Abstracts: 18th Trainee Presentation Session (26th November 2022)

No.1

Name: Dr. Chan Ka Yin, Aden

Subspecialty: Anatomical Pathology

Affiliation: Department of Anatomical and Cellular Pathology, Prince of Wales Hospital.

Combinations of single gene biomarkers can precisely stratify 1,028 adult gliomas for prognostication

Advance genomic techniques have now been incorporated into diagnostic practice in neuro-oncology in the literature. However, these assays are expensive, time-consuming and demand bioinformatics expertise for data interpretation. In contrast, single gene tests can be run much more cheaply, with short turnaround time and are available in general pathology laboratories. The objective of this study was to establish a molecular grading scheme for adult gliomas using combinations of commonly available single-gene tests. We retrospectively evaluated molecular diagnostic data of 1,275 cases of adult diffuse gliomas from three institutions where we were testing for IDH1/2 mutation, TERTp mutation, 1p19q codeletion, EGFR amplification, 10q deletion, BRAF V600E and H3 mutations liberally in our regular diagnostic work-up. We found that a molecular grading scheme of grade Group 1 (1p19q codeleted, IDH mutant), grade Group 2 (IDH mutant, 1p19q nondeleted, TERT mutant), grade Group 3 (IDH mutant, 1p19q nondeleted, TERT wildtype), grade Group 4 (IDH wildtype, BRAF mutant), grade Group 5 (IDH wildtype, BRAF wildtype and not possessing the criteria of grade Group 6), and grade Group 6 (IDH wildtype, and any one of TERT mutant, EGFR amplification, 10q deletion or H3 mutant) could significantly stratify this large cohort of gliomas for risk. 1,028 (80.6 %) cases were thus classifiable with sufficient molecular data. There were 270 cases of molecular grade Group 1, 59 cases of molecular grade Group 2, 248 cases of molecular grade Group 3, 27 cases of molecular grade Group 4, 117 cases of molecular grade Group 5, and 307 cases of molecular grade Group 6. The molecular grades Groups were independent prognosticators by multi-variate analyses and in specific instances, superseded conventional histological grades. We were also able to validate the usefulness of the grades Groups with a cohort retrieved from TCGA where similar molecular tests were liberally available. We conclude that a single gene molecular grading stratification system, useful for fine prognostication, is feasible and can be adopted by a general pathology laboratory.

No.2

Name: Dr. Li Wai Yan, Jamilla

Subspecialty: Haematology

Affiliation: Department of Haematology, Queen Mary Hospital

Unsupervised Machine Learning for Flow Cytometric Data Analysis in T-lymphoblastic leukaemia Measurable Residual Disease (MRD) Monitoring

Background and Objective

Measurable residual disease (MRD) status is strongly associated with clinical outcomes in haematological malignancies and can be monitored by flow cytometry. Conventional gating used in MRD analysis is time-consuming, operator-dependent and requires significant expertise. FlowSOM is a clustering tool that employs unsupervised machine learning for analysis of flow cytometric data. This study aimed to explore the performance of FlowSOM in analysis of T-lymphoblastic leukaemia (T-ALL) MRD flow cytometric data.

Methods

Flow cytometric data files from samples sent for T-ALL MRD testing from January 2021 to March 2022 were retrieved. FlowSOM was applied retrospectively for automatic clustering of events and the antigen expression profile for each cluster was reviewed by qualified pathologist/flow cytometrist to identify cluster(s) representing residual disease. Results were compared with those obtained using manual gating.

Results

A total of 142 tubes from 36 samples were analysed. Residual disease was positive in 14 and negative in 22 samples by conventional analysis. Analysis by FlowSOM achieved a 100% concordance rate in terms of positivity / negativity call for each sample. Residual disease was quantifiable in 62 tubes by conventional analysis and in 60 tubes by FlowSOM. In 23 tubes, FlowSOM analysis outperformed human analysis in terms of quantification accuracy. MRD levels derived from conventional analysis and FlowSOM analysis showed clinically acceptable agreement and high degree of correlation (R2 = 0.997).

Conclusion

FlowSOM facilitates quick, accurate and reproducible analysis of flow cytometric data in T-ALL MRD monitoring and shows potential as an alternative or supplementary method to conventional analysis in the clinical laboratory.

