The Hong Kong College of Pathologists
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No.1

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Emergence Of Staphylococcus Lugdunensis As A Cause Of Urinary Tract Infection: Results Of The Routine Use Of MALDI-TOF MS

Abstract

While Staphylococcus saprophyticus is a well-known cause of cystitis in young female, with the implementation of MALDI-TOF MS (Matrix-assisted laser desorption/ionization Time-of-flight Mass spectrometry) in routine microbiology practice, a new association of Staphylococcus lugdunensis with urinary tract infections (UTIs) in male with underlying urological system abnormalities was found in this study. We analyzed the incidence and the clinical and laboratory characteristics of S. lugdunensis UTIs during a 10-year period (2009–2018) and compared them with those of S. saprophyticus UTIs. A total of 38 and 162 episodes of S. lugdunensis and S. saprophyticus UTIs were observed. The number of S. saprophyticus UTIs was stable throughout the 10 years, whereas there was an obvious surge in the apparent number of S. lugdunensis UTIs since 2014, coinciding with the commencement of a routine use of MALDI-TOF MS. Univariate analysis showed that male sex ($p < 0.001$), advanced age ($p < 0.001$), hospital-acquired infections, ($p < 0.001$), upper UTI ($p < 0.005$), polymicrobial infections ($p < 0.05$), hypertension ($p < 0.001$), solid-organ malignancies ($p < 0.001$), renal stones ($p < 0.001$), urinary stricture ($p < 0.05$), vesicoureteral reflux ($p < 0.001$), and presence of a urinary catheter ($p < 0.001$) were significantly associated with S. lugdunensis UTI. Multivariable analysis revealed that S. lugdunensis UTI was associated with male sex (OR = 6.08, $p < 0.05$), solid-organ malignancies (OR = 12.27, $p < 0.01$), and urological system abnormalities (OR = 7.44, $p < 0.05$). There were significant differences in the patient population affected and predisposing factors between S. lugdunensis and S. saprophyticus UTIs.

No.2

Name: Dr Sin Ching-Tai Eugene
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A Risk Stratification Model for Vancomycin-Resistant Enterococcus Colonization Amongst Traced Hospital Contacts

Abstract

Background
Vancomycin-Resistant Enterococcus (VRE) has re-emerged in Hong Kong as hospital infection control effort has focused on the COVID-19 pandemic. Contact tracing is a cornerstone of hospital infection control measures, yet challenges arise in tackling large number of contacts in outbreak setting. A predictive model for risk stratification would be desirable.

Method
Records of VRE contact tracing in the New Territories West Cluster is reviewed, and linked with data from the electronic medical record to obtain characteristics of the VRE contacts. Risk factors for subsequent positive VRE screening is measured with logistic regression using Stata. A risk stratification model is developed with Random Forest using Python and Tensorflow.

Results
From Jan-2019 to Sept-2021, there were 153 VRE cases requiring contact tracing. 3229 contacts (2773 unique patients) were identified, of which 1908 had their VRE status determined with screening culture while the others were either discharged or dead prior to specimen collection. The overall screening positive rate was 5.9%. Sensitivity of single set of urine/stool screening is 82% compared to the aggregate results of multiple sets of specimens. Risk factors for VRE colonization amongst contacts include use of Vancomycin within the last 7 days (OR=5.7 [95% CI: 3.3-9.9]), use of antibiotics other than Vancomycin within the last 7 days (OR=3.1 [95% CI: 2.1-4.6]), and contact with multiple index cases (OR=5.2 [95% CI: 3.5-7.8]). Elderly home residency and tube feeding are not statistically significant risk factors (p=0.94 and p=0.51). The risk stratification model has an Area-Under-Curve(AUC) of Receiver Operator Curve(ROC) of 0.80. The contacts were stratified into high risk (6% of contacts), intermediate risk (75%) and low risk (19%), with their risk of subsequently being screened positive being 30%, 6% and 2.8% respectively.

Conclusion
Further refinement and validation of the model may be fruitful before it can be utilized to guide infection control priorities.

