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# The International Congress of Pathology & Laboratory Medicine 2023: Precision Medicine: Revolutionizing Pathology in Genomic Era, organised by the College of Pathologists, Academy of Medicine of Malaysia and at World Trade Centre Kuala Lumpur on 20-22 September 2023

**ICPALM 2023: International speakers**

**1. Anatomical Pathology**

**Molecular classification of gastric carcinoma**
Corrado DÁrrigo
*Poundbury Cancer Institute*.

During the past two decades there has been significant improvement of cancer outcomes due, at least in part, to increasing use of biological therapies. This requires the identification of specific subgroup of patients that may benefit from particular targeted treatment. The classical morphological classification of tumours is inadequate to support this transformation of treatment modalities. New molecular classifications have emerged for a number of cancer sites, based on comprehensive analyses of large number of parameters ("multi-omics"). In order to make it accessible to all patients, multi-omics classifications have been implemented into the histopathology diagnostic routine using a handful of on-slide tests.

Such implementation has yet to happen in gastric cancer (GC) and patients access to effective targeted treatment remains limited. We present an overview of the current molecular classification for gastric cancer and a study to assesses the feasibility of implementing a molecular classification based on 4 groups of on-slide tests. These are ISH for EBER (for the identification of GC EBV+), IHC for MLH1 and MSH2 (for the identification of GC MMR-deficient), IHC for E-cadhering and β-catenin (for the identification of GC EMT or epithelial-mesenchymal transformation) and IHC for p53 (for the identification of p53 mutated and p53 wild type GC). The prognostic and predictive implications for GC patients will be discussed.

**Rewriting the Her2 testing handbook**
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Histopathologists have been providing Her-2 status for breast cancer (BC) patients for over 4 decades. Testing aimed at identifying a small (12-15%) proportion of BC patients that have Her2 gene amplification as a main oncogenic driver in their cancer. Direct blocking of the Her2 receptor with mAb-based therapy is an effective treatment only in patients with Her2 over-expression or amplification.

Recently, targeting Her2 with specific antibodies that deliver cytotoxic payloads inside the tumour cells (ADC or antibody-drug conjugates) has shown effectiveness also in BC that has low level expression of Her2 but lacks amplification. Regulatory approval of this treatment means de facto that the traditional binary classification (positive/negative) has to be replaced with a new ternary classification (high/low/zero) and that the interpretation of the IHC staining needs to be re-focused to recognise the new thresholds.

We developed focused algorithms and training programmes for the interpretation of Her2 IHC in the new diagnostic landscape. We will be discussing the re-evaluation of the scope and parameters for Her2 testing in BC with particular focus on the analytical performance of current tests, the identification of various staining patterns and their significance, the interpretative algorithm and the new (2023) release of the ASCO-CAP and RCPath guidelines.

**Surgical pathology of low-grade epilepsy-associated neuroepithelial tumors (LEAT): role of molecular genetic testing and surrogate immunohistochemical markers**
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Low-grade epilepsy-associated neuroepithelial tumors (LEAT) is a generic term for CNS WHO grade 1 to 2 or equivalent tumors, with epileptic seizures as the main symptom developing mostly by the age of 15 years, and 88% of patients show a favorable postoperative seizure outcome, representing a clinicopathological concept distinct from the WHO classification of brain tumors. A past survey reported that the majority of LEAT consisted histopathologically of neuronal and mixed neuronal-glial tumors frequently localized in the temporal lobe, with ganglioglioma (GG) and dysembryoplastic neuroepithelial tumor (DNT) being the most common histopathological diagnoses comprising 60 to 90 % of cases. However, disagreement between experts on diagnosing GG and DNT was not uncommon, particularly when specific histological features were not

organs appeared normal. Histological examination supported these findings. Further investigations revealed persistence growth of Escherichia coli in the blood, peritoneal and spleen tissue culture. *Discussion:* Although the mortality is low due to the advent of antibiotic, death still occurred in cases with delayed diagnosis. This is given to its non-specific symptoms and absence of predisposing factors commonly associated with peritonitis. This case highlights specific risk factors and pathological findings associated in the case of paediatric primary peritonitis.

