (TIN) are a main component of inflammatory cells in tumour microenvironment. They play essential roles in many tumours and associate with the prognosis of patients. But, its prognosis in muscle-invasive urothelial bladder carcinoma (MIUBC) is still undefined.
Methods: A retrospective study on MIUBC cases treated in our institution during 4 years. TIN's quantification was performed by two pathologists on HE-stained slides. Its density was based on the abundance of neutrophils in the stroma at high magnification. Two groups were defined: low and high TIN. Associations between TIN density and clinicopathological parameters were examined using the Chi square test.
Results: Our series included 72 patients with MIUBC. There were 65 males and 7 females, with a male-to-female ratio of 9.28%. The mean age was 68.13 years. All patients underwent a radical cystectomy. The density of TIN was low in 44 cases (61.1%) and high in 28 cases (38.9%). A statistically significant association was found between TIN density and vascular invasion (p=0.001), lymphovascular invasion (p=0.001), perineural invasion (p=0.008), tumour margin status (p=0.005), pT stage (p=0.0001) and pN stage (p=0.035). There were no significant associations between gender, age, tumour size, grade, histological variant, concomitant carcinoma in situ, budding and the density of TIN.
Conclusion: Our study found that a high TIN density was associated with a worse prognosis. These findings confirm that TIN are an important marker in predicting the prognosis of bladder cancer patients. In conclusion, TIN could be used as an independent prognostic factor. Incorporation of TIN into TNM system could further stratify patients with different prognosis.

E-PS-27-021
Tumour-infiltrating lymphocytes and neutrophils predict survival in urothelial bladder cancer
Y. Ben Romdhane*, Z. Lajmi, A. Bdioui, A. Mahmoudi, O. Belkacem, S. Mestiri, S. Hmissa
*University Hospital Sahloul, Tunisia

Background & objectives: Despite surgical treatment and chemotherapy, tumour progression and death occur in approximately half of the cases of muscle-invasive urothelial bladder carcinoma (MIUBC). Therefore, the role of the pathologist is crucial in identifying new prognostic factors.
Methods: A retrospective study on MIUBC cases, treated in our institution from 2019 to 2022. TILs and TIN quantification was performed by two pathologists on HE-stained slides. TILs were scored following the guidelines established by the International TILs Working Group. Overall survival (OS) curves were calculated using the Kaplan-Meier method and compared by the log-rank test.
Results: There were 65 males and 7 females. The mean age was 68.13 years. All patients underwent radical cystectomy. The median OS was 27.1 ±2.3 months for patients with high TILs and significantly higher than in patients with low TILs (19.1 ±2.7 months, p=0.015). The median OS was 28.1 ±2.2 months for patients with low TIN and significantly higher than in patients with high TIN (16.2 ±2.6 months, p=0.003). In univariate analysis, we found that a positive surgical margins, a concomitant carcinoma in situ and the presence of perineural invasion and lymphovascular invasion were significantly associated with a decreased OS ($p<0.05$).
Conclusion: Tumours infiltrating immune cells play essential roles in tumour microenvironment. TIN and TILs are important indicators in tumour infiltrating immune process. In our study, we found that a High density of TILs and a low density of TIN were associated with longer OS in patients with MIUBC. In conclusion, TILs and TIN are a reliable tool to stratify the survival of patients with MIUBC undergoing radical cystectomy.

E-PS-27-022
MiT/TFE family renal cell carcinoma: 10 years review in University Hospital of Asturias
V. Blanco Lorenzo*, M.L. Berrios Hernández, E. Higueras Mora, M. Rubiera Valdés, S. Merino Baamonde, J.R. Riera Velasco
*University Hospital of Asturias, Spain

Background & objectives: MiT family translocation renal cell carcinoma (tRCC) accounts for 1–5% of sporadic RCCs in adults. Fluorescence in situ hybridization (FISH) assays for the detection of chromosomal rearrangements involving TFE3 and TFEB are considered the gold standard for tRCC.
Methods: We collected a cohort of 47 cases of kidney tumours suspicious for tRCC based on clinical, morphologic (papillary, polygonal cells with voluminous cytoplasm, prominent nucleoli, abundant psammoma bodies, biphasic morphology and basement membrane material) and immunophenotypic (pan-cytokeratin, CAIX and melanocytic markers) information from 2014 to 2023. 47 TFE3/TFEB FISH assays were performed on kidney tumour suspicious for MiTF aberrations.
Results: 598 RCCs were diagnosed at our institution between 2014 and 2023. Based on morphologic and immunophenotypic features, 47 TFE3/TFEB FISH assays were performed on kidney tumours suspicious for MiTF aberrations. In total, 2 of 47 (4,2%) kidney tumours were confirmed for TFE3-rearranged; 3 of 47 cases (6,3%) were confirmed for TFEB-rearranged. Patient age for these positive cases ranged from 24 to 65 years (median, 48 years). The group consisted of 2 male and 3 female patients. No TFEB-amplified carcinomas were identified. No paediatric cases were found. Immunohistochemical workup demonstrated negative or focal positivity CAIX and pan-cytokeratin in all cases; melanocytic markers (Melan-A and HMB45) were only positive in TFEB-rearranged.
Conclusion: Approximately 40% of paediatric RCCs and 1.6–4% of adult RCCs are TFE3-rearranged. TFEB- rearranged are less common than TFE3-rearranged. TFEB-amplified are very rare RCCs. The morphologic features of tRCC have been well described in the literature, but an immunohistochemical analysis using minimum antibody panel (CAIX, HMB-45 and Melan-A, pan-cytokeratin, cytokeratin-7, AMACR) could be advised routinely for every case of RCC. FISH assays for the detection of chromosomal rearrangements involving TFE3 and TFEB are considered the gold standard for tRCC.

E-PS-27-023
Lymph node metastases and lymph node count in 290 bladder cancer surgeries
M. Bonert*, P. Major, S. Salama, I. El-Shinnawy, B. Shayegan
*McMaster University, Canada

Background & objectives: Lymph node metastases (NMs) are a poor prognosticator in bladder cancer. Prior to the use of neo-adjuvant therapy, lymph node count (LNC) was also a predictor of outcome. This work examines the relation between NMs and LNC.
Methods: All in-house bladder cancer resections with synoptic report accessioned 2011-2020 were retrieved. The LNC, nodal stage and y staging modifier (YS) were extracted. The node negative rate was plotted against LNC. Logistic regression (LR) was done to assess both variables (YS, LNC) separately and simultaneously. Varied binning, spline fitting, and looped LR was done to estimate a minimum suggested LNC.
Results: The time period had 290 bladder resections. The cohort by stage was 3/209/24/34/20 for pNX/pN0/pN1/pN2/pN3. 114 of 290 cases had a y staging modifier. NM rate increased from 11% to 30% for LNC 5 to 15. NM rate was stable at approximately 30% for LNC 15 to 25. pN1-3 was predicted by LNC (p=0.0034) but not by YS (p=0.37). An analysis with multiple predictors for pN1-3 suggests no interactions between LNC and YS. A varied NM rate was seen for LNC >25; however, the number of cases were limited. Varied binning, spline fitting, and looped LR suggest a minimum LNC of 13 to 15.
Conclusion: The y staging modifier does not appear to significantly influence lymph node positivity in bladder cancer. Based on the relationship between LNC and nodal stage, approximately 15 lymph nodes or more should be retrieved to avoid possible under-staging. Evaluation of the LNC and nodal stage in conjunction with outcome data, in the neoadjuvant era, may provide further insights.

E-PS-27-025
A transcriptomic approach through immunohistochemistry in non-muscle invasive and invasive bladder cancer: clinicopathological characterization and neoadjuvant predictivity in bladder cancer
T. Cano Barbadilla*, M. Álvarez Pérez, E. Matas Rico, J.D. Prieto Cuadra, G. Paz Lopez, B. Herrera Imbroda, I. Hierro Martín
*Hospital Juan Ramón Jiménez Huelva, Spain

Background & objectives: Bladder cancer (BC) exhibits heterogeneous clinical behaviours. This study aims to characterize molecular subtypes using immunohistochemical approaches, delineating their distinct clinicopathological characteristics and evaluating the predictability of neoadjuvant chemotherapy (NAC) through transcriptomic analyses.
Methods: In this retrospective study, 141 cases of muscle invasive bladder cancer (MIBC) and non -muscle invasive bladder cancer (NMIBC) patients were included. Immunohistochemical analysis for KRT20, KRT5, KRT14, FOXA1, FGFR3, GATA3, p53, and Ki67 markers was performed on tissue arrays. A K-means clustering approach identified molecular subtypes. Statistical analyses included survival assessments and correlation with 65 NAC-treated patients.
Results: Four tumour subtypes were identified: Basal, Basal KRT14High, Luminal, and Mixed. Luminal demonstrated the highest survival rate at 79.4%, while Mixed had the lowest at 63.5%. Basal CK14High showed the most significant survival advantage at 92.2% (p=0.04). Grouped into three clusters, Luminal subtypes showed the best survival, followed by Basal and Mixed, with a non-significant trend. Basal clusters and Basal KRT14High were associated with advanced

stages and squamous differentiation. NAC response correlated significantly with survival (p=0.01). The Basal subtype showed pronounced survival benefits with NAC, whereas Luminal and Mixed exhibited lesser effects. The Basal cluster had a higher proportion of non-responders to NAC, with only 21.5% achieving pathological complete response.
Conclusion: Our study successfully classified bladder tumours into basal and luminal subtypes using immunohistochemical markers. We also identified a mixed subtype and a basal subtype enriched with CK14 expression, sharing clinicopathological features with basals. An immunohistochemical algorithm was established as a surrogate for molecular profiling. Basal subtypes showed a significant association with NAC response, aligning with existing literature. Importantly, mixed subtypes benefitted similarly to basals from NAC treatment, highlighting the need for future implementation of molecular classification in current clinical practice.

E-PS-27-026
Immunohistochemical subtyping of T1 high-grade NMIBC in a cohort of 59 patients: insights into progression, prognosis and survival
T. Cano Barbadilla*, A. Alvarez Guerrero, L. Valle Rodriguez, M. Álvarez Pérez
*Hospital Juan Ramón Jiménez Huelva, Spain

Background & objectives: Non-muscle invasive bladder cancer (NMIBC), predominantly T1 high-grade (HG), shows high recurrence and progression rates. Despite BCG treatment, many need radical cystectomy. This study aims to taxonomically categorize these NMIBC using immunohistochemistry, offering insights into progression, prognosis, and survival.
Methods: A retrospective cohort study included 59 T1 HG NMIBC patients diagnosed in TURBT at Provincial Hospital from 2019-2023. Formalin-fixed samples from TURBT were used to construct tissue microarrays with hepatic tissue controls. Immunohistochemical staining employed GATA3 and CK5/6 antibodies. Interobserver variability was assessed by two pathologists. Statistical analysis included univariate descriptive methods, survival analysis, and quantitative and qualitative variable evaluations.
Results: The study dataset included 59 patients, with a mean age of 73.2 years (56-90), predominantly male smokers (69.5%). Urothelial histology was prevalent, with 66.1% exhibiting papillary patterns. Lymphovascular invasion was rare (1.7%). Immunohistochemical analysis using GATA3 and CK5/6 identified four molecular subtypes: basal (2), luminal (47), mixed (9), and double-negative (1). Kaplan-Meier survival analysis revealed significant differences among these subtypes: luminal (134.79 months, 95% CI: 79.91-189.68), basal (12.00 months, 95% CI: 0-31.60), mixed (34.98 months, 95% CI: 21.95-48.01), and double-negative (90,000 months). The luminal subtype exhibited the highest median survival, supported by GATA3 and CK5/6 as prognostic markers, validating the classification by IHC.
Conclusion: T1 HG NMIBC represents an aggressive subtype with notable recurrence and progression rates. Molecular characterization offers potential for improved management and prognosis. Immunohistochemistry, particularly with GATA3 and CK5/6 markers, serves as a practical surrogate for molecular subtyping. This approach simplifies categorization without the complexities and limitations of molecular analysis, suggesting its value in routine clinical practice for risk stratification in NMIBC. However, the study's limitations, such as sample size and lack of gene expression profiling, warrant further validation studies.

E-PS-27-027
Emerging biphasic squamoid alveolar renal cell carcinoma: a unique variant of papillary renal cell carcinoma
G. Carrola*, N. Chiote, A.P. Rodrigues, J.R. Vizcaíno
*Anatomic Pathology Service, Pathology Department, Unidade Local de Saúde de Santo António, Portugal

Background & objectives: Biphasic squamoid alveolar papillary renal cell carcinoma (BSA-RCC), a newly recognized renal tumour, identifies as a distinct and rare morphological subtype of papillary renal cell carcinoma (PRCC). Our objective was to investigate a recent case study conducted in our department.
Methods: We present the case of a 33-year-old male with a history of stage V chronic renal disease due to IgA nephropathy. In 2022, multifocal papillary renal cell carcinoma, type 1, grade 2, was diagnosed in the left kidney, after total nephrectomy. Subsequent imaging in 2024 revealed a new lesion in the right kidney, prompting right nephrectomy and histopathologic assessment.
Results: We received a nephrectomy specimen containing a 2.4 cm mass with solid, yellow-tan cut surface located in the middle third. Microscopic analysis revealed a neoplasm with a distinct biphasic cell population, featuring alveolar-like structures formed by small, uniform neoplastic cells with clear cytoplasm and round low-grade nuclei, alongside solid nests of larger squamoid cells with eosinophilic voluminous cytoplasm and prominent nucleoli. The latter transitioned to a predominant classical component of grade 3 papillary renal cell carcinoma (WHO/ISUP). Immunohistochemistry revealed CK7, AMACR, and CK34βE12 expression, with negativity for CAIX. Cyclin D1 highlighted the squamoid cell islands. Ongoing molecular analysis includes assessment of MET status.
Conclusion: Recently, biphasic squamoid alveolar papillary RCC has been recognized as a morphological variant of papillary RCC. Our patient, currently presenting with bilateral multifocal PRCC, including a component of BSA-PRCC, is under ongoing investigation. Chronic renal disease, with long-term dialysis, is a documented PRCC risk factor, especially multifocal. Additionally, MET has been identified as a significant oncogenic driver gene in both BSA-PRCC and classical PRCC, suggesting potential benefits from anti-MET targeted therapies. A personalized approach is crucial in managing these patients.

E-PS-27-028
Primary serous carcinoma of testis - a case report
I. Catalina-Fernandez*, N. Maira González, J. Sanz Repetto, M.J. Añón Requena, A. Hens Perez
*Hospital Universitario Puerto Real, Spain

Background & objectives: In comparison to its counterpart in ovary, primary serous carcinoma of testis is a rare entity with a very few cases described up to date in the English literature.
Methods: We present a case of a 65-years old man who had undergone a varicocele surgery in left testicle in 2013. In 2023, the patient returned with testicular pain- Ultrasound revealed significant alteration of the scrotal structures showing a cystic lesion with an intramural component. The patient underwent radical orchiectomy.
Results: Grossly, the orchiectomy specimen displayed a mutilocular cystic lesion measuring 5 x 2,5 cm replacing the testicle with a solid component measuring 1 cm. Microscopically, the cyst was lined by atypical cuboidal and ciliated cells identifying glandular structures in its wall and intraluminal papillae with psammoma bodies. The solid component showed cells with clear malignant nuclear features and atypical mitotic figures and a high proliferation index Ki-67 (95%). Immunohistochemistry the neoplastic cells demonstrated positive staining for WT1, PAX8, CK7, ER, PR, EMA, BerEP4 and p16 with negative staining for CD117, PLAL, GLYPICAN 3, CD30, OCT3/4, CK20, SALL4 and CDX2. The patient is disease-free one year post-surgery.
Conclusion: Regarding the 2022 WHO classification of male genital tumours, ovarian epithelial tumours are classified in the group of tumours of the testicular adnexa. Its origin is debatable with several proposed hypotheses: Müllerian ducts remnants, mesodermal epithelium or Müllerian metaplasia of the mesothelium of the tunica vaginalis. Given the rarity of these tumours in men, other diagnosis

such as malignant mesothelioma and adenocarcinoma of rete testis or epididymis should also be considered but taking note of then when evaluating testicular masses.

E-PS-27-029

Study of concordance in budding, til and cd8 measurements in invasive urothelial carcinoma

I. Catalina-Fernandez*, M. Corrales Cuevas, A. Caro Romero, M.J. Añón Requena, N. Maira González
*Hospital Universitario Puerto Real, Spain

Background & objectives: Budding tumour, tumour-infiltrating lymphocytes (TIL) and percentage of CD8 lymphocytes are new research variables due to their impact in invasive urothelial carcinoma. Our objective is to assess the concordance of measuring these variables by to independent pathologists.
Methods: A total of 211 patients with invasive urothelial carcinoma has been included. These variables were quantitatively measured by two independent pathologists and then categorized into two groups. Concordance was assessed using the intraclass correlation coefficient (ICC) for quantitative measures and Cohen's Kappa test (K) for qualitative measures. P-Value ≤0.05 was considered statistically significant.
Results: For budding tumour, strong concordance was proven for both quantitative (ICC 0.823, p<0.001) and qualitative measures (K=0.740, p<0.001). Concerning TIL, a moderate agreement was observed for quantitative measures (ICC 0.693, p<0.001) and a significant but lower level of concordance for qualitative measures (K=0.398, p<0.001). CD8 percentage concordance was statistically significant but with poor reliability for both quantitative (ICC 0.406, p<0.001) and qualitative measures (K=0.258, p<0.001).
Conclusion: Determining budding tumours and TIL showed good reliability among observers. This represents the first step in considering the usefulness of these variables in future prognostic studies. By contrast, measuring CD8 percentage revealed poor concordance, suggesting caution in its potential application.

E-PS-27-030

Incidence of hypospermatogenesis and preserved spermatogenesis in testicular specimens during physical adaptation of male to female

S. Cerović*, B. Kovačević, B. Jovanović, M. Đorđević, V.Š. Škuletić, S. Milenković
*Institute of Pathology and Forensic Medicine, Military Medical Academy, Belgrade, Serbia

Background & objectives: Physical adaptation of male-to-female transition is related to preoperative hormone therapy. The hormone activity induces different disorders of spermatogenesis. We aim to analyse the effect of hormone therapy on histological changes and spermatogenic activity in testicular tissue after bilateral orchiectomy.
Methods: We analysed clinicopathological and microscopic parameters of spermatogenesis in the testicular tissue after bilateral orchiectomies for gender reassignment. The study included persons with coordinated hormonal preparation for at least 1 year diagnosed in our institution in the four years (2019-2023). Cases with concomitant presence of germ cell tumour and/or germ cell neoplasia in situ were not included in the study.
Results: The study included 117 persons aged 18-66 years (average, 31.71±11.74). The mean length of hormone therapy was 28.78±31.23 months. Mean testicular mass was 13,97±4,50g (right) and 13,79±5,32g (left). Hypospermatogenesis was present in 44(37.6%) cases. In the 4 (3.4%) cases, spermatogenesis was completely preserved. Thickening of the basement membranes of the seminiferous tubules and edema were found in all testicular samples. Sertoly cells occurred in 114(97,4%) cases. The fibrous obliteration of seminiferous tubules was present in 30 (25,6%) cases. All results were statistically significant (p<0,0001). There was no statistical significance between the length of hormone therapy and the pathological changes in testicular tissue.
Conclusion: Histological changes of spermatogenesis during physical adaptation of male-to-female transition are heterogeneous, commonly combined, and not related to the length of hormone therapy. According to our results, hypospermatogenesis (37.6%) is the most frequent finding with higher frequency compared to the results of other studies (18%-20%). Contrary, preserved spermatogenesis (3.4%) had a lower prevalence compared to other results (4%-40%). Our findings, as a rare institutional experience, are valuable information for knowledge of histological changes during physical adaptation to hormone therapy

E-PS-27-031

Immunohistochemical analyses of the immune tumour microenvironment in metastatic renal cell carcinoma patients receiving immunotherapy

G.D.L. Crudele*, F. Galuppini, S.E. Rebuzzi, A. Caliò, G. Martignoni, A.P. Dei Tos, G. Fornarini, M. Brunelli
*Pathology Unit, Department of Medicine (DIMED), University of Padua, Italy

Background & objectives: Identifying patients who are likely to benefit from immunotherapy is a pressing clinical effort, as there is a critical lack of predictive biomarkers for metastatic renal cell carcinoma (mRCC) patients receiving immunotherapy
Methods: Patients were categorized as responders (progression-free survival ≥ 12 months) and non-responders (progression-free survival < 3 months) after receiving ≥ 2nd line nivolumab. Immunohistochemical analysis of the immune tumour microenvironment focused on T markers (CD3, CD4, CD8), macrophages (CD68), ph-mTOR, CD15 and CD56 expression assessed on tumour cells and PD-L1 expression was performed on both tumour and immune cells
Results: Differences between the two patient groups were considered statistically significant with a p value < 0.05. Overall, 161 tumour tissue samples (57.1% primary tumours, 42.9% metastases) were analysed. Responders' tumour tissue (N = 90, 55.9%) was associated with a significantly lower CD4 expression [median(IQR): 30 (14-60) vs 60 (20-80), p = 0.014], higher CD56 expression [median(IQR): 10 (0-90) vs 0 (0-15), p = 0.046] and a higher CD8/CD4 ratio [median(IQR): 1.5 (0.67-2.70) vs 1 (0.31-2.10), p = 0.030] compared to non-responders (N = 71, 44.1%). Other parameters, including PD-L1 expression, did not reach statistical significance
Conclusion: This analysis highlights the emerging significance of CD56 as a putative biomarker for immunotherapy, suggesting a critical role for regulatory CD4+ cells over cytotoxic CD8+ cells.