No. 3

Name: **Dr Lam Wing-Kit**
Subspecialty: **Haematology**
Affiliation: **Department of Clinical Pathology, Tuen Mun Hospital**

MYD88 Mutation In Diffuse Large B-cell Lymphoma: Single Centre Study in Hong Kong

Abstract

Background
Myeloid differentiation primary response gene (MYD88) mutation is present in up to 35% of activated B-cell-like (ABC) diffuse large B-cell lymphoma (DLBCL) but is uncommon in germinal centre B-cell-like (GCB) DLBCL. However, local data on the clinicopathologic characteristics of MYD88 mutation in DLBCL in Hong Kong are limited.

Objective
To study the clinicopathologic characteristics of MYD88 mutation in DLBCL patients in Tuen Mun Hospital.

Methods
Archived diagnostic samples of DLBCL from 2014 to 2018 were analysed. They were classified into GCB and non-GCB subtype by Hans algorithm. Allele-specific polymerase chain reaction (ASPCR) for MYD88 L265P mutation and Sanger sequencing on MYD88 exon 5 were performed on the samples. Patients with and without MYD88 mutation were compared.

Results
A total of 72 samples from DLBCL patient were tested, with 24 samples showing invalid molecular results. From the analysable cases, MYD88 L265P mutation was identified in 15% (7 of 48) of DLBCL, and appeared to be more common in non-GCB DLBCL than GCB DLBCL (21% (6 of 29) vs 5% (1 of 19), $p = 0.219$). Central nervous system (CNS) involvement was more frequent in cases with MYD88 mutation than those without MYD88 mutation (3 of 7 vs 1 of 41, $p = 0.008$). There was no significant difference in overall survival in patients with or without MYD88 mutation.

Conclusion
MYD88 L265P mutation occurs at higher frequency in non-GCB DLBCL. Besides, MYD88 L265P mutation was also more prevalent in DLBCL with CNS involvement, which is in line with other studies.

No.4

Name: **Dr Lam Ki**
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Single sIgE For Dermatophagoides Pteronyssinus (Dp) Is A Good Screening Tool For Atopic Sensitization

Abstract

Background
Only a limited number of publications had evaluated the Phadiatop application for aeroallergen screen in allergic respiratory diseases (ARD) in the Chinese population. In our retrospective cohort, through studying the Phadiatop versus total IgE use in aeroallergen workups, and local aeroallergen sensitisation profiles by reviewing aeroallergen sIgE, we aimed to derive a cost-effective algorithm for ARD workup.

Methods
We have retrospectively identified 694 patients with ARD in 2010-2019, and reviewed their Phadiatop test performed in our tertiary immunology laboratory. Other associated workups including total IgE, and/or allergen specific sIgE (sIgE), if available, were retrieved and analysed. Besides, a further review was performed on 53 consecutive samples collected during January 2021, for aeroallergen screening. Cost effectiveness of the existing protocol (Phadiatop screening followed by individual aeroallergen characterisation) was compared with a new testing algorithm, which started with dust mite (Dermatophagoides pteronyssinus, Dp) allergy detection.

Results
Phadiatop positivity was 67.3%, while total IgE positivity was 66.7% in the 366 patients with the test done. Overall, the agreement of these two tests was 73.5%. Asthmatic patients can be screened positive with total IgE than Phadiatop (34.9%-45.6%). Dp was the most prevalent aeroallergen (> 90%), and its sIgE level correlated best with the Phadiatop sIgE level ($R = 0.99$, $p < 0.001$). Comparing to the existing screening using Phadiatop, initial Dp detection is both sensitive and cost effective for ARD in our locality.

Conclusions
Screening by Dp sIgE is as sensitive as Phadiatop in aeroallergen screen but of lower running cost. It should be the approach in our locality.

No.5

Name: **Dr Hung Ling-Yin**
Subspecialty: **Chemical Pathology**
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X-Chromosome Inactivation And PCDH19-Associated Epileptic Encephalopathy: A Novel PCDH19 Variant In A Chinese Family

Abstract

Background
Developmental and epileptic encephalopathy 9 (DEE9, MIM #300088) is an early onset seizure disorder associated with cognitive impairment and behavioral disturbances. It is caused by mutation in protocadherin 19 with an unusual X-linked inheritance selectively involving heterozygous females or mosaic hemizygous males. Cellular interference was the postulated mechanism underlying the unusual inheritance pattern. Non-random X-chromosome inactivation is expected to play a role in the penetrance of PCDH19-related seizure disorder.

