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Meeting Summary

35th Australian and New Zealand Society for Neuropathology (ANZSNP) Scientific Meeting 2024

Saturday 31 August - Sunday 1 September 2024
Hotel Crowne Plaza
Queenstown, New Zealand

Meeting Abstracts

ANZSNP
THE AUSTRALIAN & NEW ZEALAND
SOCIETY FOR NEUROPATHOLOGY

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The ANZSNP scientific meeting 2024 was held in the scenic city of Queenstown, New Zealand on 31 August and September 1. Dr Fouzia Ziad, President of the ANZSNP and Dr Laveniya Satgunaseelan, Secretary /Treasurer of the ANZSNP were the convenors of the meeting. The meeting was co-badged with the Australasian Winter Conference on Brain Research (AWCBR) 2024. There were 55 registrants from Australia, New Zealand, USA, Europe and Asia.

The academic program covered a wide range of neuropathology topics ranging from neuro-trauma to neuro-oncology. The neuro-oncology sessions featured a series of lectures on updates in the classification and diagnosis of various CNS tumours delivered by keynote speaker Prof Arie Perry, UCSF. Dr Thomas Robertson presented an approach to frozen sections in surgical neuropathology. An interactive session on the RCPA Neuropathology Quality Assurance Program (QAP) was organised with the QAP convenor, Dr Barbara Koszyca. Prof David Capper delivered the plenary lecture on "*DNA methylation profiling and its practical implications*" during the combined session with AWCBR attendees. Combined sessions also featured presentations on non-neoplastic conditions such as neurotrauma and neurodegeneration, comprising of presentations from invited faculty including Prof Michael Buckland, Dr Helen Murray and Prof Glenda Halliday. Four scientific research papers and 3 interesting cases were selected for oral presentation by the scientific committee. The meeting concluded with a plenary lecture delivered by Prof Arie Perry on "*Biomarkers in Neuro-oncology*".

Two of the research paper presentations were eligible for the Bill Evans Memorial award for postgraduate students or trainees. The prize was awarded to Dr Monish Maharaj for his presentation "*DNA Methylation Profiling to categorise meningioma recurrence risk: optimisation of resource allocation for patient selection*".

The feedback from the participants suggested that the meeting was well organized and appreciated for its educational content.

Meeting Abstracts

Research paper oral presentation abstracts

Abstract 1: Saliva Swabs: A game-changer for concussion diagnosis and management

Abstract 2: Identification of recurrent genetic alterations in epigenetic pineoblastoma subtypes by high-resolution whole genome cytogenetics and DNA panel sequencing

Abstract 3: DNA-Methylation Profiling to categorise meningioma recurrence risk: optimisation of resource allocation for patient selection

Abstract 4: Cell-free DNA in adult diffuse glioma – clinical utility and IDH mutation analysis

Interesting case presentation abstracts

Case presentation 1: CNS Neuroepithelial tumours with PATZ1 fusion

Case presentation 2: Two interesting, rare cases of Erdheim Chester disease (ECD)

Case presentation 3: Unusual cerebellar vermian lesions – a short case series

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Meeting Abstract

Research paper oral presentation abstracts

Abstract 1

Saliva Swabs: A game-changer for concussion diagnosis and management

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Introduction: Rugby is a physically demanding sport, as a result the injury of concussion is prevalent among players. Concussions are highly individual injuries and challenging to diagnose, leading to underdiagnosis and inadequate management among community rugby players. The Sport Concussion Assessment Tool (SCAT6) is currently recommended for concussion diagnosis in rugby, alongside clinical evaluation. However, this assessment is not feasible during a typical 15-minute general practitioner appointment. Additionally, SCAT6's reliability varies, with players often showing performance fluctuations even without a concussion. It also depends on players self-reporting symptoms, which often overlap with those experienced in the general population. Therefore, a quick, simple test identifying physiological markers and indicating physiological recovery is needed. Small non-coding RNAs (sncRNAs), which regulate gene expression, have shown promise as biomarkers for concussion.

Aims: This study aims to validate the ability of a panel of 14 sncRNAs to diagnose concussions in community and adolescent rugby players. Furthermore, it seeks to determine the right time for a player to return to play post-concussion using the a sncRNA test.

Methods: Data is collected at the Otago Concussion Clinic. Medical information and saliva swabs from players are obtained 48 hours and 19 days after injury. SncRNA analysis of the saliva samples will be conducted by Marker Health.

Conclusion: This research has the potential to improve diagnosis of concussions in community rugby players using a simple saliva test. Therefore, it might improve outcomes for players affected by concussions and reduce the risk of subsequent concussions, thereby enhancing overall player safety.

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Meeting Abstract

Abstract 2

Identification of recurrent genetic alterations in epigenetic pineoblastoma subtypes by high-resolution whole genome cytogenetics and DNA panel sequencing

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Genome-wide methylation analyses recently revealed distinct epigenetic pineoblastoma (PBL) subtypes. The aim of the study was to characterize genetic alterations underlying the pathogenesis of pineoblastoma subtypes.

