49. PRIMARY LOW-GRADE B-CELL LYMPHOMA OF THE CENTRAL NERVOUS SYSTEM: PRESENTATION AND DISCUSSION OF A CASE

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Background: Primary central nervous system lymphoma (PCNSL) is a rare extranodal non-Hodgkin lymphoma involving the brain, leptomeninges, spinal cord or eyes without evidence of systemic disease. It accounts for 3–4% all primary brain tumours. Diffuse large B-cell lymphoma (DLBCL) is the most common subtype, and low-grade PCNSL are rare, probably <5% of all cases of PCNSL.

Aim: We present and discuss a case of primary CNS low-grade B-cell lymphoma.

Case report: A 40-year-old female presented with left hemiplegia and paraesthesia. MRI brain showed signal abnormality in the deep periventricular white matter of both cerebral hemispheres without mass effect. Biopsy showed prominent perivascular infiltrate of small lymphocytes. Immunostains showed most of the lymphocytes to be CD20-positive B-cells. They were positive for BCL2 and showed lambda light chain restriction on kappa and lambda ISH. They were negative for CD10, BCL6, CD5, CD23, cyclin D1, CD138, cMYC and EBV ISH. The Ki-67 proliferation index was low. She underwent a course of chemotherapy without neurological improvement, and subsequently transferred to palliative care.

Discussion: Primary CNS low-grade B-cell lymphomas are poorly understood due to their rarity and heterogeneity. Marginal zone lymphoma and lymphoplasmacytic lymphoma in immunocompetent patients represent the majority of cases reported in the literature. It is important to exclude reactive causes (such as vasculitis and encephalitis), secondary involvement of the CNS by systemic lymphoma (including Waldenstrom macroglobulinaemia and Bing-Neel syndrome), and high-grade B-cell lymphomas (particularly T-cell-rich large B-cell lymphoma and EBV-associated lymphoproliferative disorders).

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50. ROLE OF INTRAOPERATIVE CYTOLOGY IN THE GAMUT OF SELLAR-SUPRASELLAR LESIONS: ENIGMAS UNEARTHED, LESSONS LEARNT

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Background: Intraoperative diagnosis of sellar-suprasellar tumours plays an important role in planning the extent of surgical resection and further management. Imprint and squash cytology in correlation with radiological findings are useful to provide rapid diagnosis in most of these lesions.

Aim: The present study was conducted to analyse the spectrum of cytomorphological features of various tumours of sellar-suprasellar region.

Methods: A two year retrospective study was conducted in the Department of Pathology of a tertiary care hospital. Rapid haematoxylin and eosin stained slides of imprint and squash smears of all the sellar-suprasellar lesions were retrieved. The findings were correlated with histology and radiology whenever available.

Results and conclusion: Sixteen cases of sellar-suprasellar tumours were identified in the current series. Pituitary adenoma and craniopharyngioma were commonly encountered lesions accounting for 5 (31%) cases each. Other less common tumours included meningioma, low grade glioma, lymphoma and germinoma. On radiology, pituitary adenomas and craniopharyngiomas presented as solid-cystic lesions while others were solid masses. On corroboration with histology, diagnostic accuracy of cytology smears was 94%. To conclude, intraoperative cytological evaluation plays an important role in the rapid diagnosis of sellar-suprasellar tumours, especially in cases where there may be overlapping radiological features. In addition to confirming clinical-radiological findings, intraoperative cytology is useful to detect uncommon entities that can help the surgeon to plan appropriate therapeutic strategies.

51. ADULT BRAINSTEM ANAPLASTIC ASTROCYTOMA WITH AN UNUSUAL MOLECULAR PROFILE

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Background: Adult brainstem diffuse astrocytomas are relatively rare, with molecular profiles including *IDH1* or *H3F3A* mutations in association with *ATRX* and *TP53* mutations in some cases. More unusual combinations of mutations have been described but are yet to be formally classified by the WHO. Such cases are currently difficult to evaluate by immunohistochemistry and small sequencing panels alone.

Aims: To demonstrate the molecular profile of an unusual adult brainstem astrocytoma which did not fit any of the current WHO (2016) diagnostic classifications and to evaluate these data in the context of astrocytomas reported in the cBioPortal database and the scientific literature.

Methods: Routine histopathology and immunohistochemistry for *IDH1*, *ATRX*, *p53* and *H3K27M* was evaluated. Hybrid-capture sequencing of 386 genes was performed on tumour DNA extracted from FFPE sections and germline DNA extracted from blood using an Illumina NextSeq sequencer.

Results and conclusions: Histopathology showed a grade 3 astrocytoma, IHC negative for IDH1, p53, and H3K27M but demonstrating ATRX loss. Sequencing confirmed wildtype status for *IDH1/2* and *H3F3A* and showed an unusual combination of mutated genes (*ATRX*, *NF1* and *RAF1*) and *CDKN2A* deletion. *ATRX* and *NF1* mutations typically show a high degree of mutual exclusivity in astrocytomas (cBioPortal <http://cbioportal.org>). The currently described case has a very similar molecular profile to a recently reported series of the so-called 'anaplastic astrocytoma with piloid features',¹ which is yet to be included in the WHO classification of CNS tumours, and has a unique methylation profile and clinical outcome.