Case report
We report a Chinese girl who presented with severe treatment refractory seizures at 26 months of age. Next generation sequencing detected a heterozygous novel missense variant NM_001184880.2:c.488T>A p.(Val163Glu) in PCDH19, which is considered to be likely pathogenic according to Association for Clinical Genomic Science and American College of Medical Genetics and Genomics guidelines. Her younger sister, who was also heterozygous for the variant, was asymptomatic with normal development at the time of reporting at 37 months of age. X-chromosome inactivation statuses of the siblings in genomic DNA from peripheral leucocytes were studied by digestion with methylation-specific restriction endonucleases followed by polymerase chain reaction and capillary electrophoresis of the polymorphic tandem repeats in exon 1 of the AR gene. The proband was found to have somewhat skewed (75:25) X-chromosome inactivation while the asymptomatic younger sibling was extremely skewed (91:9).

Conclusion
The findings from X-chromosome inactivation study and clinical presentation of the siblings may be in line with the theory of cellular interference. Further studies are required to determine the potential role of X-chromosome inactivation on the phenotypic variability and patient outcomes.

No.6

Name: **Dr Tsang Yat-Ming**
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Evaluation Of Nanopore-based 16S rDNA Amplicons Sequencing For Detection Of Bacteria On Culture-Negative Specimens With Clinical Evidence of Infection

Abstract
Culture-negative infection remains a diagnostic challenge in clinical microbiology necessitate the incorporation of molecular diagnostic tools into the routine diagnostic workflow. Nanopore-based 16s rDNA amplicons sequencing likely has tremendous potential given its high sensitivity, simple sample preparation, quick turnaround time and being relatively inexpensive. In this study, we used this technique to identify bacterial species form culture-negative specimens from a wide spectrum of infections including meningitis, septic arthritis, prosthetic joint infection, pleural infection and peritoneal dialysis-related peritonitis and compare the result to Microseq-based Sanger sequencing. Twenty clinical samples were tested and nanopore identified significant bacterial species in 11 of these samples, compared to 2 by Microseq. Five of these samples with positive pathogens detected by nanopore could be confirmed by culture, nucleic acid amplification test or Sanger sequencing, showing good result correlation. Overall nanopore-based 16s sequencing is promising in identifying pathogens from culture-negative infections provided that a careful workflow planning and strict quality control measures are implemented throughout the sequencing process to avoid false-positive results issued. A more large-scale prospectively study to further assess the performance of nanopore sequencing by comparing the results with another next generation sequencing platform is warranted to establish the analytical sensitivity and specificity.

No.7

Name: **Dr Li Ting-Hon Stanford**
Subspecialty: **Haematology**
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A Retrospective Observational Study On The Red Cell Morphological Changes And Changes In Haematological Parameters Associated With Alectinib

Abstract

Background
Alectinib is a second generation anaplastic lymphoma kinase (ALK) inhibitor indicated for ALK mutated non-small cell lung cancer. Recently the association between alectinib and red cell morphological abnormalities has been reported in a few case series. This retrospective observational study aims to determine the frequency of occurrence of acanthocytosis in patients taking alectinib, and to evaluate the red cell indices, biochemical markers of haemolysis and eosin-5-maleimide (EMA) binding assay results in patients receiving alectinib.

Methods
Patients who were on alectinib and had a complete blood count test performed in Queen Elizabeth Hospital haematology laboratory between 1st May 2021 and 31st August 2021 were included in the study. All the diagnostic haematological investigations that had been performed as a part of clinical investigation before and after commencement of alectinib were reviewed.

