

# 6<sup>th</sup> Annual Conference of the Neuropathology Society of India

(NPSICON)

Virtual Conference

## Meeting Abstracts

February 23–25, 2023



Submitted: 12 May 2023

Accepted: 12 May 2023

Published: 06 June 2023

**The 6<sup>th</sup> Annual conference of the Neuropathology Society of India, (NPSICON 2023)** was held in a virtual mode, from 23<sup>rd</sup> to 25<sup>th</sup> February 2023, hosted by the Division of Neuropathology, Department of Pathology, Christian Medical College Vellore. Dr Geeta Chacko was the organizing Chairperson. The pre-conference workshop was on Fluorescence in situ hybridization with nearly 90 registrants. The workshop was conducted by NIMHANS Bangalore with Dr Shilpa Rao, Dr Vaishali Suri, Dr Vani Santosh and Dr Geeta Chacko as resource persons. There were 253 National registrants and 7 International registrations. The conference had participation from reputed national (34) and international (8) faculty and covered a wide range of topics in both neoplastic and non-neoplastic Neuropathology including sessions on perinatal pathology, epilepsy, neuromuscular pathology and several sessions in Neurooncology. There were five symposiums with several sessions of cases-based discussion. The first Prof Ashru K Banerjee oration was delivered by Dr Kenneth Aldape, from NIH Bethesda on: "Practical Aspects of Methylation-Based Diagnostics in Central Nervous System Tumors". The first Prof SK Shankar oration was delivered by Dr Avindra Nath, NIH Bethesda on "Neuropathology of two pandemics: AIDS and COVID". The Presidential oration was delivered by Dr Chitra Sarkar. The key note speakers included Dr Monika Hofer, Dr David Capper, Dr Takashi Komori and Dr Maysa Hussein. There were 28 papers for oral presentation and 38 posters. A highlight of the conference was a lively Quiz competition, which was held as the penultimate session. Despite being a virtual conference, there was active participation from all the delegates and the conference was very well received.

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## Free Papers - Abstract 1

Free Neuropathol 4:9:5

Meeting Abstract

## Insulin-like growth factor 2 mRNA binding protein 3 (IMP3) immunoreactivity in Pilocytic astrocytoma and Pilomyxoid astrocytoma- Does it help to differentiate?

Sridevi Koduru<sup>1</sup>, Shilpa Rao<sup>1</sup>, Vani Santosh<sup>1</sup><sup>1</sup> Department of Neuropathology, NIMHANS, Bangalore

**Background:** Pilomyxoid astrocytoma (PMA), located mainly in the hypothalamic/chiasmatic region, is a subtype of Pilocytic astrocytoma (PA) with subtle histomorphological differences. PMA also harbors similar molecular alterations of PA including MAPK pathway alterations. However, PMAs are known for higher rates of local recurrences. Few studies have shown a difference in their gene expression profiles and from these studies, Insulin-like growth factor 2 mRNA binding protein 3 (IMP3), has been identified as a gene helpful in differentiating the two tumors.

**Objectives:** To assess the value of IMP3 in differentiating PMA from PA.

**Materials and methods:** Retrospective study was carried out on cases histopathologically diagnosed as PA and PMA between years 2015 and 2021, including review of clinical, histological and IHC features. All tumors were stained for OLIG2, SOX10, p16, BRAFV600E, Ki67 and IMP3 expressions. IMP3 Immunoreactivity was scored as 0, +1 and +2, based on intensity. Labeling index was calculated only with 2+ intensity.

**Results:** Nine cases of PMA were diagnosed during the study period, and nine age and site matched PA were included. The mean age at diagnosis was 7.3 years (1-17), with male preponderance (M:F – 2.6:1). Most common site was hypothalamic/chiasmatic region. PMA and PA showed the well-described histomorphological features and both showed similar diffuse immunoreactivity for OLIG2, SOX10, p16 and IMP3 with a low Ki67 labeling index. BRAFV600E IHC was positive in one case of PA.

IMP3 immunoreactivity was noted in both PMA and PA. Median labeling index for IMP3 in PMA was 30% (10%-70%) and 50% (10%-70%) in PA which was not statistically significant (p=0.283).

**Conclusion:** Although there are reports that suggest IMP3 to be a useful maker of PMA, our study does not support this observation. There are no specific IHC markers to distinguish PMA from PA on a routine basis and the diagnosis predominantly depends solely on histomorphology. Our observation also points to the fact that PMA could just represent a less mature form of PA.

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## Free Papers - Abstract 2

Free Neuropathol 4:9:6

Meeting Abstract

### Series of 4 cases of Subependymal giant cell astrocytoma

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**Background:** Subependymal giant cell astrocytoma (SEGA) is a slowly growing tumor of unknown histogenesis with incidence of 0.027 per 100,000 person-years<sup>1</sup>. It mainly arises in the periventricular regions adjacent to the foramen of Monro, which causes increased intracranial pressure, seizures, and focal neurologic signs.

**Objectives:** To study the age-distribution, clinical features and microscopy of SEGA in patient having clinical symptoms of tuberous sclerosis.

**Material and methods:** All four-biopsy received as multiple brown soft tissue structure aggregate each measuring 2.1x1.9x0.6 CM<sup>3</sup>, 1.5x1x0.2CM<sup>3</sup>, 3.7x0.8x0.3XCM<sup>3</sup>, 2.4x1.9x0.2CM<sup>3</sup>. Sections were fixed with 10% neutral buffered formalin solution and processed by routine tissue processing and paraffin embedding. Haematoxylin & Eosin-stained sections were studied microscopically.

**Results:** We reported four cases of SEGA over a period of two years with all having the clinical symptoms of tuberous sclerosis. Out of four cases two were male and two were female. Out of four cases three were adult and one was adolescent. On microscopic findings Sections show fascicle of spindle shaped cells with admixture of large gemistocyte like cells with homogenous eosinophilic cytoplasm and prominent nucleoli with eccentric nucleus. Histomorphological findings are suggestive of subependymal giant cell astrocytoma WHO Grade -1.

**Conclusion:** SEGA is a rare tumour of the central nervous system and diagnosis is based on clinical, radiological, histopathology findings. It should be included in the differential diagnosis of mass near the foramen of Monro even if there are features of tuberous sclerosis present or not.

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## Free Papers - Abstract 3

Free Neuropathol 4:9:7

Meeting Abstract

## Diffuse meningeal melanocytic neoplasms of the brain- Morphological and molecular analysis of BRAF and KRAS mutations

Neha Bhardwaj<sup>1</sup>, Debajyoti Chatterjee<sup>1</sup>, Renu Madan<sup>2</sup>, Navneet Singla<sup>3</sup>, Bishan Radotra<sup>1</sup><sup>1</sup> Department of Histopathology, Post Graduate Institute of Medical Education and Research, Chandigarh<sup>2</sup> Department of Radiotherapy Post Graduate Institute of Medical Education and Research, Chandigarh<sup>3</sup> Department of Neurosurgery, Post Graduate Institute of Medical Education and Research, Chandigarh

**Background:** Primary meningeal melanocytic tumors (MMT) of the central nervous system (CNS) can be circumscribed or diffuse. The latter arise from leptomeningeal melanocytes with predilection for spinal canal and posterior fossa. Their sub-categorization into melanocytoma and melanoma is based purely on histomorphology. Due to their rarity, not much prognostic information or molecular data is available at which this study is aimed.

