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CATEGORY: RESEARCH

1. Cord blood C-reactive protein and procalcitonin in histologic chorioamnionitis

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Introduction: C-reactive protein (CRP) and procalcitonin (PCT) are the common inflammatory biomarkers tested in non-pregnant adults and paediatrics, however, their utility in pregnancy has yet to be determined. Here we reported our findings on the cord blood CRP and PCT levels in cases of histological chorioamnionitis (HCA) versus non-HCA cases, and the expression of PCT in various placental cells. Methods: A prospective cross-sectional study of 99 singleton pregnant women with risk factors for chorioamnionitis in Hospital Canselor Tuanku Muhriz from May 2021 to May 2022. Cases were classified into HCA (n=72) and non-HCA (n=27). The cord blood CPR and PCT levels were compared across groups and the expression of PCT was evaluated by performing PCT immunohistochemistry (IHC) staining on a full-thickness paraffin-embedded tissue section of placenta. Results: None of the HCA negative cases had elevated CRP level (p=0.103). The levels of PCT were found to be higher in groups with higher stages of maternal inflammatory response (MIR) (p=0.231) and foetal inflammatory response (FIR) (p=0.054). Despite PCT immuno-expressed decidual cells were significantly higher in HCA group compared to non-HCA (p=0.008), there was no statistically significant difference in the cord blood PCT levels between PCT immuno-expressed vs non PCT immuno-expressed groups (p=0.237). Discussion: PCT expression was significantly higher in the HCA group, but there was no significant difference between the cord blood CRP and PCT levels between HCA and non-HCA groups. As the number of cases with higher FIR stages were low in our study, a larger study is needed to validate our findings.

2. Pertussis in children: Diagnostic clues in the peripheral blood film

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Introduction: Pertussis (whooping cough) is a respiratory infection caused by bacterium Bordetella pertussis. This report highlights the clues in the peripheral blood film which can aid in diagnosing the infection while awaiting confirmatory tests. Methods: Seven children with pertussis infection, confirmed by PCR in 2022 were studied retrospectively, focusing on their peripheral blood film (PBF) findings including the blood count. Information on demography, clinical presentation with laboratory results were obtained from clinical notes and laboratory information system. Results: The patients were 2 months to 2 years of age; 86% were unvaccinated and presented with respiratory tract infection symptoms such as fever, cough, and tachypnoea. All patients had leucocytosis (34-117 x 10^3/μL), neutrophilia (10-46 x 10^3/μL) and 86% had lymphocytosis (15-60 x10^3/μL). The characteristic small, mature lymphocytes with cleaved/clefted nuclei present in the PBF of all patients and more prominent in 71% of them with predominant lymphocytosis (Neutrophil: lymphocyte ratio < 1). Discussion: The clues to support early diagnosis of pertussis infection in children are leucocytosis, lymphocytosis with characteristic morphology of small, mature lymphocytes with clefted/cleaved nuclei in the PBF which are in keeping with similar published reports. Thus, patients could be treated earlier based on finds in PBF while awaiting the confirmatory tests.

3. Re-audit of B3 and B3 with atypia percentage in screening and symptomatic breast cores

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Introduction: The Royal College of Pathologists (RCPath) in the United Kingdom require all breast core biopsies to be categorized from B1 to B5. 'B3' lesions are of uncertain malignant potential and require subcategorization into those showing epithelial atypia and those without epithelial atypia. A previous audit in our department revealed our B3 and B3 with atypia percentage was low compared with the published guidance and we conducted a re-audit of the same parameters. Methods: All breast core biopsy reports and subsequent surgical excisions were retrospectively reviewed over a consecutive 12-month period to derive the percentage of B3, B3 with atypia, upgrade risk of B3 and the upgrade risk of B3 with atypia. Results: There were 73 B3 cases in the cohort out of 1289 cases (5.7%). Among the B3 cases, 13 were diagnosed as cancer (upgrade risk 17.8%). Fourteen of the B3 cases showed atypia (19.2%) and among those B3 with atypia, 4 were diagnosed as cancer (upgrade risk 28.6%). Discussion: Our departmental B3 percentage is now within the RCPath acceptable range (4-9%), however the subcategorization of B3 with atypia is still low and the corresponding high upgrade risk would suggest that our threshold for diagnosing atypia is too high.

4. Evaluation of androgen receptor expression in benign prostatic hyperplasia

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Introduction: Benign prostatic hyperplasia (BPH) is a significant aetiology of morbidity in aging men, causing lower urinary tract symptoms and acute urinary retention. Androgen/androgen receptor (AR) signalling plays an important role in the progression of BPH. The detailed mechanism of androgen/AR signalling, especially its role in the pathogenesis of BPH, is still debatable. Methods: 56 samples of BPH were collected from the Anatomic Pathology laboratory in Padang, Indonesia. By immunohistochemistry (IHC), AR expression was analysed using the semi-quantitative immunoreactive score (IRS). Strong staining in the epithelial and stromal cells implied a high expression of AR. Results: The mean age of patients was 68.59 ± 6.85 years. Most samples of BPH showed high AR expression at 98.21% (55 cases) in the epithelial cells and 82.14% (46 cases) in the stromal cells. Discussion: Activation of AR signalling is crucial for the progression of BPH. High AR expression was revealed in most epithelial and stromal cells of BPH. Both epithelial and stromal cells that express AR may be involved in this disease. AR pathway in the stromal cells alters intercellular signalling and results in resurrection of the embryonic mesenchyme. An increase in the ratio of stromal to epithelial components in BPH when it is compared to the normal adult prostate may influence disease outcome.

5. p16, cyclin E, and PRAME help differentiate melanocytic nevi and melanomas

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Introduction: Melanoma is a notorious tumour of skin with poor prognosis. Differentiating it from benign melanocytic nevus is important. This study was undertaken to compare the expression of p16, cyclin D1, cyclin E, and PRAME in benign and malignant melanocytic lesions. Methods: Fifty cutaneous melanomas and 50 benign intradermal melanocytic nevi were retrieved from archived paraffin blocks. Immunohistochemistry was used to analyse the expression using the streptavidin-biotin-peroxidase complex method. The scoring of immunoexpression was defined as negative for < 1% of expression and positive for 1%-100% of expression. Results: Melanocytic nevi were positive for p16, cyclin D1, cyclin E, and PRAME in 50 (100%), 42 (84%), 8 (16%), and 0 (0%), respectively. Melanomas were positive for p16, cyclin D1, cyclin E, and PRAME in 34 (68%), 48 (96%), 42 (84%), and 31 (62%), respectively. The expression of p16, cyclin E, and PRAME between melanocytic nevi and melanomas showed statistical significance ($P < 0.001$). However, there was no statistical significance in cyclin D1 expression ($P = 0.092$). Discussion: Our findings indicate the potential use of p16, cyclin E and PRAME in differentiating benign and malignant melanocytic lesions.

6. Primary malignant glandular tumour of vulva: An Indian tertiary care experience

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Introduction: Vulvar cancer has an incidence of 2-3 per 100,000 women and accounts for 5 % of all female genital tract malignancies. About 90% of them are squamous cell carcinoma. Primary malignant glandular tumours of the vulva (PMGTV) are rare, diverse tumours with different prognoses and differentials. We present four cases of PMGTV diagnosed at our institution over a 10-year period in the present study. Methods: It was a retrospective observational study from 2013 to 2022. Hospital intranet and medical records provided required clinical, histopathology, and immunohistochemistry data. Results: The age ranged from 31 to 86 years and the size varied from 2 to 6 cm. The most common presentation was a painful mass growing rapidly. A spectrum of variable entities was diagnosed, namely poorly differentiated adenocarcinoma, adenoid cystic carcinoma, adenocarcinoma intestinal type and adenocarcinoma of mammary gland type. Discussion: PMGTV are rare entities and resemble morphologically and immunophenotypically tumours of other systemic sites, making exclusion of any primary malignancy mandatory. A large panel of immunohistochemistry is needed to typify them. Due to the rarity of the disease, no definite treatment guidelines are present.