Results
50 patients were evaluated in this analysis. 100% of patients showed 3+ acanthocytes (>20%) according to the International Council for Standardization in Haematology (ICSH) grading criteria on the peripheral blood smears. 16.0% (8/50) of them showed grade 2 or above anaemia (haemoglobin concentration <10 g/dL), and 65.3% (32/49) of them showed reticulocytosis (>2%). Complete blood count results before the commencement of alectinib were available in 47 patients. When compared with the test results before starting alectinib, the post-alectinib blood tests showed a significantly lower haemoglobin concentration (11.4 g/dL vs 12.5 g/dL, $p < 0.001$), red blood cell count (3.92 x 10^12/L vs 4.50 x 10^12/L, $p < 0.001$) and haematocrit (HCT) (0.333 vs 0.384, $p < 0.001$); and a significantly higher mean corpuscular haemoglobin (MCH) (29.3 pg vs 28.2 pg, $p < 0.001$), mean corpuscular haemoglobin concentration (MCHC) (34.2 g/dL vs 32.5 g/dL, $p < 0.001$) and red cell distribution width (RDW) (14.7 vs 13.7, $p = 0.001$). There were no significant differences in mean corpuscular volume (MCV) (85.9 fL vs 85.2 fL, $p = 0.619$) between the two time points. The results were compatible with the development of a more spherocytic and anisopoikilocytic morphology. Moreover, the blood tests after commencement of alectinib showed a significantly higher bilirubin level (18.6 µmol/L vs 7.0 µmol/L, $p < 0.001$) when compared with those before the start of alectinib. The biochemical changes may suggest chronic haemolysis induced by alectinib. EMA binding assay was performed in 19 patients. All the patients showed a marked reduced in mean channel fluorescence (MCF) when compared with normal control (MCF ratio: 0.41 – 0.68, median = 0.57).

Conclusion
Our cohort revealed that alectinib caused significant acanthocytosis in all patients. Alectinib was also associated with changes in red cell indicies and biochemical markers of haemolysis, compatible with a spherocytic and anisopoikilocytic morphology with haemolysis. Patients on

alectinib had reduced eosin-5-maleimide binding. Given the anticipated increase in utilization of alectinib in oncology patients, it is critical for pathologists to recognize the red cell morphological changes and changes in haematological parameters associated with this novel agent.

No.8

Name: **Dr Fung Ching-Ki**
Subspecialty: **Anatomical Pathology**
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Uterine Sarcoma With MEIS1-NCOA2 Fusion - A Case Report And Review Of The Literature

Abstract

Spindle cell sarcomas harbouring MEIS1-NCOA2/1 fusions have been reported at various anatomical locations in some recent studies, but the morphological and immunohistochemical features of these neoplasms are yet to be completely characterized. We hereby report a case of uterine sarcoma with MEIS1-NCOA2 fusion in a 31-year old lady. She initially presented with shock and hemoperitoneum, and was found to have a ruptured uterine tumor measuring 15 cm across upon emergency laparotomy. Histology revealed a neoplasm composed of spindle cells with alternating cellularity. The tumour cells were arranged in different patterns like fascicles and whorls, featuring moderate nuclear atypia and focally prominent nucleoli. Rhabdomyoblastic and adipocytic differentiation was also identified. The immunohistochemical profile included diffuse positivity of CD10 and CD99, while estrogen receptor showed heterogeneous expression and myogenin was positive in scattered rhabdomyoblasts. The pathologic findings did not fit into any currently recognized subtypes of uterine sarcomas and raised the differential diagnosis of high grade endometrial stromal sarcoma and rhabdomyosarcoma. RNA sequencing identified a chimeric transcript of MEIS1-NCOA2, involving the fusion of exon 8 of MEIS1 gene with exon 12 of NCOA2 gene. The genetic finding was further supported by break-apart fluorescence in situ hybridization which demonstrated gene rearrangement for MEIS1. The patient underwent total hysterectomy and bilateral salpingo-oophorectomy with no residual tumour identified, followed by radiotherapy. She was clinically well with no evidence of recurrence upon follow up for six months. Our case has provided additional information to the expanding morphological and immunohistochemical spectra of this emerging entity. A literature review of MEIS1-NCOA2/1 fusion–positive sarcoma is presented.

No.9

Name: **Dr Li Xin**
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Asymptomatic Shedding Of SARS-CoV-2 In Conjunctival Secretions

Abstract

Background
Conjunctivitis is an uncommon presentation of SARS-CoV-2 infection. Detection of SARS-CoV-2 has been reported from conjunctival secretions and conjunctival / ocular swabs of patients with or without clinically apparent conjunctivitis. The prevalence and significance of viral shedding in conjunctival secretions of patients without ocular symptoms is currently unknown.

Objective
To evaluate the presence of SARS-CoV-2 nucleic acid and viable virus in conjunctival secretions from patients without ocular symptoms.

Methods
Conjunctival swabs were prospectively collected from laboratory-confirmed COVID-19 patients without ocular symptoms for reverse transcription-polymerase chain reaction (RT-PCR) and viral culture.