**Material and methods:** The cases of MMT were retrieved from surgical database over a period of 9 years, and re-evaluated for histomorphology and immunohistochemistry (HMB-45, Melan A, S100 and ki67). DNA was extracted from formalin-fixed, paraffin-embedded tissue and real time polymerase chain reaction was performed using EntroGen (KRBRRT-50) kit for *BRAF* V600E and *KRAS* (exon 2, 3 and 4) hotspot mutations.

**Results:** Six cases of melanocytomas and nine cases of melanomas were included with mean age of 35.3 years and 46.6 years, respectively. Melanocytomas were identified in spinal, posterior fossa, and basitemporal locations in 2 cases each. Melanomas were identified in spinal and cerebral location in 2 and 7 cases, respectively. No case of melanoma showed any other primary on further workup. Melanomas showed nuclear pleomorphism, mitotic activity, and coagulative necrosis in contrast to melanocytoma. No case showed *BRAF* V600E or *KRAS* mutation.

**Conclusion:** *KRAS* and *BRAF* mutations are uncommon in MMTs, hence suggesting that their mutational profile is different as compared to systemic melanomas. Meticulous histological examination along with Ki-67 help to differentiate meningeal melanoma from melanocytoma.

## Free Papers - Abstract 4

Free Neuropathol 4:9:8

Meeting Abstract

## Histopathological spectrum of Astrocytoma in tertiary care hospital

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**Background:** Astrocytoma is most common primary central nervous system (CNS) tumor that arise from the cells that form supportive tissue of the brain. Astrocytoma is a subset of glial tumors, usually affecting the brain and sometimes the spinal cord. The two major categories of astrocytic tumors are the diffusely infiltrating astrocytoma (WHO grade II to IV) and the more localized astrocytoma which is pilocytic astrocytoma (WHO grade I).

**Objectives:** To identify frequency of various histopathological types of astrocytoma. To study age, sex, site wise distribution and clinical presentation.

**Materials and methods:** A Retrospective study is conducted from January 2022 to December 2022. For histopathological study, the specimens were fixed in 10% formalin, subsequently dehydration, clearing, embedding in paraffin wax were carried out. The sections were cut and stained using routine hematoxylin and eosin stain.

**Results:** In present study, most common astrocytic tumor was diffuse astrocytoma (42%). Pilocytic astrocytoma comprises 20% of cases and Anaplastic astrocytoma comprises of 14% cases. Most cases belonged to age group between 31-40 years followed by 21-30. 58% of the cases were males and the rest were females. 82% of astrocytic tumors were supratentorial origin and 18% were infratentorial origin.

**Conclusion:** Most common astrocytic tumor was Diffuse Astrocytoma followed by Pilocytic Astrocytoma. Most common symptom was headache followed by convulsion, weakness, giddiness and vomiting. Combining histopathological and molecular features helps in the definitive diagnosis and management of astrocytic tumors.

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## Free Papers - Abstract 5

Free Neuropathol 4:9:9

Meeting Abstract

### Study of ZFTA and YAP-1 fusion in Supratentorial Ependymomas

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**Background:** Ependymomas are classified according to a combination of histopathological and molecular features along with anatomical sites. They occur in three anatomical compartments of the central nervous system- supratentorium, posterior fossa and spinal region. Supratentorial Ependymomas are relatively rare, shows considerable genetic heterogeneity and are molecularly stratified into 2 subtypes- ZFTA fusion and YAP-1 fusion positive Supratentorial Ependymomas.

**Objectives:** To perform molecular characterization of ST-EPN according to WHO CNS 2021 classification.

**Material and methods:** A total of 50 cases of Supratentorial Ependymomas were retrieved from departmental archives between 2018-2022. Histopathological examination and immunohistochemistry for L1CAM, p65 were done. L1CAM immunopositive tumors were evaluated for ZFTA fusion. Tumors which were negative for ZFTA fusion and L1CAM negative tumors were subjected for YAP-1 rearrangement by fluorescence in situ hybridization.

**Results:** Our study included 26 female and 24 males, and the tumors were commonly located in frontal and parietal lobes in the paraventricular region. On immunohistochemistry, 35 cases were L1CAM positive and 25 cases were p65 positive. Out of these 35 cases, 34 were positive for ZFTA fusion. One ZFTA fusion negative and 15 L1CAM negative cases were tested for YAP-1 rearrangement and 2 cases showed YAP-1 rearrangement. WHO grade was assigned for cases that are not molecularly defined.

**Conclusion:** Supratentorial Ependymomas have distinct molecular profiles and an integrated histopathological and genetic workup is needed for precise diagnosis. YAP-1 fusion tumors are rare. Some cases cannot be diagnosed based on this classification system and further research is needed to find out other molecular alterations to understand their oncogenesis.

## Free Papers - Abstract 6

Free Neuropathol 4:9:10

Meeting Abstract

## The many facets of astrocytes and blood-brain-barrier alterations in fungal infections of central nervous system

Aditi Goyal<sup>1</sup>, Shilpa Rao<sup>1</sup>, M Netravathi<sup>2</sup>, Arivazhagan A<sup>3</sup>, Jitender Saini<sup>4</sup>, Anita Mahadevan<sup>1</sup><sup>1</sup> Departments of Neuropathology, NIMHANS, Bangalore<sup>2</sup> Departments of Neurology, NIMHANS, Bangalore<sup>3</sup> Departments of Neurosurgery, NIMHANS, Bangalore<sup>4</sup> Departments of Neuroimaging, NIMHANS, Bangalore

**Background:** Astrocytes, most abundant cells in CNS, are diverse in morphology and function. Alterations following cellular injury, leads to dysfunction and blood-brain-barrier (BBB) permeability. Astrocytic response in CNS infections has not been systematically evaluated. We sought to study astrocytic and BBB alterations in fungal infections of CNS, incidence of which is rising due to increasing immunosuppression, ecological changes etc.

**Objectives:** To evaluate morphological patterns of astrocytic response and changes in BBB in CNS fungal infections.

**Material and Methods:** Clinico-demographic and neuropathological changes of twenty-nine patients with CNS fungal infections were reviewed. Immunohistochemistry for GFAP and aquaporin-4 (AQP4) was performed for astrocytic and BBB alterations.