E-PS-27-032

Unconventional histologies in prostate adenocarcinoma: a mono-institutional experience

G.D.L. Crudele*, F. Zattoni, F. Dal Moro, A.P. Dei Tos, F. Galuppini
*Pathology Unit, Department of Medicine (DIMED), University of Padua, Italy

Background & objectives: To date, the incidence, molecular characterization and clinical history of each individual Unconventional Histologies (UH) have not yet been extensively investigated.
Methods: A retrospective cohort was performed on consecutive PCa discovered after prostate biopsy or prostatectomy between January 2018 and January 2023. In the series the new diagnosis of UH were searched and re-evaluated by an expert uropathologist.
Results: The series included 2100 consecutive PCa. 255 cases (12.1%) of UH were identified, in particular 8 (3.14%) cases of atrophic pattern, 11 (4.31%) cases of foamy-gland pattern, 10

(3.92%) of ductal PCa, 193 (75.69%) of intraductal PCa, 1 (0.39%) microcystic pattern, 1 (0.39%) mucinous pattern, 5 (1.96%) sarcomatoid subtype and 26 (10.20%) signet-cell-like subtype. According to 2022 WHO, UH are defined as prostatic intraepithelial neoplasia (PIN)-like carcinoma, signet-cell-like adenocarcinoma, sarcomatoid carcinoma and pleomorphic-giant-cell adenocarcinoma of the prostate as true subtypes of acinary PCa. Other forms are termed unusual histological patterns and include atrophic, foamy-cell, microcystic, pseudohyperplastic and mucinous patterns. Moreover, unusual histotypes as ductal and intraductal PCa were identified

Conclusion: The most important effort in the study of UH of PCa is their correct diagnostic identification. Underestimation is possible, especially with regard to subtypes that appear similar to benign lesions. Their correct framing is essential for the correct therapeutic timing.

E-PS-27-033

Oncocytic renal neoplasm: a diagnostic conundrum

D. Das*, B.V. Rao, M.K. Pasam, S. Indulkar, S. Kodandapani, R. Sharma, S.R. Thammineedi
*India

Background & objectives: Oncocytic renal neoplasm is a broad spectrum of tumours ranging from benign to malignant differing in their managements. The new WHO has tried to classify these tumours based on IHC and molecular workups. We present the case with diagnostic challenge.

Methods: This is a case of 50 years old man presented with haematuria. The MRI showed the presence of bilateral renal masses. Intraoperative findings: a 4X3 cm tumour arising from mid part of left kidney and a 1X1 cm tumour arising from the lower pole of the right kidney. Rest of the solid and hollow viscera, peritoneum and omentum were normal.

Results: Grossly, bilateral tumours were brown, solid and cystic with focal yellowish areas.

Histopathological examination revealed a solid cystic tumour with cells showing round nucleus, mild nuclear pleomorphism, prominent nucleoli and abundant eosinophilic granular cytoplasm. Differentials of clear cell RCC, oncocytic papillary RCC, eosinophilic solid and cystic RCC, Chromophobe RCC, oncocytoma and epithelioid angiomyoipoma were considered. Immunohistochemistry showed positivity for AMACR with Ki67 index of 8% and negativity for CD10, CK7, CD117, CA IX, CK20 and HMB45. Tumour mutation study was suggested which showed deletion of FLCN gene causing frame shift mutation. A final diagnosis of bilateral oncocytic renal neoplasm with folliculin gene mutation was given.

Conclusion: The present case highlights the thorough work up is essential for diagnosing this rare entity. Most affected individuals with Birt-Hogg-Dube syndrome harbour germ line mutations in the coding region of FLCN between exon 4 and 14. The prognosis is good with low malignant potential. However, patient may rarely also develop clear cell RCC, and in that case they will have worse prognosis. Hence, a proper follow up is essential.

E-PS-27-034

Serous borderline tumour of the paratestis arising within a mesothelial cyst of the tunica albuginea. A unique case

C. Dastamani*, A. Gravvani, M. Mousia, G. Galanopoulos
*Karditsa General Hospital, Greece

Background & objectives: Serous borderline tumour (SBT) of the testis and paratestis is a rare neoplasm which shares similar histological features to its ovarian counterpart. It usually arises from tunica albuginea in middle-aged men.

Methods: An 86-year old man was admitted with progressive painless enlargement of his right hemi-scrotum. Serum AFP and β-HCG were within normal limits. A right orchiectomy was performed. Sections revealed a multilocular cystic lesion measuring 5 cm in maximal diameter adjacent to the testis. The cysts were filled with gelatinous material. Within the largest cyst, a solid papillomatous tumour was observed.

Results: Histologically, the tumour consisted of multiple papillary fronds with fibrovascular cores lined by columnar cells with focal stratification. The cysts were lined by flattened cells with intervening areas of columnar cells. Nuclear atypia was mild, mitoses were scarce. Psammoma bodies, hemorrhage and necrosis were absent. No stromal invasion was identified. The testis appeared atrophic with no direct connection to the cystic lesion. Immunohistochemically, the columnar cells were positive for CK7, CKAE1/AE3, ER and PR. The flattened cells were positive for CK5/6, CKAE1/AE3, WT1 and Calretinin. Ki-67 was low (<5%). A diagnosis of serous borderline tumour arising within a mesothelial cyst of the tunica albuginea was made.

Conclusion: Ovarian-type epithelial tumours of the testis and paratestis are very rare entities with SBTs being the most common type. They are believed to arise from either Müllerian metaplasia of mesothelial cells or Müllerian remnants. They have favourable prognosis with no recurrence or metastases. This unique case demonstrated the Müllerian metaplasia of the lining of a mesothelial cyst upon which a SBT developed.

E-PS-27-035

Proteomic analysis provides evidence for metabolic reprogramming in clear cell renal cell carcinoma

K. Denning*, A. Valluri, C. McCallister, L. Lawrence, R. Russell, J. Denvir, J. Jensen, T. Salisbury
*Marshall University/Marshall Health, USA

Background & objectives: A change in cellular metabolism is a hallmark of cancer. However, the specific protein expression changes in clear cell renal cell carcinoma (ccRCC) tissue that mediate and maintain the metabolic shift in ccRCC are still an important knowledge gap.

Methods: We collected ccRCC and pair-matched normal renal tissue (N=22), WHO/ISUP Histologic Grade 1-4, confirmed on H&E, and conducted a proteomic study. Mean differences of Log2 protein expression between tumour and normal were computed and paired t-tests were conducted to test for significant difference for each protein and phospho-protein. Benjamini–Hochberg was used to calculate adjusted p-values.

Results: The expression of 274 of 450 proteins was significantly different in ccRCC relative to normal renal tissue. Among these 274, 140 showed a change greater than 20%, 47 showed a change of more than 50%, and 15 showed a change greater than 2-fold in tumours relative to normal renal tissue. Three of the five top-upregulated proteins promote glycolysis, and two of the top five downregulated proteins are components of the mitochondrial respiratory chain. The top-upregulated (by ~ 5-fold) protein was hexokinase II, a rate-limiting enzyme in glycolysis. The top-downregulated (by ~ 6-fold) protein was mitochondrial-encoded cytochrome C oxidase, a required component of complex IV of the mitochondrial respiratory chain.

Conclusion: Prior reports indicate that ccRCC exhibits increased utilization of aerobic glycolysis and lactic acid accumulation to provide rapid energy for metabolism at the expense of oxidative phosphorylation. We extend these studies by showing which specific glycolytic proteins are upregulated, and which mitochondrial proteins that are important for oxidative phosphorylation are downregulated in ccRCC relative to pair-matched normal renal tissue. Future signaling studies will address whether the observed changes in protein expression are linked to the consequence or cause of ccRCC.

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E-PS-27-036

Revelations during organ procurement: multiple renal (including intraglomerular) angiomyolipomas in an organ donor with unknown tuberous sclerosis complex disease

L. Di Sciascio*, S. Chillotti, B. Fabbrizio, D. de Biase, F. Vasuri, D. Malvi
*School of Anatomic Pathology, Department of Biomedical and Neuromotor Sciences, University of Bologna, Italy

Background & objectives: This case report describes a peculiar case of multiple renal lesions(including the very rare intraglomerular angiomyolipoma) in a discarded kidney of a 34-year-old male donor during organ procurement. The donor was an unaware carrier of Tuberous Sclerosis Complex(TSC), not diagnosed.
Methods: TSC was suspected due to the presence of an endo-ventricular SNC lesion and multiple kidney lesions at procurement. Kidneys were discarded: macroscopic examination revealed multiple yellow-whitish nodules. Histopathological evaluation and immunohistochemistry for cathepsin-K, HMB45, SMA, SF1, and S100 were performed to characterize the lesions, alongside a molecular investigation with the Pan-somatic and Leio panels on both pathological and normal tissue.
Results: Histopathology uncovered multiple renal lesions with mostly a triphasic appearance(spindle-shaped myoid cells, mature adipose tissue, and abnormal thick-walled neoarteries), with epithelioid or cystic appearance and both a parenchymal and intraglomerular localization. Cathepsin-K, HMB45, and S100 were diffusely positive, suggesting multiple angiomyolipomas. Molecular analysis confirmed the presence of mutations in genes TSC1 and TSC2, on both normal and pathological samples. These findings suggest a complex histological composition of angiomyolipomas, with the molecular results supporting an undiagnosed TSC. SNC lesion was suspected to be a central neurocytoma or a subependymoma. The donor was considered as "non-standard/negligible" risk for transmission: the liver and the heart were donated; kidney and banked tissues were discarded.
Conclusion: The unexpected finding of multiple renal(and extrarenal) angiomyolipomas in a solid organ donor underscores the importance of a thorough evaluation during procurement. Intraglomerular angiomyolipomas are extremely rare, and previously mentioned only thrice in the literature, involving patients with TSC.

The identification of mutations in genes TSC1 and TSC2 highlights the diagnostic value of molecular analysis in confirming underlying TSC, even in cases where clinical manifestations were absent or overlooked during the patient's lifetime.

E-PS-27-037

Blue nevus: unusual prostate localization

G.A. Dumbravă*, L. Sticlaru, I. Creciun, V. Mitroi, L. Nichita
*Colentina University Hospital, Department of Pathology, Romania

Background & objectives: Melanocitic lesions of the prostate are exceedingly rare, with only 30 blue nevi cases reported until 2024. We report the case of a 63-year-old patient known with prostate adenoma in conservative treatment and incidental lesions of blue nevus.
Methods: Transurethral resection of prostate was performed. Tissue specimens, weighing 35 grams, were processed according to routine histological techniques. Special techniques like Perls' Prussian blue stain and immunohistochemical (IHC) stains: S100 protein, Melan A and Tyrosinase (T311) were performed. Because of the cells heavy loading with brownish pigment, for IHC stains we used red chromogen.
Results: Microscopic examination of the HE stained slides revealed glandular stromal hyperplasia and elongated, fusiform cells with brown granular intracitoplasmatic pigment in the stroma and focal between glandular basal cells. The pigment was negative for iron. The pigmented stromal cells were positive for S100 and T311 and negative for Melan A. After two years of follow-up the patient was free of any disease. The differential diagnosis included melanocitic lesions such as melanosis and malignant melanoma and stromal deposition of other pigments: lipofuscin and hemosiderin.
Conclusion: Blue nevus of the prostate is a rare incidental finding, but its recognition and reporting is important in order to know the real incidence of the lesion, possible associations with other injuries and clinical implications.

E-PS-27-038

An audit of reporting testicular germ cell tumours in radical orchidectomy specimens in a tertiary centre

L. English*, A. Haider
*University College London Hospital, United Kingdom

Background & objectives: The majority of testicular tumours in men under 45 years are germ cell tumours. This audit was undertaken to ensure that testicular germ cell tumours within radical orchidectomy specimens are reported according to the Royal College of Pathologists dataset.
Methods: Testicular tumour reports within radical orchidectomy specimens should assess for 100% of core macroscopic and microscopic data items. We used SNOMED codes for testis/testes and for urological resections to collect data for radical orchidectomy specimens between 1st January 2021 to 31st December 2023. This search yielded 15 cases for 2021, 19 cases for 2022, 19 cases for 2023.
Results: Tumour location was stated in 100% of cases (n=53). In 2021, 1/15 (7%) cases did not have a macroscopic description of the tumour. This was a 35mm seminoma. In 2023, all macroscopic core data items were reported apart from 1/15 cases (7%) where cord invasion was not stated. 100% of microscopic core data items were reported across all three years. Of one frozen section in 2022 and one frozen section in 2023, there was 100% concordance between the frozen section results and the microscopic examination; one seminoma (2022), and one mixed germ cell tumour (2023). Cases sent for opinion at supra-regional testicular centre had 100% concordance (2021-2023).
Conclusion: The findings from our audit are encouraging as we demonstrate compliance with the royal college of pathologist recommendations for reporting radical orchidectomy specimens for germ cell tumours. We had 100% concordance between frozen section and microscopic examination. Core items which were missed include tunica vaginalis and cord status, and tumour focality during macroscopic examination. We need to continue to re-audit these reporting of these resection cases and to also continue examination of concordance with frozen section.

E-PS-27-039

Correlation with cystic renal tumour pathology with of Bosniak classification 2019: a single-centre retrospective analysis of ten years

G. Escuer-Albero*, V. Macarrón, S. Morón Hodge, E. García Fernandez, P. González-Peramato
*La Paz University Hospital, Spain

Background & objectives: The Bosniak classification was updated with a new version in 2019. The aim of our study was to assess the prevalence and distribution of cystic tumour pathology and simple cysts according to Bosniak classes (I-IV).

Methods: A retrospective analysis was performed on cystic renal masses with biopsy and preoperative renal mass protocol of imaging from the last decade in our centre. We went through the electronic medical records of the patients to reclassify the masses according to the Bosniak 2019 version. Statistical analysis were performed using the R statistical programme.
Results: Thirty masses were included in this study (17 females and 13 males; median age 54.50 years, range from 7 months to 84 years). The five paediatrics masses, without Bosniak classification, were two cystic nephromas and three simple cysts. In adults, 21 were simple cysts (18 Bosniak I, 2 Bosniak IIF and 1 Bosniak III). The other four masses were diagnosed by tumour pathology (2 Bosniak IV and 2 Bosniak III) with a wide spectrum of entities: clear cell renal cell carcinoma with extensive cystic transformation, multilocular cystic renal neoplasm of low malignant potential (MCRNLMP) and two cases of clear cell papillary renal cell tumour.
Conclusion: The Bosniak classification version 2019 shows a good and statistically significant correlation with the tumour pathology diagnosed mainly in Bosniak III-IV masses. The cystic neoplasms showed a wide and heterogeneous range of malignancy from aggressive tumours, such as clear cell renal cell carcinoma, to more indolent ones - such as clear cell papillary renal cell tumour, (MCRNLMP) and cystic nephroma. A third of the Bosniak III masses were diagnosed as simple cysts and I-II masses were almost exclusively simple cysts.

E-PS-27-040
Descriptive study of the sites of renal cell carcinoma metastases diagnosed in a tertiary hospital over a ten-year period
I. Fernández De La Prieta*, A. Azueta Etxebarria, L. Aguirrezabal Marcotegui, R.I. Alvarado Cuenca, A. Ugalde Olano
*Hospital Universitario de Basurto, Spain

Background & objectives: Renal cell carcinoma (RCC) with distant metastases to other organs most often involves lungs, liver, bone, brain and adrenal glands. Our aim was to compare the sites of RCC metastases diagnosed in our hospital to literature data.
Methods: We checked our database and selected every RCC organ metastasis diagnosed over ten years (2014-2024) in the Pathology Department of our hospital, which resulted in a total of 36 cases. The sites of the metastases were recorded, as well as the histologic type of the primary tumour. Clinical information regarding age and gender of the patients was also obtained.
Results: The most frequent sites of metastases were lungs (30%) and bone (25%), followed by liver (11%), adrenal glands (8%) and soft tissues (8%). Other less common sites were thyroid (6%), omentum (6%), pleura (3%) and brain (3%). Concerning the locations of bone metastases, the skull and thoracic vertebrae were slightly more prevalent. Bone was the most frequent site of metastasis (36%) in patients under 60 years of age, while lung metastases were the most common (50%) in patients aged 75 years and older. Clear cell RCC was the most frequent histological type (72%). Regarding clinical data, 81% of the patients were male, and the mean age was 66,5 years.
Conclusion: According to our results, lung, bone and liver are the organs where RCC most frequently metastasizes, which is supported by scientific literature. It should be noted that soft tissue metastases were relatively prevalent in our study, compared to other studies. Conversely, although it is a common site of tumour spread, there was only one case of brain metastasis. However, this might be explained by the higher difficulty a brain biopsy involves or because these biopsies were performed at another centre.

E-PS-27-041
Myeloid sarcoma of the testis - case report and literature review
V. Filipovski*, D. Jasar, K. Kubelka-Sabit, E. Stojkoska, D. Petrovski
*Clinical Hospital Acibadem-Sistina, North Macedonia

Background & objectives: We present a case of a 29-year-old male that presented with a left-sided testicular tumour. Orchifuniculectomy was performed and the specimen was received for pathological analysis.
Methods: Macroscopic analysis revealed enlarged testis weighing 95 grams. On cut sections a tumour mass with a diameter of 4 cm was found, indistinct from the surrounding testicular tissue. The tumour was soft with grey-yellow color. Samples were taken for microscopic examination. From the paraffin blocks slices were made and stained with Hematoxyllin-Eosin. Additional slices were made for immunohistochemical analysis.
Results: Microscopy revealed a cellular-rich lesion made up of cells resembling myeloblasts. In particular we found large mono-nuclear cells containing, granular eosinophilic cytoplasm and part of these cells contained segmented nuclei. Immunohistochemical analyses using the following antibodies: Inhibin, Androgen Receptor, Ki67, LCA, CKAE1/AE3, PLAP, TdT, CD20, CD3, CD79, bcl-2, bcl-6, CD34, PAX-5, c-kit, CD68, CD15, CD99, CD56 and CD30 showed the myeloblastic nature of these cells. Latter data revealed that the patient was previously diagnosed with and treated for acute myeloblastic leukemia 6 years ago. The previous diagnosis was Acute myeloid leukemia with inv(16)(p13.1q22). This was the first manifestation of the relapse of the disease presented as a testicular tumour mass.
Conclusion: Literature shows that myeloid sarcoma of the testis is a rare first manifestation of acute lymphoblastic lymphoma, both as a primary manifestation of the disease or as a primary site of relapse from the disease. Abnormalities of chromosome 16 are found in about 5-8% of acute myeloid leukemia (AML). Testicular myeloid sarcoma can cause great diagnostic confusion particularly if the pathologists are not informed about the patient history.