No.3

Name: Dr. Lee Chung Ho, Anson

Subspecialty: Microbiology

Affiliation: Department of Microbiology, Kwong Wah Hospital

Direct Detection of Extended-spectrum b-lactamases (CTX-M) from Blood Cultures by NG-Test CTX-M MULTI Immunochromatographic Assay

Abstract

Extended-spectrum b-lactamases (ESBLs) production is among one of the most prevalent resistant mechanisms by Enterobacterales encountered clinically. ESBLs are enzymes which can hydrolyse penicillins, aztreonam, first, second and third-generation cephalosporins, sparing only carbapenems and cephamycins, and therefore substantially limit the choice of effective antibiotics. In Hong Kong, there is evidence of an increasing burden for bacteraemia due to ESBL-producing organisms, with greater than 90% of the ESBL-producing organisms producing CTX-M1. Delay in effective antibiotic administration in invasive infections due to ESBL producers is associated with poor clinical outcomes2. Therefore, there is a need for rapid detection of ESBL from clinical specimens in order to guide timely escalation of antibiotic therapy. Compared with standard antibiotic susceptibility testing by disk diffusion test and detection of ESBL production using the combination

disk test or broth microdilution method as suggested by the Clinical Laboratory and Standard Institute (CLSI) guidelines3, which takes at least 16-20 hours, a significant reduction in testing time can be achieved with direct detection of ESBL from positive blood cultures. In this study, we evaluated the use of NG-Test CTX-M MULTI immunochromatographic assay on blood cultures positive for Gram negative bacilli for direct detection of the presence of CTX-M. 180 blood culture samples from Kwong Wah Hospital, a peripheral hospital in Hong Kong, between 29 April 2021 and 4 March 2022 were tested. The sensitivity and specificity with 95% confidence intervals were 100% (95% CI 92.60% - 100.00%) and 98.98% (95% CI 95.85% - 99.98%), respectively. One false-positive result was noted, which was likely to be due to cross-reactivity between the patient's blood with the monoclonal antibodies used in the test. In conclusion, he NG-test CTX-M MULTI assay offered a rapid and reliable way for direct detection of CTX-M from positive blood cultures due to Gram negative bacilli.

No.4

Name: Dr. Lam Tony
Subspecialty: Forensic Pathology
Affiliation: Forensic Pathology Service, Department of Health

A case of hypertrophic cardiomyopathy presenting with sudden death at age of 55 days

Hypertrophic cardiomyopathy is a rare form of cardiac muscle disorder. Over the past 2 decades, hypertrophic cardiomyopathy was given as the cause of death in 246 cases in public mortuaries in Hong Kong, 7 of them were paediatric cases, and 3 of them (including this case) were below the age of 1 year. This is a case of sudden death of a 55-day-old female infant. She was born full term by normal spontaneous delivery. Medical and family history was unremarkable. She developed repeated vomiting during breast feeding and shortness of breath on the material day. She appeared dull-looking, and turned unresponsive upon arrival of ambulance, and CPR was begun. She was conveyed to hospital for resuscitation but finally in vain. External examination showed body growth parameters at about 75th percentile. No dysmorphic feature. Therapeutic needle marks were noted on her limbs, and no external injury noted. Autopsy showed a grossly enlarged heart (54.5 g), which is around the mean heart weight of a 2-year-old child. The heart chambers appeared thickened, with left ventricular free wall and septal wall both around 1.1 cm-thick. Heart valves and coronary arteries were unremarkable. Histology examination showed hypertrophic myocardial cells, with areas of disarray, and areas of waxy myofibres. Other organs were normal. Genetic studies showed one heterozygous variant in TNNT2 gene, and one heterozygous variant in TTN gene. Both TNNT2 and TTN genes are associated with cardiomyopathy, including both dilated and hypertrophic cardiomyopathy. Considering both the morphology (phenotype) and genetic study (genotype), the cause of death was given as 'hypertrophic cardiomyopathy'.

No.5

Name: Dr. Tseung Sik Bit, Jeremiah
Subspecialty: Chemical Pathology
Affiliation: Department of Pathology, Princess Margaret Hospital

Tiletamine as an emerging ketamine analogue of abuse: case series of acute poisonings in local Hong Kong population

Ketamine, an arylcyclohexylamine derivative, has been a popular drug of abuse in our locality. In the recent years, novel psychoactive substances (NPS) with close structural homology to ketamine have emerged. Among them are deschloro-N-ethyl-ketamine (2-oxo-PCE) and 2-fluorodeschloroketamine (2F-DCK), which caused a cluster of acute poisonings in year 2017 and 2019. The current report describes the emergence of tiletamine, another ketamine analogue, with its identify confirmed by liquid chromatography-mass spectrometry. Both multiple reaction monitoring (MRM) and quadrupole time-of-flight (QTOF) accurate mass analysis techniques were employed. Between February 2019 and July 2022, 20 cases of tiletamine exposure were encountered. Laboratory analysis confirmed the presence of tiletamine and/or its metabolite in the urine of all patients. Urine bedside immunoassay for ketamine was found not to cross-react with tiletamine. Up to 86% cases were known ketamine abusers. Co-ingestion was observed in 95% of patients, with ketamine (85%) and cocaine (50%) constituting the majority. Zolazepam, which was commonly used together with tiletamine as a veterinary formulation, was not detected. Most patients presented with delirium and confusion (30%), agitation and bizarre behavior (20%); 20% cases developed convulsion and 60% required benzodiazepine sedation. The rate of neurological complications was substantially higher than previously reported cases of ketamine, 2-oxo-PCE and 2F-DCK poisoning. Rhabdomyolysis also occurred frequently in 70% cases. Management was mainly supportive, and uneventful recovery was observed in all patients. Overall, tiletamine is postulated to have a potency approximating 2-oxo-PCE, which is five times more potent than ketamine; and have a longer duration of action. Tiletamine is a dangerous and emerging NPS. Frontline healthcare and laboratory personnel should stay vigilant in the lookout for tiletamine and other ketamine analogues.