**Results:** Pathological patterns of 29 cases [mucormycosis-11, aspergilloma-7, invasive aspergillosis-2, cryptococcoma-2, cryptococcal meningitis-2 and chromoblastomycosis-4, and candida-1 infection] were classified as granulomatous [aspergilloma and cryptococcoma], abscess [mucormycosis and dematiaceous fungi], diffuse cerebritis [invasive aspergillosis and mucormycosis], microabscesses [Candida], and minimal inflammation [Cryptococcal meningitis (CM)]. Astrocytes' phenotype was dictated by pathology pattern. Granulomatous inflammation and abscess were similar with loss of astrocytes and AQP4 within necrotic centres, dysmorphic astrocytes with fragmented and beaded processes with perivascular accentuation of AQP4 in periphery of lesion and hypertrophic astrocytes in adjoining parenchyma with diffuse AQP4 distribution. In diffuse cerebritis, stellate astrocytes with marked loss of AQP4 expression was seen, whereas in CM, stellate astrocytosis with increased perivascular AQP4 was seen.

**Conclusion:** Tissue patterns were associated with distinct astrocytic phenotypes and BBB integrity. Perivascular accentuation of AQP4 in perilesional zone in granulomas and CM correlate with milder perilesional edema in contrast to loss of AQP4 in suppurative inflammation with extensive perilesional edema. Understanding glial pathophysiological changes may help abrogate neurological sequelae in survivors.

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## Free Papers - Abstract 7

Free Neuropathol 4:9:11

Meeting Abstract

### Spectrum of Skeletal muscle disorders -An audit of data over four decades from a tertiary referral center

Rima S<sup>1</sup>, Nalini A<sup>2</sup>, Madhu N<sup>2</sup>, Madalambika NM<sup>1</sup>, Vani Santosh<sup>1</sup>, Anita Mahadevan<sup>1</sup>, Yasha TC<sup>1</sup>, Nandeesh BN<sup>1</sup>, Gayathri N<sup>1</sup>

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**Background:** Diseases of skeletal muscle constitute a significant proportion of neurological disorders. The developments in investigative procedures and the advent of molecular diagnostic techniques have improved our understanding, clinical and diagnostic approach.

**Objectives:** To describe the spectrum of Neuromuscular disorders (NMDs) over four decades in a tertiary neuropathology referral center, and the changing trend if any.

**Material and methods:** Review of muscle biopsies from patients of NMDs received in the department of Neuropathology. These biopsies were evaluated by histology and special tests (enzyme histochemistry, electron microscopy, immunohistochemistry and immunoblot, wherever indicated). The data is collated from NIMHANS Myobank data base from 1983-2022.

**Results:** During the period 1983-2022, a total of 28,506 muscle biopsies were received. The major categories of muscle disorders diagnosed include muscular dystrophies (n=9027;31%), neurogenic atrophy (n=6111;21%), inflammatory disorder (n=3836;13%), congenital myopathies (n=388;1.3%), Mitochondrial disorders (n=556;1.9%), miscellaneous (non-mitochondrial metabolic, myofibrillar and others). A notable change observed was a decline in the number of biopsied muscular dystrophy cases over the past two years (2021&2022), which formed 14% of biopsies, in contrast to 33% (2000-2020) in the previous years. Contrastingly, an increase from 12% to 20%, in inflammatory myopathies was observed.

**Conclusion:** The present study observed reduction in the biopsies for conventional inherited myopathies and an increase in acquired myopathies, probably reflecting the advancement and application of genetic tests. Review and regular audits of the biopsies are required to study the spectrum of disease prevalence, pattern and the associated changes (trend). This will facilitate our understanding, preparation and management. Hence there is requirement for adopting new testing platforms in the diagnosis of NMDs for optimal patient care.

## Free Papers - Abstract 8

Free Neuropathol 4:9:12

Meeting Abstract

## Does the macrophage subtype drive the immunological subtypes of leprous neuropathy?

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**Background:** Leprosy caused by *Mycobacterium leprae*, is a common cause for infective neuropathies in India. The host's immune response determines the pattern and progression of disease. Macrophages are the main cell types directly infected by the bacillus. Recently, macrophage subsets with distinct functions have been described. M1 macrophages are proinflammatory, M2 anti-inflammatory and M4 are related to the formation of foam cells described in atherosclerosis. No studies have evaluated macrophage subsets in leprous neuropathy.

**Objectives:** To determine macrophage subtypes in immunological subgroups of leprous neuritis (LN)

**Material and methods:** Leprous neuritis (n=47) diagnosed between January 2021 to May 2022 were reviewed and subtyped using Ridley-Jopling criteria. Immunohistochemistry for subtyping T- lymphocytes (CD3, CD4, CD8), B- lymphocytes (CD20) and macrophages (M1=CD68+CD163<sup>+</sup> IFN<sup>+</sup>; M2=CD68+CD163<sup>+</sup> TGF-beta<sup>+</sup>; M4 = CD68+CD163<sup>+</sup>, MRP8<sup>+</sup>) was performed and correlated with LN subgroup.

**Results:** Tuberculoid tuberculoid (TT) and chronic leprous neuritis (CLN) showed predominance of M1 macrophages with TNF $\alpha$  and small proportion of M2 > M4 macrophages. B- cells were absent in endoneurium but found around epineurial vessels with CD4 & CD8+Tcells. Borderline tuberculoid (BT) was similar to TT with M1 macrophages, but admixed M4 > M2 macrophages. In Borderline borderline (BB), Borderline Lepromatous (BL) and Lepromatous leprosy (LL), there was equal proportion of M1 and M4 macrophages.

**Conclusion:** Macrophage subtype dictates LN subgroup. The paucibacillary forms (TT, BT and CLN) with florid inflammation and nerve destruction have pro-inflammatory phenotype (M1), multibacillary forms (BB, BL, LL) with scant inflammation have anti-inflammatory macrophages (M2) with M4. Deciphering macrophage subtype in LN immunobiology has therapeutic implications to develop immunomodulatory therapies to limit nerve damage.

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## Free Papers - Abstract 9

Free Neuropathol 4:9:13

Meeting Abstract

### Study of ki67 PI amongst meningiomas of different WHO grades & its association with OS & recurrence

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**Background:** Meningiomas comprise 39% of CNS tumours and all grades are known to recur. WHO histopathological grading of meningiomas does not always correlate with, did not always correlate with chances of recurrence or progression and molecular diagnostics are not available everywhere. We studied the ki67 PI in different grades of meningiomas.

**Material and methods:** This was a retrospective study of ki67 PI in 100 meningiomas received at a tertiary hospital in central India, over 4-year period and its correlation with histopathological parameters of grading (as per WHO 2021 criteria), overall survival (OS in months) and recurrence where data was available.