E-PS-27-042
Do basal type non-muscle-invasive urothelial carcinomas exist?
M. Gándara Cortés*, A.M. Castro Iglesias, C. Gómez-de María, E. López Díez, J.A. Ortiz Rey, C. Álvarez, T. García-Caballero, P. San Miguel Fraile

*Pathology, Complexo Hospitalario Universitario de Pontevedra, Spain
Background & objectives: Stage pT1 urothelial carcinomas constitute an heterogeneous group with different risk of progression that raise a dilemma for the follow–up and therapeutic approach. Our objective is to characterize a group of pT1 urothelial carcinomas in the molecular subtypes using IHC.
Methods: Immunohistochemistry was performed on paraffin sections from tissue arrays containing a total of 378 samples from 171 different pT1 high grade urothelial carcinomas. Prediluted antibodies against CD44 (Clone SP37), CK20 (Clone SP33), all of them from Ventana, and a concentrated anti-CK5 (Clone XM26, Novocastra, 1:200) were used. Heat antigen retrieval was performed on the automatic stainer.
Results: 101 (59 %) and 8 (5 %) cases were categorized as luminal (CK 5 and CD44 -, CK20+) and basal (CK 5 and CD44 + , CK20 -) subtypes respectively. 53 cases (28.9%) had overlapping results or no immunoexpression and they were not classificable. 3 of the 8 basal cases and 38 of the 101 luminal tumours with follow-up recurrenced. While 13 of the 101 luminal cases and 2 of the 8 basal tumours with follow-up progressed to pT2. Only 9 of 101 luminal cases died from their urothelial carcinoma compared to 2 of the 8 basal tumours who died.
Conclusion: Immunohistochemistry is useful to classify urothelial carcinomas as basal or luminal types although the results cannot be conclusive in a proportion of cases. Most of the pT1 urothelial carcinomas are of luminal type. Our basal cases had apparently a higher risk of progression than the luminal. However the number of cases is too low and inconclusive. Larger studies are needed to elucidate a possible relevance for the treatment or follow up of the few cases of basal type.

E-PS-27-044

Prostatic type polyp of the bladder- a diagnostic challenge

A. Georgescu*, T. Jaswal, D. Cretoiu, T. Georgescu
*University of Medicine and Pharmacy "Carol Davila" of Bucharest, Romania

Background & objectives: Prostatic type polyp, also known as ectopic prostatic tissue or adenomatous polyp with prostatic type epithelium, is a benign lesion that is usually seen in the urethra, but rarely it can also be observed in the bladder.
Methods: We report two cases, one from a 42–year-old that presented as a solitary polypoid mass in the trigone which was referred to our institution with the suspicion of clear cell adenocarcinoma of the bladder and one from a 64-year old, that had two separate lesions. Immunohistochemistry tests (NKX3.1, PSA, AMACR, PAX8, p63 and Ki67) have been subsequently performed.
Results: The two examined cases had similar morphological aspects, revealing a papillary lesion, with columnar cells with pale cytoplasm and basally located nuclei, that formed focally acini with corpora amylacea inside the lumen. The two lesions were positive for NKX3.1 and PSA and negative for AMACR and PAX8, excluding a clear cell adenocarcinoma of the bladder and a nephrogenic adenoma; p63 was immunoreactive in rare areas of urothelial metaplasia and both lesions had a Ki67 proliferation index of less than 2%. Additionally, the 64-year-old patient had a separate lesion in the bladder with features of a non-invasive, low-grade urothelial carcinoma. Clinical follow-up did not show recurrences for any of the patients.
Conclusion: Prostatic type polyps represent a rare non-neoplastic lesion that poses differential diagnosis with clear cell adenocarcinoma of the bladder and with nephrogenic adenoma. Despite their uncommon occurrence, the morphological features (papillary structures lined by prostatic type epithelium without cytologic atypia) together with the immunohistochemical features (NKX3.1 and PSA reactivity) and low nuclear proliferation index can help one reach the correct diagnosis. These lesions are occasionally associated with other pathologies of the bladder, as shown in one of the presented cases.

E-PS-27-045

A case report of Kaposi sarcoma of the penile urethral meatus

T. Georgescu*, M.V. Olinca, A. Georgescu
*Carol Davila University of Medicine and Pharamcy Bucharest, Romania

Background & objectives: Kaposi sarcoma is a malignant vascular tumour usually affecting the lower limbs in patients of all ages. There are only a few case reports in the literature which describe Kaposi sarcomas arising in unusual locations such as the urethral meatus.
Methods: We report the case of a 60-year-old male that presenting to the urology department with an ulcerated polypoid lesion protruding out of the urethral meatus. The lesion was excised and the specimen was sent to our Pathology Department for histopathological analysis. Hematoxilyn-eosin slides followed by immunohistochemistry stains (CD31, AE1/AE3, SMA, Ki67, HHV8) have been subsequently performed.
Results: Histopathological examination revealed a fibro-conjunctive tissue covered by non-keratinizing epithelium which featured a nodular subepithelial lesion made out of spindle cells with discrete cytological pleomorphism, atypical mitoses (3M/10 HPF) and occasional intracytoplasmic hyaline globules. The immunohistochemical stains revealed diffuse immunoreactivity for CD31 and HHV8, while SMA and AE1/AE3 were negative. Ki67 revealed a proliferation rate of 30%. From a histopathological point of view a noteworthy differential diagnosis is represented by pyogenic granuloma, a benign lesion that can be seen at the urethral meatus, but which does not feature HHV8 immunoreactivity, similar to Kaposiform hemangioendothelioma, another atypical vascular lesion, which could mimic Kaposi sarcoma. Clinical tests revealed no HIV infection.
Conclusion: The presented case reveals a relatively common tumour in an extremely rare location, which can pose a diagnostic challenge and which has multiple differential diagnoses in this location: spindle cell squamous carcinoma, leiomyosarcoma, pyogenic granuloma or angiosarcoma. A close histopathological examination reveals hyaline intracytoplasmic globules and a peritumoural plasma cell infiltrate that may aid in the diagnosis, features which together with diffuse HHV8 immunoreactivity confirms the correct diagnosis. Establishing the correct diagnosis is ery important due to possible unfavourable outcome.

E-PS-27-046

ALK re-arranged renal cell carcinoma – a case highlighting the importance of pathological review in difficult to classify renal tumours

C. Girleanu*, E. Elhassan, P. Kelly, D.G. Power, L. Browning, P. Sweeney, R.M. Bambury, N. Mayer
*Mater Misericordiae University Hospital, Ireland

Background & objectives: Anaplastic lymphoma kinase rearranged renal cell carcinoma (ALK-RCC) is a rare molecular subtype recently included as a novel entity in the 2022 WHO classification of kidney tumours. We present the case of an unusual kidney tumour retrospectively diagnosed as ALK-RCC.
Methods: A 57-year-old male underwent right nephrectomy in 2015 for a kidney tumour, classified at that time as combined tubulocystic and collecting duct carcinoma. In 2020 he had a retroperitoneal lymph node dissection and in 2022 removal of a right psoas mass including a right hemicolectomy, both for recurrent disease. Subsequent liver metastases were identified on CT scan.
Results: Histologically, the nephrectomy tumour had a heterogenous appearance, with tubulocystic, cribriform, sieve-like architecture and a lesser papillary component, prominent stromal mucin and occasional psammomatous calcifications. Rhabdoid or sarcomatoid changes were not seen. Tumour was positive for PAX8, CK7, 34beta E12, p63 and CEA and negative for AMACR and OCT 4. INI-1 was retained. The diagnosis at that time was combined tubulocystic and collecting duct renal carcinoma. Following the 2022 recurrence and the atypical clinical behaviour for collecting duct carcinoma, more recently described renal tumours were considered and the tumour was re-classified as ALK-RCC after external referral which confirmed positive ALK-IHC and ALK rearrangement by FISH analysis.
Conclusion: Recognition of ALK-RCC based on morphology is difficult due to its heterogenous appearance which mimics various renal tumours. Our case highlights the importance of histologically reviewing previously difficult to classify renal tumours and considering novel and emerging molecular subtypes in the WHO classification , particularly in cases with an atypical clinical behaviour. It also demonstrates the clinical importance of diagnosing ALK-RCC, since the patient had a complete radiological response after commencing ALK-TKI therapy (Alectinib) for metastatic liver disease.

E-PS-27-047

Epididymal cholesterol granuloma resembling a testicular tumour: case report

N. Goishvili*, M. Jangavadze, I. Kirvalidze, I. Khakhutaishvili, K. Tsomaia
*TSU Aleqsandre Natishvli Institut of Morphology, Georgia

Background & objectives: Epididymal cholesterol granuloma is a rare benign pathology. It is not a neoplasm but it is locally aggressive and difficult to distinguish it from testicular cancer. We present a case of this rare entity in a young Caucasian man.

Methods: A 31-year old male patient presented with complaints of an enlarging painless right scrotal mass, that had been present for about one year. No history of scrotal trauma, prior surgery and any exposure to tuberculosis. Physical examination revealed a 10-cm hard, non-tender and non-transilluminating scrotal mass. Serum testicular tumour markers were negative. Scrotal Doppler ultrasonography revealed a 95x87x79-mm solid mass
Results: Further CT scan revealed the right scrotal mass of 8,7 x 9,3 cm with fluid density and the surrounding calcified ring. Radical inguinal orchiectomy was performed. Grossly the mass was about 15 cm in size and firm in its consistency. Histopathological examination revealed a cystic lesion in the right epididymis that contained many hemosiderin-laden macrophages. Cholesterol clefts formed by cholesterol crystals were diffusely present within the fibrinoid material and between lymphocytes, which were the predominant component of inflammatory infiltrate clusters . Hemosiderin-laden macrophages were seen around the area of cystic degeneration. Spermatogenesis in the testis was intact. The specimen also contained 7 lymph nodes which were negative for malignancy.
Conclusion: Cholesterol granuloma is a fibrogranulomatous lesion that develops secondary to a foreign body reaction to cholesterol crystals and exhibits the accumulation of foreign body giant cells. It can be very difficult to preoperatively distinguish testicular tumours from cholesterol granulomas of the testis or epididymis. If in doubt, surgical exploration and histopathologic examination are absolutely necessary. Although solid neoplasms of the epididymis are generally rare, cholesterol granuloma should be considered in differential diagnosis in patients with large, non-tender scrotal masse

E-PS-27-048
Could tubulocystic renal cell carcinoma be a hybrid tumour? Two cases report and review of the literature
Ö. Gökbaşı*, A. Namal, Ç. Demirdağ, İ. Gürses

*Cerrahpasa Medical Faculty, Turkey
Background & objectives: Tubulocystic renal cell carcinoma (TCRCC) is a rare renal cell carcinoma (RCC) subtype. It represents less than 1% of renal tumours. The World Health Organization identified it as a newly recognized renal tumour in 2016.
Methods: We reported two cases administered in our centre to contribute to the literature. The first case diagnosed as TCRCC, the second one as renal cell carcinoma with papillary and tubulocystic features.
Results: Both patients were male and aged 53 years and 63 years, respectively. They were treated by partial nephrectomy. The tumours measured 4.5 cm and 3.5 cm, respectively. Macroscopically, both tumours were described as variable-sized cystic lesions with septations filled with serous fluid to gelatinous material. On histopathological examination, cysts were lined by a single layer of flat, hobnail and cuboidal cells with high grade nuclear features. In addition, the second tumour had 3% papillary structure. Both tumours were immunoreactive for PAX8, CD10, CK8, CK19 and Vimentin; but were not for CK7 and CD117. While both tumours had similar macroscopic and immunohistochemical features, just second one had papillary component.
Conclusion: TCRCC is an uncommon, recently characterized RCC subtype with unique gross and microscopic features. It has variably been reported to be related to other renal cell carcinomas, such as papillary renal cell carcinoma. These two entities share same pathologic and cytogenetic features. According to our current information, renal carcinomas have tubulocystic features with papillary component should not be reported as TCRCC.

E-PS-27-049
Intraductal carcinoma of the prostate – wolf in lamb's skin or paper tiger?
D.A. Grubišic*, M. Ćorić, V. Pešutić Pisac, M. Duvnjak, T. Čeprnja, K. Vilović
*Croatia

Background & objectives: Intraductal carcinoma of the prostate (IDC-P) is histologically characterized by enlarged glands with hyperchromatic nuclei, prominent nucleoli, and discontinuous basal layer. We present a 70-year-old patient who underwent three TRUS-biopsies from 2021 to 2023 with the same diagnosis of IDC-P.
Methods: During that period, his PSA level ranged from 5.81 to 7.47 ng/ml. On digital rectal examination prostata was gradus I/II. On MSCT slides two lesions were described as PI-RADS 4 - 0.7 cm size lesion on the left side and a 1 cm size poorly delineated lesion on the right side. Skeletal scintigraphy showed no pathological accumulation of radiopharmaceuticals.
Results: After two years of the previously mentioned follow-up period, there was no clear evidence of widespread or metastatic disease. MDT suggested radical prostatectomy which was performed in January 2024. The histopathology report confirmed extensive IDC-P, but grade group 3 predominantly ductal morphology prostatic adenocarcinoma (PCa) with 80% of Gleason 4 component was found in 20% of the left lobe of prostate. Two types of IDC-P are morphologically indistinguishable, first one is typically associated with high-grade and high-stage acinar PCa representing a late colonizing event - the so-called retrograde spread. However, the second type of IDC-P is observed without PCa or with grade group 1 PCa – the so-called precursor pathway.
Conclusion: IDC-P in our patient is not the first mentioned type of IDC-P because the associated PCa is predominantly high-grade ductal PCa for which is hard to assume that has been dormant for two years. Also, it is not type two of IDC-P because, in our case, the associated PCa is not low-grade. Therefore, since there are molecular differences between the mentioned groups (PTEN and ERG status, driver mutation in MAPK/PI3K genes), it would be interesting to do a molecular analysis.

E-PS-27-050
Urine for a surprise: primary malignant melanoma of the urinary bladder
C. Guerin*, J. Moyle, R. Wong, I. Cheema, L. Grogan, E. Leen
*Ireland

Background & objectives: Malignant melanoma develops at mucosal sites in only 1.3% of cases; of these, melanoma of the urogenital tract accounts for just 2.8%. We report a case of invasive malignant melanoma of the urinary bladder in an 82 year old female.
Methods: A previously healthy 82 year old female presented with frank haematuria and recurrent urinary tract infection. Ultrasound and CT imaging demonstrated a 5.3cm lobulated intravesical mass which was confirmed on cystoscopy. She underwent a transurethral resection of bladder tumour.
Results: Microscopic examination revealed multiple fragments of partially necrotic tumour showing muscle invasion. The tumour cells have vesicular nuclei and variably prominent nucleoli and focally cytoplasmic melanin pigment. On immunohistochemistry, tumour cells are diffusely positive with melanA and HMB45 and focally to diffusely positive with S100. They are negative with cytokeratins (AE1/3, CK5/6 and 34BE12), p63, CD45, CD20 and CD30. CD138 is very focally positive. The features are of an invasive malignant melanoma. Molecular analysis detected a KRAS mutation. BRAF mutation was not identified. The patient had no signs of current or regressed cutaneous melanoma. No other sites of disease were detected on CT thorax, abdomen and pelvis (CT TAP).

Conclusion: The patient was diagnosed with primary invasive malignant melanoma of the bladder. Repeat CT TAP performed 2 months after initial presentation showed new lymphadenopathy and sacral metastasis. She died within 6 weeks of commencing radiotherapy and nivolumab treatment. The aetiology and pathogenesis of this rare condition have not been definitively established. The limited number of cases reported in the literature illustrate a condition which is often aggressive and fatal, as in our case.

E-PS-27-051
Mucinous tubular and spindle cell renal carcinoma - a case report series
E. Higueras Mora*, S. Merino Baamonde, M. Rubiera Valdés, F.J. Pérez Rastrollo, C. Fuente Díaz, C. González Rodríguez, M. García Martínez, A. Soria Montoya, A. de la Huerga, J.R. Riera Velasco, V. Blanco Lorenzo
*Hospital Universitario Central de Asturias, Spain

Background & objectives: Mucinous tubular and spindle cell renal carcinoma (MTSCC), is a rare renal carcinoma (<1% of renal neoplasms), mainly affecting females, and typically located in the renal cortex. We evaluated MTSCC cases at a tertiary referral centre from 2013 to 2024.
Methods: A search was made in our institution's archives and 5 patients with a diagnosis of MTSCC were identified from 2013 to April 2024. The following variables were studied: Surgical procedure, gender, age, pTNM classification and clinical outcome.
Results: MTSCC typically presents with a prominent tubular architecture, featuring small, uniform, columnar epithelial cells in solid or anastomosing tubular patterns. Tumour cells exhibit regular nuclei, eosinophilic cytoplasm, and may reside in a myxoid or mucinous stroma. Mucinous components vary, occasionally with spindle cells. Four total nephrectomies and one partial nephrectomy were performed, with a mean age of 73.2 years. Our case series, consistent with literature, shows a female predominance (4/5). Four cases were confined to the kidney (pT1 and pT2), one with renal sinus involvement (pT3a). A patient with stage pt2b developed peritoneal metastasis five years later. Currently, all patients are alive without disease.
Conclusion: MTSCC is an exceedingly rare tumour, typically low grade, diagnosis was often made without additional immunohistochemical techniques. A proliferation characterized by elongated tubules, and particularly the presence of extracellular mucin were often enough in reaching the final diagnosis. In tumours that are low in mucin, overexpression of VSTM2A would be useful in distinguishing MTSCC from other renal tumours.

Tumours with high-grade transformation are frequently associated with distant metastasis, although rare cases with classic morphology may develop metastases.

E-PS-27-052
Changes in glycosylation patterns are observed alongside prostate neoplasia
P. Janega*, A. Janegova
*Institute of pathological anatomy, Comenius University, Faculty of medicine in Bratislava, Slovakia

Background & objectives: Prostatic cancer is one of the most common malignancies worldwide and it is the third leading cause of dead from oncological malignancies in men in Slovakia. New diagnostic and therapeutic markers opens new opportunities for soon diagnostics herapy of patients.
Methods: Abnormal glycosylation of cell structures is important part of the neoplastic transformation process. The aim of presented study was to evaluate the changes of glycosylation pattern in neoplasia of prostatic tissue. The fluorescent lectin histochemistry, using the lectins specific for sialylated (SNA, MAL) and fucosylated (UEA, AAL) glycoconjugates, was used for the evaluation of glycosylation changes in the prostatic cancer.
Results: Neoplastic transformation in prostatic tissue is accompanied by changes of tissue glycosylation pattern. The increased expression of fucose residues, characterized by increase of UEA positivity, is present in all samples of prostatic carcinoma. The sialylation of the tissue glycoconjugates is significantly decreased in prostatic cancer compared to the normal prostatic glands, characterised by the decrease of both SNA and MAL positivity.
Conclusion: The shifts in glycosylation patterns may affect the functional properties of neoplastic cells, including the survival, invasiveness and metastatic potential of cells. A deeper comprehension of these mechanisms could pave the way for the development of innovative diagnostic and therapeutic modalities.

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E-PS-27-054
Primary extranodal marginal zone lymphoma of bladder: a rare cause of hematuria in a young male
S. Kaushal*, A. Narwal, V. Aggarwal, A. Seth
*Department of Pathology, India

Background & objectives: Lymphoma of the urinary bladder (LUB) is rare. Here in we present a case of primary extranodal marginal zone lymphoma of the bladder presenting as a haematuria in a young male.
Methods: A 45-year-old male came to the OPD with complaints of painless gross hematuria. The patient had a history of urethral stricture repair; 20 years back after a road traffic accident. MRI showed a diffuse circumscribed thickening in the bladder mucosa. A transurethral biopsy of the bladder was performed.
Results: Hematoxylin and eosin-stained slides showed a tumour arranged in sheets comprising small to intermediate-sized atypical lymphoid cells. On immunohistochemistry, these cells were diffusely immunopositive for CD 20, CD 43, and focally for BCL2 while they were negative for cytokeratin, GATA 3, CD 10, BCL6, CD 3, and CD 5. Dendritic meshwork was highlighted by CD 23 immunostain. Ki 67 labelling index was low. A diagnosis of primary extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue was rendered. A bone marrow biopsy was also performed which showed hematopoietic elements of all three series and no malignancy was identified in the sections examined.
Conclusion: Primary extranodal marginal zone lymphoma of the urinary bladder is an uncommon lesion, and its diagnostic features may not be well known to the unaccustomed practitioner. Potential misdiagnosis of poorly differentiated urothelial carcinoma or chronic cystitis can occur and accurate diagnosis depends upon comprehensive immunohistochemical and molecular work-up.