No.6

Name: Dr. Loong Chi Wang, Thomson
Subspecialty: Anatomical Pathology
Affiliation: Department of Clinical Pathology, Tuen Mun Hospital

Paediatric type mesothelioma with ALK translocation: A case report

Malignant mesothelioma usually presents in older adults, but it may rarely occur in children or young adults. Previous publications have shown that paediatric type mesothelioma has different clinical behavior and mutational profiles. We

report a case occurring in an 18-year old woman who presented with abdominal distension and a large pelvic mass, subsequently confirmed to be malignant mesothelioma. Similar to previously reported cases, the tumour harboured an ALK translocation. Her condition remained stable initially with debulking surgery and chemotherapy, but she developed late recurrence and widespread metastases. There was mixed response towards ALK inhibitors, and she passed away at age 31, 13 years after the initial diagnosis. This case further reinforces that paediatric type mesothelioma is distinct to the conventional type, and further studies are required to identify the potential for targeted therapy in these patients.

No.7

Name: Dr. Ling Cheuk Nam
Subspecialty: Anatomical Pathology
Affiliation: Department of Pathology, United Christian Hospital

Asymptomatic patient: Incidental finding of lipoprotein glomerulopathy with ApoE Kyoto mutation

Lipoprotein glomerulopathy is an unusual kidney disease with clinical presentation of proteinuria and renal insufficiency. The diagnosis is based on histological examination, featuring lipoprotein thrombi in glomerular capillaries. We present here an unusual case of lipoprotein glomerulopathy detected during pre-employment checkup. Histopathology examination confirmed the diagnosis, and subsequent genetic test revealed ApoE Kyoto mutation.

No.8

Name: Dr. Tsang Cheuk Ho
Subspecialty: Anatomical Pathology
Affiliation: Department of Pathology, Queen Elizabeth Hospital

Primary T-cell lymphoma of the central nervous system mimicking a brain abscess

Primary T-cell lymphoma is extremely rare in the central nervous system. We report a case occurring in an elderly Chinese male patient with underlying myeloproliferative disorder, who presented with fever and focal brain lesion on imaging mimicking brain abscess. Histological examination of the excised lesion showed extensive necrosis of brain tissue accompanied by marked perivascular infiltration of small to mid-sized lymphocytes with subtle nuclear atypia, while microbiological work up was negative and extensive immunohistochemical and histochemical staining failed to identify any pathogen. Immunohistochemistry revealed that the atypical lymphocytes were CD3+ CD56- EBER- T cells with attenuated BCL2 and CD2 expression. T-cell receptor analysis by PCR study confirmed monoclonal TRG gene rearrangement. The case highlights the importance of the awareness of T-cell lymphoma as a differential diagnosis of solitary brain tumour, despite its rarity and the need of attentive analysis of the histomorphology and immunophenotype and integration of molecular findings for accurate diagnosis. Recent findings on primary T-cell lymphoma of the central nervous system are discussed.

No. 9

Name: Dr. Tsang Chui San Zara
Subspecialty: Anatomical Pathology
Affiliation: Department of Pathology, Kwong Wah Hospital

Multiple chorangiomas of placenta: a case report

Chorangioma is a relatively common benign villous capillary lesion of the placenta. It is characterized by a nodular proliferation of capillaries with intervening perivascular stroma surrounded by trophoblasts. The aetiology is debated, with postulated causes including a reactive response to hypoxia and a hamartomatous proliferation. Most chorangiomas are small and clinically incidental. Large lesions (>4-5 cm in size) can result in significant antenatal and perinatal complications, including foetal anaemia and thrombocytopenia, high output cardiac failure, intrauterine growth restriction and hydrops fetalis which can lead to adverse outcomes such as pre-term birth, low birth weight and intrauterine death. In this case report, we describe a case of extensive placental involvement by multiple chorangiomas associated with hydrops fetalis and low birth weight presenting incidentally at 33 weeks' gestation with abnormal ultrasound findings. The patient underwent emergency Caesarean section and was delivered of a neonate with low APGAR scores and birth weight in the 10th percentile for gestational age. Significant placental abnormalities were noted at operation. On pathological assessment, the gross and microscopic findings were consistent with multiple chorangiomas which occupied most of the surface area of the placenta. On subsequent clinical-pathological correlation, there were features suggestive of multiple chorangioma syndrome as well as foetal anaemia and thrombocytopenia. The clinical and pathological findings are presented and discussed. Relevant medical literature is briefly summarized and evaluated.