7. International medullary thyroid carcinoma grading system: An institutional experience

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Introduction: Medullary carcinoma (MTC) is a rare neuroendocrine thyroid neoplasm. The International Medullary Thyroid Carcinoma Grading Scheme (IMTCGS), which has prognostic significance, has been introduced recently. The study evaluated IMTCGS using our MTC cases. Methods: All MTC thyroidectomy cases from 2016 to 2021 were evaluated. Low-grade (LG) and high-grade (HG) cases were compared. Survival analyses included loco-regional free survival (LRFS) and distant metastasis-free

survival (DMFS) analyses. Results: Of 32 cases, 31.25% were HG and 68.75% LG. The mean age was 44.0 years. The male to female ratio was 1:1.146. HG patients were older and had tumour cells with prominent nucleoli and frequent distant metastasis. IMTCGS did not affect LRFS. Univariate log-rank test analysis showed that cohorts with HG (p<.001), Ki67 >5% (p<.001), and coagulative necrosis (p<.001) had worse DMFS. Further multivariate Cox regression analysis, adjusted for age and gender, showed significant association with IMTCGS (p=0.026) and coagulative necrosis (p=0.04). However, when adjusted for other variables, neither was independently associated with DMFS. Discussion: This is the first Indian study evaluating IMTCGS. In univariate analysis, HG MTC had poor DMFS. However multivariate analysis showed IMTCGS carried prognostic significance only when adjusted for age and gender but lost its significance when other variables were considered.

8. Abnova probes performance by modified fluorescence *in situ* hybridisation protocol

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Introduction: Accurate assessment of *MDM2* and *CDK4* gene amplification status is essential for effective targeted therapy. Here, we presented a modified fluorescence in situ hybridisation (FISH) protocol that allows optimal performance of Abnova *MDM2* and *CDK4* probes on formalin-fixed paraffin-embedded (FFPE) liposarcoma tissue. Methods: FISH was performed on representative FFPE sections following standard manufacturer protocol, with several modifications. The main differences that were made include deparaffinisation, digestion, denaturation, and hybridisation steps. The results obtained with the modified protocol was compared with standard protocol in terms of background and signal quality. To validate the applicability of developed protocol, modified FISH was performed on FFPE lymphoma and liposarcoma tissue sections using Vysis *IGH* and *C-MYC* break-apart probes, and the quality of signals obtained were analysed. Results: The modified version has significantly reduced background fluorescence and enhanced the Abnova probes signal intensities compared to standard protocol. Prolonged deparaffinisation, optimised digestion condition specific to tissue type and higher denaturation temperature contributed to the positive results obtained. Good hybridisation signals were observed when modified protocol was tested with Vysis probes. Discussion: Our improved FISH protocol is effective in achieving interpretable hybridisation signals and it can also be applied on other probes for various cancer diagnosis.

9. Soft tissue tumours of the oral cavity: A 20-year analysis

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Introduction: Soft tissue tumours represent a group of neoplasms with overlapping morphological features and variable differentiation. Due to its rarity in the oral cavity, it may become a diagnostic challenge for the oral pathologists. Furthermore, there is a lack of this data in Malaysia. The aim of this study was to evaluate all soft tissue tumours of oral cavity reported by Stomatology Unit, Institute for Medical Research from year 2000 to 2020. Methods: Data regarding the histopathological diagnoses and immunohistochemistry findings were retrieved from the computerized record. Information regarding patients' demographics and clinical information were extracted from the histopathological examination request form. Results: A total of 410 cases comprised of 194 female and 216 male patients; the age ranged from 3 months to 87 years old. Majority of patients were Malays (56.1%), followed by Chinese (16.6%), Indian (11.2%) and other ethnicities (13.4%). Based on histological classification, the most common cases were of nerve sheath, adipocytic, vascular and fibroblastic/myofibroblastic tumour. Discussion: Soft tissue tumours of the oral cavity are rare with only 1.09% cases reported in our facility over a 20-year period. 213 of the cases required immunohistochemistry as an ancillary study while 64 cases were referred to another pathologist for a second opinion.

10. Hepatocellular carcinoma: A 5-year institutional review

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Introduction: In Malaysia, hepatocellular carcinoma is the eighth most common cancer and fifth most common cancer in males. Risk factors and aetiologies show geographical variation. We reviewed a total of 142 liver biopsy and resection specimens received at the Histopathology Unit, Hospital Sultanah Bahiyah, Malaysia. Methods: This is a retrospective hospital-based study looking at histopathological reports from 2015 to 2019. Epidemiological factors, risk factors and histopathology findings were studied. Results: A male predominance (Male=97 [68%]; Female = 45 [32%]) with a peak incidence in ages 60 to 70 years (44%) was observed. 104 of patients had available Hepatitis B/C status; 49% having either Hepatitis B/C. From a total of 116 cases, 49% showed Grade 3 (n=57) tumour grades in the Edmondson-Steiner system. In resection specimens, a majority were > 5 cm in size. Out of 79 cases reviewed for background liver assessment, 57 showed steatosis, 13 cases had hepatitis activity and 23 cases showed steatohepatitis activity. Overall, 71 cases showed established cirrhosis. Discussion: This review gives an insight on epidemiological trends, risk factors and histomorphological features of HCC and background liver. Cirrhosis secondary to viral hepatitis is the most significant risk factor. Knowledge of these factors in the Malaysian setting will help to improve current concepts for prevention, screening, and management of hepatocellular carcinoma.

11. Korean forensic medical practitioners' attitude and expectation on digital pathology

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Introduction: National Forensic Service (NFS) of South Korea implemented its first digital pathology (DP) system in 2021. This study aimed to investigate the attitudes and expectations for DP in the field of forensic medicine among forensic medicine practitioners in NFS. Methods: An electronic survey consisting of 10 yes/no and multiple questions was designed and distributed to 53 medical examiners and medical technologists in NFS. Results: A total of 50 forensic medicine practitioners responded to the survey. The majority (82%) of respondents revealed interest in DP. Consultation (46.9%) was answered as the most expected use of technology in the field. The greatest perceived advantage of DP was permanent data retention (22.1%), while cost (39%) was the most cited disadvantage. The most favored option for slide storage was digital image (58%) and the majority (94%) felt a need for an online digital library. In order to adopt DP in practice, increasing the number of forensic medicine practitioners (29.7 %), lowering of prices (28.7%) and establishment of pathology DICOM (26.7%) were the top three most considered priorities. Discussion: The forensic medicine practitioners in NFS presented overall positive attitudes toward DP, as well as high expectations for the introduction of technology in the field of forensic medicine.

12. Spectrum of histopathological diagnosis of skin lesions: A 5-year institutional review

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Introduction: Skin-related diseases place a significant burden on the world's health; thus, a histopathological (HPE) evaluation is necessary to establish the right diagnosis for the patients' best therapy. We analysed the histopathological diagnosis of skin biopsies in Hospital Universiti Sains Malaysia (USM). Methods: Information was gathered from the Laboratory Information System of the Department of Pathology, Hospital USM over a 5-year period (from December 2017 to December 2022) using the keywords 'skin lesion, melanoma, squamous cell carcinoma, and basal cell carcinoma'. The parameters included were the histopathological diagnosis, age, gender, and ethnicity. Results: 297 skin cases were identified with 75.4% non-neoplastic, 8.4% benign, 14.8% malignant and 1.3% metastatic carcinoma. The median age was 50.7 years with female preponderance (60.2%). Majority were Malay (91.6%). The most diagnosed benign skin lesions included acrochordon (35.3%), naevus (8.9%) and seborrheic keratosis (8.5%). The most common malignant skin neoplasia were basal cell carcinoma (45.5%) and squamous cell carcinoma (43.2%). Discussion: Commonly benign skin lesions are biopsied for diagnostic confirmation or as cosmetic removal. For malignant lesions, histopathological validation is mandatory to determine further management. Future studies should include other centres for a better understanding of our local skin cases.