E-PS-27-055
Case report of a sarcomatoid squamous cell carcinoma of the penis with an osteosarcomatous component
O. Kouroukli*, E.H. Kourea
*Evaggelismos General Hospital, Athens, Greece

Background & objectives: Sarcomatoid squamous cell carcinoma (SCC) is an uncommon variant of HPV-independent squamous carcinoma of the penis. We present a case of a penile sarcomatoid SCC with a rarely reported osteosarcomatous component in order to highlight this rare but interesting finding.
Methods: We received in consultation 25 H&E slides and 2 paraffin blocks from a partial penectomy for a glans and foreskin lesion in

a 76-year-old patient. Microscopic evaluation of the slides was performed, along with immunohistochemical studies for the following markers: p40, vimentin, SMA, MSA, Desmin, h-caldesmon, CD31, CD34, ERG, SATB-2, S100, p16 and SOX-10.
Results: Microscopic examination revealed a well-differentiated SCC originating from the surface epithelium. The carcinoma transitioned abruptly into a hypercellular and atypical spindle-cell proliferation with a fascicular growth pattern that occupied most of the tumour. Osteoid deposition and foci of calcification were identified. Immunohistochemistry for p40 was positive in the well-differentiated component and negative in the spindle-cell component. The latter expressed vimentin, SMA, MSA and SATB-2 and was negative for the rest of the immunohistochemical markers. The diagnosis of sarcomatoid HPV-independent SCC with an osteosarcomatous component was made. The tumour invaded into corpus spongiosum.
Conclusion: The sarcomatoid component in this case was easily recognized as sarcomatoid carcinoma, as it was juxtaposed to a conventional, notably well-differentiated SCC. Epithelial-to-mesenchymal transition is the underlying mechanism of sarcomatoid transformation. Heterologous elements, bone in our case, are rarely reported in penile SCC, further highlighting the plasticity of tumour cells. Penile sarcomatoid carcinomas are unusual and aggressive tumours with high risk for metastasis. The significance of the osteosarcomatous component has not been defined due to the scarcity of relevant reports.

E-PS-27-056
A rare case of somatic type malignancy of high-grade neuroendocrine carcinoma in metastatic mixed non-seminomatous germ cell tumour
A. Kret*, M. Cumberbatch, R. Young, S. Conroy, K. Benes
*Sheffield Teaching Hospitals NHSFT, United Kingdom

Background & objectives: A man in 30s presented with hypertension. During routine workup, a complex groin mass and retroperitoneal lymphadenopathy have been identified. There was no significant testicular abnormality seen on the ultrasound scan.
Methods: The histology of the groin mass biopsy revealed a tiny group of cells with hyperchromatic nuclei and eosinophilic cytoplasm. Lesional cells expressed AE1/3, CK8/18 and HCG, and did not express LCA, OCT4, CD30, Melan A, PLAP and AFP. The histological findings were concordant with serum tumour markers (elevated bHCG and LDH, normal AFP). The provisional diagnosis of choriocarcinoma was made.
Results: The patient underwent chemotherapy and serum bHCG decreased to normal range. The subsequent retroperitoneal lymph node dissection of the residual tumour demonstrated large necrotic areas and viable tumour with morphological features and immunohistochemical profile of a teratoma. There was no evidence of choriocarcinoma, seminoma, yolk sac tumour or embryonal carcinoma. There was a separate district component demonstrating glandular to solid growth of basophilic pleomorphic cells with prominent mitoses. This component expressed AE1/3, CD56, 'punctate' staining of CAM5.2 and focal synaptophysin. Ki-67 was over 70%. There was no expression of Chromogranin, CD99, GFAP and S100.
Conclusion: The overall findings are of metastatic mixed Non-Seminomatous Germ Cell Tumour with somatic type malignancy of high-grade neuroendocrine carcinoma. The combination of choriocarcinoma and teratoma in mixed Non-Seminomatous Germ Cell Tumours is well recognised. An associated somatic type malignancy is rare and predicts worse survival. The cases involving teratomatous component transforming into high-grade neuroendocrine carcinoma are extremely rare.

E-PS-27-057
Centralized prostatectomy with intra-operative NeuroSAFE surgical margin assessment improves surgical margin control
L. Kroon*, S. Remmers, M. Busstra, M. Gan, S. Klaver, J. Rietbergen, M. van der Slot, E. Hollemans, C. Kweldam, C. Bangma, M. Roobol, G. van Leenders
*Erasmus MC Cancer Institute, The Netherlands

Background & objectives: This study investigates surgical margins in prostate cancer patients who underwent robot-assisted radical prostatectomy (RARP) with intra-operative neurovascular structure-adjacent frozen-section analysis (NeuroSAFE) in a centralized operation clinic and evaluates differences compared to patients who underwent radical prostatectomy (RP) without NeuroSAFE.
Methods: Between Sept-2018 and Jan-2021, 962 patients underwent centralized RARP with NeuroSAFE. Positive NeuroSAFE prompted secondary resection to achieve negative margins at final pathology. A retrospective cohort of 835 patients had undergone RP in a tertiary centre without NeuroSAFE between Jan-2000 and Dec-2017. We performed multivariable logistic regression to evaluate differences in risk of PSM and length, controlling for clinicopathological variables.
Results: Patients operated with NeuroSAFE in the centralized clinic had 29% PSM at final pathological RP examination. The median cumulative length of definitive PSM was 1.1 mm (interquartile range (IQR) 0.4-3.8). Among 275 men with PSM, 136 (49%) had a cumulative length ≤1mm and 198 (72%) ≤3mm. After controlling for PSA, pT-stage, pN-stage, Grade Group and cribriform pattern, patients treated in the centralized clinic with NeuroSAFE had significantly lower odds on PSM (odds ratio (OR) 0.70, 95% confidence interval (CI) 0.56-0.88; p=0.002), as well for PSM length >1mm (OR 0.14, 95% CI 0.09-0.22; p<0.001) and >3mm (OR 0.21, 95% CI 0.14-0.30; p<0.001)
Conclusion: NeuroSAFE was primarily developed to aid urologists in optimizing nerve bundle sparing RP to improve postoperative continence and erectile function, potentially at the cost of increased PSM. In this study, consistent with previous literature, centralization with NeuroSAFE was associated with significantly lower PSM risk. Additionally, this study is the first to present evidence that centralization with NeuroSAFE is associated with shorter cumulative PSM lengths, indicating improved control of surgical margins.

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E-PS-27-058
Histopathological characteristics of prostate cancer lymph node metastasis with false-negative PSMA-PET/CT findings
L. Kroon*, C. Kweldam, G. van Leenders
*Erasmus MC Cancer Institute, The Netherlands

Background & objectives: This study evaluated the histopathological characteristics of metastasis at pelvic lymph node dissection (PLND) in prostate cancer (PCa) patients with false-negative nodal status on prostate-specific-membrane-antigen positron-emission-tomography (PSMA-PET)/computed-tomography (CT).
Methods: Twenty-seven men who after PSMA-PET/CT underwent robot-assisted radical prostatectomy with positive PLND between September 2018 and February 2021 were included. We assessed the following histopathological features: total number LN removed, number of positive LN, tumour diameter, largest contiguous tumour diameter, Gleason score (GS), morphological pattern, extranodal extension (ENE), and PSMA-PET/CT detection.
Results: The median number of removed LNs was 16, with most patients having one positive LN (56%). Of the 47 positive LNs, 32%

were detected via PSMA-PET/CT, 60% were not, and 8.5% could not be correlated. The median pathological tumour diameter of detected LN metastasis was 7.0mm (range 0.8-28mm, continuous 6.0mm (0.8-28mm)); larger than the diameter of undetected LN (2.3mm 0.2-8.0mm, contiguous 1.9mm, 0.2-7.5mm). In undetected LN, tumour diameter exceeded 3.5mm in 46%. All detected LN had cribriform pattern, compared to half of the undetected LN (54%). No significant differences were found in GS or ENE. PSMA staining was performed in 64%, revealing moderate-strong expression in both detected and undetected metastases.
Conclusion: Although PSMA-PET/CT undetected LN metastases were on average smaller, approximately half (46%) had diameters exceeding 3.5mm. No difference in GS or ENE was found, but all detected metastases had cribriform pattern. The lack of variance in PSMA expression between detected and undetected LN metastases in PSMA-PET/CT suggests that PSMA immunohistochemistry on prostate biopsy may not reliably identify potential false-negative PSMA-PET/CT results. Limitations are different PSMA-PET/CT tracers and evaluations, and a small sample size preventing mixed model analysis.

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E-PS-27-059
How to handle prostatic ductal adenocarcinoma in the urethra prostatica?
L. Kroon*
*Erasmus MC Cancer Institute, The Netherlands

Background & objectives: Ductal adenocarcinoma (DAC) of the prostate may manifest as an exophytic papillary/polypoid whitish mass near the verumontanum at the urethra prostatica, observed during urethrocystoscopy. It is unclear whether transurethral resection (TUR) alone is sufficient therapy, or further treatment is necessary.
Methods: Patients with DAC diagnosed on TUR or urethral biopsy (UB) between 2013-2022 were identified via Dutch national pathology registries (DNTP-group, NKR, IKNL). After histopathological revision 27 cases were included, and clinicopathological and follow-up information was collected.
Results: Median age and PSA at diagnosis were 78 years and 3.2 ng/mL (ranging 0.8-70.5). Pure DAC was present in 73%, the remaining had mixed DAC and acinar adenocarcinoma. At diagnosis, tumours had high GS (3.8% 4+3=7, 73% 4+4=8, 19% 4+5=9) and 22.2% contained necrosis. Upon presentation, 14.8% had nodal metastasis and 11.1% had distant metastasis, resulting in hormonal therapy. Eight patients received no initial therapy, of whom 62.5% later underwent a TUR for suspicious lesions (2 within 6 months, 2 within 1.5 years and 1 after 6.5 years) which all showed high volume DAC. Two untreated patients died after 565 and 1329 days; one survived after 180 days.
Conclusion: The DAC tumours presenting on TUR or UB have aggressive characteristics. The majority of patients with no initial therapy underwent secondary TUR due to suspicious lesions in the urethra which revealed high-volume DAC. Therefore, it seems insufficient to give no other treatment after diagnosis of DAC in TUR/UB. Limitations of this study include small sample size due to rarity of the phenomenon and unknown comorbidities and cause of death.

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E-PS-27-060
Sarcomatoid variant urothelial carcinoma of the bladder in a patient previously treated for prostate cancer
M.A. Krupinska*, R. López Henríquez, J.S. Marrero Afonso, C.N. Hernández León, S. García Hernández
*Hospital Universitario de Canarias, Spain

Background & objectives: Sarcomatoid urothelial carcinoma is a very rare variant estimated to represent about 0.3% of all urothelial cancers and associated with poor prognosis.
Methods: An 82-year-old male with a history of prostate cancer treated with radiotherapy presented with haematuria and anemia. Edema of the bladder mucosa was the only cystoscopic finding. Samples were obtained via transurethral resection.
Results: Microscopically, the bladder wall was massively infiltrated by a neoplastic growth composed of discohesive atypical cells immersed in myxoid stroma. The tumour cells had predominantly spindled morphology with irregular hyperchromatic nuclei and variable amounts of amphophilic cytoplasm. Frequent typical and atypical mitotic figures were noted. The tumour was strongly immunoreactive for GATA3 (diffusely) and p63 (patchy). Limited, focal staining for EMA, CK(AE1/AE3), and SMA was observed. NKX3.1, CAM5.2, desmin, CD34, STAT6, NTRK, ROS1, and ALK stains were negative.
Conclusion: Sarcomatoid variant urothelial carcinoma consists of high-grade spindle cells, and exhibits morphological and immunohistochemical evidence of both epithelial and mesenchymal differentiation. Risk factors include previous exposure to radiotherapy and intravesical cyclophosphamide treatment.

E-PS-27-061
Cystic trophoblastic tumour in retroperitoneal lymph node metastasis
O. Şahin, S. Ekmekci, B.G. Özamrak, T. Degirmenci, Ü. Küçük*
* Izmir Provincial Health Directorate, Izmir City Hospital, Department of Pathology, Turkey

Background & objectives: The cystic trophoblastic tumour (CTT) was first reported by Ulbright et al. in 1988 as "choriocarcinoma-like tumours" that developed after the diagnosis of nonseminomatous germ cell testicular tumours(GCT).In their series of 17 cases in 2004, they defined it as CTT.
Methods: Most cases reported in the literature occur after chemotherapy(CT).Though its pathogenesis remains unclear,it's widely believed that it originates from the spontaneous regression or CT-induced regression of choriocarcinoma.Here, a case of CTT associated with teratoma detected in a patient who received CT after the diagnosis of GCT and developed retroperitoneal lymph nodes(RPLN) metastasis during follow-up is presented with its clinical,radiological, histopathological features.
Results: A 19-year-old patient who underwent surgery for testicular mass at an external centre, diagnosed with mixed GCT and later found to have undergone CT.The case was referred to our hospital after RPLN of pathological size were detected on positron emission tomography imaging.Histopathological examination of the excised lymph nodes revealed a tumour mostly compatible with teratoma.Cystic structures vary in size and collapsed among teratoma tumour components. The cells lining the cysts had eosinophilic cytoplasm and smudged nuclei. Although the cells were single row in most areas,small cell groups were also observed.The cells showed positive reaction with hCG, GATA3, Inhibin immunohistochemical markers. It was reported as "CTT and teratoma metastasis in lymph node"
Conclusion: Cystic trophoblastic tumour is a rare lesion that can easily be overlooked when not carefully evaluated. Since it is often accompanied by teratoma, due to its cystic nature and cells that can appear eosinophilic and squamoid, many pathologists may classify the tumour as cystic teratoma. This entity should be kept in mind and detailed examination should be carried out with many examples.

E-PS-27-062
Paraganglioma in unusual location -a case report
R. López Henríquez*, M.A. Krupinska, J.S. Marrero Afonso
*Hospital Universitario de Canarias, Spain

Background & objectives: Paraganglioma is a neuroendocrine tumour originating from chromaffin cells of the sympathetic nervous system. Its occurrence in the bladder is very rare, constituting less than 1% of paragangliomas and only 0.05% of bladder tumours.
Methods: A 37-year-old woman underwent routine gynaecological examination, during which a lesion was identified on the anterior wall of the bladder via transvaginal ultrasound. A cystoscopy revealed an erythematous lesion, and an abdominal CT scan showed a hypercaptivating focal lesion. Subsequently, a transurethral resection was performed, revealing a solid 1 cm lesion with deep growth on the anterior bladder wall.
Results: Four irregular whitish-pink tissue fragments, measuring a total of 1.2x1x0.3 cm, were received. Histological examination revealed the bladder wall affected by a tumour proliferation forming predominantly small solid nests, with focal areas of large and irregular nests. The cells displayed oval nuclei with monomorphism and no significant atypia, with granular eosinophilic cytoplasm and a network of peripheral sustentacular cells. No necrosis, comedonecrosis, or vascular invasion was identified. Immunohistochemical analysis showed positivity for synaptophysin, chromogranin, INSM1, and succinate dehydrogenase B (preserved), with S100 positive in sustentacular cells. CKAE1/AE3 was negative, and KI67<1%. The diagnosis was bladder paraganglioma, with an intermediate-risk GAPP score.
Conclusion: Bladder paragangliomas are rare neoplasms that can be confused clinically and histologically with urothelial carcinomas. They may even mimic high-grade urothelial carcinoma with invasive solid nests, especially in transurethral resections with significant artifacts. Although most are non-functional, suspicion of paraganglioma should prompt investigation of catecholamine levels and their metabolites.

E-PS-27-063
Malignant and uncertain malignant potential primary mesenchymal tumours of the kidney in adulthood: a comprehensive review of cases since 1980
V. Macarrón*, G. Escuer-Albero, L. Hato Salmón, B. Popescu, E. García Fernandez, P. González-Peramato
*La Paz University Hospital, Spain

Background & objectives: Malignant and uncertain malignant potential primary mesenchymal tumours of the kidney are infrequent neoplasms with different biology and behaviour. Our aim is to assess the clinicopathological features of these tumours in adults diagnosed at our hospital since 1980.
Methods: Our investigation focused on pathological reports of nephrectomies performed at our hospital since 1980 in order to identify malignant and uncertain malignant potential primary mesenchymal tumours in patients over 18 years, excluding metastatic cases. The clinicopathological features we gathered were age at diagnosis, gender, affected kidney and kidney location.
Results: Among the 4603 nephrectomies performed at our centre in these years, only 10 cases were malignant or uncertain malignant potential primary renal mesenchymal tumours (<0,01%). The majority of patients were women (60%) and the average age was 63 years. The mean tumoural size was 9 centimetres. These neoplasms more frequently located in the left kidney (71%) and in the renal lower pole (56%). The tumoural histology that was diagnosed most often was leiomyosarcoma (40%), followed by synovial sarcoma (30%). The remaining tumour types were angiosarcoma (10%), undifferentiated sarcoma (10%) and fibrous solitary tumour (10%).
Conclusion: The frequency of malignant and uncertain malignant potential primary mesenchymal tumours of the kidney in adulthood is extremely low in comparison to the total number of nephrectomies performed at our institution since 1980. However, its correct differential diagnosis is essential for optimizing multidisciplinary management of these patients. These tumours more frequently affect women and appear at older ages, except for synovial sarcoma, which affects younger individuals. Leiomyosarcoma is the most frequently diagnosed histology, as indicated by other published series.

E-PS-27-064
Evaluating the histological accuracy of percutaneous kidney biopsies in the diagnosis of renal masses
A. Malaviya*, A. Warren, S. Aldujaili
*Cambridge University Hospitals NHS Foundation Trust, United Kingdom

Background & objectives: The role of renal tumour biopsies (RTB) has gained increasing importance. Urologists, are frequently reliant on biopsy results to guide informed treatment decisions. Here we present, a 3 year study evaluating the histological diagnostic accuracy of RTB at our centre.
Methods: All reports for RTB performed between 2017 and 2019 were retrieved from our pathology reporting system. Cases where there was no record of a subsequent resection were excluded from the study. Histology reports of RTB and the nephrectomy were reviewed; noting biopsy adequacy, tumour subtype and grading. Concordance rates were then compared with published literature.
Results: 77 cases were available to investigate; as based on the biopsy results the tumour had been resected at our institute. The diagnostic accuracy rate was found to be 90%. There were only eight non diagnostic cases. The concordance between the biopsy and the resection specimens was 97.4% for tumour subtype. Of the 77 RTB, the majority of renal masses (52) were diagnosed as Clear cell Renal cell carcinoma (RCC). Two cases were not concordant for histological subtype. Comparison of tumour grades showed a concordance of 57% in renal cell carcinomas. The 7 cases reported as urothelial carcinomas showed a 100% concordance on tumour grade.
Conclusion: The high diagnostic yield of RTB proves that this is an accurate and reliable tool in the diagnosis, management and risk stratification of renal masses. A high concordance rate of 97.4% for tumour subtype between the biopsy and nephrectomy is comparable with concordance rates published previously; establishing that reporting standards are being met. The 57% concordance for ISUP/Fuhrman grading in RCC, although on the lower side is within the range recorded in published literature and reflects tumour heterogeneity.