No.10

Name: Dr. Lung Chee Heng Cheryl
Subspecialty: Anatomical Pathology
Affiliation: Department of Pathology, Princess Margaret Hospital

Intracranial mesenchymal tumour: case report of a rare intracranial tumour with angiomatoid fibrous histiocytoma-like features and FET::CREB fusion

Angiomatoid fibrous histiocytoma (AFH) is a rare mesenchymal tumour that infrequently recurs and rarely metastasizes, mostly occurring in subcutaneous tissue in children and young adults. These tumours are characterized by a distinctive set of histological features. They most frequently harbor EWSR1::CREB1 fusion (in > 90% of cases), less commonly EWSR1::ATF1 fusion. The latest WHO classification of central nervous system tumours includes intracranial mesenchymal tumour, FET::CREB fusion-positive as a provisional entity. These tumours demonstrate a wide morphological spectrum which may or may not resemble AFH. This is a case report of an intracranial tumour with AFH-like histological features and EWSR1::CREM fusion demonstrated by RNA sequencing in a female patient in her seventh decade. The clinical presentation,

histomorphology, immunoprofile and molecular findings of this case will be discussed. The spectrum of clinical and morphological features of this entity and how it is distinguished from its differentials will be reviewed.

No.11

Name: Dr. Lau Cheuk Hei, Derek
Subspecialty: Anatomical Pathology
Affiliation: Department of Pathology, United Christian Hospital

Extragastrointestinal GIST present as vaginal mass in a 57 year old female: a case report

Extragastrointestinal GIST, which has no apparent connection to gastrointestinal tract, is a rare entity. Common site are omentum, mesentery and retroperitoneum. A case of extragastrointestinal GIST present as a vaginal mass in a 57 year old female is reported. A 57 year old female present with postmenopausal bleed which was found to have a vaginal mass at 2017 with initial negative biopsys due to superficial sampling. The repeated biopsy at 2019 showed a spindle cell meoplasm, which is positive for c-kit, DOG1, CD34, caldesmon, and negative for actin, desmin, S100 and CK MNF116. KIT mutation analysis is detected with mutation in exon 11, whereas mutation of PDGFRA is not detected. Extragastrointestinal GIST present as vaginal mass is rare, and positivity for caldesmon can added difficulty as this is positive in leiomyoma. Misdiagnosis may lead to inappropriate therapy because conventional chemotherapy and radiotherapy are not effective in the treatment of GISTs, whereas imatinib has a proven role in managing these tumors. Thus, it is important to consider extragastrointestinal GIST in the differential diagnosis for a spindle cell neoplasm in female genital tract.

No.12

Name: Dr. Fong Nga Yee, Katie
Subspecialty: Anatomical Pathology
Affiliation: Department of Pathology, Tseung Kwan O Hospital

A case report of Macrophage Activation Syndrome associated with adult-onset Still's disease

A 31 years old lady with good past health presented with sudden onset pyrexia of unknown origin, accompanied by arthralgia, pancytopenia, liver dysfunction, and increased ferritin levels for 3 weeks. Adult-onset Still's disease was clinically suspected and the patient was treated with steroids. However, liver function progressively deteriorated. Bone marrow aspiration has been performed twice and the result was unremarkable. Subsequent liver biopsy showed sinusoidal dilatation, Kupffer cell hyperplasia with hemophagocytosis of erythrocytes and leucocytes, which was consistent with Macrophage Activation Syndrome (MAS) associated with Adult-onset Still's disease. Tacrolimus has been prescribed and liver function improved. MAS is a rare but potentially fatal disorder that can be idiopathic or secondary to an infection, malignancies, autoimmune diseases, or drugs. Early diagnosis can be challenging due to overlapping symptoms, leading to late diagnosis

and death. MAS should be suspected in patients with persistent high fever, hepatosplenomegaly, coagulopathy, thrombocytopenia, hepatopathy, and hyperferritinemia. Hepatic manifestations are characterized by sinusoidal dilatation and Kupffer cell hyperplasia with hemophagocytosis. Early diagnosis is vital to prevent mortality and underlying conditions should be actively looked for in cases of MAS.

No.13

Name: Dr. Yiu Sze Wan, Rachel
Subspecialty: Chemical Pathology
Affiliation: Department of Chemical Pathology, Queen Mary Hospital

Rewriting the future of newborns with a newly treatable rare disease

Background

Allan-Herndon-Dudley syndrome (MCT8 deficiency) is an X-linked recessive condition caused by pathogenic variants in the SLC16A2 gene that encodes the monocarboxylate transporter 8 (MCT8), a crucial transporter of thyroid hormones in the brain. Affected males present with neurocognitive and neuromotor deficits, and abnormal serum thyroid function tests (TFT). In 2019, a clinical trial reported effectiveness of TRIAC in improving clinical phenotypes caused by abnormal thyroid function. Superior effect on neuromotor function associated with earlier start of treatment was found. Current newborn screening (NBS) programs will not detect affected newborns due to their normal TSH levels; whereas recent research yielded insights into the use of T3/rT3 ratio in dried blood spot (DBS) samples as biomarker predicting MCT8 deficiency in the first few days of life. We aimed to learn from the old clinical journeys of two patients born in 1987 and 1993, and propose how current technology in clinical biochemistry can be harnessed to achieve earlier diagnosis of newborns with this treatable rare disease.