13. The early-onset of breast cancer (≤ 40 years) – A single institution experience

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Introduction: Early-onset breast cancer (≤ 40 years) has aggressive clinicopathological features and poor clinical outcomes. We aimed to present the early-onset breast cancer (EOBC) pattern from a 9-year single institute experience. Methods: Clinicopathological characteristics of EOBC patients diagnosed at Hospital Universiti Sains Malaysia (USM) from January 2013 to June 2022 were retrospectively retrieved and analysed. Results: During the 9 years, 76 patients were diagnosed with EOBC at Hospital USM, making up around 13% of all breast cancer cases. Of the 76 cases, 35.5% have lymph node-positive, 31.5% present with a tumour larger than 5 cm, 21% had grade 3 tumours, 11.8% were suffering from bilateral breast cancer, 35% had luminal A subtype, 22% have luminal-B subtype, 21% have triple-negative breast cancer, and 11.9% have HER-2 over-expressed subtype. We also found 43% (33/76) had information related to distant metastasis, where 54% (18/33) had distant metastasis at the time of presentation, and the common site for metastasis was bone, followed by lung and liver. Discussion: The proportion of EOBC among Asian patients is higher than in the western population. Many patients were suffering from tumours with positive lymph nodes, which are a predictor of poor prognosis. A third of patients have large tumour size (>5cm) at presentation. Bilateral breast cancer percentage is high and finally, the distribution of molecular subtypes in EOBC differs from that of late-onset, which may indicate different risk factors. This study paves the road for further studies investigating EOBC and promotes early breast cancer detection in Malaysia.

14. Clinical-pathological characteristics of renal cancer in Malaysia: A follow-up study

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Introduction: This study looked at demographics and histopathological features of renal cell carcinoma (RCC) cases in Hospital Canselor Tuanku Muhriz (HCTM). The findings were compared with previously published study by the same institution. Methods: Demographic and histopathological data of RCC patients (n=177) treated at HCTM from 2008 to 2020 were analysed. The data was compared with the former study by the same institution that looked at 75 cases over the preceding ten years. Data evaluated were age, gender, ethnicity, tumour grade, tumour histology subtype and stage. Results: The male to female ratio was 2:1. Incidence was slightly higher in the Malay (50.8%) as compared to the Chinese ethnic group (43.5%). Mean age of patients was 58.9 (9-84) years old. Tumour histologies were clear cell (89.3%), papillary (6.2%), chromophobe (2.8%) and not otherwise specified (NOS) (1.7%). Specimens consisted of 41 (23.2%) Grade 1, 83 (46.9%) Grade 2, 24 (13.6%) Grade 3 and 8 (4.5%) Grade 4. There were 72 (40.7%) patients with Stage I disease, 24 (13.6%) at Stage II, 42 (23.7%) at Stage III and 10 (5.6%) at Stage IV. Discussion: Current data shows age influences initial diagnosis of renal cancer with less than 10% presenting at less than 40 years old. Clear cell remains the most common histological subtype with many harbouring low nuclear grades (Grades 1 and 2) and most patients present at lower disease stages (Stages I and II). Despite having more than double the number of patients as compared to the previous study, our findings concur with each other.

15. A study of the epidemiology and pathological profile of renal cell carcinoma in Hospital USM

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Introduction: Renal cell carcinoma (RCC) contributes 90% as primary tumour of the kidney. The epidemiology of RCC varies worldwide. We analysed our in-house data of RCC diagnosed in our centre. Methods: A 5-year retrospective study in Department of Pathology, Hospital Universiti Sains Malaysia. Using the keyword 'renal' and 'renal cell carcinoma', the data was retrieved from the Laboratory Information System. The clinicopathology parameters included were the clinical presentations, age, gender, staging, sites laterality, type of specimen. Statistical analysis was done using SPPS Ver 27. Results: We identified 37 cases of renal neoplasm with 35 cases were renal cell carcinoma, the remaining were epithelioid sarcoma and urothelial carcinoma. The median age was sixth decade with male predominant (68%). The most common clinical presentation was hematuria in 32%. The microscopic variants of RCC included clear cell (77%), papillary (20%) and chromophobe (3%). The most frequent pathology stage was pT3a. Discussion: Our study demonstrated that clinicopathological data in our population mimics those reported in Europe and USA. However, our patients presented with a more advanced stage. This may reflect differences in access to the healthcare worldwide. Further studies involving other local centres are recommended.

16. A study on expression of HER2/neu and Ki-67 in gastric malignancies

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Introduction: HER2/neu is gaining momentum as an imperative marker to be used in gastric cancers since it has been linked to a more aggressive outcome as well as for targeted therapy. The aggressiveness of the tumor is determined by the percentage of Ki-67 expression. Hence, immunohistochemical correlation of HER2 and Ki-67 with clinicopathological parameters of gastric carcinoma was done in this study. Methods: A total of 26 gastrectomy resection specimens received during the period of March 2020 to November 2021 were included in this study. Malignancies other than adenocarcinoma were excluded from the study. p-value of < 0.05 was considered statistically significant. Results: There was statistical association between presence of lymphovascular invasion and increase in "T" staging and "N" staging of gastric carcinomas (both p-values < 0.05). Significant correlation was observed between positive HER2 expression and the lower "T" stages (p-value < 0.001) and AJCC staging (p-value < 0.05) of gastric carcinoma when compared to the higher stages. There was no significant statistical correlation between parameters of "N" stage, "M" stage, perineural invasion and lymphovascular invasion, and both HER2 and Ki-67 index. No correlation between HER2 and Ki-67 expression was noted. Discussion: More research studies have to be done in this field of study so that better targeted therapies for HER2 and possibly Ki-67 be developed for inoperable advanced stages of gastric cancers.

17. Significance of α-SMA And FAP expression in colorectal cancer-associated fibroblasts

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Introduction: Cancer-associated fibroblasts (CAFs) are a major cellular component of the tumor microenvironment and play a pivotal role in tumor progression. α-SMA and FAP are the common markers to identify CAFs. This study aims to determine the association of α-SMA and FAP expression with colorectal carcinoma (CRC) invasion variables. Methods: α-SMA and FAP expression at the stromal invasion front of CRC was scored semi-quantitatively. Invasion variables such as depth of invasion, lymphovascular invasion, lymph node metastasis, and tumour budding (TB) were analysed. Results: Thirty-seven CRC patients aged 20 to 74 years. The male-to-female ratio was 15:22. α-SMA expression in CAFs showed a significant negative association with lymph node metastasis (p=0.013). In contrast, FAP expression showed a significant positive association with TB (p=0.022). There was no significant association of α-SMA and FAP expression with other variables. Discussion: High expression of α-SMA (>50%) in CAFs has negative lymph node metastasis (92.3%), which suggests a protective effect of α-SMA. A significant association between FAP expression and TB supports the role of FAP in inducing epithelial-mesenchymal transition and invasive behaviour of tumour cells. Further research for different biomarkers in CAFs is needed for the development of personalised therapy based on CAFs.

18. FOXP3, mismatch repair proteins and BRAF V600E status in young-onset colorectal cancer

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Introduction: This study aimed to determine the expression of Forkhead box P3 (FOXP3) with Mismatch Repair (MMR) proteins and proto-oncogene B-Raf (BRAF) V600E status among Young-onset Colorectal Cancer (YOCRC) at Hospital Universiti Sains Malaysia. Methods: This was a retrospective study of YOCRC (less than 50 years old) for 9 years (January 2013 to December 2021). Immunohistochemistry staining of FOXP3, BRAF V600E and MMR proteins expression was performed. The staining intensity and percentage of positive cells were used to evaluate the staining (Immunoreactive Scoring). The data were analysed using descriptive and correlation statistics. A p-value of ≤ 0.05 was taken as statistically significant. Results: Of 65 YOCRC patients, 53.8% had proficient MMR (pMMR) with a mean age of 41, while 46.2% had deficient MMR (dMMR) with a mean age of 35.5. The pMMR with BRAF V600E+ group expressed higher FOXP3 (54.2%) than dMMR with BRAF V600E+ group (22.9%). Patients with lower FOXP3 were observed more in dMMR with BRAF V600E- (47%) than pMMR with BRAF V600E- (5.9%). There was a significant relationship (p=0.002) between histological subtypes and expression of FOXP3. Discussion: Most YOCRC in this study expressed higher FOXP3 levels, most of which are pMMR with BRAF V600E+ than dMMR with BRAF V600E+.