Results
A total of 158 conjunctival swabs were obtained from 49 laboratory-confirmed COVID-19 patients. The median duration of illness when the first conjunctival swab was obtained was 10 days (range, 2 days to 27 days). Four conjunctival swabs from four different patients (4/49, 8.2%) were positive for SARS-CoV-2 RNA by RT-PCR. The Ct values ranged from 32.7 to 37.7 (mean, 35.4). Viral cultures were negative for all four RT-PCR-positive conjunctival swabs.

Conclusions
Conjunctival secretion of a minority of COVID-19 patients without ocular symptoms may contain relatively low levels of SARS-CoV-2 RNA, but their infectiousness remains undetermined. Appropriate infection control measures should be implemented during ophthalmological assessment of COVID-19 patients as well as other occasions with possible ocular fluid exposure to prevent potential nosocomial transmission of SARS-CoV-2.

No.10

Name: **Dr Gao Yang**
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Splenic Littoral Cell Haemangioendothelioma: Case Report

Abstract

Littoral cell haemangioendotheliomas (LCHE) are vascular tumours that originate from littoral cells lining splenic red pulp sinuses with intermediate features between benign littoral cell angioma and frankly malignant angiosarcoma. Only scanty case reports of LCHE are available in literature, including those of minimal atypical histological features, but presented with disseminated disease or with late recurrence or metastasis. We present herein a local case of LCHE. The patient was a 67-year-old female who presented with abdominal discomfort, weight loss and splenomegaly. Blood investigations showed anemia and leukocytosis. Computer tomography with contrast revealed marked splenomegaly with reduced splenic enhancement. There were scattered hyperdense haemorrhagic areas in the spleen, and small peripheral splenic hypodense regions with mild rim-enhancement. The peripheral splenic vein is poorly enhancing suggesting thrombosis. Splenectomy was subsequently performed. Grossly, the spleen was enlarged to 17.0x11.5x7.5 cm and weighed 675 gm. Cut surface showed the well-capsulated spleen was occupied by a firm red tumour, measuring 17.0x11.0x7.0 cm, with vaguely multinodular appearance and multiple focal necrosis. Histological examination shows the spleen is almost completely replaced by a vascular neoplasm which exhibits vaguely nodular growth with permeative borders. The tumour comprises spindly cells forming slit-like or sinusoidal blood vessels. The tumour cells possess obviously atypical nuclei with varying fine to hyperchromatic chromatin, focal distinct nucleoli and exhibit mitotic activity (up to 4 mitoses/10 high power fields). Scattered degenerative bizarre cells are also seen. On immunostaining, the neoplastic spindle cells are CD31+, CD8+(some), ERG+(some), HHV8- and CD34-. Rich population of perivascular myoid cells are demonstrated by SMA. The overall features are consistent with LCHE. There is no recurrence or metastasis in a one-year follow-up. This case adds another example of this rare entity. Considering the indeterminate behavior, long-term follow-up is deemed necessary, especially in view of the high-grade morphology.

No.11

Name: **Dr Lo Chun-Hai Haison**
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Myoid Differentiation In Dermatofibrosarcoma Protuberans And Its Fibrosarcomatous Variant: 10 Years' Experience In A Local Tertiary Hospital

Abstract

Dermatofibrosarcoma protuberans (DFSP) is a relatively rare, locally aggressive, dermal based fibroblastic tumour. There are several histological variants, in which the usual emphasis is on fibrosarcomatous DFSP as it acquires metastatic potential. Myoid differentiation in DFSP is rare, and more often found in fibrosarcomatous DFSP. Myoid differentiation is defined as tumour cells with brightly eosinophilic cytoplasm, well-defined cytoplasmic margins and vesicular nuclei. In this study, we try to characterize the immunostaining pattern regarding myoid differentiation in DFSP, and discuss the potential pitfall in making the diagnosis. A total of seventeen cases of DFSP were found in the past ten years in our hospital, seven of them were excluded as those were biopsy or re-excisional specimen from same tumour or patient. In the remaining ten cases, two of them show focal myoid differentiation, including the only case of fibrosarcomatous DFSP. Around 5% of the tumour area in the traditional DFSP case shows myoid differentiation, while around 10% of the tumour area in fibrosarcomatous DFSP shows myoid differentiation. The myoid areas show positive staining (albeit patchy to focal) for smooth muscle markers, such as smooth muscle actin, muscle specific actin, caldesmon and calponin. Staining for CD34 in those areas are weak or negative. This may create diagnostic difficulties with smooth muscle tumour or myofibroblastic lesions especially in small biopsy sample. In difficult cases, the detection of COL1A1-PDGFB fusion by fluorescence in situ hybridization is helpful as this is a characteristic chromosomal translocation found in the large majority of DFSP.