Case presentations

Patients 1 and 2 were Chinese males, born in 1993 and 1987, who were deceased at age 18 and 17 respectively. Their genetic diagnoses were made post-mortem through the “Undiagnosed Diseases Program”, with identification of NM_006517.4(SLC16A2):c.305dupT (p.Val103fs); and NM_006517.4(SLC16A2):c.511C>T (p.Arg171*) respectively. Patient 1 presented with GDD, head lag, dystonia and epilepsy at 6 months old; while Patient 2 presented with GDD and epilepsy. Patient 2 also had family history of intellectual disability and 3 brothers born to the same mother were deceased before age 20. There was no data on TFT nor thyroid medications for both patients.

Conclusion

From the 1980s to today, MCT8 deficiency is becoming a treatable rare disease. While universal NBS by NGS is still in hot debate, how we could harness existing clinical biochemistry to expand the power of NBS to detect affected newborns before irreversible clinical phenotypes might be key to rewrite their future.

No.14

Name: Dr. Ho Tin Wai Elson
Subspecialty: Anatomical Pathology
Affiliation: Department of Pathology, Queen Elizabeth Hospital

EBV-negative fibrin-associated large B-cell lymphoma arising in thyroid hyperplastic nodule

Fibrin-associated large B-cell lymphoma is a rare microscopic-sized tumor, typically representing an unexpected finding at anatomic sites rich in chronic fibrin deposition. It is associated with Epstein-Barr virus, and has been reported to occur in a wide variety of sites. We report a case arising in a thyroid hyperplastic nodule, only the second case reported in this location. Notably, this is only the fourth case of fibrin-associated large B-cell lymphoma that is not associated with Epstein-Barr virus. We provide a literature review on the clinic-pathological characteristics and outcome of this newly characterized and uncommon lymphoma type, which has only recently been separated out from the pathologically similar but highly aggressive large B-cell lymphomas associated with chronic inflammation.

No.15

Name: Dr. Li Yuk Wah
Subspecialty: Forensic Pathology
Affiliation: Forensic Pathology Service, Department of Health

A Case of Atypical Kawasaki Disease: Sudden Death of a 9-Year-Old Child with Ruptured Coronary Artery Aneurysm

Background
The deceased was a 9-year-old boy with no known chronic medical illness. He complained of fever, sore throat and neck pain since 2020-02-25 and attended a private hospital on 2020-02-25 and 2020-03-02. He was treated as tonsillitis and antibiotics were given. The fever was slightly improved but he then complained of skin rash, so he attended the private hospital again on 2020-03-04 and was treated as urticaria. He was found collapsed on sofa suddenly while watching TV at home on 2020-03-07, and was certified dead in Accident and Emergency Department of Ruttonjee Hospital on the same day.

Autopsy
Coroner's autopsy was performed at Victoria Public Mortuary on 2020-03-10. Externally, the eyes were a bit reddened and the lips were cracked. Palms and soles showed no desquamation. Internally, the anterior descending branch of left coronary artery showed two aneurysms, each about 1 cm in maximal dimension; one of the aneurysm was ruptured, causing haemopericardium with about 130 ml of blood clots in heart sac. Right coronary artery also showed an aneurysm, about 0.5 cm in maximal dimension. Histological examination showed abundant inflammatory cells infiltrating all layers of the coronary arteries, causing extensive destruction to the arterial wall architecture. Microbiological studies showed negative results of viral infections including Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Toxicological examination showed presence of cetirizine, an antihistamine, in blood at its therapeutic level; no significant finding was obtained by a general screening procedure for alcohol, other common drugs and poisons.

Cause of Death

In view of the available circumstances, autopsy findings and histological examination, the cause of death was given as 1(a) Cardiac tamponade, 1(b) Ruptured coronary artery aneurysm and 1(c) Atypical Kawasaki disease.

No.16

Name: Dr. Ho Cheuk Lam

Subspecialty: Anatomical Pathology

Affiliation: Department of Pathology, United Christian Hospital

Mesonephric remnants with epididymis-like morphology in a postmenopausal woman with endometrial carcinoma - A case report and review of the literature

Mesonephric remnants with epididymis-like features are rarely recognized in the female genital tract, with only isolated reports in the literature mostly in the context of exogenous hormonal manipulations. We hereby report a case of a 56-year-old lady with good past health, who presented with postmenopausal bleeding. She did not have any history of hormone replacement therapy or exogenous androgen use. The endometrial aspirate revealed FIGO grade 1 endometrioid adenocarcinoma. She underwent total hysterectomy with bilateral salpingo-oophorectomy and pelvic lymph node dissection with uneventful clinical course. An incidental microscopic finding of tubular structures is found at the right parametrium, which measures up to 3.2 mm in greatest dimension. Histology reveals small to medium-sized tubules lined by pseudostratified columnar epithelium with stereocilia on the luminal surface and a layer of basal cells, with eosinophilic secretion within the lumen. The tubules are surrounded by well-defined layers of smooth muscle cells. By immunohistochemistry, the epithelial cells at the tubules are positive for GATA3, PAX8 and androgen receptor. p63 highlights the basal cells. The epithelial cells and the basal cells are both negative for ER, PR and NKX3.1. The immunoprofile supports a mesonephric histogenesis for these tubules, the morphology of which resembling that of epididymal tubules. Our case has provided additional evidence for the biological nature of mesonephric-derived elements in the female genital tract and highlighted the differential diagnostic considerations. A literature review of previous reports of mesonephric remnants with epididymis-like morphology is presented.