19. Types of glomerular diseases: A single hospital-based study

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Introduction: Glomerular diseases are a major renal disorder worldwide. We aim to determine the types of glomerulonephritis (GN) at Hospital Universiti Sains Malaysia. Methods: This is a retrospective study of native kidney biopsies between January 2016 and December 2022. The types of GN were retrieved from the computerized system. Results: A total of 202 renal biopsies were performed at our centre (22 in 2016 to 48 in 2022). The age ranged from 3 to 68 years. Majority were children (51%) and Malays (95.5%) with a female predominance (female: male ratio = 1.5:1). The main indications for biopsy were nephrotic syndrome (51.0%), systemic lupus erythematosus to rule out lupus nephritis (LN) (15.8%), non-nephrotic range proteinuria with haematuria (14.4%), while others were less than 10%. The most frequent type of GN was LN (29.7%), followed by focal segmental glomerulosclerosis (FSGS, 25.2%), minimal change disease (MCD, 14.4%), membranoproliferative GN (10.9%), IgA GN (4.0%) and postinfectious GN (3.0%). Discussion: There was an upward trend of renal biopsy performed at our centre. The most common indication was nephrotic syndrome. LN (29.7%) and FSGS (25.2%) were the most frequent glomerular diseases followed by MCD (14.4%). This study could potentially add more information to the national database for medical renal disorders, particularly about glomerular diseases.

20. EUS-FNAC in diagnosing pancreatic lesions: A single centre experience

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Introduction: Endoscopic ultrasound-guided fine-needle aspiration cytology (EUS-FNAC) is currently the optimal method for sampling lesions of the pancreas. This study aims to review our experience with EUS-FNAC. Methods: A total of 95 cases of

pancreatic lesions with EUS-FNAC performed from January 2022 to December 2022 were included. There were nine inadequate specimens. 57 cases had final diagnosis based on EUS-FNA cell block and/or surgical pathology specimens. Results: There were 33 cases (58%) of neoplastic aspirate. The overall accuracy for the diagnosis of malignancy was 93%, with 89% sensitivity, 100% specificity, 100% positive predictive value and 83% negative predictive value. There were four false-negative cases; two cases were due to technical sampling error and the other two were camouflaged by massive amount of benign epithelial cells. Discussion: Our results were comparable with other published studies hence confirming that EUS-FNA can be considered as the first line technique for obtaining tissue diagnoses, particularly in pancreatic masses.

21. Pathologic spectrum of ossifying fibromyxoid tumour: Analysis of 19 cases

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Introduction: Ossifying fibromyxoid tumour (OFMT) is a rare soft tissue tumour of uncertain differentiation, characterized by cords and trabeculae of ovoid cells in a fibromyxoid matrix, surrounded by peripheral shell of bone. Methods: Nineteen cases diagnosed at Aga Khan University Hospital from 2013-2022 were included. Histologic type and pathologic features were assessed together with available follow-up information. Results: This study included 13 males and 6 females aged between 22 and 67 years (median: 37). Buttock was the most common location (4), followed by thigh (3) and foot (3). Tumour size range was 1.6-17cm (mean: 8cm). Diagnoses were typical OFMT (8), typical OFMT, non-ossifying variant (4), atypical OFMT (3) and malignant OFMT (4). Fifteen cases showed bone formation: 14 within the tumour and 6 at periphery. Twelve out of 13 patients with available follow-up information (range 2 to 8 years) were alive. All had surgical excision with local recurrence in 3 cases. Two recurrences involved hand and foot with typical OFMT; one of them died of lung metastasis in 2 years. The third recurrence had atypical OFMT, awaiting treatment. One malignant OFMT with available follow-up information was disease-free post treatment. Discussion: OFMT should be considered in differential diagnoses of bone-forming tumours of lower limbs. Recurrence was unrelated to worrisome histological features and observed more in hand and foot.

22. Clinicopathology of lipomatous tumours – An institutional ten-year experience

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Introduction: Lipomatous tumours are one of the most common soft tissue tumours; due to their varying clinical presentation and their heterogeneous morphology, they consistently present a diagnostic problem leading to inappropriate patient management. The study focuses on our institution's clinicopathologic aspects of large lipomatous tumours and their clinical outcome. Methods: We retrospectively collected 79 cases of archived lipomatous tumours (larger than 10 cm in size). Histopathology slides were reviewed. The clinicopathological data were retrieved from the medical records and histopathology reports. Results: Fifty-two of the 79 cases were histologically evaluated as lipomas. The remaining 27 cases were liposarcomas. Atypical lipomatous tumour/well-differentiated liposarcoma (ALT/WDLS) and myxoid liposarcoma were the two most prevalent subtypes of liposarcoma, accounting for 40.7% of cases. The overall recurrence rate for liposarcoma was 37%, with histological grade being the most significant predictor for recurrence [$\beta = 5.93$, $p < 0.001$]. There is no significant difference in the clinical outcomes of large lipomas and ALT/WDLS after surgical excision. Discussion: Due to their morphologic heterogeneity, lipomatous tumours can be challenging to diagnose. Molecular testing of the MDM2 and CDK4 genes is increasingly important to confirm the diagnosis of liposarcoma, thus reducing morbidity and mortality.

23. Evaluation of HV16/18 E6 and E7 oncoprotein expression in cervical lesions

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Introduction: High-risk human papillomavirus (HPV) strains particularly HPV16 and HPV18 have been the hallmark causative agents of cervical malignancy. Viral oncoproteins E6 and E7 play predominant roles in tumour progression notably in persistent HPV infection. This study focused on the evaluation of HPV oncoprotein expression in formalin fixed paraffin embedded (FFPE) tissue in different grades of cervical lesions. Methods: A total of 102 FFPE cervical tissues of different grades were collected from Hospital Universiti Sains Malaysia and Hospital Raja Perempuan Zainab II from the year 2014 to 2022. Immunohistochemical analysis of E6 and E7 oncoproteins of HPV16 and HPV18 were evaluated. Results: Immunohistochemical staining of HPV16-E7, HPV18-E7 and HPV 16/18-E6 was seen within both nuclear and cytoplasm of cervical epithelium. HPV18-E7 expression correlated with the increasing grades of cervical lesions from the low-grade precursors to malignancy. HPV16-E7 expression was significantly associated with histological grades of cervical lesions that had been confirmed to be HPV16-DNA positive ($p=0.001$). Discussion: A variation of HPV oncoproteins immunostaining patterns were noted in our samples in which some were concordant with the previous studies. Immunohistochemistry application in targeting specific viral oncoproteins for detection of HPV within FFPE tissue samples was feasible and applicable, especially in basically equipped laboratories.

24. Analysis of physician training needs in filling anatomic pathology request forms

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Introduction: In practice, nonconformity and poor quality of filing out a pathological request form are often observed. These nonconformities have consequences on sample management, histology report and led to additional work for pathologists due to missing information or because of the need to modify the sample management. This study aimed to analyse the physician training needs to address these issues. Methods: A total of 24 internal medicine doctors (IMD) from Sheikh Khalifa Hospital participated in this study. They underwent individual interviews and answered an open-ended anonymous survey on the difficulties encountered in filling out a request for a pathological examination and vial labelling; this followed by a Frequency, Severity, Problems (FSP) analysis grid. Results: The mean frequencies of the anatomic pathology request preparation (APRP) and labelling of vials were rated respectively at 0.79 and 0.75. Their severities were estimated respectively at 1.12 and 0.54. IMD expressed training needs in the APRP for histopathological examination. The means of cognitive skills, know-how, and knowledge being problems for the APRP corresponded respectively to 0.75, 1.29 and 1. Discussion: Surgical specimens for pathology examination must contain all required clinical information. To address this insufficiency, quality improvement plans must be implemented such as organizing training to improve the quality of the information submitted. A properly filled request form ensures quality sample management and a valid report.

