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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

AP13: CD47 expression in chorioamnionitis

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Introduction: Chorioamnionitis is the inflammation of the placental membrane with presence of neutrophilic infiltration. Currently, the mediators involved in neutrophil recruitment and migration is still under investigation. Early research has hypothesised that CD47 is involved in transmigration of neutrophils across epithelial and endothelial cells. Our objective is to examine the potential involvement of CD47 in neutrophils recruitment and migration in the placenta of patients. *Materials & Methods*: A retrospective study was conducted involving 100 cases with histological diagnosis of acute chorioamnionitis (n=20), subchorionitis (n=20), necrotising chorioamnionitis (n=20) and normal placenta (n=40) over a period of 4 years. Immunohistochemistry was done on the placenta, umbilical cord and placental membrane section. The presence of positive staining and its' intensity on these tissue sections were analysed. *Results*: CD47 positive staining was observed in syncytiotrophoblast, cytotrophoblast, and foetal vessels. A small number of cases also showed positive staining in the maternal vessel, and decidua. All of the stainings were not significantly correlated with chorioamnionitis and foetal inflammatory response syndrome (P>0.05). *Discussion*: Further experiment with a larger sample size and molecular techniques should be conducted in order to corroborate the result.

AP14: Histopathological profile of cervical biopsies in Sarawak

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Introduction: Cervical cancer is the third most prevalent cancer in women in Malaysia. Managing the disease has placed a significant economic burden of approximately RM312 million on the government each year. This study aimed to evaluate the pattern of the histopathological profile of cervical biopsies and to determine the association of risk factors with the findings of the cervical biopsies performed at Klinik Sakit Puan & Infertiliti Universiti Malaysia Sarawak (UNIMAS). *Materials & Methods:* This retrospective study was conducted in a specialist clinic in UNIMAS from January - August 2023. Data regarding the patients and the cervical biopsy findings were recorded using a pre-designed form and were analysed using Statistical Package for Social Sciences version 28.0. *Results:* The most common finding observed was chronic cervicitis (20.9%), whereas cervical intraepithelial neoplasia (CIN) lesions were observed in 20.4% of cases. Among the CIN findings, 87.23% were classified as CIN I, while CIN II and CIN III accounted for 8.51% and 4.26%, respectively. Additionally, 6.38% of the overall CIN findings were associated with HPV. However, there was no significant association between the patient's age and the cervical biopsy finding (p>0.05). *Discussion:* Our study did not observe any significant association between age or ethnicity and the cervical biopsy finding. This study highlights the importance of other sociodemographic data regarding cervical cancer, which should be obtained from all patients referred for a cervical biopsy, as this information is relevant to most healthcare interventions in terms of improving the morbidity and mortality associated with cervical cancer.

AP15: A rare variant of oncocytic mucoepidermoid carcinoma of the parotid gland: A case report

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Introduction: Mucoepidermoid carcinoma (MEC) is the most common salivary gland malignancy across all ages. This malignancy consists of a combination of squamoid, intermediate cells and mucocytes. A rare variant composed predominantly of oncocytes can be confused with benign entities. We present a case with such an associated lesion. *Case report*: A 61 years old Indian female presented with 10-year history of right preauricular swelling, with recent increase in size and pain for the past year. Cytomorphological examinations of this soft tumour yielded cystic content with no definitive diagnosis. Meanwhile, biopsy revealed a malignant tumour composed of predominantly oncocytic cells, with mucocytes exhibiting intracytoplasmic mucin evidenced by positive Mucicarmine stain and PAS-D resistance. Immunohistochemical markers p63, p40 and CK 5/6 were demonstrable within the basal layer of the intermediate cells. Tumour necrosis and mitosis were scarce with focal perineural invasion observed. *Discussion*: The diagnosis of OMEC is particularly challenging in cytological examinations since it requires at least > 50% population of oncocytic cells, where oncocytic metaplasia is also common in MEC. This variant, even though rare, still has a favourable prognosis. However, the actual challenge in diagnosis lies in differentiating this malignancy with several benign oncocytic lesions that are much more common such as, Warthin's tumour, oncocytoma, and pleomorphic adenoma with oncocytic and mucocytic metaplasia. Ancillary tools like immunohistochemical markers, special stains and molecular studies for MAML2 gene translocation are vital with aiding the diagnosis. Adequate sampling, high index of suspicion coupled with ancillary techniques are crucial to prevent misdiagnosis.

AP16: Impaired DNA mismatch repair and PD-L1 expression in triple negative breast cancers

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Introduction Effects of immune checkpoint inhibitors in triple negative breast cancers have been extensively studied. Clinical trials for triple negative breast cancers have shown clinical improvement using anti PD-L1 antibody in combination with a chemotherapy agent. Solid tumours with impaired DNA mismatch repair (MMR) system (MLH1, PMS2, MSH2, and MSH6