E-PS-27-067
Fluorescence confocal microscopy for the assessment of ureteral and urethral margins in radical cystectomy: a feasibility study
L. Mendes*, R. Almeida Magana, E. Day, A. Ta, G. Shaw, J. Kelly, A. Freeman, A. Haider
*Department of Cellular Pathology, University College London Hospital NHS Foundation Trust, United Kingdom

Background & objectives: Fluorescence confocal microscopy (FCM) allows for remote analysis of fresh-tissue with microscopic resolution within minutes,saving time and resources.Here we correlate confocal and H&E images showing the feasibility of FCM in the assessment of radical cystectomy (RC) ureteral and urethral margins.
Methods: Ten patients who underwent RC at UCLH between April 2023 and May 2023 were selected. FCM was performed using the Histolog® scanner. Image acquisition was standardised and performed by the surgical team. Images were quality checked and assessed for tumour presence by an experienced uropathologist retrospectively and compared to matching PE H&E samples.
Results: Of the 10 cases included, 6 were muscle-invasive urothelial carcinoma. Routine histological assessment showed 2 patients with ureteral margin involvement (one of which had concomitant positive urethral margin). 12 FCM images were taken per specimen (total: 120). After quality check (QC) 73% of the images were considered evaluable.

It was possible to identify CIS in all QC passed images from the 2 patients who had positive surgical margins verified on H&E. Limitations for FCM image analysis included incomplete imaging of the entire luminal circumference in some images. Image assessment took on average 7 min (range 2-20min).
Conclusion: In this proof-of-concept study FCM using the Histolog scanner for surgical margin assessment during RC appears feasible and correlates with H&E analysis. Larger studies are required to validate these results and estimate diagnostic accuracy metrics of this new technology.

E-PS-27-068
Thyroid-like follicular renal cell carcinoma: a rare presentation following neuroblastoma - a case report
T. Micsik*, R. Kiss, M. Csoka, S. Szabo, Z. Jenövari, G. Bedics, G. Vujanic, L. Kuthi
*Semmelweis University Budapest, Hungary

Background & objectives: After neuroblastoma diagnosis, some patients may develop secondary kidney tumours. Thyroid-like follicular renal cell carcinoma (TLFRCC), an emerging but rare subtype, has not been reported in post-neuroblastoma patients. We aim to highlight TLFRCC in this context.
Methods: Our patient had stage 1 neuroblastoma in his early childhood, treated only with radical surgery due to favourable histology. Sixteen years later, he was presented with abdominal pain, revealing a left kidney tumour with hemorrhage on MRI. Despite tumour rupture, negative lymph nodes facilitated successful abdominal surgery. However early local relapse was detected which needed oncological treatment.
Results: Histological analysis revealed predominantly haemorrhagic tissue with eosinophilic tumour cells arranged in follicles, resembling thyroid tissue. Immunohistochemistry showed positivity for PAX8, Cyclin D1, MelanA, and TFE3. Negative markers included TTF1, Thyroglobulin, p63, and ALK. Fluorescent in situ hybridization showed no alterations in TFE3 and EWSR1 genes. Next-generation sequencing (NGS) identified an EWSR1::PATZ1 fusion, confirming the diagnosis of TLFRCC in stage pT1b, pN0.
Conclusion: Our case presents unique features: 1. First TLFRCC reported in a post-neuroblastoma patient. 2. Paediatric TLFRCC cases are exceptionally rare. 3. MelanA expression, unusual in TLFRCC, could mislead toward other diagnoses. 4. NGS identified the characteristic fusion gene, aiding in accurate diagnosis. Our case underscores the importance of considering TLFRCC in post-neuroblastoma kidney tumours, especially when unusual histological features are present.

E-PS-27-069
Epidemiological and histopathological characteristics of urothelial carcinoma of the bladder in women
M. Mohamed lamine*, A.Z. Latreche, K. Chaita, M. Atrous, A. Mahdjoub, S. Bensaci
*EPH Bordj Bou Arreridj, Algeria

Background & objectives: Bladder cancer, predominantly seen in older men, also significantly affects women, often diagnosed with advanced-stage tumours. This study aims to review the histopathological and epidemiological features of bladder urothelial carcinoma (UC) in the female population.
Methods: This retrospective study encompasses 83 cases of female urothelial bladder tumours registered in our department over a period of 8 years and 6 months, from January 1, 2015, to June 30, 2023.
Results: The prevalence of UC tumours among women, in comparison to the total bladder tumour patient population, was 10%. The average age of our patients was 61.65 years, with ages ranging from 22 to 90 years. Cystoscopy was performed on all patients, and histological analysis confirmed urothelial carcinoma in all cases. 12 patients exhibited tumours that infiltrated the bladder muscle, while 77 patients had non-muscle invasive disease. Anterior pelvectomy was conducted in 12 patients, and a single case required cystectomy. The recurrence rate stood at 28%. 4 cases progressed from stage pT1 to pT2, and 6 cases evolved from low grade to high grade.
Conclusion: Our study largely aligns with the existing literature. Bladder cancer, though rare in women, can affect females of any age. Predominantly, patients exhibit high-grade but non-invasive disease, accompanied by a high risk of recurrence.

E-PS-27-070
Urothelial carcinoma associated with carcinoma in situ: epidemiological and pathological characteristics
M. Mohamed lamine*, A.Z. Latreche, K. Chaita, M. Atrous, A. Mahdjoub, S. Bensaci
*EPH Bordj Bou Arreridj, Algeria

Background & objectives: Carcinoma in situ represents a non-invasive, flat malignant neoplasm strictly confined to the urothelial lining.It commonly occurs alongside a bladder tumour.This term is applied to non-invasive lesions that exhibit marked anaplasia of the epithelium without the formation of papillary structures.
Methods: This retrospective study reviewed 43 cases of bladder tumours diagnosed as urothelial carcinoma with associated CIS lesions registered in our department over a period of 8 years and 6 months, from January 1, 2015, to June 30, 2023.
Results: The incidence of urothelial carcinoma associated with CIS lesions was 4%. The age of patients ranged from 42 to 88 years, with an average age of 66.21 years. The cohort consisted of 40 men (93%) and 3 women (7%), indicating a significant male predominance with a male-to-female ratio of 13:1. At diagnosis, 95.1% of the cases were identified as high-grade carcinomas. Among the tumours, 20.9% infiltrated the muscle (stage pT2), while 7% were classified as stage pT3 and another 7% as stage pT4.
Conclusion: The detection of carcinoma in situ in bladder tumours is crucial as it is frequently associated with a poorer prognosis and higher risks of recurrence and progression. Pathologists play a vital role in identifying these lesions to facilitate early intervention strategies.

E-PS-27-071
Renal mass biopsy - about a series of 470 cases
K. Mokeddem*, S. Loughreib, Z.C. Amir
*Pathology Department Mustapha Hospital University Algier, Algeria

Background & objectives: The evolving role of renal mass biopsy and current recommendations.Histologic interpretation of renal mass biopsy: Morphology-based diagnostic approaches.
Methods: Our study revolves around a series of consecutive cases of kidney mass diagnosed at the pathology department of Mustapha University Medical Hospital (Algiers) over a period of five years (January 2012-December 2023). The biopsies come from the imaging department of the same hospital. The indication of the biopsy was made during the multidisciplinary team meeting of onco-urology.
Results: 470 cases, One patient presents VHL disease. 50ù discovered incidentally during Imaging exams. Bilaterality:4 cases.Synchronous metastases:30 % .
Our serie contains different histological types of the WHO 2022 classification:
Clear cell renal carcinoma (70%), papillary carcinoma (10%), chromophobe carcinoma(8%). others: Translocation carcinoma, mucinous tububular and spindle cell carcinoma, collecting duct carcinoma, unclassified carcinomas, clear cell papillary tumours, invasive urothelial carcinoma, nephroblastoma, Well differenciated liposarcoma, solitary fibrous tumour, lung metastatic adenocarcinoma,

mixed epithelial stromal tumour, extramedullary hematopoiesis, leiomyoma with endometriosis,.lymphoma. oncocytoma, angiomyolipoma (one epithelioïd subtype) and metanephric adenoma. Imunohistochemistry and molecular stydies were used in somes cases.
Conclusion: The renal mass biopsy plays an important role in the managment of kidney tumour. Pathologic evaluatios is also important in active surveillance of small renal masses

E-PS-27-072
Tertiary lymphoid structures in socially important prostate diseases
A. Mollova-Kyosebekirova*, M. Koleva, A. Bivolarska, M. Stoilova, D. Dikov
*Department of General and Clinical Pathology, Medical Faculty, Medical University, Plovdiv, Bulgaria

Background & objectives: Tertiary lymphoid structures (TLS) are lymphoid aggregates formed in non-lymphoid tissues in the context of chronic inflammation,autoimmunity or cancer, with unclear value.We examined the presence ofTLS in NIH-categoryIVprostatitis, benigh prostatic hyperplasia (BPH) and prostate adenocarcinoma (PCa).
Methods: We investigated TLS in 152 different cases of prostatic inflammatory and normal specimens, in the context of basic prostate pathology – BPH, prostatic adenocarcinoma PCa, and HP, scored in low and high grade (LG and HG) using the severity of inflammation.
Results: TLS of « classical » type is detected in 46.4% from the patients s HP. It was established an evident connection between the incidence of TLS in the prostate and the degree of HP. In none of the control patients, with normal or low-grade inflammatory prostate, is found TLS. We observed presence of TLS in50.6% of the patients with BPH and 46.7% of the patients with PCa. Statistical analysis shows a significant correlation of the presence of TLS with HG-HP ($p<0.001$). There is lack of significant correlation between the presence TLS with BPH ($p=0.128$) and PCa ($p=1.00$).
Conclusion: We present the first quantitative study of prostate TLS in association with socially important prostate diseases.The results revealed a significant association of the presence of TLS and the degree of HP.TLS present integral part of HG-HP.In the present study, we confirm that TLS are not a constitutive feature of the healthy human prostate. The presence of TLS is induced by antigenic stimuli and external factors and reflects the chronic inflammatory prostate microenvironment.

E-PS-27-073
Bladder paraganglioma: a rare incidental finding
M. Nadia*, M. Hamdani, M. Walha, K. Bel Haj Ali, M. Manita, A. Khabir
*Habib Bourguiba University Hospital of Medicine,Tunisia

Background & objectives: Paraganglioma is a non-epithelial neuroendocrine neoplasm rarely found in the bladder. It can cause haematuria and irritative symptoms associated in some cases with catecholamine-related symptoms. Given the rarity of this tumour, we report a case of Paraganglioma of the bladder.
Methods: A 64-year-old male with a history of benign prostatic hyperplasia presented with painless haematuria. Physical examination revealed only a firm enlarged prostate on digital rectal exam. Ultrasound showed a one centimeter mass developing at the expense of the bladder. The presumptive diagnosis was an urothelial bladder tumour. The patient underwent trans-urethral-resection of bladder tumour (TURBT)combined with trans-urethral-resection of prostate (TURP).
Results: Histological examination of the TURBT specimen revealed epithelioid cells with granular eosinophilic cytoplasm and ovoid nuclei with infrequent mitosis or atypia. These cells were arranged in a nested pattern. They were separated by fibro vascular septa. Immunohistochemistry revealed positivity of tumour cells for chromogranin, S100-Potein, synaptophysin and GATA3. Rare cells showed positivity for Ki67. Paraganglioma of the bladder was the final diagnosis. Accessorily, histological examination of TURP specimens showed stromal and glandular hyperplasia.
Conclusion: Despite its rarity, paraganglioma of the bladder should be suspected in patients with bladder mass associated with catecholamine-related-symptoms. It should be considered in the differential diagnosis of bladder neoplasms. Total cystectomy can be avoided by early diagnosis. Follow-up after tumour removal is recommended due to its frequent recurrence.

E-PS-27-074
Unusual double differentiation in a germ cell tumour
M. Narváez Simón*, A. Remón Love, A. González Fábrega, A. Carrero Castaño, R.M. Ríos Pelegrina
*Upigap-Hospital de Baza-HUVN, Spain

Background & objectives: Postpuberal teratoma has been described to metastasize either as pure teratomatous or as mixed-type germ cell tumour(GCT).Development of somatic-type malignancy is a rare finding.We report a case of a testicular pure teratoma presenting with mixed-GCT with somatic-type malignancy(SM) retroperitoneal metastasis.
Methods: A 21-year-old male with long-term lower back pain presented with a palpable abdominal mass and 8kg weight loss in 6 months. Abdominal Computed Tomography scan revealed a heterogeneous 65mm retroperitoneal mass with microcalcifications. In a testicular ultrasound, a 3mm solid nodule with calcifications was identified in the left testicle. Unilateral orchiectomy and resection of the retroperitoneal mass were performed.
Results: Histological examination of the orchiectomy specimen revealed postpuberal teratoma with mature glandular and squamous epithelial component limited to testis. The retroperitoneal mass was diagnosed as a metastasis of mixed GCT with embryonal carcinoma component (10%) and teratoma (90%) with somatic-type malignancy consisting of areas of chondrosarcoma and nephroblastoma with epithelial and blastema component.
Conclusion: Up to 37% of pure teratomas present with metastases,which may exhibit any type of GCTs.Somatic-type malignant transformation in mixed-GCTs occurs in around 3–6%, with carcinomas being the most common malignancy in metastasis followed by rhabdomyosarcomas.Larger tumour size has been correlated with malignant transformation.However,despite having a 3mm primary tumour,our patient presented a 65 mm metastasis with SM-transformation to chondrosarcoma and nephroblastoma.The association between those two malignancies has been infrequently described and it seems to have an aggressive potential and worse prognosis.

E-PS-27-076
Testicular lymphoma: a 5-year retrospective of a Portuguese University Hospital and reference centre for testicular pathology
S. Neves*, N. Chiote, D. Sá, F. Emanuel Costa, N. Jorge Lamas
*Unidade Local de Saúde de Santo António (ULSSA), Portugal

Background & objectives: Malignant lymphoma is a rare testicular neoplasm, comprising up to 5% of the cases. The majority are Diffuse Large B-cell Lymphoma of the testis (T-DLBCL), accounting for 80-90% of all primary testicular lymphomas, usually harboring a non-germinal centre immunophenotype (70-90%).
Methods: We identified five testicular lymphoma cases diagnosed at our institution from 2019 to 2024. The patients were between 64 and 78 years old, the majority below 70 years old. Four of the cases were restricted to the testicle, while one also had intra-abdominal involvement.

Results: In our series four cases were diagnosed as T-DLBCL and one had T/NK cell lymphoma. Half of the T-DLBCL had a germinal-centre B-cell–like subtype (CD10 and BCL-6 negative), while the others had an nongerminal centre B-cell–like subtype (CD10 and BCL-6 positive). The cytogenetics study for MYC gene rearrangement was negative in the 3/3 cases in which the test was performed. The T/NK lymphoma showed positivity for CISH EBER. Since this patient had a poorly described previous history of hard palate tumour dating 23 years before, the possibility of a nasal-type extranodal T/NK cell lymphoma relapse was also equated, but its long evolutionary time makes this hypothesis very unlikely.
Conclusion: In line with the literature nearly all of testicular lymphoma cases in our series were T-DLBCL. Notwithstanding the sample size, more of the germinal centre B-cell–like subtype T-DLBCL were diagnosed, when compared to other studies. One patient had T/NK lymphoma, possibly of the extranodal nasal-type. All of the patients were submitted to radiotherapy during a short period of time and are currently under chemotherapy. Their condition remains stable.

E-PS-27-077
Papillary urothelial carcinoma with grade heterogeneity: concordance between manual assessors, automated image analysis and urine cytology
N.J. Nguyen*, E. Olkhov-Mitsel, C. Sherman, J. Sweet, T. van der Kwast, M.R. Downes
*Department of Laboratory Medicine and Pathobiology, University of Toronto, Canada

Background & objectives: Papillary urothelial carcinoma with at least 5% high grade (HG) component is classified as HG per WHO 2022 recommendations. We assessed the interobserver reproducibility of percent HG, and evaluated the concordance between manual assessors, automated image analysis and urine cytology.
Methods: Four uropathologists and one resident independently and blindly assessed for percent HG of twenty papillary urothelial carcinomas with/without heterogeneity (1 H&E slide/case). Slides were scanned at 20X on Aperio Scanscope AT and analysed by QuPath v0.3.2, which generated automated percent HG based on urothelial nuclear enlargement (50 um diameter threshold). Concordance with urine cytology was evaluated using Mann-Whitney U tests.
Results: Original reported grades were: low grade (LG)-4, HG-5, heterogeneous-11. Assessment of percent HG as a continuous variable yielded substantial agreement for 5 manual raters (Fleiss κ 0.890). The pure LG and HG cases had the highest reproducibility. With percent HG estimates between 2-10%, the interobserver agreement was the lowest. Moderate interrater agreement was achieved (κ 0.407) when a binary grading at 5% cut-off was employed. Automated estimates using QuPath showed substantial agreement with manual interpretation when assessing grade as a continuum (κ 0.862), and fair agreement with the 5% threshold (κ 0.234). Urine cytology (negative, n=11; atypical, n=8) did not correlate with mean/median manual estimates (p=0.840) or automated estimates (p=0.492).
Conclusion: Interobserver reproducibility and concordance with automated analysis were excellent when percent HG was assessed as a continuum, but moderate and fair when using binary classification at 5% cutoff. Our findings also demonstrated that urine cytology cannot detect high grade components in heterogeneous cases. The lack of reproducibility in classifying papillary urothelial carcinoma as LG or HG per WHO 2022 recommendations has downstream clinical implications. Further assessment and refinement of algorithms may contribute to rectifying this discordance.

E-PS-27-078
How does smooth muscle invasion quantification of transurethral resection of bladder tumour specimens influence staging outcome on cystectomy?
S. Niculae*, L. Mitrache, G. Berdan, A. Petrescu
*Department of Pathology, Colentina University Hospital, Bucharest, Romania

Background & objectives: The purpose of this study is to determine if the smooth muscle fibers quantity identified on transurethral resection of bladder tumour (TURBT) specimens can predict the staging outcome in patients who underwent radical cystectomy for invasive urothelial carcinoma.
Methods: This paper is a retrospective-comparative study that selected 24 patients diagnosed with pT2 urothelial carcinoma on TURBT. The patients were diagnosed between 2021-2023 in a single urology centre. The 24 patients were divided into two groups according to the pathological staging on cystectomy specimens: "under" pT2 group with 8 cases and "at least" pT2 group with 16 cases.
Results: In order to integrate all data, the TURBT slides were collected and examined under microscope. Using eyeballing measurements, the percentage of smooth muscle fibers in the total mass resected was counted and how much of it was tumour invaded. The two groups were statistically compared. The total amount of smooth muscle fibers in the two groups had almost the same average: 45,11% ("under" pT2) and 51,21% ("at east" pT2). It was observed that the less smooth muscle invasion, the lower the cystectomy stage. Moreover, 75% of patients in the first group had less than 60% tumour invaded fibers, whereas all patients in the second group had more than 60%.
Conclusion: Quantification of tumour invaded smooth muscle fibers on transurethral resection of bladder may predict the pathological staging outcome later on radical cystectomy, however, all these data should be validated in larger studies.

E-PS-27-079
Mucinous, tubular, and spindle cell renal cell carcinoma - importance of accurate diagnosis: case report
G. Nikolic*, Đ. Radisavčević, M. Miler, S. Radojevic Skodric, V. Mijajlovic
*Institute of Pathology, Faculty of Medicine University of Belgrade, Serbia

Background & objectives: Mucinous, tubular, and spindle cell carcinoma of the kidney is a rare and distinct subtype of renal cell carcinoma characterized by unique morphological features. This entity is classified under the category of low-grade renal epithelial neoplasms with generally favourable prognosis.
Methods: Here we present a 66-year-old woman who was admitted to the hospital because of the presence of a non-homogeneous, expansive, subcapsularly localized and opacified tumoural change, in the upper pole of the kidney, 46 mm in diameter. The described tumour was detected accidentally, during a regular systematic examination. A biopsy was performed, and the specimen was sent for pathohistological examination.
Results: Histological examination revealed tumour composed of admixed tubular formations and spindle cells embedded in a mucinous stroma. Tumour was localized within the kidney, without perirenal, hilar of vein expansion. Immunohistochemical analysis revealed positivity for AMACR, CD10, CK7, CK19, PAX-8 and Vimentin. The morphological findings, in accordance with immunohistochemical analysis, corresponded to a mucinous tubular and spindle cell renal cell carcinoma (MTSRCC).
Conclusion: Mucinous, tubular, and spindle cell carcinoma represents a unique subtype of renal cell carcinoma with predominantly indolent behaviour and favourable outcomes. Accurate diagnosis through careful histological and immunohistochemical examination is crucial for distinguishing MTSCC from more aggressive forms of kidney cancer. Awareness of this rare subtype is important for optimizing patient management and avoiding overtreatment.