No.17

Name: Dr. Ho Wai Leung

Subspecialty: Anatomical Pathology

Affiliation: Department of Pathology, Prince of Wales Hospital

Reliability of the nonalcoholic steatohepatitis clinical research network and steatosis activity fibrosis histological scoring systems

Background and aim: We aimed to determine whether lobular inflammation and ballooning grades in the Non-alcoholic

Steatohepatitis Clinical Research Network (NASH CRN) scoring system can be directly translated into the same for the Steatosis Activity Fibrosis scoring system (SAF) and to look at intra-observer and inter-observer agreement for each individual histological component and for diagnosis of non-alcoholic steatohepatitis (NASH) using the two scoring systems.

Methods: Four pathologists from two Asian centers scored 20 digitalized slides, twice using the NASH CRN, twice using the SAF. Intra-observer and inter-observer agreement was analyzed using Fleiss' kappa, weighted kappa, or Cohen kappa, where appropriate.

Results: The intra-observer discrepancy rate when using the NASH CRN compared with the SAF was higher than when using the individual scoring system for lobular inflammation (15% comparing both scoring systems vs 10% and 1.8% for the NASH CRN and the SAF, respectively) and hepatocyte ballooning (33.8% vs 12.5% and 5%, respectively), but not for diagnosis of NASH (6.3% vs 6.3% and 0%, respectively). Intra-observer and inter-observer agreement was substantial to almost perfect, except for inter-observer agreement for lobular inflammation and diagnosis of NASH, which was only fair to moderate in most instances.

Conclusion: These findings do not support the direct inter-translation between the NASH CRN and the SAF. However, the diagnosis of NASH during examinations using the NASH CRN may be comparable with diagnosis of NASH using the SAF, vice versa. The inter-observer agreement for lobular inflammation and NASH diagnosis needs to be improved.

No.18

Name: Dr. Li Xin

Subspecialty: Clinical Microbiology and Infection

Affiliation: Department of Microbiology, School of Clinical Medicine, Li Ka Shing Faculty of Medicine, The University of Hong Kong

Risk factors for slow viral decline in COVID-19 patients during the 2022 Omicron wave

Background

For the control of COVID-19 outbreak, home isolation is an important public health measure to reduce community spread, while cohort or single-room isolation can prevent nosocomial transmission within healthcare facilities. Formulating termination of isolation (de-isolation) policies requires up-to-date knowledge on viral shedding dynamics. However, current de-isolation policies are largely based on viral load data obtained before the emergence of the Omicron variant. We sought to determine the viral shedding kinetics and investigate the host factors associated with viral shedding during the 2022 Omicron wave.

Method

We conducted a retrospective cohort study involving adult patients hospitalised for COVID-19 between January and February 2022. We retrieved serial saliva specimens and monitored viral shedding using real-time RT-PCR. Univariate and multivariate analyses were performed to determine host factors affecting viral decline.

Results

A total of 104 patients between the age of 47 and 76 years were included. Chronic medical illness was present in 70.2% (73/104) of patients, and 49% (51/104) were fully vaccinated. Whole viral genome sequencing showed that 90.4% (94/104) and 9.6% (10/104) were infected with the Omicron and Delta variants, respectively. The viral load was highest (Ct value was lowest) on day 1 and 2 post-symptom-onset (PSO), and gradually declined. Older age, hypertension, hyperlipidemia, and chronic kidney disease were associated with slow viral decline in the univariate analysis on both day 7 and day 10 PSO, while incomplete vaccination was associated with slow viral decline on day 7 PSO only. However, older age was the only risk factor that remained statistically significant in the multivariate analysis (Day 7: P=0.016; Day 10: P=0.018).

Conclusions

Older age is an independent risk factor associated with slow viral decline in this study conducted during the Omicron-dominant 2022 COVID-19 outbreak. Transmission-based precaution guidelines should take age into consideration when determining the timing of de-isolation.

No.19

Name: Dr. Mok Ka Kin

Subspecialty: Forensic Pathology

Affiliation: Forensic Pathology Service, Kwai Chung Public Mortuary, Department of Health

A Case of Coronary Fibromuscular Dysplasia

Fibromuscular dysplasia (FMD) is a rare non-atherosclerotic non-inflammatory vasculopathy often involving medium-sized vessels. It is well-known to present with non-atherosclerotic stenosis of renal arteries and hence hypertension. Involvement of other arteries, including the carotid arteries, illiac arteries and visceral arteries have also been reported. Fatality due to involvement of heart vasculature has also been described in both literature and local coroner cases.