No.12

Name: Dr Hau Man-Nga
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Intestinal Ganglioneuromatosis: An Unusual Presenting Feature In MEN2B Syndrome As Acute Toxic Megacolon

Abstract

Multiple neuroendocrine neoplasm type 2B syndrome is characterized by frequent occurrence of phaeochromocytoma, medullary thyroid carcinoma, and intestinal ganglioneuromatosis. Although gastrointestinal symptoms are common among patients with MEN 2B syndrome, acute toxic megacolon as the presenting feature is not common. On the other hand, intestinal ganglioneuromatosis is a rare condition among the various causes of intestinal dysmotility, and it can be associated with MEN2B syndrome, neurofibromatosis, and Cowden syndrome. Here we present a case of toxic megacolon due to diffuse intestinal ganglioneuromatosis in a previously healthy adult man, raising the suspicion for MEN2B syndrome, which was eventually confirmed by the identification of pheochromocytoma and medullary thyroid carcinoma, and genetic studies.

No.13

Name: **Dr Wong Yuen-Sze Sivia**
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Microscopic Colitis: Report Of Two Cases Of Collagenous Colitis

Abstract

Microscopic colitis is a relatively common yet under-recognized chronic inflammatory bowel disease. It causes watery non-bloody diarrhea, leading to urgency and ultimately fecal incontinence, which can have a great impact on the quality of life. Epidemiologic studies show a comparable incidence and prevalence between microscopic colitis and inflammatory bowel disease (Crohn's disease and ulcerative colitis). Studies have also revealed an increase in risk of incidence of inflammatory bowel disease among patients with microscopic colitis. The endoscopic finding in cases of microscopic colitis is largely unremarkable. The diagnosis of microscopic colitis is based on the histological findings in the appropriate clinical context. We report two cases of collagenous colitis and their clinicopathologic analysis. Correct diagnosis and appropriate treatment can typically lead to satisfactory control of symptoms and improvement of quality of life.

No.14

Name: **Dr Li Wai-Yan Jamilla**
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Langerhans Cell Sarcoma: A Case Report

Abstract

Langerhans cell sarcoma (LCS) is an extremely rare haematogical neoplasm. It is a tumour derived from Langerhans cells (LC) and shows the characteristic LC immunophenotype. In contrast to Langerhans cell histiocytosis, LCS displays an overtly malignant cytology and also behaves more aggressively clinically. Patients with LCS often present with multi-focal disease, with the most common sites of involvement including skin, bone, lymph nodes, lung, liver and spleen. We herein report a case of LCS occurring in an adult patient presenting with fever, cough and shortness of breath for 1 month. PET/CT imaging revealed hepatosplenomegaly, widespread lymphadenopathy and diffuse ground glass opacities in the lungs. Bone marrow examination was performed. While the marrow aspirate was aparticulate, occasional giant multi-nucleated cells were present. Trephine biopsy showed a prominent infiltration by medium to large sized abnormal mononuclear cells with pleomorphic appearance. They were negative for common haematolymphoid markers but were positive for CD1a, Langerin and S100, consistent with Langerhans cell sarcoma. Subsequent para-aortic lymph node core biopsy revealed similar findings. Broncho-alveolar lavage also yielded isolated and loose aggregates of malignant cells. BRAF V600E mutation was negative. The patient was initially treated with cladribine but experience resurgence of fever and repeat imaging after 2 cycles showed disease progression. She was switched to GDP chemotherapy (gemcitabine, cisplastin and dexamethasone) with partial response on PET/CT, while bone marrow biopsy showed residual disease involvement. She then underwent myeloablative matched sibling haematopoietic stem cell transplant (HSCT). Although occasional malignant cells were still found on bone marrow biopsy, the patient remains clinically well 10 months post-HSCT.

