SESSION 1 – Jean Campbell Prize trainee presentations

Paediatric orbital lipoblastoma: A case presentation

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Case: We present a case of a 7-month-old male, with a left orbital tumour of three months of evolution. The patient presents left exophthalmos and limited abduction of the left eye. An orbitotomy was performed. The histopathological examination showed a mesenchymal tumour composed of hypocellular lobules with a mixture of adipocytes of various stages of maturity and myxoid stroma separated by prominent fibrous septa, suggesting a differential diagnosis between the several types of adipocytic orbital tumours, especially liposarcoma. However, the lack of significant atypia and the lobulation of the tumours ruled out liposarcoma and confirmed the diagnosis of orbital lipoblastoma in the paediatric age.

Key Words: lipoblastoma, paediatric
Abstract Category: Clinical case report with an ocular pathology theme.

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Recurrent periorbital cellulitis: a sinister NK/T cell lymphoma

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Introduction: Extranodal NK T-cell lymphoma (ENKTL)is an aggressive type of lymphoma of NK T-cell lineage. ENKTL divided into nasal and extra-nasal subtypes according to the site of primary tumour. The nasal type represents the most common subtype accounting for 80% of cases and non-nasal type is 20%. Its more prevalent in East Asia and Latin America and rare in Western countries. Commonly affects adult patient with male predominance but have been reported in younger patients.
Most patients with ENKTL, nasal type present with midfacial destruction. Other clinical presentation includes epistaxis, purulent discharge and nasal obstruction. The main characteristics of this lymphoma are vascular destruction, necrosis, cytotoxic phenotype and association with Epstein Barr virus (EBV). We describe a rare case of periorbital cellulitis caused by ENK T-cell lymphoma.
Case Report: An 18-year-old female presented to a regional eye unit with left eye periorbital swelling and a watering eye for 2 months. Initially, she was diagnosed with periorbital cellulitis, and she received multiple courses of antibiotics with no improvement. MRI scan demonstrated nasolacrimal duct obstruction. The clinical diagnosis was periorbital cellulitis secondary to dacryocystitis. She was admitted and initiated on intravenous antibiotics. The swelling improved and she was listed for a dacryocystorhinostomy (DCR) procedure as an outpatient. Subsequently, 2 weeks later, she presented with a recurrence of periorbital swelling. OCT orbit scan was performed and showed severe mucosal disease, and thinning of the medial wall of left orbit. Otolaryngology review was requested, and a functional endoscopic sinus surgery was undertaken with biopsies. The morphological examination of the biopsies demonstrated an infiltrative malignant tumour with angio-destruction and extensive necrosis. The morphological and immunohistochemical examination confirmed the diagnosis of extranodal NK/T cell lymphoma, nasal type.
Conclusion: ENKTL, nasal type is an aggressive and locally destructive lymphoma with a poor prognosis. A high index of suspicion should be maintained in a patient presenting with non-resolving periorbital cellulitis that fails to improve with treatment. A CT sinus should always be considered in such patients.

Key Words: Extranoda NK/T-cell lymphoma, EBV, cellulitis
Category: Clinical case report with an ocular pathology theme.

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An unusual phenotypic presentation of ocular Erdheim-Chester disease

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Introduction: Erdheim-Chester Disease (ECD) is a rare systemic non-Langerhans histiocytic disorder resulting from mutations in the mitogen-activated protein kinase pathway causing uninhibited cell survival and proliferation of histiocytes. The resulting infiltration of various tissues leads to end-organ dysfunction. Ophthalmic involvement may be the presenting feature, occurring in around a quarter of patients, usually with painless intraconal orbital mass and, rarely, intraocular involvement. We present a case with an unusual phenotype of choroidal and sub-conjunctival involvement.
Methods: A 64-year-old Caucasian male with stable ECD affecting lung, skin and bone, managed with weekly peginterferon and filgrastim was referred for ocular oncologist review of asymptomatic symmetrical macular choroidal mass lesions. Examination revealed xanthelasma-like subtle bilateral orange subconjunctival infiltrative lesions in the fornices and bilateral amelanotic macular choroidal calcified mass lesions with no associated sub- or intra-retinal fluid. Multimodal imaging did not detect orbital involvement. The patient underwent subconjunctival incisional biopsy.
Results: Histology demonstrated the same bubbly histiocytic infiltrate as was in the patients' previous lung and skin biopsies, positive for CD163 and negative for S100, CD1a and Langerin, confirming a malignant histiocytic disorder, entirely consistent with ECD.
Discussion: Our case is the first to describe concomitant calcified choroidal and subconjunctival lesions in ECD. Literature review revealed ophthalmic phenotypic similarities between other histiocytic disorders and ECD, despite pathophysiological and genetic differences, including Langerhans histiocytosis and Rosai-Dorfman disease. Ophthalmologists need to be aware of the potential for ophthalmic involvement by ECD and the other histiocytoses, as early diagnosis can improve survival and visual prognosis.