**Results and Conclusions:** Amongst 100 meningiomas studied M:F was 1:2. Mean age of presentation was 45 years. The different WHO grade 1/2/3 meningiomas and their median **mitoses, ki-67 indices, OS** (available in 68 cases) and recurrence (data available 70 cases) rates were noted: **grade 1** (n=65) - mitoses median 1/10 hpf, ki-67 PI median 3.5%, OS median 32 months, recurrence 10.76% (n=7); **grade 2** (n=28) - **grade 2A** n=12 (mitoses <4/10 hpf) median 1/10hpf, ki67 PI median 6.5%, OS median 28 months, recurrence 16.7% (n=2); **grade 2B** n=15 cases (mitoses >4-19/10hpf) median mitoses 5/10hpf, ki-67 PI median 10%, OS median 19 months, no recurrence, **grade 3** (n=7): median mitotic count 21/10 hpf, ki-67 PI median 20%, OS median 10 months, recurrence 29% (n=2). Mitotic count was not an independent predictor of recurrence in our cohort while ki67 PI was. Ki-67 was significantly associated with OS in our cohort.

## Free Papers - Abstract 10

Free Neuropathol 4:9:14

Meeting Abstract

## Utility of immunohistochemistry in subtyping Posterior fossa group A ependymoma

Abhishek Chowdhury<sup>1</sup>, Shilpa Rao<sup>1</sup>, Nandeesh BN<sup>1</sup>, Vani Santosh<sup>1</sup><sup>1</sup> Department of Neuropathology, National Institute of Mental Health and Neurosciences

**Background:** Posterior fossa ependymomas (PF-EPN) have been classified into posterior fossa group A (PFA) and posterior fossa group B (PFB) ependymomas. PFA-EPN show loss of H3 p.K27me3 expression. Further subdivided into molecular subgroup 1 (PFA-1) and subgroup 2 (PFA-2), they encompass 9 subtypes (PFA 1a to 1f and 2a to 2c). OTX2 and H3 p.K27M immunopositivity is noted in PFA-2c and 1f respectively and have prognostic implications.

**Objectives:** To assess the frequency of OTX2 and H3 p.K27M immunopositivity in PFA-EPN.

**Material and methods:** This retrospective study included PFA-EPN diagnosed at our institute from 2020 to 2022. They were diagnosed based on loss of expression of H3p.K27me3 by immunohistochemistry. In these cases, immunohistochemistry for OTX2 and H3 p.K27M was carried out.

**Results:** A total of 28 cases of PFA-EPN were encountered. Age range was 10 months to 23 years, with median age being 3.5 years. OTX2 immunopositivity was seen in 3 tumors (10.7%). Only one tumor was positive for H3 p.K27M (3.6%). The youngest patient (10-month-old girl) had the H3 p.K27M positive tumor. Two OTX2 positive tumors were seen in two 2 year old and one in a 12 year-old patient.

**Conclusion:** PFA-EPN are most common in younger children. Occasional tumors are OTX2 and H3 p.K27M immunopositive, conforming to PFA 2c and 1f. Whilst PFA 2c is known to be associated with a better prognosis, H3 p.K27M positive tumors are associated with a worse outcome. Assessment of frequency of OTX2 and H3 p.K27M immunopositivity with data on survival can help in prognostication and exploring therapeutic avenues in PFA ependymomas.

## Free Papers - Abstract 11

Free Neuropathol 4:9:15

Meeting Abstract

## Posterior fossa ependymomas - A clinicopathological study

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**Background:** The 5th edition of WHO CNS 5 has classified ependymomas into ten subgroups based on the anatomical site together with their molecular signature, of which supratentorial ependymomas with ZFTA fusion, posterior fossa ependymomas group A and spinal ependymomas with MYCN amplification are found to have a dismal outcome. This study aimed to subgroup posterior fossa ependymomas (PFE) into posterior fossa ependymoma group A (PFA) and posterior fossa ependymoma group B (PFB) as it was of prognostic significance. The objective was to assess the expression of H3K27me3 in PFE and correlate it with the clinicopathological profile.

**Objectives:** To assess the expression of H3K27me3 (Histone H3 lysine 27 trimethylation) and to assess the clinicopathological profile of posterior fossa ependymomas.

**Materials and methods:** A twelve-year study including 77 cases of posterior fossa ependymomas were subjected to immunohistochemical marker H3K27me3 and were sub-grouped as PFA and PFBs. Further, all PFAs were subjected to immunohistochemistry using the EZHIP antibody. Demographic details, site of the tumour, extent of surgery, and adjuvant therapy were obtained from the medical records.

**Results:** The prevalence of the PFA and PFB subgroup in this study population was 36.4% and 63.6% respectively. PFA tumours were more common in the younger age group, whereas PFB tumours were more common in the adult age group. PFA tumours were predominantly high-grade WHO CNS grade 3 tumours; in contrast, PFB tumours were predominantly WHO CNS grade 2 tumours. It was found that age (<10 years), WHO CNS grade 3, MIB1 labelling index >10% and the PFA subgroup had significantly poorer progression-free survival.

**Conclusion:** It is important to subgroup PFE based on their molecular signature as it is an independent indicator of outcome.

## Free Papers - Abstract 12

Free Neuropathol 4:9:16

Meeting Abstract

## Clinicopathological study of ependymomas with special reference to L1CAM expression in prognosis and survival

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**Background:** Ependymomas exhibit heterogeneity across age, location, histology, molecular nature and survival. The CNS WHO classification (2021), identifies nine different molecular sub-groups of ependymomas based on DNA methylation studies thus suggesting an epigenetic component its pathogenesis. Studies suggests that these molecular sub-types remain stable throughout the course of disease. Immunohistochemical expression of L1CAM, has been identified as a surrogate marker for ZFTA/c11orf95-RELA fusion in supratentorial ependymomas.

**Objectives:** This study aims at realising the utility of L1CAM as a surrogate marker for ZFTA/c11orf95-RELA fused supratentorial ependymomas specially in resource-poor setups.

**Materials and methods:** Forty-three histopathologically-proven cases of ependymoma under treatment over the period of two and half years from December 2019 to June, 2022 were selected. Histopathological examination followed by IHC staining for GFAP, S-100, EMA and Ki-67 in all cases and L1CAM in the supratentorial ependymomas. We have followed-up most cases during our study period. IHC expression was correlated with various clinico-pathological parameters, including survival.

**Results:** In our study the commonest location for ependymomas was the spine in adults and posterior fossa in the pediatric age group. Majority cases belonged to CNS WHO Grade 2 both in adults and in the paediatric age group. Supratentorial location of ependymomas with positive immuno-reactivity for L1CAM and a higher Ki-67 labelling index were associated with poor survival.

**Conclusion:** The study revealed that L1CAM was an effective surrogate marker for supratentorial ependymomas possibly carrying the ZFTA Fusion gene product. The L1CAM immuno-reactivity also corresponded with the survival data. However, larger population-based studies amongst the Indian population are required to validate these results further.