E-PS-27-080
Undifferentiated renal cell carcinoma with medullary phenotype or medullary renal cell carcinoma - what is the difference? A case report
G. Nikolic*, L. Ćuković, J. Stefanović, V. Mijajlovic, S. Radojevic Skodric
*Institute of Pathology, Faculty of Medicine University of Belgrade, Serbia

Background & objectives: Renal medullary carcinoma is a severe type of non-clear cell kidney cancer predominantly found in young adults. It is closely linked with the sickle cell trait. The prognosis for RMC is dire, with surviving less than a year on average.
Methods: We report the case of a fifteen-year-old female, who presented with hematuria and abdominal pain. A nodular mass on the right kidney with lymphadenopathy, and scattered nodules in the lungs was observed on CT. Radical nephrectomy with regional lymphadenectomy were performed. On gross examination, the tumour was 80 mm in maximal diameter, whitish in color with necrosis and hemorrhage.
Results: Histologically, the tumour was composed of large cells with prominent nucleoli, high degree of pleomorphism, and mitotic activity. A dense fibrous stroma and desmoplastic reaction surrounded the tumour cells, and osseous metaplasia was noted, infiltrating perirenal fat tissue. Immunohistochemically, the tumour showed positivity for CKAE1/AE3, Pax-8, Pax-2, CK 7 focally, EMA, GLUT-1, Vimentin, and AMACR. The loss of INI-1 (SMARCB1) expression was noted. A diagnosis of undifferentiated renal cell carcinoma with a medullary phenotype was made. Although the age, presence of metastasis, histopathological, and immunohistochemical findings are in favour of SMARCB1 deficient renal medullary carcinoma, a definitive diagnosis could not be made due to the lack of information about hemoglobinopathy.
Conclusion: This case highlights the diagnostic challenges associated with undifferentiated renal cell carcinoma with a medullary phenotype. In our case, the absence of definitive genetic information, such as hemoglobinopathy status, left the diagnosis presumptive despite strong suggestive evidence. This emphasizes the importance of comprehensive genetic testing in the diagnosis of renal medullary carcinoma.

E-PS-27-081
A challenging case about testicular tumour of adrenogenital syndrome: a clinico-pathological report
M. Njima*, A. Ben Mabrouk, S. Mabrouk, S. Ben Hammouda, A. Bellalah, A. Zakhama
*Fattouma Bourguiba University Hospital, Monastir, Tunisia

Background & objectives: Testicular tumour of adrenogenital syndrome (TTAGS) is a rare, benign anomaly usually presenting as bilateral testicular masses in young men with endocrine disorders. Histologically it resembles Leydig cell tumour (LCT). Consequently, distinction between these tumours can be challenging for pathologist.
Methods: A 16-year-old male with a history of precocious puberty and polycythemia without confirmed endocrine disorder. He was admitted to the Urology Department at the University Hospital of Monastir for the management of two palpable bilateral testicular masses. Testicular ultrasonography demonstrated these lesions as hypoechoic infiltrative nodules with invasion of the spermatic cord. These lesions were managed by tumour enucleation.
Results: On macroscopy, all the surgical specimens were nodular well circumscribed, with pale-tan color and measuring between 1cm and 2 cm in diameter. A frozen section was carried out and showed aspects of LCT of the testis. The final histological analysis confirmed the initial diagnosis. It showed aggregates of tumour cells separated by bands of dense fibrous tissue. The cells were large, with finely abundant granular eosinophilic cytoplasm. The nuclei were round, showing focal marked atypia. There was no mitotic activity or necrosis. But considering the patient's history and clinical presentation coupled with the histologic findings, TTAGs was ultimately concluded.
Conclusion: Our case, although dealing with a rare case, illustrates the importance of careful follow-up examinations and observation when treating patients with adrenogenital syndrome. Patients are generally young men with endocrine disease presenting with bilateral orchialgia and palpable testicular lesion. The close histological similarity between TTAGS and LCT has been described by numerous authors. The diagnosis of TTAGS is determined by patient history and clinical presentation. Differentiation between these tumours is of critical importance because their behaviour dictates different management strategies.

E-PS-27-082
A paratesticular mass diagnosis supported by molecular pathology
G. Nogueira Fontinha*, J. Amaral, A.C. Lai, R. Almeida, V. Sousa
*Institute of Anatomical and Molecular Pathology, Faculty of Medicine of the University of Coimbra, Coimbra, Portugal

Background & objectives: Paratesticular rhabdomyosarcoma is a rare tumour mainly affecting children. It encompasses the embryonal, alveolar, pleomorphic and spindle cell/sclerosing subtypes and several chromosomal abnormalities have been reported such as gains of the 2, 8, 11,12 and 20.
Methods: 17-year-old male presenting with painless tumefaction of the scrotum with 4 months without other symptoms. Ultrasound: solid vascularized paratesticular mass with 7.4cm compressing the testi. CT-scan: mass with well-defined limits and preservation of scrotal tunics with necrotic areas. PET/CT-scan: suspicion for secondary location in interaortocava lymph nodes. Radical orchidectomy is perfomed with lymph node and bone marrow staging.
Results: Gross examination: preserved epididymis and testi; paratesticular 7.5cm yellowish and elastic mass with congestive areas. Histology: mass composed predominantly by medium cells with scant cytoplasm and irregular large nuclei with prominent nucleoli in sheets or nodules; presence of multinucleation and focal anaplasia as well as rhabdomyoblastoid cells; necrosis and fibrosis are 20% of the mass; infiltration of the epididymis and vascular invasion; expression of vimentin, desmin, glypican and myogenin with negative germinal cell tumours markers. FISH: no FOXO1/PAX3/PAX7 rearrangements; amplification of c-MYC and MDM2 (after CGH). CGH array: gains of chromosomes 8, 20 and 12q15 region. Lymph nodes and bone marrow were clear of neoplasia.
Conclusion: In the light of the histological examination and molecular analysis the diagnosis of paratesticular embryonal rhabdomyosarcoma was made. Molecular testing is particularly important in rhabdomyosarcoma because embryonal rhabdomyosarcoma lack PAX3::FOXO1 and PAX7::FOXO1 fusions while alveolar rhabdomyosarcoma usually harbours them and they are of negative prognostic significance. The study of lymph nodes is key for the IRS staging that is highly predictive of outcome. Our patient was staged as Group I (IRS) and has started chemotherapy.

E-PS-27-083
Pure yolk sac tumour in retroperitoneum - primary or secondary?
D. Oflas*, M.F. Hant
*Erzurum City Hospital, Department of Pathology, Turkey

Background & objectives: Yolk sac tumours (YSTs) are malignant neoplasms originating from germ cells. YSTs can manifest either primarily or secondarily in extragonadal sites, with retroperitoneal occurrence being rare. Herein, we present a case of pure YST retroperitoneal metastasis.
Methods: A 28-year-old male presented to the emergency department with abdominal pain. Physical examination revealed a palpable retroperitoneal mass. Computed tomography (CT) scan showed a solid mass adjacent to the right vena cava, measuring 100x90 cm. Pathological evaluation identified a mass in the patient's right testicle radiologically.
Results: Macroscopically, the mass appeared ill-defined, fragmented, with solid grayish-white areas and mucoid secretion-filled cystic regions. Histological examination revealed extensive necrosis and various growth patterns (microcystic, myxomatous, endodermal sinus, and solid). Neoplastic cells exhibited diverse features, including flattened cells forming anastomosing cords, spindle/stellate cells in a myxoid

background, Schiller-Duval bodies, and sheets of polygonal clear to amphophilic cytoplasmic cells. Nuclear pleomorphism and atypical mitotic figures were prominent. Immunohistochemically, pancK, AFP, and glipican 3 stained positive in neoplastic cells. Despite the postpubertal period, no accompanying germ cell neoplasia was detected.
Conclusion: Retroperitoneal YSTs are rare primary or secondary malignant germ cell neoplasms. In our case, a testicular mass was identified by scrotal ultrasound following the pathological diagnosis, but surgical intervention was precluded due to advanced disease. Although pure YST metastasis to the retroperitoneum is uncommon, it should be considered in the differential diagnosis of retroperitoneal tumours. Clinical and radiological assessments aid in distinguishing between primary and secondary lesions.

E-PS-27-084
An infrequent diagnosis in an unusual location: a case report
A. Ordoñez*, B. Aguiar, M. Manrique, M. Rezola, M. Conde, S. De Burgos González, A. Val-Carreres Castellote, I. Ruiz Díaz
*Hospital Universitario Donostia, Spain

Background & objectives: Paratesticular tumours are uncommon entities. Ovarian-type paratesticular lesions are called Müllerian-type, which origin is not well known. There are theories attributed to a Müllerian metaplasia of the tunica vaginalis and others that originate from Müllerian remains of paratesticular soft tissues.
Methods: An 18-year-old male, with a previous left orchidopexy in 2013, consulted for pain and an increase in size of the left testicle. Imaging studies revealed a 7 cm intra-scrotal extra-testicular mass, and it was decided that a left orchiectomy should be performed. The material was widely sampled and fixed in formaldehyde. Haematoxylin-eosin and immunohistochemical stainings were performed.
Results: The histological sections showed an intra-scrotal neoplasm of extra-testicular location that respected the testis, rete testis, epididymis, and spermatic cord. The lesion presented as a neoplastic proliferation of infiltrative solid-cystic architecture with a papillary-tubular growth pattern, embedded in a stroma with myxoid change. The epithelial lining consisted of columnar cells, with slight pleomorphism, broad eosinophilic and, in other areas, pale-clear cytoplasm with nuclear atypia and loss of polarity. Calcifications and few foci of mucinous material were observed. The immunohistochemistry techniques results confirmed the diagnosis of paratesticular ovarian type serous cystadenocarcinoma.
Conclusion: Paratesticular tumours are uncommon, and ovarian type tumours are even less common. Specifically, paratesticular serous cystadenocarcinomas of ovarian type are rare lesions. Given their low frequency and the limited knowledge about them, their clinicopathological and therapeutic management remains an enigma.

E-PS-27-086
Reporting the status of non-neoplastic testicular parenchyma in tumoural radical orchiectomies (ROs) as screening for infertility factors: a study of 56 consecutive cases with corresponding semen analysis (SA)
G. Paner*, J.W. Kwon
*Department of Pathology and Reproductive Endocrinology and Infertility Clinic Laboratory, University of Chicago, USA

Background & objectives: A higher proportion of testicular cancer patients has infertility issues. NCCN recommends sperm banking but a substantial number opts not to undergo SA. We assessed the value of histologic evaluation of non-neoplastic testis in ROs to predict sperm count.
Methods: 56 RO patients had corresponding SA results. Cases were reviewed for seminiferous tubules: 1) containing sperm cells & 2) showing maturation to at least spindled spermatids. Presence of sperm cells and maturation were quantified as +1 (1-10%), +2 (11-50%) and +3 (>50%). For SA, definitions for oligospermia (mild, moderate or severe) and azoospermia were based on the 6th WHO definitions.
Results: The patients were 16-45 years old (mean 27). The tumours included seminoma (41%), NSGCTs (55%) or others (4%). SA showed 70% normal sperm count and 30% abnormal sperm count showing mild (5%), moderate (2%), severe (14%) oligospermia, or azoospermia (9%). Histologically, 71% (40/65) of ROs showed seminiferous tubules with +3 sperm maturation. 82% (33/40) of these ROs with +3 sperm maturation had normal sperm count. No ROs with +3 sperm maturation showed azoospermia. Of 16 with no normal seminiferous tubules, 62% (10/16) had abnormal sperm count and 31% (5/16) had azoospermia. All 5 cases of azoospermia had similar histologic pattern revealing atrophic seminiferous tubules with no cells in tubular lumen.
Conclusion: In this first ever study, there is good correlation between histologic presence of sperm maturation in tubules and sperm cell count in SA. The study suggests that tubular sperm status in tumoural testis may predict the status in the contralateral testis. If further validated, this study highlights the value of commenting on the spermatogenesis status in the non-neoplastic parenchyma in ROs as a cost-effective screening tool for sperm cell count.

E-PS-27-088
Prostatic adenocarcinoma with focal pleomorphic giant cell features is prone to microsatellite instability
S. Peng*, C. Wu, M. Hou, L. Zhao, L. Lei, X. Qiu, J. Yang, Y. Fu
*China

Background & objectives: Prostatic adenocarcinoma with focal pleomorphic giant cell features is rare and clinically highly aggressive. Here we aim to elaborate on the clinicopathologic characterization of prostatic adenocarcinoma with this rare feature, and explore the relationship between this subtype and microsatellite instability.
Methods: Since these focal pleomorphic giant cell features are more likely to appear in prostate cancer tissues with high Gleason scores, we searched our pathological tissue bank and 1812 cases of Gleason pattern 5 (including 1489 biopsy and 323 radical prostatectomy samples) were retrieved. Clinical Information are collected, IHC and 2nd generation sequencing are used to analysis the samples.
Results: We identified 13 cases of prostate carcinoma with focal (5~30%) pleomorphic giant cell features. All 13 samples had a Gleason pattern 5. Five of 13 (41.7%) patients received preoperative neoadjuvant therapy and they had partial or no therapeutic response. Four of the cases showed a loss of DNA mismatch repair (MMR) proteins expression and two more cases showed a decreased expression of them, and MMR proteins were relatively reduced expressed in the component of pleomorphic giant cell. Besides, 4 of 13 patients possessed high microsatellite instability (MSI-H), and another 1 patient showed low microsatellite instability (MSI-L). DNA damage repair gene mutations are also common in this rare subset of tumours.
Conclusion: Prostatic adenocarcinoma with focal pleomorphic giant cell features is prone to microsatellite instability. Microsatellite stability/MMR defects should be considered as a standard test in this situation for subsequent personalized treatment strategies like PD-L1 antagonists and other immunotherapies.

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E-PS-27-089

In search of identity: a case report of an enigmatic oncocytic kidney tumour

M.C. Popelea*, A. Borda, M. Decaussin-Petrucci, A. Loghin
*Mures Clinical County Hospital, Romania

Background & objectives: In recent years, enhanced comprehension of renal tumours has been achieved through advancements in molecular pathology. This progress has led to the introduction of several entities, particularly within the "oncocytic tumours" classification, as outlined in the WHO 2022 classification system.
Methods: A 52-year-old female patient presented in November 2023 at the Urology Department for a 4 cm tumoural mass located in her right kidney. A partial nephrectomy was performed, and the specimen was sent to our Pathology Department for microscopical examination and final diagnosis. On gross examination the tumoural mass was relatively well-defined, non-encapsulated, measuring 44 mm at its maximum diameter.
Results: Microscopically, the tumour presented solid and tubular architecture, consisting of cells with eosinophilic, granular cytoplasm and round, relatively uniform nuclei with visible nucleoli at 20x magnification. Focally, the tumoural cells presented scarce cytoplasm and „hobnail" appearance, with foamy macrophages among these structures. The tumoural cells were positive only for PAX8 and CKAE1/AE3 and were negative for CD117, CK7, AMACR, CD10, TTF1, Vimentin, CK20, TFE3, ALK, Melan A and HMB45, while the expression of FH and SDHB was preserved. Molecular analysis with a large panel using NGS (Next Generation Sequencing), did not detect any genetic alterations, and all clinically significant somatic variants, including mTOR and TSC1/2, were absent.
Conclusion: Due to the immunohistochemical and molecular profile, this tumour could not be classified into any of the subtypes already described in the category of "other oncocytic tumours of the kidney". However, since the presence of mTOR mutation is not an essential diagnostic criteria, this tumour could be part of this heterogeneous group of tumours, having an indolent behaviour. Even though the understanding of renal tumours has improved greatly, the current case is a major example that further research is needed.

E-PS-27-090

Hemangioblastoma of the kidney – clinical, pathological, and genetic features

B. Pósfai*, F. Sánta, A. Jenei, G. Forika, A. Fintha, Á. Somorácz, B. Dénes, F. Salamon, K. Eizler, N. Giba, D. Semjén, I. Illyés, A. Kovács, G. Munkácsy, L. Kuthi
*Hungary

Background & objectives: Hemangioblastoma (HB) is a benign central nervous system (CNS) tumour typically associated with mutations in the von Hippel-Lindau (VHL) gene. Although rare outside the CNS, the pathological and genetic features of such cases remain poorly understood.
Methods: We analysed four kidney parenchyma-derived HBs. Demographics, clinical presentation, and follow-up data were extracted from medical records. Hematoxylin-eosin stained slides were assessed, and immunophenotyping was conducted using CA9, inhibin, AE1/AE3, CD10, CD56, PAX8, S100, MelanA, HMB45, CD117, FH, SDHB, and brachyury antibodies. Mismatch repair (MMR) deficiency was examined through MMR protein expression. Whole-exome sequencing was performed to detect pathological mutations.
Results: Our cohort comprised 3 male and 1 female patients, with a median age of 49 years (range: 35-65 years). No data on VHL disease were available. Tumours, with a median size of 25.5 mm (range: 24-42 mm), displayed clear vacuolated cytoplasm with a vascular component. Each tumour exhibited well-defined boundaries, encapsulated by a thick pseudocapsule. Immunostaining consistently revealed expression of PAX8, inhibin, AE1/AE3, S100, and cytoplasmic brachyury. CA9 positivity was noted in three tumours. MMR proteins remained intact across all cases. WES analysis detected no pathogenic mutation in VHL or other cancer-related genes. No cancer-related deaths or progressions were observed in any patients.
Conclusion: Renal HB is a rare tumour posing a diagnostic challenge. Histologically, renal HB resembles to low-grade clear cell renal cell carcinoma (ccRCC) and shares expression of PAX8, pancytokeratin, and CA9. However, renal HB uniquely exhibits diffuse positivity for inhibin, S100, and lacks VHL mutation. Its favourable prognosis underscores the importance of distinguishing it from ccRCC to prevent unnecessary treatment interventions. Further research is warranted to elucidate the underlying genetic mechanisms.

E-PS-27-091

Case series of micropapillary urothelial carcinoma: a rare and aggressive subtype of bladder cancer

A. Raicea*, A. Tătar, A. Loghin, A. Borda
*George Emil Palade University of Medicine, Pharmacy, Science and Technology of Târgu Mureș, Romania

Background & objectives: Micropapillary urothelial carcinoma of the urinary bladder (MPUC) is a rare subtype of urothelial carcinoma (UC), accounting for 0.6-2.2% of all bladder cancers. It is characterized by its aggressive nature, with a high metastatic potential.
Methods: We present seven cases of MPUC from 1133 cases of UC diagnosed at the Pathology Department of Mures Clinical County Hospital, Târgu Mureș, Romania, between 2017-2021. In four cases the characteristic aspect of MPUC was present on transurethral resection of the bladder (TURBT) and in three cases only in the cystoprostatectomy specimens. All specimens were processed in the Pathology Department.
Results: On microscopy, the tumoural cells were arranged in small nests and micropapillae lacking fibrovascular core, surrounded by lacunae resembling vascular invasion. Multiple nests in the same lacunar space were common. The cells had peripherally located nuclei and marked atypia, focally with intracytoplasmic vacuoles, forming ring-like structures. All 7 patients were male, with a median age of 63 years old. On cystectomy specimens, all 3 cases were associated with urothelial carcinoma in situ; the pathological stage was advanced (pT3a and pT4), with lymph node metastasis.
Conclusion: MPUC is a rare subtype of UC, characterized by specific morphological features. Considering that most of MPUC are muscle-invasive at the time of diagnosis frequently with lymph node metastasis, the preferred treatment for all these patients is radical cystectomy with lymph node dissection, even if no invasion of the muscularis propria is observed in TURBT specimens. Any amount of micropapillary feature within UC must be reported due to its association with aggressive behaviour and unfavourable prognosis.

