

The Annual Scientific Meeting of College of Pathologists, Academy of Medicine of Malaysia: Opportunities and Challenges in Laboratory Medicine, was held at Riverside Majestic Hotel, Kuching, Sarawak on 27-28 June 2019. Abstracts of K. Prathap Memorial Lecture, plenary, symposium and paper (poster) presented are as follows:

K Prathap Memorial Lecture:

Opportunities and challenges for laboratory professional in patient safety

Yasmin Ayob

National Blood Centre & National Heart Institute, Kuala Lumpur, Malaysia

Pathology has been the engine of healthcare system in understanding diseases and in the last few decades in monitoring therapy. However, the approach and technique we use remain very much the same. As we move into the future of the digital age and artificial intelligence, the challenge is should we continue doing the same or do we need to change and reinvent the discipline and the service we provide. To remain relevant, we have to embrace the change and move with the times. The digitization of pathology laboratories makes the specialty more efficient, specimen more reproducible and the work of pathologists less cumbersome. New technologies that produce biomedical “big data” (next generation sequencing, multiparameter / multiplex flow cytometry, high-throughput proteomics and metabolomics, systems biology analysis) have also caused us to rethink the best approach to diagnostics. While these opportunities and challenges seem daunting, we still have to grapple with old challenges of funding and leadership.

Plenary 1:

Challenges in diagnosis of monoclonal gammopathy

Pavai Sthaneshwar

University of Malaya (UM), Kuala Lumpur, Malaysia

The monoclonal gammopathies (MG) are a group of disorders characterised by the proliferation of clonal plasma cells to produce resulting in a detectable abnormality called monoclonal component or M-protein or paraprotein. Direct measurement of the M-protein spike by electrophoresis and immunochemical measurements of specific isotypes or free light chains pairs has provided useful information about the quantity of M-protein. Nonetheless, quantitation of M-protein by electrophoretic method gives suboptimal measurements on small M-proteins. In addition, measurements by electrophoresis of M-proteins migrating in the β - and α -regions are difficult due to the presence of normal serum proteins in those regions. The nephelometric quantitation of immunoglobulins (Igs) is a simple automated method that uses anti-human Ig antigen binding fragments (Fabs) that target the constant region of Ig. The method measures both monoclonal and polyclonal immunoglobulins, and therefore, its diagnostic use for identification of monoclonal proteins is not recommended and is also of no value for biclonal and triclinal gammopathies. Use of the serum free light chain (FLC) immunoassay, has led to improvements in the diagnosis and monitoring of patients with plasma cell dyscrasia and other monoclonal gammopathies. Not all MG secrete excess FLC. Abnormal serum FLC ratios have only been detected in 90–95% of intact Ig multiple myeloma and 40% of MGUS. Since these two patient groups can be easily diagnosed by serum M-proteins by protein electrophoresis, a combination of tests is needed to detect all MGs. Nephelometric methods using antisera specific for Ig heavy and light chain epitopes separately quantitate IgG kappa and IgG lambda, IgA kappa and IgA lambda, and IgM kappa and IgM lambda and may be useful for monitoring monoclonal proteins migrating in the beta fraction. The heavy-light, isotype-specific kappa to lambda ratio has been proposed as a potential monitoring method for IgA or IgM M-proteins migrating in the beta fraction. Although the assay is not sensitive enough to use as a routine screening method for MM, a 97% sensitivity observed in IgA MM and IgA MGUS indicates that almost all IgA MM patients can be monitored by HLC for both detection of the disease clone and quantitation using the IgA HLC assay. A 24-hour urine collection allows the quantitation of both the albumin and M-protein that has been rapidly cleared by the kidneys. The potential broad use of mass spectrometry for MG has been recently demonstrated by the application of matrix assisted laser desorption ionization – time of flight instruments (MALDI-TOF) for detecting monoclonal proteins. The Mayo Clinic group performed a large retrospective study in which patients with an assortment of plasma cell proliferative diseases had SPE, IFE, and FLC as well as urine protein electrophoresis and IFE performed at the time of diagnosis. The study shows patients would have had M-proteins detected by the various tests singly or in combination and if urine assays are removed from the diagnostic panel, there is no decrease in sensitivity. This and other studies have led the IMWG to recommend a panel of serum protein electrophoresis, immunofixation electrophoresis and FLC to screen for a MG; the inclusion of diagnostic urine testing is only recommended if amyloidosis is suspected, which simplifies collection for the patient and workflow for the laboratory and reduces costs as well.

liquid chromatography (HPLC). The results showed levels of Hb A, Hb A₂ and Hb F were 62.3%, 1.9% and 1.4% respectively. Additionally, an abnormal Hb peak, X, with a value of 29.4% was observed at the retention time of 1.43 minutes. This abnormal Hb was also seen at zone 12 capillary electrophoresis (CE), which was similar to Hb J variant (*i.e.* Hb J-Singapore, Hb J- Meerut). Further molecular study using amplification refractory mutation system (ARMS) and Gap-Polymerase Chain Reaction (Gap-PCR) to detect known deletions and point mutations were negative. The direct DNA sequencing revealed the CGT>CCT mutation at codon 141 of $\alpha 2$ -globin gene identified as heterozygous Hb Singapore. Three other family members (mother, a brother and a sister) also had the variant. However, both siblings had co-inheritance of heterozygous $\alpha 3.7$ deletion with higher presentation of Hb variant fraction, X>35%. **Learning Points:** Hb Singapore has similar HPLC pattern and CE migration time with Hb J variants which is a potential pitfall for misinterpretation. The confirmatory diagnosis can only be made by DNA sequencing. Therefore, the knowledge of this Hb variant is important to be used in diagnosis, management and counselling of patients.