## Free Papers - Abstract 13

Free Neuropathol 4:9:17

Meeting Abstract

## GFAP and SOX10 Expression in Neonatal Cerebral White Matter Injury: A Postmortem Minimally Invasive Tissue Sampling Study

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**Background:** Cerebral white matter injury (WMI) due to hypoxia-ischemia is the most type of neurological injury seen in term and preterm infants resulting in cerebral palsy. Two pathogenetic pathways have been described that include the upper pathway where severe hypoxia-ischemia results in pan-cellular death of neurons as evidenced by severe white matter necrosis, microcysts and loss of glia and axons and the lower pathway where mild hypoxia-ischemia causes selective death of the preoligodendrocyte progenitors (preOL) resulting in reactive gliosis.

**Objectives:** To study the utility of GFAP and SOX10 in cerebral white matter injury.

**Material and methods:** 50 postmortem brain cores of neonates with suspected neurological injuries were obtained following parental consent. The brain cores were studied for evidence and patterns of neurological injury. Immunohistochemical markers GFAP and SOX 10 were used as surrogate markers to demonstrate loss of glial cells and preoligodendrocytes or reactive gliosis respectively

**Results:** The various changes observed in the biopsies included anoxic neurons, reactive gliosis, cystic change, microgliosis, microglial nodules, meningitis, germinal matrix, intraventricular and white matter hemorrhage and subarchnoid hemorrhage. GFAP was increased in 31 preterm and 8 term neonates and reduced or absent in 6 preterm and 1 term baby. SOX 10 was absent in 35 preterm and 5 term infants and retained in 4 preterm and 6 term infants.

**Conclusion:** The above findings demonstrate that both pathways are involved in preterm and term infants with WMI and identifying the patterns of injury would aid in early therapeutic interventions and prediction of outcomes.

## Free Papers - Abstract 14

Free Neuropathol 4:9:18

Meeting Abstract

## Olig2-positive cell density in MOGHE versus other epilepsy surgical samples: A morphometric study

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**Background:** Abnormalities in oligodendroglia are reported in surgical samples of patients with drugresistant epilepsy. "Mild Malformation of Cortical Development with Oligodendroglial Hyperplasia (MOGHE)" described mostly in patients with frontal lobe epilepsy is characterized by significantly higher degree of oligodendroglial hyperplasia.

**Objectives:** To compare the density of Olig2-positive cells in white matter between MOGHE and other types of epilepsy specimens.

**Material and methods:** 59 epilepsy surgical samples comprising 6 groups (10: focal cortical dysplasia, 7: gliosis, 19: hippocampal sclerosis, 4: MOGHE, 10: oligodendrogliomas, 9: others) were included in the study. Olig2-positive cell density/mm<sup>2</sup> area in the white matter was determined on Olig2-immunostained sections using Image J software. One-way ANOVA test was used to compare the Olig2-positive cell densities between different groups (P < 0.05 significant).

**Results:** The mean density of Olig2-positive cells in the white matter in the six groups was: Focal cortical dysplasia: 1094/mm<sup>2</sup>, Gliosis: 1080/mm<sup>2</sup>, Hippocampal sclerosis: 1426/mm<sup>2</sup>, MOGHE: 2138/mm<sup>2</sup>, Oligodendrogloma: 2300/mm<sup>2</sup> and Others: 1198/mm<sup>2</sup>. The P-value (one-way ANOVA) between groups was 0.002. To further understand which groups were different, multiple comparisons test was performed. As the group of interest was MOGHE, the mean Olig2-positive cell density of each group was compared with the mean Olig2-positive cell density of MOGHE group. The mean Olig2-positive cell density/mm<sup>2</sup> was significantly different between MOGHE and all other groups (P: < 0.05), except oligodendrogloma (P: 0.71).

**Conclusion:** The mean density of Olig2-positive cells/mm<sup>2</sup> in white matter in MOGHE was significantly higher than in other epilepsy samples and was like that of oligodendrogloma.

## Free Papers - Abstract 15

Free Neuropathol 4:9:19

Meeting Abstract

## Significance of emerging prognostic markers in meningiomas

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**Background:** Meningiomas are the most common primary intracranial tumours. WHO CNS5 classification updates has incorporated prognostic biomarkers like pTERT promoter mutation and CDKN2A/B homozygous deletion. Expression of p16 is being correlated with CDKN2A gene alterations in gliomas and can be detected via immunohistochemistry.

**Objectives:** To assess the significance of prognostic markers (pTERT, CDKN2A homozygous deletion, and p16 expression) in meningioma to identify their biological and clinical utility.

**Material and methods:** 200 cases (93 males and 107 females) of Grade 1 (n=107), 2 (n=78), and 3 (n=15) were included. They were assessed for pTERT mutation (C228T/C250T) using Sanger Sequencing; CDKN2A deletion by FISH, and p16 expression by IHC.

**Results:** There were 192 adult and 8 paediatric cases. Only **5%** (10/200) of meningiomas showed pTERT C228T mutation. All were histopathologically grade 2. Histopathological grade 2 meningiomas with pTERT mutation survival varied from 7 to 64 months with mean survival of 26 months while without pTERT alteration grade 2 meningiomas varied from 10 to 91 months with mean survival of 36 months. **62%** (124/200) of cases showed total and **29.5%** (59/200) showed partial loss of p16 expression. Only a **small fraction** of meningiomas (2.5%, 5/200) showed CDKN2A homozygous deletion including histologically grade 3 (4/5) and 2 (1/5) tumours.

**Conclusion:** Integrated diagnostic protocol simplifies meningioma categorization and provides improved accuracy in predicting outcome and recurrence. There is no association between CDKN2A deletion and p16 expression. Further, the predictive power of pTERT and CDKN2A status identifies aggressive meningiomas and provides biomarker for new therapeutic interventions.

## Posters - Abstract 1

Free Neuropathol 4:9:20

Meeting Abstract

## Glioblastoma with predominant sarcomatoid differentiation: a rare case report

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**Background:** Is a rare primary malignant tumor of central nervous system with biphasic morphological pattern, glial and malignant mesenchymal components and is considered as variant of glioblastoma multiforme. Located in the cerebrum, involving the temporal, parietal, frontal, and occipital lobes in decreasing order of frequency.

**Objectives:** To correlate frozen section findings with histopathological examination and Immunohistochemistry for exact histogenetic typing.

**Material and methods:** Received one reddish brown soft tissue measuring 2.5x2x0.3cm<sup>3</sup> in normal saline during ongoing surgery, processed as frozen section with cryostat machine. Another three greyish brown soft tissue were received in 10% neutral buffered formalin total measuring 2.8x2.6x1.5 cm<sup>3</sup> which was processed by routine tissue processing. After paraffin embedding, Hematoxylin and eosin- stained section were studied microscopically. IHC for GFAP, Vimentin, EMA and p53 was performed.

**Results:** Frozen section showed histology of high grade glioma -Glioblastoma with small cell component and pleomorphic spindle cell component WHO Grade-IV. On biopsy, microscopy showed glial component with pleomorphic astrocytic cells showing nuclear atypia, mitosis, pseudopalisading necrosis and microvascular proliferation. Sarcomatous component shows spindle shaped cells with nuclear atypia. This showed impression of Glioblastoma with predominant sarcomatoid differentiation-WHO Grade IV. IHC was positive for P53, Vimentin and negative for GFAP in areas with sarcomatoid differentiation, EMA negative which confirmed the case as Gliosarcoma.