Cytogenetic alterations of 83 FFPE materials from patients with PBL confirmed by central reference neuropathology and methylation-based subtyping were analyzed by high-resolution genome-wide molecular inversion probe (MIP) analysis. Mutational status was assessed by next-generation DNA panel sequencing. Clinical follow-up information of 54 patients was available.

According to epigenetic consensus PBL subtypes (Liu et al., 2021), our cohort consisted of 48 PBL-miRNA1 (1A, 40; 1B, 8), 19 PBL-miRNA2, 8 PBL-MYC/FOXR2, and 8 PBL-RB1 samples. PBL-miRNA subtype tumors had characteristic, mutually exclusive alterations in microRNA-processing genes; *DICER1* mutations (n = 19) and homozygous deletions of the *DROSHA* locus (n = 17) were most abundant, followed by *DROSHA* (n = 12) and DGCR8 (n = 2) mutations. The most frequent cytogenetic aberrations in PBL-miRNA were whole chromosome 7 gain (n = 31). PBL-miRNA2 subtype was significantly associated with chromosome 14 loss and *DICER1* mutation. In contrast, PBL-miRNA1A/B showed frequent gains of chromosome 14 (n = 21) and also focal gains of the *OTX2* oncogene on chromosome 14q (n = 8). In the miRNA subtypes 1A/B, 16 cases cases had polyploid cytogenetics. Survival analysis did not show differences in the PBL-miRNA subtypes 1A, 1B and 2.

The epigenetically defined PBL-miRNA subtypes are characterized by distinct cytogenetic alterations and mutational events. Frequent gain of *OTX2* may indicate a role of this oncogene in the pathogenesis of PBL. A possible prognostic role of genetic alterations requires investigation in prospective clinical trials.

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Meeting Abstract

Abstract 3

DNA-Methylation Profiling to categorise meningioma recurrence risk: optimisation of resource allocation for patient selection

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Background: The emergence of an integrated classification including morphology, DNA-methylation profiling and copy number changes is leading towards significant changes in meningioma patient management. Global accessibility to methylation profiling remains costly and limited to the research setting in many countries. This requires the development of a strategy to optimise clinical utility.

Aims:
(1) To determine histopathological factors that may influence discordant classification.
(2) To examine patient factors that may influence benefit from further methylation testing.

Methods: DNA extracted from FFPE samples of 71 patients with resected WHO CNS Grade 2 meningioma using the Infinium HD FFPE Restore Protocol and methylation profiling with the Illumina EPIC (850k) Human Bead Chip (Illumina, San Diego, USA) was conducted. Meningiomas were sub-classified using the integrated system published by Mass SLN et al (2021). Factors including histopathological features, gross total resection, adjuvant therapy, mitotic activity and ethnicity were examined using standardised statistical methods.

Results: >50 % of the WHO CNS 2 cohort (n = 71) was classified into the integrated low risk group. Classification demonstrated good correlation with recurrence (p = 0.004). Those without a gross total resection were more likely to recur (55 % vs 26 %). Chordoid subtype was common in Maori population but segregated across all risk groups. Interestingly brain invasion correlated with a more benign methylation class (p = 0.05).

Conclusion: The implementation of integrated methylation testing carries significant implications on patient treatment and health economics. Potential WHO CNS 2 subgroups that may merit profiling include those with brain invasion, subtotal resection and certain histopathological subtypes.

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Meeting Abstract

Abstract 4

Cell-free DNA in adult diffuse glioma – clinical utility and IDH mutation analysis

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Background: Cell-free DNA (cfDNA) has found utility in diagnosis and management of malignancies with scant literature in Adult Diffuse Gliomas (ADG).

Aims: This study aimed to quantify baseline values and serial cfDNA levels in the sera of patients with ADG undergoing radiation therapy comparing responders vs non responders and further to detect *IDH1* mutation in cfDNA.

Materials and Methods: The study group comprised of histologically confirmed ADG (n = 50), -grade 2 (n = 15), 3 (n = 08), 4 (n = 27) and controls (n = 15). CfDNA was extracted using a ChargeSwitch gDNA 1 ml Serum Kit (Invitrogen) and quantified using SYBR-based qPCR. *IDH1* mutation was detected using a castPCR assay, Sanger's sequencing and Next Generation Sequencing.