HM-51. Bone marrow histoplasmosis in a renal transplant patient

Lee Jia Haur¹, Khamisah Mohd Gaus¹, Madzlifah Ahadon², Tan Rui Xin³, Nur Izati Mustapa³

¹Haematology Unit, Department of Pathology, Sarawak General Hospital; ²Department of Pathology, Faculty of Medicine & Health Sciences, Universiti Malaysia Sarawak; ³Microbiology Unit, Department of Pathology, Sarawak General Hospital, Malaysia

Introduction: Fungal infections remain an important cause of mortality and morbidity in post solid organ transplant patients due to chronic immunosuppression. **Case Report:** A 58-year-old renal transplant recipient presented to the hospital with a four-day history of fever with chills. A full blood count revealed pancytopenia (haemoglobin 8.9 g/dL, white cell count $2.7 \times 10^3/\mu\text{L}$, platelet count $51,000/\mu\text{L}$). Blood films for malarial parasite, serological studies for dengue and cytomegalovirus were negative. Peripheral blood film showed presence of intracellular organisms within the monocytes and neutrophils. Many intracellular organisms were seen in the bone marrow aspirate, which were positive for Periodic Acid-Schiff. Intracellular fungal bodies in the trephine sections stained positive for Gomori Methenamine-Silver stain. Fungal culture of the bone marrow aspirate was positive for *Histoplasma capsulatum*. **Discussion:** In solid organ transplant recipient, disseminated histoplasmosis can occur either as a primary infection, as a reactivation of latent infection or as a donor-transmitted infection. The incidence of histoplasmosis in solid organ transplant recipients is low and there have only been a few case series involving renal and liver transplant recipients. Prolonged fever is the main clinical feature of histoplasmosis among organ transplant recipients. Splenomegaly, hepatomegaly and mucocutaneous lesions which are associated with features of disseminated histoplasmosis have also been reported to be quite common in renal transplant recipients. Majority of cases occur within the first 18 months of surgery. Post-transplant histoplasmosis can be established by performing culture or histopathological examination. However, *Histoplasma* urine antigen test or the *Histoplasma* serological test may provide rapid results. Detection of the antigen in the urine is currently the most sensitive serological test available for disseminated histoplasmosis. **Learning Points:** This case illustrated the importance of having a strong clinical suspicion of a disseminated fungal infection in an organ transplant patient, presenting with non-specific symptoms of infection.

HM-52. A child with pancytopenia: Is this childhood myelodysplastic syndrome?

Muhammad Haizie Ibrahim¹, Azly Sumanty Ab Ghani¹, Wan Amal Hayati Wan Hassan¹, Alawiyah Awang Abd Rahman¹, Nazzlin Dizana Din², Ahmad Toha Samsudin³

Departments of ¹Pathology & ²Paediatrics, Hospital Sultanah Nur Zahirah, Terengganu; ³Department of Pathology, Hospital Queen Elizabeth, Sabah, Malaysia

Introduction: Pancytopenia is not uncommon in children. The cause for pancytopenia in children varies, it can either be benign as in infections or malignant as in acute leukaemias and myelodysplastic syndrome (MDS). MDS is very uncommon in childhood and accounts for only less than 5% of all hematopoietic neoplasms in children below the age of 14 years old. Here, we describe a child who presented with pancytopenia and suspected to have MDS. **Case Report:** An 8-year-old girl was referred to our centre for pancytopenia, with haemoglobin of 9.4 g/dL, neutrophil count of $0.85 \times 10^9/\text{L}$ and platelet of $12 \times 10^9/\text{L}$. She has been having this problem for the past 2 years. On clinical examination, she had multiple small cervical lymph nodes and hepatomegaly. There was no other significant finding. Peripheral blood film showed pancytopenia with no blast cells. Bone marrow (BM) aspirate showed hypocellular marrow with presence of significant dyserythropoiesis and dysmegakaryopoiesis. Trephine biopsy findings favoured MDS with excess blasts. However, marrow cytogenetic was unable to proceed due to low count. This patient is currently managed supportively, by giving blood transfusion whenever necessary. Being the only child, finding a matched donor for haematopoietic stem cell transplant (HSCT) is not easy. **Learning Points:** This case highlights MDS as a cause for pancytopenia in children. Even though uncommon, a diagnosis of MDS should be considered in a child presenting with pancytopenia. Due to its rarity, diagnosing MDS in childhood is a challenge to clinicians as well as pathologists. Comprehensive and intensive work-up is required to confirm the condition. Cytogenetic testing in MDS not only aids the diagnosis but also useful for prognosis.