In our experience, the most common fatal FMD leading to sudden death involves the atrioventricular nodal artery, with a frequency of 10 cases over the last 20 years. A case of fatal stroke due to FMD has also been performed in our centre several years ago.

Recently, there was a case involving major coronary artery leading to coronary occulsion and death.

The case was a 37-year-old male with good past health and unremarkable family history who collapsed at home. Autopsy showed significant non-atheromatous occulsion of the anterior descending branch of left coronary artery. No recent or old myocardial infarcts were noted. Histology of the artery showed disruption of the internal elastic lamina, pronounced intimal proliferation and no sign of inflammation. Other organs showed no remarkable gross or microscopic findings. Toxicology examination was unremarkable.

Conclusion: This is the first reported fatal case due to FMD of major coronary artery in our centre. Both clinicians and pathologists should be aware of the possibility of non-atherosclerotic coronary occulsion and the potential fatal outcome.

No.20

Name: Dr. Wong Yuen Sze Sivia
Subspecialty: Anatomical Pathology
Affiliation: Department of Clinical Pathology, Pamela Youde Nethersole Eastern Hospital

Carcinosarcoma of gallbladder: a case report

Gallbladder cancer is an uncommon neoplasm. Carcinosarcoma of the gallbladder is a rare entity with less than 100 cases reported. Carcinosarcoma is defined by the presence of both carcinomatous and sarcomatous components in the tumour. We report a case of carcinosarcoma of gallbladder in a 75 years old lady. She has a history of adenocarcinoma of lung with lobectomy performed in 2015. Follow-up imaging in 2020 showed distended gallbladder with irregular poorly-defined enhancing densities and apparent wall infiltration over the fundus. Cholecystectomy and partial liver resection was performed. Macroscopically, the gallbladder was distended by a 10 cm exophytic tumour filling the gallbladder cavity. The tumour was largely soft with focal bony hard areas. Histology revealed both adenocarcinoma and sarcomatoid component, the latter featuring cartilage with malignant chondrocytes and sheets of malignant mesenchymal cells. The liver shows no tumour involvement. No lymph node metastasis was found. Adjuvant chemotherapy was given.

No.21

Name: Dr. Cheung Yee Ting
Subspecialty: Chemical Pathology
Affiliation: Department of Pathology, Princess Margaret Hospital

Glycerol intoxication mimicking toxic alcohol ingestion: A case report

Introduction

Glycerol is traditionally considered to be of low toxicity and is a widely-available food additive.

Case presentation

A 47-year-old male was found with impaired consciousness after consumption of query spirit. Acute kidney injury (Creatinine 479 umol/L) and lactic acidosis (pH 6.73, lactate 28.2 mmol/L) were noted. There was an elevated osmolal gap of 77 mOsm/L with concurrent serum ethanol concentration of 32 mmol/L. Analysis for toxic alcohols and glycols were unrevealing. Pseudohypertriglyceridaemia of 19.8 mmol/L was detected in a plasma specimen with low turbidity, which was found to be secondary to significantly elevated glycerol levels. The patient required ICU care and renal replacement therapy to correct the severe acid-base disturbance. The patient remained dialysis-dependent two weeks after presentation.

Discussion

The current case of glycerol toxicity mimicked toxic alcohol ingestion. Review of previous suspected cases of toxic alcohol consumption with negative toxicological findings found increased signal of glycerol in assays in some. This may represent a under-diagnosed condition given availability of products with high glycerol content. Glycerol intoxication should be highly suspected in cases presenting in a similar manner as toxic alcohol poisoning with pseudohypertriglyceridaemia. Wide availability of triglyceride assays in clinical laboratories would timely diagnosis and treatment of the under-recognised condition.

No.22

Name: Dr. Wong Ho Yan
Subspecialty: Forensic Pathology
Affiliation: Forensic Pathology Service, Department of Health

Sudden/Unattended deaths due to diabetic ketoacidosis in Hong Kong

Diabetic ketoacidosis (DKA) is a serious complication of diabetes mellitus which can be fatal. It is commonly precipitated by underlying stress, infection, myocardial infarction or lack of insulin administration. Typical presentations of DKA include vomiting, abdominal pain and polydipsia. However, DKA may result in sudden or unattended death without any prior symptoms noted.

There were 63 cases of sudden or unattended deaths by DKA transferred to public mortuaries in Hong Kong between 2016 and 2021. Mean age was 55.1 years and there was a slight predominance in male over female (37 male cases as compared with 26 female cases). Over half of the cases (37 cases; 58.7%) were presented with sudden collapse and no complaints were noted before death. Most cases DKA-related deaths had long-standing history or poor control of diabetes mellitus, though DKA cases with no known history of diabetes mellitus could also be found.

