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Background: Pancreatic cancer is one of the most lethal and molecularly diverse malignancies. Although *HER2* amplification occurs in pancreatic cancer, it is inadequately characterised to define its clinical relevance and to exploit the potential of anti-*HER2* therapies.

Aims: We aim to characterise the clinicopathological features of *HER2* amplified pancreatic cancer. Our work extends the clinical relevance of our effect as part of the Australian Pancreatic Cancer Genome Initiative (APGI) in cataloguing genomic aberrations that characterise pancreatic cancer.

Methods: 469 cases of surgically resected pancreatic ductal adenocarcinoma (PDAC) from 12 institutions associated with the APGI from 1990 to 2012 were assessed for *HER2* overexpression by immunohistochemistry and *HER2* gene amplification by *in situ* hybridization. 55 of these cases were also assessed for DNA copy number changes and mRNA expression.

Results: *HER2* amplification was found in 10 of 469 (2.1%) of samples. *HER2* gene amplification was found in 100% (7/7) of *HER2* 3+, 11% (3/27) of *HER2* 2+ and none of 1+ overexpressing tumours. In all but one case, *HER2* overexpression was uniform throughout tumours rather than showing clonal heterogeneity. *HER2* amplification was associated with moderately differentiated tumours with distinctive macroglandular morphology. *HER2* amplified tumours were also distinctive in their pattern of metastasis, with involvement of the lung $\pm$ brain without liver metastasis.

Conclusions: *HER2* amplification occurs in 2% of PDAC and has distinct clinicopathological features with implications to clinical practice. The molecular heterogeneity of PDAC implies that even an incidence of 2% represents an attractive target for anti-*HER2* therapies, as options for PDAC are limited. Recruiting patients based on *HER2* amplification rather than organ of origin could make clinical trials of anti-*HER2* therapies more feasible but needs to be well defined with robust diagnostic assays.

11. *ROS1* GENE REARRANGEMENTS IN NON-SMALL CELL LUNG CARCINOMA – A NEW GENETIC TARGET

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Background: Targeted therapies aimed at specific molecular genetic alterations are revolutionising cancer treatment, particularly in non-small cell lung cancer (NSCLC). Driver mutations

involving translocation of the *ROS1* gene have recently been identified in NSCLC and show promise as a target for tyrosine kinase inhibitors.

Aim: To investigate the incidence and clinicopathological features of NSCLC harbouring *ROS1* rearrangements and the accuracy of IHC compared to FISH at identifying these tumours.

Methods: We tested for *ROS1* translocations using a FISH break-apart probe and immunohistochemistry (IHC) in (1) tissue micro-arrays from a retrospective cohort of 308 early stage adenocarcinomas, (2) a prospective cohort of 23 NSCLC, selected on clinical grounds for mutation testing.

Results: Only 1 of 308 cases was positive by FISH in the retrospective cohort giving a 0.3% incidence of *ROS1* gene rearrangements. *ROS1* IHC was positive in 7 (2.3%) of these cases, including the FISH+ case (sensitivity 100%, specificity 98%). In the prospective cohort, three cases with *ROS1* rearrangement were identified by FISH (all IHC positive). All 4 cases of *ROS1* gene rearrangement identified by FISH occurred in adenocarcinomas that were *EGFR*-wild-type, *ALK*-negative, from non-smoking females (age range 33–81 years, mean 59). Two were of Asian ethnicity.

Conclusions: *ROS1* gene rearrangements occur in a very small percentage of lung adenocarcinomas and are mutually exclusive with *EGFR* and *ALK* alterations. Screening with IHC may be a suitable method of reducing the number of cases requiring FISH.

12. PREVENTION OF CISPLATIN-INDUCED NEPHROTOXICITY BY DICHLOROACETATE

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Background: There is a continuing need to improve the efficacy of anticancer agents and to reduce the toxicity associated with them. Recently, reversal of the glycolytic phenotype of cancer cells with novel agents such as DCA (dichloroacetate) has been recognised as an important new target for cancer therapy. DCA is currently being assessed as a novel chemotherapeutic in clinical trials. It is anticipated that DCA will be used in combination with other well-established chemotherapeutic drugs. It is therefore critically important to determine the effects of DCA on therapeutic efficacy, and off-target effects of existing frontline anti-cancer drugs. We have recently discovered that DCA induces glutamate cysteine ligase, the rate-limiting step in glutathione (GSH) synthesis, a major cellular antioxidant. We hypothesised that the ability of DCA to stimulate GSH-synthesising capacity could reduce cisplatin-induced nephrotoxicity, which is thought to be mediated in part by oxidative stress.

Aims: To determine whether DCA can attenuate cisplatin-induced nephrotoxicity, and to determine if DCA influences the anti-cancer properties of cisplatin.

Methods: 120 Balb/c mice were injected subcutaneously with the syngeneic 4T1 breast cancer cell line and then co-treated with DCA and cisplatin weekly for 1 month. Controls included treatment with cisplatin alone, DCA alone, or normal saline injections. Serum blood urea nitrogen (BUN) and creatinine were measured and kidney damage was assessed histologically. Tumour size was monitored throughout.