Key Words: Erdheim-Chester Disease, Non-langerhans histiocytosis, ocular involvement
Abstract Category: Clinical case report with an ocular pathology theme.

SESSION 1 – Jean Campbell Prize trainee presentations

The xylem's in the details

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Case: A 53-year-old Caucasian intravenous drug user attended after allegedly tripping over a tree branch and falling, while under the influence of cocaine. Globe rupture was initially suspected, due to the protrusion of gelatinous sticky black material, which was thought to be prolapsed uveal tissue. He was taken to theatre for an examination under anaesthetic and repair. No scleral rupture was found, but the black material extended far posteriorly behind the equator, with extensive conjunctival rupture and involvement. The material was cleaned as best as possible, but a significant portion of conjunctiva needed to be excised. The remaining defect was closed with an Omigen(R) graft. The history and appearance of the black foreign material fit with a working diagnosis of "street herion," which has a black tar-like appearance. However "black tar" heroin is rare in the United Kingdom, as the predominant form is a brown powder. Histopathology identified the substance to be plant material, as xylem tubules, plant structures responsible for transporting water and minerals, were visualised.

Category: Clinical case report with an ocular pathology theme.

SESSION 1 – Jean Campbell Prize trainee presentations**MBD4 – are heterozygous carriers of loss of function variants predisposed to cancer?**

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Introduction: Patients with homozygous loss of function (LoF) variants in MBD4 were recently identified as having a muti tumour predisposition syndrome with an unusual tumour spectrum, including AML, colorectal cancer and uveal melanoma. Somatic samples from these show distinctive features, reflecting the biologic function of MBD4, including high tumour mutational burden (TMB) and extremely high cosmic mutational signature 1, which is characterised by C-T changes from spontaneous deamination of methylated cytosine to thymidine. MBD4 has a crucial role in Base Excision Repair of these thymidines. We therefore wanted to know if there was a phenotype for patients with heterozygous LoF variants in MBD4.
Methods: Participants with variants in MBD4 were identified from the Genomics England 100,000 Genomes project (100kGP) Whole Genome Sequencing dataset. Variants were filtered, reviewed and categorised by sequency ontology term. Data was combined with clinical information and somatic genomic data. The signature 1% in tumours was compared between groups based on MBD4 germline status. We also identified any tumours with extremely high signature 1 (>90%), and reviewed MBD4 status. Finally, we reviewed signature 1% and TMB for all uveal melanomas in the 100kGP dataset.
Results: Among the 15237 participants in the cancer arm of 100kGP, there were 46 participants with a germline heterozygous LoF variant in MBD4. Among the rare disease arm of 100kGP, there were 141 LoF variants among 64908 genomes (OR in cancer arm 1.4, (95%CI=1-1.94)). Comparing those with a LoF variant to those without any variant, there was a different distribution of signature 1% in tumours in the LoF variant group (Mann-Whitney U test, W=232320, p=0.00010). There were 7 tumours (15%) in the LoF variant cohort with a "very high signature 1" above 90%, which was found in 0.02% of tumours when there was no MBD4 germline variant. These comprised 3 sarcomas, 3 breast carcinomas and 1 uveal melanoma. All had somatic second hit of the other MBD4 allele. Searching for all very high signature 1 tumours, without regard to MBD4 germline status, yielded 11 tumours, 7 of these being those already described above. Of the 4 without a germline variant, one had a somatic biallelic inactivation of MBD4. The other three had only single copy somatic loss of MBD4. There were 17 uveal melanomas sequenced. Of the 16 without a germline MBD4 variant, Signature 1% ranged 12-29% (median 19.5%, mean 19.75%). TMB ranged from 0.25-4.48 variants/Mb (median 0.52, mean 0.75). In contrast, the case with an MBD4 LoF variant had a TMB of 6.62 variants/Mb and a signature 1% of 100%.
Discussion: Heterozygous MBD4 LoF variants appear to confer a slightly increased risk of cancer. Tumours of any type, including uveal melanomas, where mutational signature 1 is >90% are likely to have a heterozygous MBD4 LoF germline variant. There is some emerging evidence that MBD4 deficient tumours are particularly sensitive to immunotherapy, and potentially chemotherapy with cytidine analogues. Identification of these tumours may provide therapeutic options.

Key Word: Whole Genome Sequencing; Uveal melanoma; MBD4
Category: Brief research paper report relevant to disease of the eyes.