**Conclusion:** Frozen section plays crucial role in deciding staging of tumor and determining margin for resection. Biopsy and IHC has important role in confirmation of diagnosis and prognosis.

## Posters - Abstract 2

Free Neuropathol 4:9:21

Meeting Abstract

## Does MIB-1 labelling index correlate with WHO grade and outcome in spinal meningiomas? – A clinicopathological study

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**Background:** Spinal meningiomas are slow growing indolent tumours. The histological grade and extent of resection do not reliably predict prognosis. The MIB-1 labelling index is known to be a useful prognostic marker.

**Objectives:** To assess MIB-1 labelling index (MIB-1 LI) in spinal meningiomas, and to correlate it with WHO grade, histological parameters, and outcome.

**Material and methods:** This was an ambispective study on 115 cases of spinal meningiomas diagnosed between January 2012 and June 2021. Based on WHO (2021) criteria, these tumours were assigned into benign, atypical, and anaplastic categories. MIB-1 immunostaining was performed on all these cases. Outcome (recurrence) was correlated with the WHO grade, histological parameters, and MIB-1 LI.

**Results:** Of the 115 cases, 65 were CNS WHO grade 1, and 50 were CNS WHO grade 2. There were no CNS WHO grade 3 tumours. CNS WHO grade 2 meningiomas had a higher MIB-1 LI compared to grade 1 tumours, with a threshold index of 5% exhibiting highest diagnostic validity at a sensitivity/specificity of 98% / 41.5% respectively. This cut-off also had significant correlation with certain 'atypical' features, namely, sheeting, small cell change, prominent nucleoli, and necrosis. Follow-up was available for 66.9% of cases, with a mean duration of 26 months. Only one patient with a CNS WHO grade 2 meningioma had recurrence.

**Conclusion:** MIB-1 LI threshold of 5% distinguished grade 2 from grade 1 meningiomas and had a significant correlation with certain individual 'atypical' features. Association with recurrence could not be ascertained due to limited follow-up, and a low incidence of recurrence.

## Posters - Abstract 3

Free Neuropathol 4:9:22

Meeting Abstract

## Non-Hodgkins lymphoma - NK/T cell type of nasal cavity : A rare case report

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**Background:** Rare, Aggressive and predominantly extranodal lymphoma of NK / T cell origin characterized by angiotropism, angiodestruction, necrosis and association with Epstein-Barr virus (EBV). Also known as midline malignant reticulosis, polymorphic reticulosis, nasal T-cell lymphoma, lymphomatoid granulomatosis and angio-centric T cell lymphoma.

**Objectives:** To study a rare case for its clinical features, microscopic findings and Immunohistochemistry for exact histogenetic typing and to rule out remote possibility of Embryonal Rhabdomyosarcoma-small cell type and High-Grade Neuroblastoma.

**Material and methods:** Received multiple greyish white soft tissue structure aggregate total measuring 0.8x0.6x0.2 cm<sup>3</sup> in Histopathology section of pathology department, B J medical college. Sections were fixed with 10% neutral buffered formalin and processed by routine tissue processing. After paraffin embedding, Haematoxylin & Eosin-stained sections were studied microscopically.

**Results:** Serial sections from received small, fragmented biopsy specimen shows markedly cellular and necrotic tumor tissue with diffusely arranged monomorphic population of poorly differentiated round to oval cells with dense hyperchromatic nuclei, scant cytoplasm and extensive areas of necrosis. Histopathological findings are suggestive of Undifferentiated Malignant Round Cell Tumor –Possibly Non-Hodgkins Lymphoma-NK/T cell type, with remote possibility of other round cell tumor- Embryonal RMS. Immunohistochemistry done for further confirmation and rule out other possibilities.

**Conclusion:** Histopathological findings give clue for diagnosis of NK/T cell non-hodgkins lymphoma and Immunohistochemistry is confirmatory.

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## Posters - Abstract 4

Free Neuropathol 4:9:23

Meeting Abstract

### A case of papillary tumor of pineal region – A rare entity

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**Background:** Tumors of the pineal region comprises 1% or less of all intracranial neoplasms. Papillary tumor of pineal region (PTPR) is a very rare entity, arising from specialized secretory ependymocytes of the subcommissural organ. Headache is the common presenting symptom occurring due to increased intracranial tension as a result of compression of the aqueduct. This is a case report of a 17-year-old male, presenting with headache and altered sensorium, subsequently diagnosed with Papillary tumor of pineal region.

**Objectives:** To study about the cause, symptoms, histological pattern and its differentiating feature from other tumors of pineal region.

**Materials and methods:** Excised Specimen was received in histopathology department. Specimen was then preserved in 10% neutral buffered formalin, processed in automated tissue processor, embedded in paraffin blocks, stained using H&E stain following which microscopic examination was performed.

**Results:** Histopathology revealed oval to columnar tumor cells arranged in pseudorosettes formation and papillary architecture with fibro-vascular core and small foci of tumor cells arranged in group. Immunohistochemistry study showed strong reactivity for Vimentin and S-100 protein. EMA and GFAP were negative. Overall histomorphological appearance was suggestive of Papillary tumor of Pineal Region WHO Grade 2.

**Conclusion:** Papillary tumor of the pineal region is a neuroepithelial tumor with distinct morphological and immunohistochemical features. IHC is used to differentiate it from other primary and metastatic tumors in this region. It's potential for disease progression, frequent local recurrence and CSF dissemination warrants early diagnosis and early aggressive therapy in these patients.

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## Posters - Abstract 5

Free Neuropathol 4:9:24

Meeting Abstract

## A rare case of Atypical Teratoid/Rhabdoid tumour: case report

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**Background:** Atypical Teratoid Rhabdoid Tumour is a rare, malignant, highly aggressive paediatric intracranial neoplasm. It comprises 1-2% of all paediatric brain tumours and 10–20% of CNS tumours up to 3 years of age, with male preponderance. It originates mostly from cerebral and cerebellar hemispheres, cerebellopontine angle and brain stem, and is easily misdiagnosed as medulloblastoma on CT/MRI. The tumour progression is associated with loss of INI-1 expression in the neoplastic cells and immunohistochemistry helps confirming the diagnosis. This is a case report of a 4-year-old male presented with complain of vomiting, lethargy and macrocephaly. CT/MRI suggestive of trigeminal schwannoma and surgical excision was performed.

**Objectives:** To study the histopathology and immunohistochemistry in a case of Atypical Teratoid Rhabdoid Tumour.

**Material and methods:** Specimen of the excised greyish-white soft tissue aggregates was received and fixed in 10% neutral formalin. After gross examination, sections were taken and processed by automated tissue processing. Slides were stained using H&E stain, and microscopic examination was performed.