CATEGORY: CASE SERIES

1. Light chain proximal tubulopathy with crystalline cast nephropathy: Two case series

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Introduction: Light chain proximal tubulopathy (LCPT) is a rare form of paraprotein-related kidney disease in which monoclonal free light chains damage the proximal renal tubular epithelial cells. Combined LCPT and crystalline light chain cast nephropathy (LCCN) is even rarer with less than 20 cases reported worldwide. We describe 2 unusual cases of combined LCPT and LCCN. Case Presentation: Case 1 is a 41-year-old man who presented with acute kidney injury (AKI) and nephrotic range proteinuria. Further work-up confirmed the diagnosis of multiple myeloma. Case 2 is a 28-year-old man presented with nephrotic syndrome and AKI. Limited blood and bone marrow examinations revealed lack of evidence of paraprotein, plasmacytosis or atypical lymphoid cells. Patient lost to follow-up subsequently. Results: Both renal biopsies showed focal intracytoplasmic crystalline inclusions within proximal tubular epithelial cells and prominent crystalline and noncrystalline casts within distal tubules. Congo red stains for amyloid deposition were negative. Immunofluorescence and immunohistochemical studies showed Lambda light chain restricted staining within the intratubular casts and proximal tubular epithelium focally. Ultrastructural studies were unavailable for both cases. Discussion: To the best of our knowledge, this is the first case series of simultaneous LCPT and crystalline LCCN reported in Malaysia. Despite the rarity, correct diagnosis is crucial as it initiates proper haematological work-up for appropriate patient management.

2. Epstein-Barr virus-associated smooth muscle tumour: A case series

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Introduction: Epstein-Barr virus-associated smooth muscle tumour (EBV-SMT) is a rare neoplasm recognized in immunocompromised patients including HIV-infected patients. Case Presentation: Case 1: A 41-year-old male with underlying HIV infection, presented with abdominal pain. CT abdomen showed multiple rounded hypodense lesions in the liver. He underwent CT guided liver biopsy. Case 2: A 31-year-old male with underlying HIV infection, presented with right sided lower limb pain. MRI spine showed an oval, homogenously enhancing intrathecal extramedullary nodule at level L3/L4 causing nerve root compression. He underwent tumour excision. Results: Microscopically, the tumours from both patients were composed of bland spindle cells arranged in fascicles. These spindle cells were immunoreactive to smooth muscle marker i.e., SMA or Caldesmon, and positive for EBER transcripts by in-situ hybridization. Discussion: EBV-SMT is a rare tumour occurring over a wide age range and in any location in the body. The presenting features may be nonspecific or not related to the site of involvement. Therefore, it is recommended that this entity be always included in the differential diagnosis of a mesenchymal tumour arising in any organ in immunocompromised patients of all ages.

3. Adrenocortical carcinoma: A look at 3 cases and review of literature

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Introduction: Adrenocortical carcinoma (ACC) is a rare and aggressive malignant epithelial tumour of the adrenal gland. Three cases are discussed in this series observing the different demographic, clinicopathological features and outcomes. Case Presentation: The first case was a 16-year-old boy with features of hypercortisolism, initially diagnosed as adrenal cortical adenoma. Histopathological examination confirmed ACC. The second case was a 22-year-old woman treated for multiorgan failure secondary to cortisol-producing ACC. Despite adrenalectomy, she had resistant hypercortisolism. The third case was of a 66-year-old woman being treated for endometrial carcinoma, incidentally found to have an adrenal mass. She defaulted follow-up but presented 2 years later with a larger adrenal mass. Results: All three cases consisted of large adrenal masses (8 to 15cm) with malignant morphology, invasive growth and increased proliferative activity on histopathological examination. All the patients eventually developed disseminated diseases. One of the patients succumbed, while two others were lost to follow-up. Discussion: Most ACC develops through somatic mutations while some are related to genetic susceptibility. The 5-year overall survival rate is 37-47% but only a few patients survive up to the mark, since many of them present with disseminated disease, as demonstrated in our case series.

4. Orbital Langerhans cell histiocytosis: A series of two cases

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Introduction: Langerhans cell histiocytosis (LCH) is a clonal disorder characterised by proliferation of Langerhans cells. LCH is clinically classified by extent of organ involvement (single vs multisystem). There is poorer outcome if high-risk organs are involved. We hereby present two cases of orbital LCH in children. Case Presentation: Case 1 is a 1-year-old boy, presented with unilateral eye proptosis for 2 months. Case 2 is a 2-year-old boy, presented with bilateral eyelid discharge and worsening of right eyelid swelling. Biopsies were performed. Results: Both cases showed atypical mononuclear cells admixed with eosinophils, neutrophils, and small lymphocytes. These atypical cells showed round to oval pale-looking nuclei with irregular contour, nuclear grooving, and eosinophilic cytoplasm. The cells were positive for CD1a, S100 protein and Langerin (CD207). Diagnosis of LCH was confirmed. Hepatomegaly was detected by abdominal ultrasound in the second patient. Discussion: Orbital lesion is one of the presentations of LCH in children. Differential diagnosis includes reactive processes. After diagnosis is made, systemic workup is beneficial to evaluate possible multisystem involvement and risk organ involvement. LCH harbours active somatic BRAF V600E mutation and MAP2K1 gene mutations. The use of BRAF inhibitor in refractory cases has been described in literatures recently.

5. Pathology of gastric fungal infections in immunocompetent hosts: A report of 2 cases

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Introduction: Fungal infections of the stomach are extremely uncommon in immunocompetent hosts. The pathological diagnosis is sometimes challenging due to the lack of characteristic features in the clinical data and endoscopic findings of these unusual infections. Methods: Two cases of gastric fungal infections in immunocompetent hosts were retrieved from the archive. Clinicopathological characteristics of these cases were described. Results: The first case was a 27-year-old man without any underlying diseases who presented with severe abdominal pain and septic shock. Exploratory laparotomy revealed gastric gangrene, resulting in a subsequent proximal gastrectomy. Histologically, acute necrotizing gastritis with well-formed granulomas and a fungal infection were noted. GMS and PASD stains show abundant septate hyphae with dichotomous branching, consistent with invasive gastric aspergillosis. The second case involved a 50-year-old woman with dyspepsia who underwent esophagogastroduodenoscopy. Endoscopic findings showed yellow-white plaques in the stomach. Gastric xanthoma was suspected. The biopsy specimen revealed gastric mucosa without significant active inflammation containing several budding yeasts and pseudohyphae, consistent with gastric candidiasis. Discussion: Clinicopathological features of two cases of gastric fungal infections in the immunocompetent host were described. Due to non-specific clinical data and endoscopic findings, a thorough pathological assessment is required to arrive at a definite diagnosis in these cases.

6. Malignant transformation of mature cystic teratoma: Our encounters in Sarawak

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Introduction: Malignant transformation of ovarian mature cystic teratoma (MCT) is rare, with the occurrence rate of 0.17 to 2%. Squamous cell carcinoma (SCC) is the most common type. We present three such cases encountered in Sarawak General Hospital (SGH); one transformed to clear cell carcinoma (CCC) and two to SCC. Case Presentation: The first case was a 50-year-old lady,

underwent total hysterectomy, bilateral salpingo-oophorectomy (TAHBSO) for a huge complex left ovarian tumour. The second case was a 53-year-old woman who had TAHBSO for an ovarian mass associated with ascites and intraabdominal keratin flake seeding. The third case was a 32-year-old woman who had left salpingo-oophorectomy for ovarian tumour. Results: Histologically, the ovarian MCT of the first case showed malignant transformation of cuboidal epithelium into neoplastic clear cells forming tubulocystic and solid patterns. The latter two cases showed malignancy arising from squamous epithelium of MCT. All three MCTs were large, measuring more than 15 cm at the largest dimension; the cyst wall was variably thickened and nodular with necrosis. Discussion: A large MCT should prompt extensive and thorough examination to exclude malignancy. Patients with MCT with malignant transformation will require additional management such as staging laparotomy or adjuvant therapy.