Results: Serum cfDNA levels were considerably higher in patients with ADG (Median: 113.50 ng/mL; IQR: 44.66–243.20) than in healthy controls (Median: 53.33 ng/mL; IQR: 40.67–73.87) (p = 0.02). cfDNA values were highest in grade 4 (353.53 ± 601.22 ng/mL) followed by grade 2 (201.93 ± 245.35 ng/mL) and 3 (153.67 ± 162.83 ng/mL). The cfDNA level was significantly higher in $IDH1^{WT}$ cases (157.83 ng/mL; IQR: 92.55–667.65) than in $IDH1^{MT}$ cases (69.55 ng/mL; IQR: 49.08–188.35) (p = 0.04). In non-responders, the cfDNA level (Median: 255.6 ng/mL) was significantly higher than that in responders (Median: 66.70 ng/mL) (p = 0.005). In cfDNA of IDH^{MT} ADG, castPCR assay detected the $IDH1^{R132H}$ mutation in 3/26, Sanger's sequencing failed to detect (0/20) while NGS was positive in 4/7 cases.

Conclusion: cfDNA quantity in ADG increases in proportion to the grade of the tumor, responders show higher levels, but the trend is inconsistent across cases. NGS is most sensitive for IDH mutation detection in cfDNA.

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Meeting Abstract

Interesting case presentation abstracts

Case presentation 1

CNS Neuroepithelial tumours with PATZ1 fusion

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CNS neuroepithelial tumours with PATZ1 fusions comprise a heterogenous group. We present two of these tumours, illustrating the diverse clinical presentation and morphology of these lesions. The first occurred in the cervical cord of an 8-year-old and was thought initially to be an ependymoma. The second case was a left frontal tumour in a 54-year-old, and the initial impression was of a high-grade glioma, possibly a gliosarcoma. The histology and genetics of this entity are discussed.

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Meeting Abstract

Case presentation 2

Two interesting, rare cases of Erdheim Chester disease (ECD)

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Case 1: This 51-year-old lady presented with diabetes insipidus in 2001(at the age of 28 years) and diagnosed as case of empty sella syndrome. In 2008 developed pericardial effusion which was tapped thrice and was given a course of ATT without any improvement. In 2013 developed signs and symptoms of raised intracranial pressure and MRI of brain revealed a SOL in pineal region. Subtotal excision of the lesion was done. In 2020 this mass increased in size and subtotal excision of lesion was done. This mass again increased in size and radiotherapy was given. Currently patient is bed ridden and mass has grown into left lateral ventricle.

Case 2: A 38-year-old man presented with signs and symptoms of raised intracranial pressure. MRI brain showed multiple extra axial meningeal bases lesions and was suspected to be a case of NF2 with multiple meningiomas. One of the suprasellar lesion was excised and subjected for histopathological examination.

Pathological examination revealed similar features in both cases. Microscopic examination revealed sheets of foamy cells admixed with lymphocytes, plasma cells and fibroblasts. Emperipolesis of lymphoid cells was absent. An occasional tuoton giant cell was noted in second case. Foamy cells were immunopositive for CD163 and CD68 but negative for CD1a, Langerin & S100. Ratio of IGG4 to IGG immunopositive cells was normal. Foamy cells were immunopositive for BRAFv600. BRAF mutation was confirmed by Sanger-sequencing.

Conclusion: ECD is a rare histiocytic disorder characterised by admixture of foamy histiocytes and inflammatory cells. Involvement of central nervous system is extremely uncommon and poses a diagnostic dilemma. High index of suspicion is required for its diagnosis and differentiation from other close mimics.

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Meeting Abstract

Case presentation 3

Unusual cerebellar vermian lesions – a short case series

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Introduction: The central nervous system is known for its anatomical uniqueness and immune privileges. Despite this, this organ becomes a host for many neoplastic and non–non-neoplastic lesions. Some non-neoplastic lesions occur in such brain regions and present with clinicopathological features that mimic neoplastic conditions. The present study describes a short series (3 unique cases) of rare lesions involving the cerebellum and masquerading other lesions, including a neoplasm.

Clinical details: Three cases aged 11, 50, and 67 years presented with headache, vomiting, and cerebellar signs of 2, 8, and one-week duration. The 2nd case was a known case of seronegative myelopathy on oral steroids and mycophenolate; the 3rd case was a known case of B – CLL (diagnosed two years back) and post-chemotherapy. The first case was negative for any investigated risk factors. The clinical/radiological diagnoses in all three cases included a tumor (medulloblastoma in the first case) and inflammatory/ infective/ deposits.

The histology of the lesions revealed irregular confluent necrosis, including the blood vessels and mixed inflammatory cell infiltrate, along with histiocytic aggregates (ill-formed granulomas) and giant cells. All three cases showed typical amoebic trophocytes and cyst forms, indicating a diagnosis of granulomatous amoebic encephalitis (GAE).

Discussion: GAE, a rare protozoal infection of high mortality, is caused by Acanthamoeba spp. and Balamuthia *mandrillaris*. Hence, it is essential to understand the clinicopathological characteristics of this rare infection and offer a timely and accurate diagnosis. Thus, it becomes necessary to consider GAE in the differential diagnoses of an atypical necrotic lesion and (even in an immunocompetent patient) search for the pathogen.