E-PS-27-092

Mucinous tubular and spindle cell carcinoma, with spindle cell-dominant morphology: a diagnostic challenge

M. Rodrigues*, I. Andrade
*Unidade Local de Saúde da Lezíria, Portugal

Background & objectives: Mucinous Tubular and Spindle Cell Carcinoma (MTSCC) is a rare (less than 1% of renal neoplasms), indolent renal neoplasm. Cases with spindle cell–dominant morphology require differentiation from sarcomatoid change in renal cell carcinoma, emphasizing the significance of accurate diagnosis.
Methods: We submit a case of a 69-year-old woman who presented to the emergency department with abdominal pain and decreased urinary output. A CT scan revealed a 20x17.5x15.3cm left renal mass with

well-defined contours, predominantly cystic, with contrast-enhancing solid peripheral areas, suggestive of malignancy (Bosniak Class IV renal cyst). A radical nephrectomy was performed.
Results: A left radical nephrectomy specimen weighing 3450g revealed a well-circumscribed tumour measuring 23x25x11cm. Central necrohaemorrhagic regions contrasted with yellow-brown solid peripheral areas, pushing against the renal capsule without infiltration. Microscopic analysis showed a neoplasm primarily comprising spindle cells with mild nuclear pleomorphism and occasional prominent nucleoli. Epithelial elements were focal, appearing as tubular structures with slit lumens, within a myxoid stroma with foamy macrophage clusters. No mitosis nor lymphovascular invasion was observed. Immunohistochemistry indicated tumour cell expression of CKAE1/AE3, CK7, Vimentin, PAX8, and focal P504S, with negativity for CD10, SMA, HMB-45, MART-1, Synaptophysin, and Chromogranin A. The diagnosis rendered was MTSCC. Follow-up (6 months) showed no signs of disease recurrence.
Conclusion: MTSCC is a rare neoplasm, exhibits distinct pathogenesis and variable morphologic variants, including the spindle cell-dominant morphology. High-grade MTSCC features increased mitotic count, necrosis, vascular invasion, high-grade nuclei, and adverse growth patterns, often associated with CDKN2A/CDKN2B deletion. Surgical intervention remains pivotal due to its indolent nature. Awareness of MTSCC's diverse presentation is crucial to avoid misdiagnosis and ensure appropriate treatment, given its differential diagnosis spanning from benign (e.g. angiomyolipoma) to aggressive (e.g. sarcomatoid change of renal cell carcinoma) neoplasms.

E-PS-27-093
Statistical analysis of the incidence of malignant neoplasm of the prostate gland in the Sumy region
A. Romaniuk*, M. Yasnikova, Y. Kudriavtsev, A. Ponyrko, R. Mychailenko, A. Yaremenko
*Sumy State University, Ukraine

Background & objectives: Prostate cancer (PCA) is one of the most common cancers in the world. According to the World Health Organization, it accounts for 14.5% of all cancers in men.
Methods: Study of statistical data on the incidence of prostatic hyperplasia in the population of Sumy region for the period from 2019 to 2023. The work used the methods of multifocal biopsy of the prostate, histology and immunohistochemistry of prostate tissues, and MRI of the pelvic organs with contrast.
Results: During the period from 2019 to 2023, 2,430 people with prostate cancer and 5,735 people with benign prostatic hyperplasia were diagnosed in the Sumy region. According to the epidemiological distribution of prostate adenoma and prostate cancer in the Sumy region, the city of Sumy and the Sumy district have the highest incidence rates. Mortality rates from prostate cancer in Ukraine are 41 cases per 100,000 population.
Conclusion: Statistical indicators of the incidence rate of prostate cancer depend on the level of accessibility of patients to qualified medical care.

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E-PS-27-094
Sarcomatoid urothelial carcinoma with heterologous components: case report of a rare and aggressive subtype of urothelial carcinoma
D. Sá*, S. Neves, M. Mexia, X. Wen, F.E. Costa, J.R. Vizcaíno
*Anatomic Pathology Service, Pathology Department, Unidade Local de Saúde de Santo António, Portugal

Background & objectives: Sarcomatoid urothelial carcinoma is a rare and aggressive subtype of urothelial carcinoma. It is characterized by areas that are indistinguishable from sarcoma with features varying from the nondescript spindle cell pattern to those of an undifferentiated pleomorphic sarcoma.
Methods: We report a case of a 66-year-old man that was referred to a urology consultation due to symptoms of dysuria and polyuria and a polypoid lesion found on vesical ultrasound. Cystoscopy showed a 5cm lesion on the right lateral wall of the bladder. Cytological examination of the bladder washing was positive for high grade urothelial carcinoma.
Results: Following the cytological result the patient was submitted to a transurethral resection of the bladder tumour (TURBT). We received a TURBT specimen with 40g comprising multiple irregular and tan fragments. Histologic examination showed a urothelial carcinoma with papillary and solid patterns and focal divergent glandular differentiation. There was necrosis and sarcomatous areas with heterologous components such as osteosarcoma and chondrosarcoma. The carcinoma invaded the subepithelial connective tissue and there was no evidence of muscularis propria invasion. Immunohistochemistry revealed expression of CK7, GATA3, CK20 (weak) and p53 (mutant-type) in the epithelial component and for SATB2 in the osteosarcoma heterologous component and no immunoreaction of PAX8 and WT1.
Conclusion: Sarcomatoid urothelial carcinoma can infrequently have heterologous components, the most common being osteosarcoma, followed by chondrosarcoma, rhabdomyosarcoma, leiomyosarcoma, liposarcoma and angiosarcoma. Heterologous components should be acknowledged in the pathology report as it has been suggested they can impart a more adverse behaviour. Sarcomatoid urothelial carcinoma frequently presents as advanced disease and has a poor outcome with a reported 5-year cancer-specific survival of 28% and a median overall survival of 14 months. Our patient is still alive 5 months after surgery.
E-PS-27-095

Succinate dehydrogenase-deficient renal cell carcinoma: case report of a rare kidney neoplasm
D. Sá*, G. Carrola, N. Chiote, F.E. Costa, J.R. Vizcaíno
*Anatomic Pathology Service, Pathology Department, Unidade Local de Saúde de Santo António, Portugal

Background & objectives: Succinate dehydrogenase-deficient renal cell carcinoma (SDH-DRCC) was first described as an emerging and provisional renal entity in 2013 by the ISUP. SDH-DRCC has been reported in patients of all ages but occurs more commonly in the young.
Methods: We herein report a case of a 35-year-old woman that was referred to a urology consultation due to a palpable and visible left flank mass without pain or haematuria. A CT scan was performed and showed a 12cm, lobulated, heterogeneous renal lesion with calcifications. The patient was then submitted to a total nephrectomy.
Results: We received a total nephrectomy specimen showing a solid capsulated neoplasia on the lower pole of the kidney with 11,5 cm and a heterogeneous cut surface with white and tan areas. The neoplasia was friable, showed calcification and was limited to the kidney. At histologic examination the neoplasia presented solid and tubular architecture, cells with eosinophilic and sometimes vacuolated or flocculent cytoplasm and inconspicuous nucleoli (grade 1 WHO/ISUP). Immunohistochemistry revealed positive reaction for PAX8 in the neoplastic cells and negativity for CAIX, CD117, CK7, CK20, CK34βE12, SMA, HMB-45, TFE3 and RCC. There was loss of expression of SDHB in the neoplastic cells.
Conclusion: Immunohistochemistry for SDHB is negative whenever there is biallelic inactivation of SDHA, SDHB, SDHC, SDHD, or SDHAF2, which is rarely a somatic-only event and almost always occurs in the setting of germline mutation. Most cases are indolent, but high-grade transformation (found in up to one third of cases), tumour

necrosis, and sarcomatoid change are associated with a high risk of metastasis—up to 70%. Our patient was referred to a genetic consultation and is alive 6 months after the surgery.

E-PS-27-096

Uncommon testicular tumours: a Tunisian centre experience

G. Sahraoui*, M. Ben Thayer, A. Khemir, I. Abbes, M. Dkhil, R. Doghri, H. Azaiez, L. Charfi, K. Mrad
*Pathology department Salah Azaiez institute Tunisia / Precision Medicine and Oncology Investigation Laboratory, Tunisia

Background & objectives: Testicular sex cord-stromal tumours (TSCST) are rare primary testicular neoplasm, accounting for less than 4% of all testicular tumours.They include a wide spectrum of tumours. We aimed to review and discuss the clinicopathological characteristics of TSCT diagnosed in our institution.
Methods: We retrospectively assessed all the cases of patients operated on for TSCST in Salah Azaiez Institute in a 10-year period (2013-2023). All the histopathology reports of the enrolled patients were reviewed for data collection.
Results: We reported four cases of TSCST. Three patients were children aged respectively of one year, two and eight years. Only one patient was an adult of 54 years. In one case the testis. In one case, the testis was ectopic in an intra-abdominal position. Mean tumour size was: 2.8 [1.5-4.5cm]. Tumours consisted in Sertoli Leydig tumour in one case and juvenile granulosa tumour in two cases. In the two remaining cases, the diagnosis of TSCT corresponding either to a juvenile granulosa tumour or a Sertoli tumour was made. Albuginea was invaded in one case. In all cases, no nodal involvement was detected.
Conclusion: TSCST are rare and occur both in children and in middle-aged adults. Their symptoms are non-specific and there are no pathognomonic radiological features. The pathological examination is therefore the key for diagnosis. However, diagnosis might be challenging. It is not always easy to distinguish between the different subtypes of TSCST. These tumours generally do not have aggressive behaviour. The treatment is still controversial but is based on surgery.

E-PS-27-097

A single-centre case series of a new entity: low-grade oncocytic tumour

F.G. Salman*, M. Oktay, E. Karakök, F. Aktepe, İ. Türkmen
*Memorial Hospitals Group, Turkey

Background & objectives: The differential diagnosis of renal tumours with oncocytic features is broad and new entities have been defined under the heading "other oncocytic tumours of the kidney" in the latest WHO classification. Low-grade oncocytic tumours have been included in this subgroup.
Methods: Nine cases diagnosed as low-grade oncocytic tumour (LOT) between 2021 and 2023 were reviewed retrospectively for their demographic and histopathological features.
Results: Median patient age was 71 (range 45-78 years) with a female-to-male ratio of 1:2. The majority of patients (55.6%) underwent partial nephrectomy. All were unifocal and tan/yellow-brown solid tumours. The median tumour size was 4.5cm (range 1.8-13cm) and 7 (77.8%) of 9 were located in the right kidney. All but 1 case were limited to the kidney. The case with perinephric fat involvement also had the largest tumour diameter. Microscopically, all tumours consisted of uniform oncocytic cells with low-grade nuclei. None of the cases exhibited lymphovascular invasion, tumour necrosis. Immunohistochemically, all were CK7 positive, CD117 and vimentin negative. Only 2 tumours had higher stage than pT1 (1 each: pT2a, pT3a).
Conclusion: Since LOT has indolent behaviour, it is important to be aware of this newly defined entity. The typical immunoprofile is helpful in the differential diagnosis. In our case series, perinephric fat invasion, which is not expected to be seen in LOT was found in 1 case. Larger tumour series and further studies are needed to fully understand this emerging entity.

E-PS-27-100

Uncommon histological features of succinate dehydrogenase-deficient renal cell carcinoma: an experience of 3 cases

F. Sánta*, B. Pósfai, B. Vasas, L. Kaizer, A. Jenei, B. Scheich, V. Téglási, K. Bíró, A. Maráz, S. Mavrogenis, H. Butz, K. Pivovarčíková, A. Dabaghian, M. Akgul, L. Kuthi
*Department of Pathology, Albert Szent-Györgyi Medical School, University of Szeged, Szeged, Hungary

Background & objectives: Succinate dehydrogenase-deficient renal cell carcinoma (SDH RCC) is a rare subtype, primarily affecting younger individuals, characterized by germline mutations in SDH genes, particularly type B. Histologically, it features eosinophilic cytoplasm cells forming solid nests or microcysts, sometimes entrapping normal tubules.
Methods: We investigated 3 cases of SDH RCC exhibiting uncommon histological features. Demographic parameters, clinical presentation, and follow-up data of the patients were retrieved from medical records. Hematoxylin and eosin-stained slides, along with immunohistochemical assays, were reviewed. Next-generation sequencing was utilized to study mutations of the SDH genes.
Results: Patient 1, a 32-year-old male, presented with a 55 mm tumour with high-grade eosinophilic cells forming tubulo-papillary structures. Patient 2, a 49-year-old male, exhibited a 60 mm mass in the right kidney, with focal high-grade appearance, composed of basophilic mitotically active cells. Patient 3, a 79-year-old male, was diagnosed with a 125 mm tumour, with biphasic appearance mimicking TFEB rearranged RCC. All tumours lacked SDHB expression and harbored pathological germline SDHB mutations.
Conclusion: Similar to other molecularly-defined RCC, SDH RCC exhibits a wide spectrum of morphologic diversity. SDH RCC should be in the differential diagnosis in kidney tumours with unconventional morphology. Given its association with germline mutations, identifying SDH RCC has significant clinical implications. This study underscores the importance of recognizing the spectrum of histological presentations in SDH RCC to guide appropriate management and genetic counseling for affected individuals.

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E-PS-27-102

Adult nephroblastoma case detected during acute coronary syndrome - Georgian rare case report

V. Shonia*, g. Burkadze, T. Mosidze, S. Kepuladze
*Tbilisi Medical university, Georgia

Background & objectives: Nephroblastoma is the most common malignant renal tumour in children. Less than 3% of all the reported Wilms' tumour cases occur in adults. Due to rare occurrence and lack of differentiating features its diagnosis is delayed or often misdiagnosed.
Methods: The H&E method was used, and differential diagnosis included papillary renal cell carcinoma and rhabdoid tumour. IHC was planned. Histopathological diagnosis and immunohistochemistry using

a panel of antibodies (WT1 ; PAX8 CK8/18 ; EMA ; CD56 ; Vim ; Ki67, Glypican 3; AMACR;FLI1, synaptophysin, chromogranin) were reviewed and recorded.
Results: Panel of antibodies revealed: Positive stains: WT1 ; PAX8 CK8/18 ; EMA ; CD56 ; Vim ; Ki67 – positive in 80% Negative stains : Glypican 3 ;AMACR;FLI1, synaptophysin, chromogranin, Staging criteria for Wilms tumour in SIOP and COG- TNM classification-pT3NxMx Molecular testing revealed TP53 (17p13).
Conclusion: The preoperative diagnosis of adult WT is extremely difficult because there are no specific radiographic findings that can distinguish it from the more common adult malignant renal neoplasms. The possibility of an adult Wilms' tumour should be considered when a patient presents with pain in the flank and a renal mass. Although the prognosis is poorer than outcome for adult patients diagnosed with Wilms' tumour is steadily improving. Adjuvant chemotherapy is initiated and patient is followed up the his oncologist.

E-PS-27-103
Unusual localization and diagnostic challenge: a case series of four patients with leiomyomas of the urinary tract
I. Stanišić*, Ž. Panić, T. Vasiljević, T. Lakić, V. Trivunović, S. Trivunić Dajko
*University clinical centre of Vojvodina, Novi Sad, Serbia

Background & objectives: Leiomyomas are benign mesenchymal tumours that rarely occur in the urinary tract. There are small asymptomatic lesions or large tumours clinically manifested as flank pain or gross haematuria. The average age of presentation is 42 years, more often in women.
Methods: We present a case series of four urinary tract leiomyomas diagnosed and treated at our insitution during the past 7 years. Three female patients aged 54, 55 and 67 years were diagnosed with kidney leiomyomas (KL). The fourth case was a 63-year-old male patient diagnosed with ureteral leiomyoma (UL).
Results: KL were asymptomatic and incidentally detected by abdominal ultrasonography and computed tomography as a small size (1-3.2 cm), sharply defined, rounded lesions projecting in the upper pole of the right kidney in all three cases. The appearances were suggestive of renal cell carcinoma on imaging. After preoperative diagnosis, patients underwent laparoscopic partial nephrectomy. A male patient complained of left flank pain and frequent urination. Computed tomography urography showed hydronephrosis of the left kidney and a mass diameter of 3.9 cm located in the upper end of the left ureter. These finding were consistent with a tumour suspicious for malignancy; thuse, open nephroureterectomy with partial cystectomy was defined as a treatment.
Conclusion: Urinary tract leiomyomas were radiologically indistinguishable from other, more common neoplasma, and the definitive diagnosis were achived by histopathological and immunohistochemical evaluation after surgical interventions. In the presented case series, immunohistochemical analysis showed positive staining with smooth muscle actin, caldesmon and calponin, whereas negative staining with cytokeratin, vimentin, HMB 45, and melan A, which is the methods used in the differential diagnosis of leiomyomas.

E-PS-27-105
Immunoprofiling of mucins (MUC1, MUC2, MUC4, MUC5ac and MUC6) in a rare case of urachal mucinous neoplasm of low malignant potential
C. Taverna*, F. Montefiore, F. Bonini, F. Tava, A. Di Marco, R. Gaeta
*Pathology Unit, Local Hospital ASLAL, Ospedale san Giacomo Novi Ligure, Italy; Department of Health Sciences, University of Eastern Piedmont "Amedeo Avogadro", Italy

Background & objectives: Urachal mucinous cystic tumour of low malignant potential (MCTLMP) is an occasional entity among neoplasms of the urachus, a vestigial remnant of foetal development. Herein we present a case with mucin profile assessment, exploring their distribution and potential prognostic implications.
Methods: A 3.3x3 cm lesion filled with mucinous material, incidentally discovered during cholecystectomy screening in an 80-year-old woman, was sampled, embedded in paraffin, and analysed using an immunoistochemical mucin panel comprising MUC1, MUC2, MUC4, MUC5ac, and MUC6 (Cell MarqueTM, Sigma-Aldrich, Rocklin, CA, USA)
Results: Microscopical examination revealed a single layer of mild atypical and pleomorphic mucinous cuboidal to columnar cells, showing tufting, pseudostratification and crowing patterns with rare mitoses. Therefore, a diagnosis of MCTLMP was made. The lesion exhibited positive expression of CK20 and CDX2 and negative expression of ER and PGR, aligning with data on other malignant mucinous lesions of the urachus reported. Among mucins, MUC1 and MUC6 showed negative stain. MUC2 was strongly and diffusely expressed, with cytoplasmatic and membrane stain. MUC4 displayed positive membrane staining, with varying intensities ranging from mild to moderate. Furthermore, MUC5 exhibited strong expression, observed both in cytoplasm and in cellular membrane.
Conclusion: The MCTLMP herein reported showed a similar mucin immunoprofile to the intestinal type pancreatic intraductal papillary mucinous neoplasms (IPMN). This is the first report of complete mucin assessment in this type of lesions, as previously only one study assessed MUC2 expression in a group of urachal carcinomas, with 2 mucinous cystadenocarcinomas showing positive stain. Conversely, the normal urachal residual shows negative MUC2 expression. MUC2 positivity in our case suggests a close relation with the malignant counterpart

E-PS-27-106
Fumarate hydratase deficiency occurring in malignant Leydig cell tumours
N.P. Tenace*, M. Barella, B. Paolini, G.M. Pini, G. Sabella, M. Colecchia
*Department of Pathology, Vita-Salute San Raffaele University, Milan, Italy

Background & objectives: Molecular pathogenesis of testicular Leydig cell tumours (LCT) is poorly understood. Some LCT are associated with fumarate hydratase (FH) mutations. Acosta et al. proposed to reclassify these tumours, characterized also by FH immunohistochemical loss of expression, as FH deficient LCT.
Methods: 15 cases FH on testicular LCTs with metastatic behaviour, surgically resected during the calendar years 2000 to 2018, were seen among consultation cases by senior author (MC) and were tested by IHC for FH on formalin-fixed paraffin-embedded sections. Molecular assay is under evaluation for the pathogenetic variant in FH gene.
Results: Overall, 15 malignant testicular LCTs were available for IHC. All cases showed retained FH IHC except one (6,6%), where the normal pattern of staining was present only in endothelial cells. This case showed FH loss both in primitive as in metastatic presentation in retroperitoneal lymph nodes and high-grade morphologic features detailed in a previous publication as high risk LCT. All the other cases had retained FH expression.
Conclusion: FH deficiency is relatively rare in LCT probably occurring in <5% of malignant LCT. Its occurrence is reported in cases associated with more aggressive behaviour. It is not associated with any unique morphologic feature unlike other FH deficient neoplasms.