7. Cutaneous lymphoid hyperplasia: A report of two cases

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Introduction: Cutaneous lymphoid hyperplasia (CLH) is a reactive lesion of benign T or B lymphocyte infiltrates. Often it is due to variety of stimuli such as drugs, microorganism, or foreign bodies. It is important to exclude cutaneous lymphoma as this condition may simulate the malignant counterpart. Case Presentation: We report two cases of CLH diagnosed in our centre. Case 1 was a 34-year-old female presented with a 3-month history of a 1x1cm cystic lesion in the right breast. Case 2 was a 39-year-old male with underlying chronic myeloid leukaemia, presented with a 2-month history of increasing size of a 5x5cm erythematous mobile lesion on the right elbow. Results: Microscopic examination of both lesions showed a few clusters of reactive lymphoid follicles with expanded germinal centres within the subcutaneous tissue. CD20 and CD3 identified both B and T lymphocytes in their respective locations. Proliferative Ki-67 index was low in both cases. Negative CD30, CD23, CD5 and cyclin D1 excluded other cutaneous lymphomas. Discussion: Clinical history and tissue biopsy with ancillary tests are important for an accurate diagnosis. Distinguishing CLH from other cutaneous lymphomas is important as both have different prognosis and treatment.

CATEGORY: CASE REPORT

1. Epstein-Barr virus-positive diffuse large B cell lymphoma, not otherwise specified

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Introduction: Epstein-Barr virus-positive diffuse large B cell lymphoma, not otherwise specified (EBV+ DLBCL, NOS) is characterised by frequent extranodal involvement, associated with systemic symptoms and poorer prognosis. We hereby report a case of EBV+DLBCL, NOS. Case Presentation: A 54-year-old Chinese male suffered from sore throat and B symptoms for three months. Clinically, he showed left tonsillar ulceration and systemic lymphadenopathies. Biopsy of left tonsil was performed. Results: The tonsillar tissue showed diffuse infiltration of large atypical lymphoid cells. These cells were positive for CD19, CD20, CD79a, PAX5, MUM1, OCT 2, BOB1 and CD30. T and NK cell markers were negative. EBV-encoded small RNAs (EBER) *in situ* hybridisation showed positivity in tumour cells. EBV+ DLBCL, NOS was confirmed. He died of disease progression in one month. Discussion: Incidence of EBV+DLBCL, NOS is higher in some Asian countries (up to 8-10%) compared to the West. Differential diagnosis includes Classic Hodgkin Lymphoma and T cell-rich B cell lymphoma. When encountering a diffuse polymorphic or monomorphic B cell lymphoproliferative disorder that contains Reed Sternberg-like cells, plasmacytic morphology, angioinvasion, tumour necrosis and non-germinal centre B (non-GCB) immunophenotype, EBV testing would be helpful in identifying this rare entity.

2. Diagnostic dilemma: A case of glandular odontogenic cyst

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Introduction: Glandular odontogenic cysts (GOCs) are rare developmental odontogenic cysts. They possess distinct clinical, radiographic, and microscopic features which assist in distinguishing them from other mimickers. We present a case of GOC arising from the mandible. Case Presentation: A case of 62-year-old man presented with mandibular swelling. CECT showed a cystic lesion in the body of the left mandible, causing cortical expansion associated with cortical break and submandibular collection. Results: Histologically, a unilocular cystic lesion lined by predominantly ciliated mucous-secreting epithelium and focally by non-keratinising stratified squamous epithelium of variable thickness was seen, associated with supportive microscopic features such as eosinophilic cuboidal cells, clear vacuolated cells, mucous goblet cells with microcysts and tufting. The tumour lied close to the root apex of teeth and there was no association with unerupted tooth, rendering dentigerous cyst unlikely. The lack of nuclear palisading excluded odontogenic keratocyst and unicystic ameloblastoma. The cyst wall lining, lined predominantly by ciliated epithelium with focal microcyst, made central mucoepidermoid carcinoma less likely. The patient underwent segmental resection of mandible, and a diagnosis of GOC was established. Discussion: GOCs are rare entities and mostly arise from the mandible. It is important to distinguish them from other more common odontogenic cysts for appropriate management.

3. A challenging case of jejunal malignant gastrointestinal neuroectodermal tumour

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Introduction: Malignant gastrointestinal neuroectodermal tumour (GNET) is a rare sarcoma involving the gastrointestinal tract with neuroectodermal differentiation. The tumour resembles clear cell sarcoma but shows no specific evidence of melanocytic differentiation. We present a case of malignant GNET arising from the jejunum. Case Presentation: A 23-year-old lady presented with persistent iron deficiency anaemia and examination revealed a left hypochondriac mass. OGDS showed a large friable mass at D3 and biopsies were obtained. CTTAP showed a heterogeneously enhancing mass arising from D4 and proximal jejunum (12cm in widest dimension). The differentials included lymphoma, GIST, and adenocarcinoma. Results: Histologically, the tumour showed nested epithelioid cells with irregular hyperchromatic nuclei, inconspicuous nucleoli and clear to vacuolated cytoplasm. Diffuse SOX10 and S100 with focal synaptophysin positivity were appreciated. A diagnosis of malignant GNET was rendered. The patient underwent resection of the tumour and diagnosis was confirmed. Discussion: Malignant GNET are rare entities and can arise at any part of the gastrointestinal tract. It is important to distinguish this entity from other more common gastrointestinal tumours such as adenocarcinoma, GIST and lymphomas for appropriate management and treatment.

4. Ovarian gonadoblastoma with 46,XX karyotype and no sex development disorder

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Introduction: Gonadoblastoma is a rare neoplasm comprising sex cord and germ cell elements, widely thought to be exclusive to patients with gonadal maldevelopment caused by genetic anomalies. We present a case of gonadoblastoma in a phenotypically normal girl with 46,XX karyotype without sexual developmental disorder. Case Presentation: A 6-year-old girl showed precocious puberty, with breast development (Tanner Stage 4b), pubic hair (Tanner Stage 2) and per vaginal spotting. An MRI brain ruled out central precocious growth. Intra-operatively, she had a reproductive-age uterus, enlarged right ovary and normal-appearing left ovary. Results: Right ovary (38x25x20mm) was excised, showing an intimate mixture of larger germ cells and sex cord derivatives (Sertoli and granulosa cells) in cellular nests. The germ cell component was CD117(+), OCT3/4(+), SALL4(+), PLAP(+), D2-40(+) and pankeratin AE1/3(+), while the sex cord component is inhibin(+) and calretinin(+). Microcalcifications were helpfully present. Discussion: Gonadoblastoma was thought to be restricted to those with gonadal maldevelopment. A significant number have been misdiagnosed as mixed germ cell-sex cord-stromal tumours (MGC-SCST). If this misconstrued notion is expelled, gonadoblastoma can be effectively differentiated by a nested pattern, contrary to the diffuse pattern and absence of calcifications in MGC-SCST. The patient is on interval follow-ups and pelvic ultrasound monitoring. She is currently well and thriving.