**Results:** Serial sections showed highly cellular embryonal neoplasm composed of sheets histology of markedly cellular, mitotically active high grade CNS Tumour-Atypical Teratoid/Rhabdoid tumour, WHO Grade-IV. Immunohistochemistry was positive for Vimentin, EMA, GFAP, but negative for INI-1 which confirmed the diagnosis.

**Conclusion:** This highly aggressive tumour can metastasize rapidly via the cerebrospinal pathway, resulting in poor prognosis. Earlier detection and adjuvant therapy can improve the prognosis. Reporting such rare tumours is of utmost importance as it provides information on clinicopathological patterns and factors that impact prognosis.

## Posters - Abstract 6

Free Neuropathol 4:9:25

Meeting Abstract

## Smoke and Mirrors: A tale of two unusual cerebellopontine angle tumors

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**Background:** Tumors of the cerebellopontine angle (CPA) are frequent; with neural tumors and meningiomas predominating the scene. However, infrequently encountered tumors, derived from adjoining anatomical structures, can be confounding to a pathologist, especially under the duress of an intra-operative frozen section. We herein describe two such unusual neoplasms, having radiologic and clinical incongruity, which led to diagnostic difficulties and eventually, a learning experience.

### Case Reports:

Case-1: A 25-year-old lady with a history of headache and gait imbalance for 3 months. The radiology profile showed a left CPA tumor measuring 3.8x3.7cm., hinting at a possibility of a neural tumor. The on-table finding prompted a meningioma. The imprint and squash cytology & section suggested an epithelial neoplasm -? metastasis. The paraffin sections showed compact, organoid nests with a granular cytoplasm and intervening vasculature, positive for synaptophysin, chromogranin, S-100 & negative for cytokeratin, Inhibin; a low Ki67 index, compatible with a paraganglioma.

Case-2: A 48-year-old man with a history of gait imbalance and dizziness for 2 months. Radiology suggested a mass lesion in the right CPA, compatible with either an epidermoid/ dermoid cyst or a schwannoma. The on-table diagnosis -? schwannoma or an epithelial cyst. The imprint and squash cytology & section showed acellular matrix with suspended epithelial cells and vacuolated cells, commensurate with the radiologic diagnosis. The paraffin sections showed lobules of large, vacuolated cells with a myxoid stroma with a pseudochondroid appearance. The IHC profile showed positivity for CK19, EMA, S100 and negative for CK7; rendering a diagnosis of a conventional chordoma.

**Conclusion:** These cases intend to highlight the lesser encountered CPA neoplasms by revisiting the intra-op devices for diagnostic clues and a better precision.

## Posters - Abstract 7

Free Neuropathol 4:9:26

Meeting Abstract

## All proliferating vessels are not haemangiomas - A case report of rare entity of sporadic meningioangiomatosis

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**Background:** Meningoangiomatosis is a rare benign disorder which can occur sporadically or in association with neurofibromatosis. Seizures are the first symptom in sporadic type whereas the one associated with neurofibromatosis is often asymptomatic. It is characterized by proliferation of fibroblasts with increased number of vessels surrounded by meningothelial cells. Very few case reports have been reported out of which most of the cases were sporadic. We present the etiology, imaging and histopathological findings of a sporadic case of meningioangiomatosis.

**Case Report:** We present a case of 8-year-old male child who was evaluated for complaints of multiple episodes of seizures, disorientation and speech disturbances. There was no significant past or family history. There was no association with neurofibromatosis. Investigations revealed parietal space occupying lesion. The boy underwent craniotomy with surgical excision. Histopathology and immunohistochemistry was consistent with Meningoangiomatosis. Within a short span, the boy came with early local recurrence.

**Conclusion:** Meningoangiomatosis can occur sporadically or in association with neurofibromatosis and it must be considered in the differential diagnosis of vascular cortical lesion.

## Posters - Abstract 8

Free Neuropathol 4:9:27

Meeting Abstract

## Extensive spherical amyloid deposition in Lactotroph pituitary neuroendocrine tumour masquerading as a primary bone tumour

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**Background:** Amyloid deposition is uncommon in PitNET. These deposits can be spherical, perivascular or stellate, commonly seen in prolactin and growth hormone-producing tumours. However, the spherical type of amyloid is rare and is exclusively described in prolactin-producing tumours. Herein, we report a rare case of prolactin-producing pituitary PitNET with extensive spheroid amyloid deposits.

**Case Report:** A 45-year-old male patient presented with a gradual diminution of vision in the left eye for three years associated with headache. MRI showed the presence of a sellar mass measuring 2.4\*2.3\*1.9cm bulging inferiorly into the sphenoid sinus. Biochemical investigation revealed elevated prolactin levels (34.9 microgram/L), for which he was treated with cabergoline for nine months. He subsequently underwent trans-sphenoidal resection of the mass. Intra-operatively, the mass was firm to hard, and differentials of clival chordoma and pituitary adenoma were considered. On microscopic examination sections from the mass revealed PitNET showing therapy related changes, in the form of shrinkage of tumor cells. There was extensive large lamellated spheroidal acellular eosinophilic deposits masking the tumor cells. The lamellated deposits showed positivity for Congo red and displayed apple green birefringence under polarised microscope, indicating amyloid in nature. On IHC, the tumour cells and spheroid collections showed exclusive positivity for prolactin.

**Conclusion:** Prolactin producing PitNET may show extensive spherical amyloid deposits, masquerading as calcification in imaging or raise a suspicion of a primary bone tumor. Microscopically, the extensive lamellated structure may deceptively camouflage the neoplastic tumour cells. Hence, awareness of this rare histological finding is essential.

## Posters - Abstract 9

Free Neuropathol 4:9:28

Meeting Abstract

### Late onset Pompe disease: role of fluorescence microscopy

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**Background:** Pompe disease is a type II glycogen storage disorder (GSD), which is caused by acid alpha-glucosidase deficiency. Onset usually occurs soon after birth, however, partial enzyme activity can result in late onset Pompe disease (LOPD) which can present as late as second decade of life. Owing to presence of storage material in lysosomes, LOPD is characterised by presence of intralysosomal lipopigment deposition, which can be depicted on immunofluorescence, aiding in diagnosis.

**Case Report:** A 15-year-old boy presented with gradual onset weakness and progressive wasting for 3 years. He complained of difficulty in getting up from squatting position, climbing upstairs and lifting heavy objects. His elder sister had history of similar symptoms, before she expired at 18-years of age with sudden onset breathlessness. Grade II ejection systolic murmur was present in mitral area. CK-NAC was 2347 U/L. Muscle biopsy was done which revealed moth eaten appearance with marked cytoplasmic vacuolation in subsarcolemmal location. These showed periodic acid Schiff- diastase (PAS-D) positive material. Lipopigment was seen as autofluorescent granules on fluorescent microscopy at 494 nm. This autofluorescence was quenched on sudan black B staining, hence confirming lipopigment deposition. Combination of above features was useful for diagnosis of LOPD which was subsequently confirmed on whole exome sequencing with homozygous mutation in GAA gene at exon 14 (c.2040G>A).