Reference

1. Reinhardt A, Stichel D, Schrimpf D, *et al.* Anaplastic astrocytoma with piloid features, a novel molecular class of IDH wildtype glioma with recurrent MAPK pathway, CDKN2A/B and ATRX alterations. *Acta Neuropathol* 2018; 136: 273–91.

52. FGFR3-TACC3: CASE REPORT AND REVIEW OF A POTENTIALLY TARGETABLE DIAGNOSTIC MARKER IN HIGH GRADE GLIOMAS

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Background: *FGFR3-TACC3* fusion has been identified in IDH wild-type WHO grade III and IV astrocytomas, with an incidence of 2–3% in most case series and a range of 1–8%. These tumours have characteristic histopathological features and a poor prognosis. The aberrant CD34 immunohistochemical staining and glial and neuronal marker co-expression may lead to a misdiagnosis of a glioneuronal tumour with a better prognosis. An immunohistochemistry antibody to FGFR3 is commercially available which may serve as a more cost-effective screening test for identification of possible *FGFR3-TACC3* cases. These tumours may also be amenable to treatment by FGFR tyrosine kinase inhibitors, or through inhibition of oxidative phosphorylation as a down-stream functional target of *FGFR3-TACC3* fusion.

Aims: A report highlighting common pitfalls in the diagnosis of high grade astrocytoma with *FGFR3-TACC3* gene fusion.

Methods: A single case study and review of the supporting literature.

Results and conclusions: A 64-year-old male with a four month history of focal sensory abnormalities had a solitary 24 mm, intra-axial, contrast-enhancing left parietal lobe brain lesion on MRI. A stereotactic craniotomy and tumour resection was performed. Histopathology showed a malignant heterogeneous tumour. The cellular morphology included gemistocytic features, larger pleomorphic cells and numerous mitotic figures. Additional findings were psammomatous calcifications and thin-walled branching blood vessels with perivascular lymphoid cuffing. Many of the lesional cells co-expressed neuronal and glial protein markers on immunohistochemistry and there was also patchy aberrant CD34 staining. *IDH1*, *IDH2* and *BRAF* genes were wild-type on molecular pathology testing. There was no loss of chromosome 1p or 19q or *EGFR* amplification by cytogenetic analysis. The Illumina TP170 next-generation sequencing assay identified a *FGFR3-TACC3* gene fusion, a *TERT* promoter mutation (C250T) and a gain of *FGFR3*. The

diagnosis of anaplastic astrocytoma, WHO grade III, IDH wild-type with *FGFR3-TACC3* fusion, *TERT* promoter mutation and *FGFR3* gain was made.

53. A CASE OF EMBRYONAL TUMOUR WITH MULTILAYERED ROSETTES, C19MC-ALTERED

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Background: Embryonal tumour with multilayered rosettes, C19MC-altered (ETMR, C19MC-altered) is a rare, aggressive central nervous system embryonal tumour with alterations including amplifications and fusions in the C19MC locus.¹ C19MC is a microRNA cluster thought to be involved in regulating gene expression, and C19MC microRNA expression is increased in ETMR, C19MC-altered. ETMR, C19MC-altered is a new entity in the WHO Classification of Tumours of the Central Nervous System, revised 4th edition. A new feature of this edition is the integration of molecular genotype, as well as histological and immunohistochemical characteristics, into the diagnostic criteria for several tumours, including ETMR, C19MC-altered.¹ We present a case of ETMR, C19MC-altered. **Aims:** The aim was to determine the histological and molecular type of tumour resected from the left frontal lobe of the patient, a 2 year old female.

Methods: Histology, immunohistochemistry and molecular karyotyping were performed on a sample from the tumour.

Results and conclusions: Histology showed a tumour composed of cells with small to intermediate-sized nuclei and coarse chromatin in a fibrillary background. Multilayered rosettes and occasional neoplastic ganglion cells were present. Immunohistochemically, the neuropil component stained for vimentin and synaptophysin, with patchy staining for Neuro T. The small cells showed retained INI1 staining, focal staining with LIN28 and CD99 staining in occasional cells. NeuN highlighted neoplastic ganglion cells. The Ki-67 index was up to 23%. Molecular karyotyping showed C19MC alteration, and copy number changes for chromosomes 2, 4, 19 and 17. ETMR, C19MC-altered was diagnosed.

Reference

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54. TOWARDS BETTER CHARACTERISATION OF MOLECULAR ALTERATIONS IN GLIONEURONAL TUMOURS

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Background: Glioneuronal tumours constitute a subtype of brain tumour characterised by neoplastic cells with both glial and neuronal differentiation. The lack of specific biomarker panels has resulted in large inter-observer variability in their diagnosis