No.15

Name: **Dr Leung Hoi Shan**
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Biotin Interference And Biotin-Depletion Protocol

Abstract

Biotin interference is not an uncommon phenomenon in assays that adopt the biotin/streptavidin-based technology. Erroneous results may lead to misdiagnosis and mismanagement of patients, and therefore it is important to recognize the pattern and undertake necessary workup to confirm the presence of biotin interference to avoid issuing misleading results. We report here a case of hypercalcaemia mimicking vitamin D intoxication, and subsequent workup confirmed the presence of positive biotin interference on total vitamin D assay. With a simple biotin-depletion protocol using streptavidin-coated microparticles, the affected results were restored to levels similar to those measured in non-biotin-based platforms.

No.16

Name: **Dr Li Ting-Hon Stanford**
Subspecialty: **Haematology**
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A Retrospective Study On Cytogenetic Features And Prognosis Of Chinese Myeloma Patients In A Tertiary Referral Centre In Hong Kong

Abstract

Background
Although frequencies and significances of different cytogenetic abnormalities in plasma cell myeloma have been well documented in the Western countries, this information is relatively lacking in Chinese population. Moreover, the use of autologous stem cell transplantation and novel agents such as proteasome inhibitors and immunomodulators has increased significantly over the past 2 decades. This may change the prognostic value of FISH abnormalities. Therefore the roles of FISH abnormalities in the prognosis of plasma cell myeloma need to be reevaluated in the era of novel agents. To address these issues, we studied the clinical, pathological and cytogenetic characteristics of plasma cell myeloma in a cohort of Chinese patients from Hong Kong.

Methods
The study is a retrospective cohort study. Newly diagnosed plasma cell myeloma patients with interphase FISH (iFISH) performed in Queen Elizabeth Hospital, a tertiary referral centre in Hong Kong, between August 2008 and March 2017 were included in the study. Information was collected via the electronic patient record (ePR) system of the Hospital Authority of Hong Kong for review.

Results
191 patents with a confirmed diagnosis of plasma cell myeloma were included in the analysis. 177/191 (92.7%) patients showed cytogenetic abnormalities on iFISH test. 1q21 (CKS1B) gain (88/160, 55.0%), del (13q) (97/190, 51.1%) and hyperdiploid (82/191, 42.9%) were the most common cytogenetic abnormalities, followed by t(4;14) (29/190, 15.3%), del(1p) (19/160, 11.9%), del(17p) (19/190, 10.0%), and t(14;16) (10/191, 5.2%).

We demonstrated that t(4;14), t(14;16), del(13q), 1q gain and del(1p) were adverse prognostic factors of PFS (progression free survival); while t(14;16), del(17p) and del(13q) were adverse prognostic factors of OS (overall survival). Hyperdiploidy was both a favourable prognostic factor of PFS and OS. Among patients with high risk cytogenetic changes according to the mSMART 3.0 stratification, those with concomitant hyperdiploidy has a significantly prolonged OS but not PFS (median OS: hyperdiploid vs non- hyperdiploid: 56.8 vs 38.5 months, p=0.013; median PFS: hyperdiploid vs non- hyperdiploid: 37.7 vs 27.5 months, p=0.106).

The effects of iFISH abnormalities on PFS and OS were further assessed after adjusting for age, ISS and first-line therapy using multivariable-adjustment COX regression models. Of these, t(14;16) (hazard ratio [HR] 2.387 [95% confidence interval, CI: 1.086-5.248], p=0.030), del(17p) (HR 1.774 [95% CI 1.063-2.960], p=0.028), del(13q) (HR 1.684 [95% CI 1.168-2.428], p=0.005) and hyperdiploidy (HR 0.649 [95% CI 0.448-0.941], p=0.022) were statistically independent predictors of PFS in multivariate analysis; while del(17p) (HR 1.818 [95% CI 1.017-3.249], p=0.044), del(13q) (HR 2.089 [95% CI 1.335-3.270], p=0.001) and

hyperdiploidy (HR 0.483 [95% CI 0.304-0.768], p=0.002) were statistically independent predictors of OS.

Conclusion

Our cohort of Chinese patients demonstrated similar patterns of FISH abnormalities compared to the western populations. The prognostic implications of FISH abnormalities were also comparable with the results found in western studies.