60 out of 63 cases underwent autopsy, in which a majority of them showed non-specific natural diseases associated with long-standing diabetes mellitus, such as coronary artery disease. There were also several cases showing underlying infection (pyelonephritis or pneumonia) in autopsy that are known to predispose to DKA. Armanni-Ebstein lesion in kidneys are not commonly seen. However, toxicological and biochemical analysis of these cases revealed significantly elevated vitreous humour glucose levels (16.5 – 54.9 mmol/L) and blood acetone levels (7 – 69 mg/100mL), which both were the main indicator for establishing diagnosis in DKA in our locality.

Conclusion
It is not uncommon for individuals dying of DKA to have no prior complaints prior to final collapse. Autopsy of these cases often revealed non-specific findings from gross and histological examination, but such diagnosis could be established by elevated blood acetone level and vitreous humour glucose level.

No.23

Name: Dr. Wong Tak Siu
Subspecialty: Anatomical Pathology
Affiliation: Department of Clinical Pathology, Pamela Youde Nethersole Eastern Hospital

Tenosynovial giant cell tumor of temporomandibular joint – A case report with literature review

Tenosynovial giant cell tumor (TGCT) is a rare tumor, arising in the synovial lining of joints, tendon sheaths and bursae. It is classified as localized and diffuse type. Localized type commonly involves digits but is also rarely found in large joint. Diffuse type commonly involves large joint of extremities. Translocation involving the CSF1 gene (colony stimulating factor 1) and overexpression of the CSF1 protein were demonstrated in some tenosynovial giant cell tumors. The incidence rate of TGCT is 29, 10, and 4 per million person-years for digit, localized-extremity and diffuse TGCT respectively. It usually occurs in patient aged from 30-50 years. TGCT involving temporomandibular joint is even rarer with only more than 100 cases being reported as of 2021. Radiological features and clinical presentation of TGCT are non-specific and there is a broad differential diagnosis. Its rarity and the lack of specific radiological and clinical features sometimes lead to a delay in diagnosis. We report a case of tenosynovial giant cell tumor involving temporomandibular joint in a 47-year-old female. She presented with blocked ear sensation on the left side for 3 years. MRI and CT scan showed a soft tissue mass extending to the middle cranial fossa and encasing mandibular head. Biopsy was performed showing a giant cell rich lesion and the lesion was later completely excised. We present the pathology finding and provide a literature review.

No.24

Name: Dr. Yeung Ka Pik, Vivian
Subspecialty: Haematology
Affiliation: Department of Pathology, Princess Margaret Hospital

Mast Cell Leukaemia: A Case Report

Mast cell leukaemia (MCL) is a very rare and aggressive form of systemic mastocytosis (SM), representing <1% of all mastocytosis and carries dismal prognosis. MCL is characterized by leukaemic expansion of immature mast cells in the bone marrow and other internal organs. Patients often present with constitutional symptoms, urticarial skin rash, gastrointestinal symptoms and hepatosplenomegaly. KIT D816V mutation, the main phenotypic driver in SM, is present in around 50% of the cases of MCL. Literature suggests the association of a haematological malignancy has negative impact on survival. We herein report a case of mast cell leukaemia associated with myelodysplastic syndrome in an elderly patient presenting with anaemic symptoms, bleeding diathesis, weight loss and fever for one month. Blood tests showed pancytopenia with occasional circulating blasts. USG abdomen revealed hepatosplenomegaly. Bone marrow examination was performed. Marrow aspirate showed 38% mast cells of immature morphology. Other findings include dyserythropoiesis, dysmegakaryopoiesis and left-shifted granulopoiesis with 8% blasts. Flow cytometry showed an abnormal mast cell population positive for CD25 and CD123 and negative for CD2. Trephine biopsy showed diffuse infiltration by atypical immature mast cells positive for CD25 and CD30, and negative for CD2 and toluidine blue. Serum tryptase was >200 ug/L. KIT p.D816V mutation was detected by DNA sequencing; trisomy 8 was detected on karyotyping. The patient was started

on midostaurin but remained pancytopenic. He suffered from gastrointestinal bleed and intracranial haemorrhage and succumbed three months after diagnosis.

No.25

Name: Dr. Yuen Wing Nam

Subspecialty: Anatomical Pathology

Affiliation: Department of Clinical Pathology, Tuen Mun Hospital

Endometrial Biopsy with Non-neoplastic Signet-Ring Cells: Potential Pitfall in Diagnosis

The presence of non-neoplastic cells with signet-ring cell-like changes in the endometrial stroma has been investigated previously. We will revisit the topic by describing a case of endometrial biopsy showing florid signet ring cell-like changes and demonstrate that they are positive for Estrogen Receptor and CD10 while negative for CD68 and pancytokeratin with the cytoplasmic vacuoles beinb negative for mucin stains. With the adjacent areas of the endometrial stroma show changes of late secretory endometrium, the signet ring cells-like change likely represents one of the morphologic changes exhibited by decidual cells and should not be confused with poorly differentiated adenocarcinoma.