**FM11: Lung chronicles: decoding granulomatous disease; role of molecular study**

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*Introduction*: Granuloma alone is a nonspecific histopathological finding, rather it comprises a group of disorders which have a wide spectrum of pathologies. The integration of histological analysis and molecular study is crucial in concluding a case in the field of forensic pathology. *Case report*: A 43-year-old Malay gentleman was found unconscious at his home. Reportedly, he has no known medical illness but was an intravenous drug user and had multiple histories of prison detention, though he was not under custody at that moment. He had a short history of fever and shortness of breath. External examination revealed a cachexic, medium body-built with no marks of injury. However, upon opening the chest, there was generalized adhesion of the pleura with cavitations of bilateral lungs and copious amounts of pus-like secretions. Histological analysis of the lung sections showed presence of few multinucleated giant cells. *Discussion*: Presence of lung cavitations grossly, together with giant cells with or without granuloma histologically, were frequently associated with mycobacteria infection. This has not always been the case, particularly in the case reported above as the sample sent for molecular study did not detect mycobacteria. What is highlighted under the microscope will somehow need to be further investigated with molecular study, either to nullify or confirm the preliminary findings.

**FM12: Silent clues: decoding autopsy case of subinvolution of placental site**

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*Introduction:* Secondary postpartum haemorrhage (PPH) accounts for 1% of maternal death and subinvolution of the placental site (SPS) is one of its uncommon aetiologies. *Case report:* A 34-year-old woman (Para1) was brought-in-death 14 days post vaginal delivery to the emergency department. Her delivery was uneventful. Antenatally, she had gestational diabetes and good glycaemic control. She was asymptomatic postnatally and stated having chills, light-headedness and vomiting two days before her death. Unfortunately, her husband was unable to quantify the amount of vaginal bleeding during the postpartum period. At autopsy, her sarong and undergarment were soaked with blood, and her body was pale. The underlying SPS was identified from the autopsy. Endometritis and urinary tract infections were also present. *Discussion:* Subinvolution of the placental site can cause significant delayed postpartum haemorrhage and if undetected may result in death. SPS is defined as delayed or inadequate physiological closure and sloughing of the superficial modified spiral arteries at the placental site (the failed process of normal involution). The diagnosis of SPS was confirmed histologically by the presence of endovascular extravillous trophoblasts and clustered myometrial arteries that were dilated and partly occluded by old and new thrombi. Although the cause of subinvolution is not known, this process may manifest an abnormal interaction between foetal-derived trophoblasts and maternal tissue. Subinvolution is an important process to recognise, as it implies an idiopathic cause of delayed postpartum bleeding. The diagnosis of SPS can be challenging as it requires a detailed autopsy including histology.

**FM13: Mesenteric haematoma as a rare complication of acute pancreatitis: a case report**

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*Introduction:* Mesentery haematoma is an uncommon and potentially life-threatening complication of acute pancreatitis in the absence of any external abdominal trauma. Despite the normal appearance of the pancreas during an autopsy, the possibility of acute pancreatitis cannot be totally excluded especially in the presence of a mesentery haematoma. *Case report:* A 40 years lady with no known premorbid presented with abdominal pain, vomiting and loose stool for two days. She was treated for gastritis prior to death. The autopsy examination showed no fatal external injuries. Abdominal examination exhibited mesentery haematoma. Although the pancreas appeared grossly normal; histopathological examination of the pancreas showed evidence of necrotic tissue with adjacent inflammatory infiltrates, haemorrhage and fat necrosis. Postmortem serum amylase revealed twenty folds increment from the normal value. *Discussion:* Acute pancreatitis is an inflammatory disease which can be associated with significant complications and these can be categorized into either early or late and local or systemic. Acute pancreatitis can be the cause of sudden unexpected death where haemorrhagic pancreatitis holds higher mortality rates. Nevertheless, the absence of typical gross pathological findings on the pancreas during autopsy may defy the diagnosis of acute pancreatitis. Hence, a higher suspicion rate towards pancreatitis in the presence of mere surrounding tissue haematoma will help in determining the underlying pathology. Furthermore, postmortem serum amylase in a fresh body would have some potential benefit in providing supportive evidence along with the histopathological changes towards determining the final cause of death especially in a case of acute abdomen presentation.