5. NUTM1 gene-rearranged neoplasms: A case report with peculiar morphology

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Introduction: NUTM1 gene-rearranged neoplasms (NRNs) are tumours characterised by chromosomal rearrangements involving the NUTM1 gene. Formerly known as NUT midline carcinomas (NMCs), they were aggressive childhood carcinomas with BRD4-NUTM1 gene fusion and nuclear NUT expression. Recent studies have shown that NRNs can occur in a broader age range, in non-midline locations, and with sarcomatous morphology. Herein, we describe a case of NUTM1-rearranged neoplasm arising from an unusual site, the mesentery of the small bowel. Case Presentation: An 18-year-old gentleman presented with left-sided abdominal pain and intestinal obstruction symptoms. Computed tomography (CT) revealed a huge left abdominal mass. The initial radiological differential diagnosis was intra-abdominal sarcoma. Results: The tumour had sarcomatous morphology with no apparent lineage differentiation, and NUT immunohistochemistry displayed weak nuclear staining. Pan-sarcoma fusion assay sequencing was negative, but molecular analysis identified a rearrangement in the NUTM1 gene, confirming the diagnosis of NUTM1 gene-rearranged neoplasms. The patient received chemotherapy but had a new lung metastasis during the latest follow-up. Discussion: The case highlights the importance of considering NRNs in diagnosing uncommon sarcomatous tumours, as they may exhibit variable characteristics. NRNs have shown good response to bromodomain and extra-terminal inhibitors, and advancements in tumour diagnosis have identified novel fusion partners and morphology.

6. A rare case of invasive primary Paget disease of scrotum

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Introduction: Extramammary Paget disease (EMPD) is a rare and aggressive cutaneous malignancy that primarily affects the anogenital region. Scrotal involvement is infrequent, with EMPD lesions mimicking other skin conditions, highlighting the importance of an accurate diagnosis to differentiate between primary and secondary EMPD for appropriate treatment. Herein, we present a case of primary extramammary Paget disease of the scrotum with invasive adenocarcinoma. Case Presentation: This is a 72-year-old gentleman with a history of benign prostatic hyperplasia who presented with a pruritic scrotal lesion that had been gradually increasing in size over three years. The lesion showed a hyperkeratotic plaque with a verrucous surface upon clinical examination. Results: Scrotal skin biopsy revealed intraepidermal tumour cells. The Paget cells exhibited acinar structure formation with dermal infiltration. Immunohistochemistry showed CK7 positivity and negative for CK20, CK5/6, and MelanA, consistent with scrotal EMPD. Discussion: EMPD frequently masquerades as benign skin conditions, necessitating early biopsy for timely diagnosis and prompt treatment. Due to the high risk of recurrence and distant metastases in invasive EMPD, vigilance is essential when dealing with eczematous lesions.

7. Reticular and myxoid non-keratinising nasopharyngeal carcinoma: A diagnostic challenge

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Introduction: Non-keratinising nasopharyngeal carcinoma (NK-NPC) is commonly associated with Epstein-Barr virus (EBV) and is characterised by distinct histologic patterns, ranging from a syncytial sheet to nests of cells mixed with lymphocytes and plasma cells. We herein present an extremely rare variant of NK-NPC, which mimics salivary gland carcinoma (SGC). Case Presentation: A 32-year-old male, presented with a left nasopharyngeal mass involving cranial nerve. CT imaging revealed a large, solid nasopharyngeal tumour with intracranial extension and nodal metastasis. Results: Histopathological examination from the biopsy showed malignant cells arranged in reticular appearance within a myxoid-rich stroma with malignant cytologic features mimicking SGC. The tumour was strongly positive for CKAE1/AE3 and p63; it also displayed strong nuclear positivity for EBV but did not express CD117 or synaptophysin. Discussion: This subtype of NK-NPC presents diagnostic challenge due to its rarity and morphological similarities with SGC. Only a few case reports have been published for this variant and the current World Health Organization classification system briefly acknowledges its existence. NK-NPC is associated with significant genetic and epigenetic alterations, and recently has been linked with JAK/STAT3 signalling pathway which offers potential therapeutic interventions. However, limited understanding of the precise molecular alterations in this subtype may restrict the implementation of the targeted therapies.

8. Clear cell carcinoma of the kidney with partial regression features: A case report

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Introduction: Spontaneous regression of malignant tumours is a rare occurrence. The incidence of spontaneous regression in metastatic renal cell carcinoma (RCC) has been estimated between 1% to 7%. This mostly applied to pulmonary metastatic RCC regression cases. We report a rare case of spontaneous RCC regression in a primary tumour. Case Presentation: A 58-year-old Malay man presented with intermittent haematuria. Computed tomography showed an irregular, heterogeneously enhancing left kidney mass, suggestive of RCC. Subsequently, he underwent laparoscopic left radical nephrectomy of a 15cm highly vascular tumour. No prior treatment such as radiation therapy or arterial embolization was given. Results: Histological evaluation showed features of renal clear cell carcinoma with the presence of tumour regression changes amounting to 60% of tumour which include sclerotic nodules ranging in appearance from a cellular fibroblastic to scar areas, residual networks of capillaries resembling haemangioma, stromal fibrosis and hyalinisation, oedematous stroma, cystic degeneration, and calcification. Focal caseating and non-caseating granulomatous reactions are also present. Discussion: Interpretation of regression in renal clear cell carcinoma may be difficult as the features are maybe non-specific or may overlap with multicystic RCC. Recognition and studying of regression changes in RCC may allow insight into tumour biology and potential treatment option in the future.

9. A rare case of anaplastic meningioma, WHO Grade 3

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Introduction: Meningioma is a known benign tumour (WHO Grade 1), even though about 25% is reported as atypical (WHO Grade 2) or 1-6% anaplastic (WHO Grade 3). The malignant type is locally aggressive with high incidence of recurrence despite a complete resection. Case Presentation: We report a case of meningioma Grade 3 in a 58-year-old male who presented with 2 years history of worsening of behavioural changes and bilateral lower limbs weakness for 3 months. Results: MRI brain

showed bifrontal extra-axial solid cystic lesion. Intraoperative findings demonstrated tumour infiltration into the adjacent tissues. Histopathological examination exhibits pleomorphic and focal anaplastic meningeal cells with high mitoses >20 mitoses per 10 high-power fields and has infiltrated into the dura, brain, and cranial bone. Ki-67 proliferative index is 30%. Discussion: Diagnosis was made based on the recent WHO Classification's criteria of: ≥ 20 mitoses per 10 high-power fields and frank anaplasia resembling sarcoma. Genetic alterations (*TERT* promoter mutation and homozygous deletion of *CDKN2A* and/or *CDKN2B*) were not ascertained due to unavailability of these molecular studies in our centre. Both male gender and deep-seated lesion are risks for a higher-grade meningioma with 0.1% of extracranial metastases. A close follow up of such patient is recommended.

10. Isolated soft tissue Rosai-Dorfman disease: An unusual entity

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Introduction: Rosai-Dorfman disease (RDD) is a proliferative histiocytic disorder typically presenting with massive lymphadenopathy involving the head and neck region. Isolated soft tissue RDD is infrequent but should be considered in the differential diagnoses of soft tissue tumours. Case Presentation: A 34-year-old male complained of a painful upper back swelling of one month duration. Examination showed a diffuse, hard, subcutaneous mass which measured 6x4cm, clinically suspicious of a lipomatous tumour. There was no lymphadenopathy. The mass was excised and submitted for histological examination. Results: Macroscopically, there was a fleshy, unencapsulated lesion with irregular borders measuring 40x30x30mm displaying pale-yellowish cut surfaces. Microscopic examination showed dense fibroblastic proliferation associated with florid infiltration by histiocytes, reactive lymphoid follicles and plasma cells. The histiocytes appeared atypical with enlarged, round, vesicular nuclei and abundant pale cytoplasms. Emperipolesis was found upon close inspection. The histiocytes were immunohistochemically positive for S100 and CD68 but negative for CD1a. Markers of lymphoma and soft tissue tumours were negative. A diagnosis of RDD was made. Discussion: Atypical presentation of RDD, coupled with dense inflammatory and fibroblastic background may cause diagnostic confusion. High clinical and pathological suspicions are required to arrive to the right diagnosis.