E-PS-27-107
The prognostic significance of peritumoural lymphocytic infiltrate in invasive urothelial carcinoma: correlation with clinical endpoints and long-term outcomes
N.P. Tenace*, D. Robesti, R. Lucianò, M. Freschi, G.M. Pini, A. Lopez Beltran, M. Colecchia
*Department of Pathology, Vita-Salute San Raffaele University, Milan, Italy

Background & objectives: The role of lymphocytic infiltrate in invasive urothelial carcinoma (UC) of the bladder is still unclear. We correlated the amount and distribution of peritumoural lymphocytes with clinical endpoints and clinical-pathological features.
Methods: We collected and reviewed 122 specimens of invasive urothelial carcinoma (UC) surgically resected in our Institution from 2008 and 2016 at first diagnosis. 93 cases of pT1 tumours were obtained. We evaluated the amount of peritumoural lymphocytic infiltrate at 20X magnification dividing it in a two-tier scoring system (0-1 low vs 2-3 high). Thus, we correlated results with clinical variables.
Results: The baseline characteristics were homogeneous in the two groups being the pT1 substage, according to the ROL system, the only statistically different parameter ($p < 0.01$). Kaplan-Meier analysis showed a higher risk of recurrence in patients with low lymphocytic infiltrate (0-1 score) when compared with those cases with high infiltrates (2-3 score) (p 0.03 at log rank test). Multivariable cox regression analysis confirmed these findings (HR 1.23, 95% CI [1.05, 1,48], p 0.02) after accounting for well-known confounding factors. No statistical difference was observed in Overall Survival, Progression Free Survival, and Radical Cystectomy free Survival.
Conclusion: The subclassification of peritumoural lymphocytic infiltrate (low vs high) in cases of pT1 UC may be an independent risk factor for early disease recurrence. Analysis over an observation period exceeding 8 years reinforces this data and confirms its limited prognostic value. The potential impact of this evaluation must be considered for the operative management of the patient.

E-PS-27-108
Penile melanoma in young patient: case report
S. Tolmachev*, M. Urezkova, A. Gogolev, D. Gazizova, I. Poliatskin, N. Anarbayev
*Kazakh Institute of Oncology and Radiology, Kazakhstan

Background & objectives: Penile melanoma is a rare tumour that predominantly develops in older patients, typically in the sixth and seventh decades of life. We report an unusual case of penile melanoma in a young adult on the penile shaft.
Methods: A 31-year-old male patient presented with an exophytic tumour on the skin surface near the frenulum of the penis, measuring 2 cm in its largest dimension. It appeared over a year ago and does not bother the patient; there is no evidence of growth dynamics. No additional studies are available.
Results: Histopathological examination indicated an ulcerated epithelioid-cell tumour with asymmetry, severe cytologic atypia, and massive pagetoid spread in the epidermis. The dermal component is presented as solid sheets of cells without maturation, with high mitotic activity, a small amount of pigment, and scant lymphoid infiltration. The Breslow thickness was 3.5 mm. Immunohistochemical staining showed patchy HMB-45 expression, dot-like p16 expression, and a Ki-67 index of approximately 15%. Our diagnosis was ulcerated penile melanoma. Genetic tests were recommended, but results are not available.
Conclusion: In summary, primary penile melanoma typically manifests in older patients and carries a poor prognosis. This case report underscores the potential occurrence of this tumour at a younger age.

E-PS-27-109
Primary neuroendocrine tumour of the kidney: case report
S. Tolmachev*, M. Urezkova, A. Gogolev, D. Gazizova, I. Poliatskin, N. Anarbayev
*Kazakh Institute of Oncology and Radiology, Kazakhstan

Background & objectives: Neuroendocrine tumour (NET) is common in the respiratory and digestive systems, but it is a rare tumour for the kidney. We report a case of a primary NET of the kidney with metastases in regional lymph nodes and the liver.
Methods: A 45-year-old female presented with left-sided backache. Computed tomography (CT) scan revealed a 9 cm renal mass in the left kidney and a 2 cm nodule in the liver. After surgery, CT exploration showed an increase in the size of the liver nodule and metastases in the paraaortic lymph nodes. The patient underwent liver resection and para-aortic lymph node dissection.
Results: Histologically, the tumour revealed features of a well-differentiated NET. The tumour presented trabecular and solid growth patterns; tumour cells are monomorphic, polygonal, with oval regular nuclei containing granular chromatin. Necroses are absent, and mitotic activity is 2 mitoses per 2 square mm. The liver masses and lymph nodes contained a similar tumour. Immunohistochemical staining showed positive Synaptophysin, CD56, and Chromogranin A expression, and a lack of TTF-1 and CDX2. Ki-67 was approximately 2%. A series of CT scans excluded any tumours of the lungs, digestive system, and ovaries.
Conclusion: In summary, primary renal well-differentiated NET is rare, and for correct diagnosis, NET of more common localizations should be excluded. In our case, after matching clinical data and histological features, NET grade 2 of the kidney was the most suitable diagnosis.

E-PS-27-110
Mucinous tubular and spindle cell carcinoma: a case report of a rare kidney tumour
R.M. Tripea*, M. Penciu, M. Cristina, R. Șoană
*Romania

Background & objectives: Mucinous tubular and spindle cell carcinoma (MTSCC) is a rare type of renal neoplasm, usually with indolent behaviour. We report the case of a 70 year old female patient with an incidental finding of a tumour in her left kidney.
Methods: Total nephrectomy was performed and the kidney was sent to the Pathology Department for examination. Macroscopically, we described a large solid tumoural mass (approximately 12 cm in diameter), well-circumscribed, confined to renal parenchyma, with cut yellow surface and areas of hemorrhage. After microscopic examination we performed a large panel of immunohistochemical tests to exclude the differential diagnoses.
Results: The histopathological examination indicates a tumour consisting of elongated tubular structures, lined by bland, cuboidal cells, focally admixed with spindle cells, both with little cyto-nuclear pleomorphism. The stroma is myxoid and slightly edematous. Frequent mucin deposits with groups of foamy macrophages in the periphery are observed. Small areas of necrosis are present. Immunohistochemical tests indicate tumour positivity for AE1/AE3, AMACR, EMA, NSE and PAX8 markers. The Ki67 index is below 1%, which shows that the tumour is not aggressive. Alcian blue was used to highlight the mucin pools. CD10, WT1 and Chromogranin were negative, which helped us exclude a metanephric adenoma, a renal papillary carcinoma or a collecting duct carcinoma.
Conclusion: Considering the histopathological and immunohistochemical results, the diagnosis was mucinous tubular and spindle cell renal carcinoma. These rare tumours are generally indolent, although a small part of them have high-grade transformation, being associated with metastases and poor prognosis. Although there were areas of necrosis, this tumour had no other aggressive characteristics, therefore it was classified as classic MTSCC. An extensive analysis of several such cases could be useful for the subclassification of the tumours that show very few high-grade characteristics.

E-PS-27-111
Adenoid cystic (basal cell) carcinoma (ACC) of the prostate: case report and literature review
O. Tzaida*, G. Galanopoulos, E. Souka, P. Bafaloukos, E. Fergadis
*Metaxa Cancer Hospital, Piraeus, Greece

Background & objectives: ACC is a rare type of malignancy, mostly involving the salivary glands. It can also be found in other less frequent sites such as the breast, skin, lung, lacrimal duct and cervix. Prostate is an extremely rare primary location site.
Methods: A 73-year-old male patient was admitted for a periprostatic nodule investigation, found during a routine prostate gland check. The PSA level remained within the normal range. A prostatic needle biopsy was performed. Four (4) core samples measured from 2.2 to 2.6 cm in length were delivered for examination to our Pathology Department.
Results: Histology revealed a malignant basal cell population with a nested and ill-defined cribriform pattern. An intraglandular eosinophilic hyaline material with inspissated secretions was also identified. Mitotic activity was mild. The surrounding stroma was fibromyxoid. The immunohistochemical analysis showed positivity for CK7 labeling the abluminal cells. There was CK903 and p63 expression at the outermost cellular layers and focal NKX3.1, PSAP, and Bcl-2 staining. AMACR, PSA were negative. Ki-67 mitotic index was low; approximately 3%. The aforementioned results established the diagnosis of a prostatic ACC. A Gleason score 8 (4+4), ISUP Grade group 4, was appointed according to the architectural pattern.
Conclusion: ACC of the prostate, a neoplasm thought to originate from the basal prostatic cells, is considered exceedingly rare. Less than 120 cases have been reported in the literature. The neoplasm is histologically identical to ACC of the salivary glands with similar molecular aberrations. Most cases occur from 65 to 84 years. Loss of PTEN expression, overexpression of EGFR and MYB translocation are frequent findings in ACC. Given the rarity of this disease, not enough data are available for optimal therapy.

E-PS-27-112
Four in a row - multiple primary malignant tumours with two of them in the urogenital tract
A. Vitan*, A. Croitor, V. Dema, A. Cumpanas, D. Herman, A. Dema
*Pathology Department, Pius Brinzeu Emergency County Hospital, Romania

Background & objectives: The prevalence of multiple primary malignant neoplasms is a very rare phenomenon. This study reports a case of a 57-year-old man who was diagnosed with four different tumours, two of them in the urogenital tract.
Methods: At the age of 37, the patient was diagnosed with high-grade sarcoma of the abdominal wall. At 55, a renal mass was discovered on ultrasound examination and later confirmed by a CT scan. Six months later, a mesenteric tumour was revealed. At 57, prostate carcinoma was suspected based on a high PSA level and a PI-RADS score of 3.
Results: All the tumours were surgically excised, with the following pathology findings. The first tumour was a high-grade sarcoma, previously diagnosed and treated in another hospital. In our hospital, the pathology report from the initial presentation revealed a clear cell renal cell carcinoma - G1 WHO, with a pathological stage of pT1aNxR0. At the second presentation, the synchronous tumour was diagnosed as a well-differentiated G1 neuroendocrine tumour of the small intestine - pT3N1LV1Pn1RO. Lastly, the metachronous tumour discovered during the most recent presentation was a prostatic acinar adenocarcinoma with a Gleason score of 6 (3+3), grade group 1 - pT2NxPn1LV0.
Conclusion: The improvement of diagnostic methods and the increasing effectiveness of cancer therapies have led to better survival rates among cancer patients, consequently resulting in the occurrence of multiple primary tumours in these patients. Including patients with malignant tumours in well-established protocols with active surveillance, leads to the early diagnosis of multiple primary tumours and increases their survival.

E-PS-27-113
Histopathological evaluation of tumour hypoxia in relation to IDC-P and cribriform pattern in prostate cancer
L. Vlatkovic*, V.E. Skingen, T. Seierstad, T. Hompland, H. Lyng
*Oslo University Hospital, Norway

Background & objectives: Tumour hypoxia is a potential biomarker of aggressive disease in prostate cancer, but its prevalence in different histological pattern is not known. We assessed relationships between hypoxia and different growth patterns in histological sections from prostate cancer.
Methods: Totally 82 intermediate- and high-risk patients receiving the hypoxia marker pimonidazole prior to radical prostatectomy were included. Hypoxic fraction and range of hypoxia levels from mild to severe were determined for the index lesion in pimonidazole-stained whole-mount sections by use of digital histopathology. HE-stained sections of punch biopsies from this lesion were applied to identify IDC-P and cribriform patterns.
Results: Most tumours contained hypoxic regions, and hypoxic fraction ranged from 0% to 71% (median 27%) across patients. IDC-P was seen in 42 patients (51%), and 19 patients (23%) had cribriform pattern. Cribriform pattern was in most cases (79%) seen in tumours with IDC-P. Comedo necrosis in many IDC-P and cribriform tumours was always surrounded by regions of severe hypoxia. The hypoxic fraction was higher in tumours with IDC-P than in the remaining tumours (P=0.01). No difference was observed for the cribriform pattern alone. Hypoxic fraction (P=0.04), presence of IDC-P (P=0.02) and cribriform patterns (P=0.006) correlated significantly with biochemical recurrence at 8 years of follow-up in univariate analysis.
Conclusion: Tumour hypoxia is an aggressive feature in prostate cancer with high prevalence in patients with IDC-P. Hypoxic fraction assessed by digital histopathology may aid identification of high-risk patients. These patients might benefit from more intensified treatment with hypoxia-targeting drugs.

E-PS-27-114
Mixed epithelial and stromal tumour of the kidney
M. Vuletic*, T. Čeprnja, J. Bezić, V. Pešutić Pisac
*University Hospital Center Split, Croatia

Background & objectives: Mixed epithelial and stromal tumour of the kidney (MEST) is a rare benign biphasic lesion composed of a mixture of stromal and epithelial elements. The histogenesis of MEST is unknown. It occurs overwhelmingly in women with history of hormone therapy.
Methods: An 29-year-old male patient was incidentally diagnosed with a lesion of the left kidney on abdominal ultrasound as part of systematic medical examination. MR imaging showed an avascular, expansive mass measuring 24 mm in the largest diameter with no other pathologic findings. He had no history of hormone therapy. Left sparing nefrectomy was performed.
Results: The tumour was well-circumscribed. Histopathological evaluation showed a biphasic tumour containing solid and cystic components with unusual immunophenotype. Multiple cysts and tubules of varying sizes were separated by focally hypocellular, partially sclerotic and collagenous stroma admixed with hypercellular areas displaying ovarian-like features. Stromal calcifications were found. The cysts and tubules were lined by single layer of flat, cuboidal and hobnail epithelium. No mitoses, atypia or necrosis were identified. Immunohistochemically, epithelial component was positive for cytokeratin-7, PAX-8, AMACR, CD10, progesterone (PR) and estrogen receptors (ER). A few stromal tumour cells were positive for CD34 and the rest of the stromal cells were negative for the WT-1, ER, PR, Inhibin and CD10.

Conclusion: The diagnosis in this case was performed according the essential histological characteristics typical for this entity (a complex solid and cystic tumour with epithelial elements in a variably cellular spindle-shaped stroma). We missed the desirable stromal immunohistochemical positivity for PR and/or ER but we decided to rely on morphology. In the same procedure we excluded other potential entities like cystic nephroma, synovial sarcoma, clear cell papillary tumour and tubulocystic renal cell carcinoma.

E-PS-27-115

Incidence and pitfalls of adipose tissue encountered in prostatic transurethral resections and related specimens

D. Wu*, J. Brooks, A. Sangoi
*Stanford Medical Center Department of Pathology, USA

Background & objectives: The incidence of adipose tissue and its involvement by prostatic cancer in transurethral resections of the prostate (TURP) is largely unexplored. The aim of this study was to investigate the incidence of adipose tissue in TURP and related specimens.
Methods: From 200 consecutive TURPs, aquablations, and laser enucleations as well as a 3-year study of all similar specimens with primary prostatic cancer, the following data was collected: presence of fat, presence of cancer within fat, and quantity of fat. Adipose tissue mimics were excluded. For cases with fat and prostatic cancer, specimen weight and tumour volume were also collected.
Results: Within 200 consecutive TURPs/aquablations/laser enucleations, adipose tissue was identified in 20%. 55% had <1 mm of adipose tissue, 29% had 1-2.5 mm of adipose tissue, and 18% had >2.5 mm of adipose tissue. The number of fragments with adipose tissue ranged from 1 to 14. No correlation between specimen weight and measured extent of adipose tissue or number of fragments with adipose tissue was identified. The amount of adipose tissue varied by procedure: 24% in TURPs, 8% in aquablations, and 18% in laser enucleations. 15 cases had both prostatic cancer and adipose tissue, with 2 cases containing large cancer volume (>90%) demonstrating involvement of adipose tissue by cancer.
Conclusion: Adipose tissue is frequently present within TURP and related specimens with variability in extent. While the exact mechanism behind encountering adipose tissue is uncertain, it could represent resection into periprostatic fat, intraprostatic fat, or bladder neck fat sampling. While encountering adipose tissue involved by cancer in TURP/related specimens may imply extraprostatic extension (pT3a), further studies are needed to corroborate these findings as well as to determine if these should be included in reported synoptics.

E-PS-27-116

Squamous cell carcinoma of the kidney: a tumour that is often missed preoperatively

M. Zghal*, O. Boudaouara, W. Ghribi, M. Mellouli, L. Ayadi, T. Sellami Boudawara, C. Chaari
*Department of Pathology, Habib Bourguiba University Hospital, Sfax, Tunisia

Background & objectives: Squamous cell carcinoma (SCC) of the kidney is a rare tumour of renal-pelvis. It is often an incidental finding in removed-nonfunctioning-kidneys. We aim through this case-series-report to highlight the pathologist role in establishing the diagnosis of SCC of the kidney.
Methods: All pathological reports of patients who underwent nephrectomy at the Urology department of Habib Bourguiba Hospital, between January 2022 and March 2024, were reviewed. A total of 4 patients with a diagnosis of SCC were identified among 47 patients in whom a renal cancer was established after final histopathological analysis.
Results: The mean age of patients was 59 years. A diagnosis of malignancy was suspected in 2 patients preoperatively; a biopsy of the renal-mass suggested a SCC. The other 2 patients were discovered incidentally to have a SCC on a presumed-nonfunctioning-pyonephrotic-kidney after a history of renal-stone-disease. Gross-examination of the 4 removed kidneys showed a grey-whitish-infiltrating-mass replacing the renal parenchyma. After careful histopathological examination of the 4 renal-masses, the diagnosis of SCC was affirmed: all the tumours showed a pure squamous morphology without any component of urothelial carcinoma. All 4 cases were staged pT3 at least with tumoural circumferential surgical margins. Regional lymph node metastases were evidenced in 2 cases.
Conclusion: SCC of the kidney is most often diagnosed postoperatively after nephrectomy for a presumed noncancerous kidney. A history of a renal stone disease raises the suspicion of SCC. Nevertheless, the final diagnosis of SCC could only be affirmed after histopathological examination of the surgical specimen.

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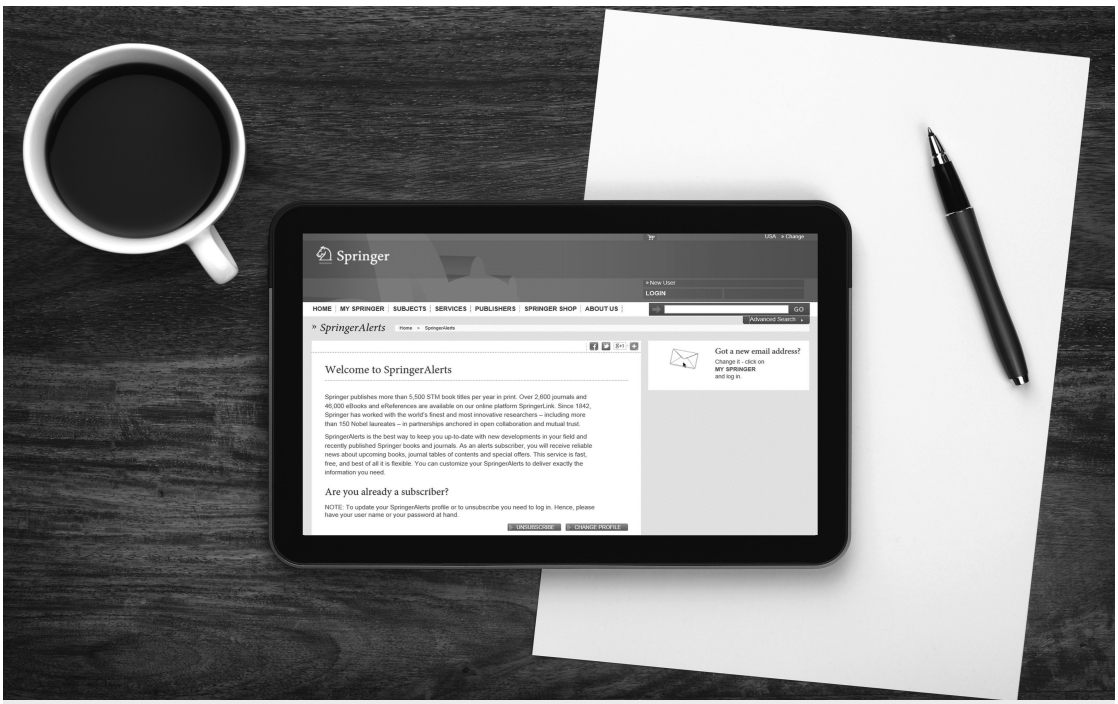

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