Results and conclusions: DCA prevented increases in serum creatinine, BUN, and renal proximal tubule apoptosis evident in cisplatin-only treated mice. The tumour size in mice in the co-treated group decreased at the same rate as the cisplatin-only treated mice. We have thus concluded that DCA largely prevents the development of cisplatin-induced nephrotoxicity, and does not attenuate its anti-cancer properties.

13. A CASE OF SEBACEOUS ADENOMA IN A SALIVARY GLAND

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Sebaceous differentiation in parotid glands is a frequent histopathological finding (approximately 20–40%), however sebaceous neoplasms occurring in parotid glands are very uncommon. Sebaceous adenomas are benign adnexal neoplasms and account for 0.1% of all salivary gland neoplasms. These adenomas occur most commonly in the parotid gland; however they have been reported in the submandibular, sublingual, and minor salivary glands. The literature describes a few cases diagnosed by fine needle aspirate cytology, however it remains a histological diagnosis in the majority of cases. Histologically, the neoplasm is characterised by abundant islands of sebaceous cells admixed in a fibrous stroma surrounded by cystic and duct like structures. There have been no reports of recurrence following adequate surgical excision. We present a case of sebaceous adenoma in a parotid gland, to draw attention to this differential diagnosis in the diagnosis of parotid masses.

14. SCLEROSING ANGIOMATOID NODULAR TRANSFORMATION (SANT) OF THE SPLEEN: A PERTH EXPERIENCE

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Background: Sclerosing angiomatoid nodular transformation of the spleen (SANT) is an uncommon, usually incidental, non-neoplastic vascular splenic lesion first described in 2004¹. Recent articles have suggested association of SANT with IgG4-related sclerosing disease and with Epstein–Barr virus RNA expression².

Aim: A retrospective review of SANT cases reported in three Perth metropolitan hospitals over the past 20 years.

Methods: A computer-assisted search of all reported SANT cases from the Perth metropolitan hospital Anatomical Pathology database for the period 1992–2012 was performed. Slides were reviewed from the identified cases and, where formalin-fixed paraffin-embedded (FFPE) tissue was available, further immunohistochemical stains were performed including CD8, CD30, CD31, CD34, D2–40, ERG, CD138, IgG, IgG4 and EBV-encoded small RNA (EBER).

Results: Four cases were identified, including three splenectomy specimens and one post-mortem specimen. All had the characteristic CD31/CD34/CD8 vascular immunophenotype¹. Endothelial expression of CD30 was found in two of the cases. Architectural derangement was highlighted by an altered pattern of ERG immunoperoxidase nuclear expression in the sinusoidal epithelium of SANT angiomatoid nodules. EBER was negative in the three cases

with available FFPE material and no convincing evidence for IgG4-related sclerosing disease was identified.

Conclusion: Four cases of SANT are described, including immunohistochemical adjuncts to their diagnosis. No evidence for an association with EBV infection or IgG4-related sclerosing disease is identified in these cases.

References

1. Martel M, Cheuk W, Lombardi L, *et al.* Sclerosing angiomatoid nodular transformation (SANT). Report of 25 cases of a distinctive benign vascular splenic lesion. *Am J Surg Pathol* 2004; 28: 1268–79.
2. Kashigawa S, Kumasaka T, Bunsei N, *et al.* Detection of Epstein-Barr virus-encoded small RNA-expressed myofibroblasts and IgG4-producing plasma cells in sclerosing angiomatoid nodular transformation of the spleen. *Virchows Arch* 2008; 453: 275–82.

15. A TWIN WITH A MOLE! A CASE REPORT OF AN EXTREMELY RARE CONDITION OF MOLAR PREGNANCY WITH A COEXISTING FETUS PROGRESSING TO A VIABLE INFANT

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Introduction: Molar pregnancy with a coexisting twin fetus is an extreme rarity. The incidence of such an occurrence ranges from 1 in 10,000 to 100,000 pregnancies and this may increase with the greater use of assisted reproductive techniques. The management of these pregnancies is difficult due to complications such as fetal death, vaginal bleeding, pre-eclampsia and an increase risk for persistent trophoblastic disease. Delivery of a viable term normal infant from this combination is even rarer.

Case report: We report a case of molar pregnancy in a 36-year-old woman with a coexisting twin fetus which progressed to delivery of a viable healthy infant at term gestation. The submitted specimen was a twin placenta comprising two separate discs joined by a dividing membrane. One of the discs was pale yellow and small. Vesicles were not evident macroscopically. Microscopic examination showed a dichorionic diamniotic twin gestation. The placenta of the viable term gestation showed no significant abnormality while the separate yellow disc showed changes of hydatidiform mole with extensive infarct-like necrosis.

Discussion: Molar pregnancy with a coexisting twin fetus progressing to a healthy infant is an extremely rare entity. The management guidelines for decision making are limited as there are only a few published reports in the literature. We present this case report to highlight the existence of this extremely rare entity. In addition, it demonstrates that, despite the presence of a coexisting molar gestation, the non-molar gestation may progress to delivery of a normal healthy term infant.

16. IS IT A GIST OR WHAT? TWO CASE REPORTS OF DESMOID TUMOUR IN PATIENTS WITH PREVIOUS GASTROINTESTINAL STROMAL TUMOUR

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Background: Gastrointestinal stromal tumours (GISTs) and desmoid-type fibromatosis (desmoid tumours) are rare mesenchymal