11. Metastatic lobular breast carcinoma masquerading as pancreatic tumour

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Introduction: Invasive lobular carcinoma (ILC) is a subtype of invasive breast carcinoma that often metastasises to the pancreas as compared to other types of breast carcinoma. Case Presentation: A 47-year-old female without a past medical history presented with obstructive jaundice and epigastric discomfort. CT scan detected a mass at head of pancreas with poor demarcation from duodenum, and peripancreatic and paraaortic lymphadenopathy. Open biopsy was done during bypass surgery for gastric outlet obstruction due to pancreatic head tumour. Results: Histopathological examination revealed mildly pleomorphic neoplastic cells infiltrating between pancreatic acini and ducts in short cords and single file patterns. The immunohistochemical profile was suggestive of breast primary (GATA3+, mammaglobin+, ER+, PR+, e-cadherin-). There was however dilemma to diagnose metastatic ILC due to lack of a prior history and no palpable breast lump at the initial presentation. The issues were conveyed to the primary team. A subsequent mammogram showed a BIRADS 5 lesion in the right breast which was confirmed to be invasive lobular carcinoma by biopsy. Discussion: This rare case highlights diagnostic challenges in distinguishing pancreatic adenocarcinoma with lobular carcinoma-like pattern from metastasis. Accurate diagnosis will only be possible with relevant clinical investigations and thorough pathological examination.

12. Histological changes in hepatocellular carcinoma post-locoregional therapy

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Introduction: Locoregional therapies are widely practiced in treatment of primary hepatocellular carcinoma and metastatic carcinoma to the liver as they provide a more targeted treatment with less side effects. Transarterial chemo-embolisation and selective internal radiotherapy (SIRT) are a few examples. However, histopathological findings after locoregional therapy of hepatocellular carcinoma are rarely reported. Case Presentation: A 61-year-old man with underlying Hepatitis B and subsequent hepatocellular carcinoma was treated with SIRT followed by wedge liver resection. Results: Macroscopically, the specimen showed a well-defined mass with areas of fibrosis and haemorrhage. Microscopic examination showed 70% tumour necrosis with numerous microspheres surrounded by multinucleated giant cells with histiocytes and chronic inflammatory cells. Currently the patient is well with regular follow-up. The latest ultrasound findings show no residual liver lesion despite liver cirrhosis. Discussion: Although assessment of treatment response following locoregional therapy based on histopathological findings are not widely practiced, recognising histopathological changes such as tumour necrosis, provide valuable insight to a patient's prognosis. Minimal to absent tumour necrosis implies poor response, limiting further locoregional therapy option. Findings of numerous microspheres might pose a diagnostic challenge as they mimic fungal organisms. Hence histological examination with aid of special stains like PAS and Grocott's methenamine silver stain may be useful.

13. C3 glomerulonephritis or infection-related glomerulonephritis? A diagnostic dilemma

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Introduction: C3 dominant deposit can be seen in infection-related glomerulonephritis (IRGN) and C3 Glomerulonephritis (C3GN). The distinction without an electron microscope study is challenging. Case Presentation: A 12-year-old boy presented with lower limb petechiae, upper respiratory tract infection, proteinuria, microscopic haematuria, elevated serum creatinine and low C3 complement. Serum ANA and ASOT were negative. Serologic testing for p-ANCA was positive. Results: Renal biopsy showed crescentic lesion with dominant C3 deposits. The differential diagnoses were IRGN and C3G. He was treated with corticosteroids, mycophenolate mofetil and hydroxychloroquine. The patient showed signs of renal function recovery with serum creatinine trended down. Discussion: Characteristics of IRGN and C3GN can overlap. Both can have haematuria, proteinuria and low C3 level. IRGN is triggered by infection, which can also be an inciting factor in C3GN. Both cases can reveal crescentic nephropathy. Our patient showed dominant C3 deposits, leading to possible C3GN diagnosis, but clinical features, improvement in acute kidney injury, normalisation of C3, ANCA positivity and resolution of haematuria supported IRGN. For a definitive diagnosis, electron microscopy is necessary. Centres performing renal biopsies should have this test available, either in-house or through collaboration with other centres.

14. Endometriosis as a large urinary bladder mass mimicking malignancy

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Introduction: Endometriosis is a common entity characterised by functional endometriotic tissue outside the uterus. However, involvement of the urinary tract is rare (1-2%), and the bladder is most affected. Here we describe a case of a young lady who presented with a bladder mass, clinically thought to be urothelial carcinoma but turned out to be endometriosis on histology. Case Presentation: A 36-year-old nulliparous lady had a previous diagnosis of well-differentiated squamous cell carcinoma of the tongue with lymph node metastasis. She presented with a 5-year history of intermittent and cyclical chronic suprapubic pain, urinary frequency and dysuria without frank haematuria. CT abdomen and pelvis revealed a large intra-luminal polypoidal mass at the left superolateral aspect of the bladder, suspicious of urothelial carcinoma. Results: Trans-urethral resection of bladder tumour was done, and histological examination showed florid endometriotic foci, characterised by presence of many endometrial glands and their stroma, embedded within the bladder wall with no evidence of malignancy. Discussion: The case highlights that bladder endometriosis presenting as a mass lesion can mimic urinary malignancy. Therefore, women of reproductive age complaining of urinary symptoms, most often during the menstrual cycle, should be investigated earlier for endometriosis. This requires close collaboration from both urologists and gynaecologists.

15. Pancreatic lymphoma: A diagnostic challenge

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Introduction: Primary pancreatic lymphoma is very rare. The commonest type is diffuse large B-cell lymphoma (DLBCL). Clinically, it is difficult to distinguish pancreatic lymphoma from the more common pancreatic ductal adenocarcinoma due to nonspecific presentation and imaging findings. Case Presentation: A 79-year-old male with underlying hypertension and diabetes mellitus, presented with worsening epigastric pain and obstructive jaundice. CT scan showed a locally advanced pancreatic head lesion, encasing portal vein and duodenal wall. There were multiple peripancreatic, splenic hilum, and para-aortic lymphadenopathy, and splenic lesions. Results: Endoscopic ultrasound-guided biopsy of the pancreatic mass shows fibrotic pancreatic tissue with extensive crush artefacts. There are poorly cohesive clusters of crushed blue cells within fibroblastic stroma and amidst haemorrhagic background. Portal lymph node biopsy reveals polymorphous lymphoid cells and many crushed large blue cells. Immunohistochemically, these blue cells are CD20+, PAX5+, CD10-, BCL6+, MUM1+, BCL2-, c-MYC+, with Ki67 index of 70-80%. They are negative for epithelial and neuroendocrine markers. A diagnosis of DLBCL was made. Review of clinical and radiological findings concurred with the impression of lymphoma. Discussion: This rare case presents an overview of challenges in diagnosing pancreatic lymphoma due to its rarity and potential pitfalls in small biopsies. It also emphasises the importance of a multidisciplinary approach in making diagnosis.

16. Bilateral primary adrenal diffuse large B cell lymphoma without adrenal insufficiency

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Introduction: Primary adrenal lymphoma (PAL) is a rare tumour that presents as bilateral adrenal gland masses in most cases. Case Presentation: A 55-year-old male patient presented with asthenia and anorexia for the past three months. Results: Laboratory tests revealed thrombopenia and elevated LDH. Plasma total cortisol, aldosterone, ACTH level and serum catecholamines were normal. Abdominal ultrasound examination and computed tomography (CT) scanning revealed a right adrenal gland mass (100×80 mm) and a left adrenal gland mass (75x80 mm). Ultrasound-guided biopsy was done. Histopathological examination and immunohistochemistry tests (CD20+, Mum1+, Bcl-2+, CD3-, CD5-, CD10-, Cytokeratins-, BCL6-, CD30-, Tdt-, C-Myc-) confirmed the lesion was diffuse large B cell lymphoma (DLBCL). Discussion: PAL without any other extra-adrenal involvement is a rare subtype of extranodal non-Hodgkin lymphoma. DLBCL is the predominant histological subtype, which represents 70% of PAL cases. Identification of bilateral adrenal glands in CT warrants ultrasound-guided biopsy for further histopathological examination coupled with immunohistochemistry tests to confirm the diagnosis. Recommended treatment regimen for PAL is R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone), a classical chemotherapy regimen.