**Conclusion:** Late onset Pompe disease is a rare entity which is characterised by lipopigment accumulation in addition to other characteristic features of GSD. Though the muscle biopsy findings of GSDs show considerable overlap, knowledge of additional role of fluorescence microscopy can be helpful in arriving at correct diagnosis and in performing targeted genetic studies, if required.

## Posters - Abstract 10

Free Neuropathol 4:9:29

Meeting Abstract

## Nemaline Myopathy: A case report

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**Background:** Nemaline myopathy is a heterogeneous group of congenital myopathies caused by autosomal dominant or recessive mutations commonly involving *ACTA1* and *NEB* genes. The spectrum of clinical presentation is broad, ranging from congenital onset muscle weakness and hypotonia to adult forms which are mostly autoimmune related. Ultrastructurally, these rod like or ovoid structures are derived from Z lines and have a similar lattice structure and protein content.

**Case Report:** We describe a case of an 18-year-old female presenting with very low body mass index since birth and proximal weakness since childhood. On examination, she had high arched palate, bilateral pedal edema, and ptosis associated with bulbar signs. Gower's sign was positive. Biochemical analysis revealed elevated serum creatinine and uric acid. Nerve conduction studies (NCS) showed sensori-motor axonal polyneuropathy. The electromyography (EMG) performed from deltoid, vastus lateralis and tibialis anterior was suggestive of myopathic pattern. Snap frozen left vastus lateralis muscle biopsy examined showed uniform myofibres with dominance of type 2 fibres. These fibres showed numerous subsarcolemmal rod shaped inclusions in the cytoplasm which stained red on modified Gomori's trichrome (MGT) stain. These regions stained negatively on NADH enzyme, thus confirming Nemaline myopathy.

**Conclusion:** Nemaline Myopathy is a rare form of congenital myopathy. Routine histology of muscle biopsy may be normal, hence, MGT and enzyme stains are essential for the diagnosis. A better recognition and understanding of the disease will pave the way for early diagnosis and development of potentially effective treatment modalities. Genetic counselling is mandatory in the affected families.

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## Posters - Abstract 11

Free Neuropathol 4:9:30

Meeting Abstract

### Cutaneous clue to amoebic encephalitis: A case report

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**Background:** Pathogenic free living amoebae can cause fatal central nervous system infections in humans. These include *Acanthamoeba* sp, *Naegleria fowleri* and *Balamuthia mandrillaris*. Of these *Balamuthia* is known to cause skin involvement with skin as one of the proposed entry routes. We present one such case report.

**Case Report:** A 28-year-old male presented with generalised tonic clonic seizures for 1 month. MRI brain was done which showed an ill-defined intra-axial cortical based SOL in left superior and middle frontal gyri with marked perilesional edema, suggestive of infectious etiology. He also had well-defined erythematous plaques over back and left arm. Biopsies were performed from both brain and skin lesions. Histopathology of brain specimen revealed features of necrotising granulomatous inflammation with presence of trophozoites of *Balamuthia mandrillaris*, confirmed on periodic acid Schiff stain with diastase digestion. Skin lesions showed pan dermal dense lymphohistiocytic infiltrate. Patient was started on multi-drug regimen, however, he continues to deteriorate. Multiple steps were included in species identification and confirmation, including pathology and microbiology consults, assessment of size of organism, presence of cutaneous lesions and PCR (which served as gold standard).

**Conclusion:** Free living amoeba are neurotropic organisms which cause rapidly fatal meningoencephalitis. Of the known species, *Balamuthia* is known to cause skin lesions. Thorough search for organisms must be performed in all cases of granulomatous inflammation of brain, as amoebic trophozoites are easily missed due to their resemblance to histiocytes. Species identification is a key aspect in diagnosis and disease management which requires multi-speciality coordination.

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## Posters - Abstract 12

Free Neuropathol 4:9:31

Meeting Abstract

# Malignant transformation of intracranial epidermoid cyst: A rare case report

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**Background:** Intracranial epidermoid cysts constitute approximately 0.2 – 1% of all brain tumours. Malignant transformation of an intracranial epidermoid cyst to squamous cell carcinoma is extremely rare and very few cases have been reported in the world.

**Case Report:** We hereby present a rare case of a 29 year old man who had presented with a new swelling on a previous surgical site and left paresis. The patient had presented three months prior with a dermoid cyst with a small focus of grade 1 SCC, for which he underwent total excision. Evaluation of the current lesion showed recurrence with significant interval growth, with imaging findings suggestive of residual lesion as well as pseudomeningocele. He underwent exploration and excision, resulting in improvement of paresis. Histopathological examination revealed a moderately differentiated squamous cell carcinoma (grade 2) infiltrating adjacent glial parenchyma.

**Conclusion:** Although malignant transformation of EC to SCC is rare, possibility of such rare entities should be kept in mind. Appropriate diagnosis with immunohistochemical and other ancillary techniques are mandatory for the treatment and management of the patient

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## Posters - Abstract 13

Free Neuropathol 4:9:32

Meeting Abstract

## Neuropathological findings in a 17-month-old boy with delayed milestones and kinky- hair

Yukim Dong<sup>1</sup>, Neha Bhardwaj<sup>1</sup>, Kirti Gupta<sup>1</sup>, Chaithanya Reddy<sup>2</sup>, Jitendra Kumar Sahu<sup>2</sup><sup>1</sup> *Departments of Histopathology, Postgraduate Institute of Medical Education and Research, Chandigarh, India*<sup>2</sup> *Departments of Pediatrics, Postgraduate Institute of Medical Education and Research, Chandigarh, India*

**Background:** Menkes disease is rare X-linked recessive disorder reported in 1 in 300000 live births. It is caused by loss of function mutation in copper transport gene, ATP7A gene located on chromosome X. Patients classically present with neurodevelopmental delay, skin with hair changes and can be successfully treated with copper supplements.

**Case Report:** We describe a case of 17-month-old boy presenting with cyanosis, breathing difficulty and seizures. There was loss of previously attained developmental milestones. On examination, he was lethargic with small head circumference. His hair was brittle with skin laxity, joint hypotonia and brisk deep tendon reflex. His elder sibling and maternal uncle died at young age with similar symptoms. Investigations revealed low levels of serum copper and ceruloplasmin. Magnetic resonance imaging revealed diffuse atrophy of the cerebrum, cerebellum along with tortuosity of intracranial vessels. Due to worsening clinical condition, the child expired on day 32 of hospital stay. Brain autopsy was performed and histopathological examination of cortex showed dense gliosis, myelin loss and significant loss of neurons. Basal ganglia and other deep grey nuclei revealed variable loss of neurons in the background of gliosis. Cerebellum showed aberrant dendritic arborization, somal sprouts and axonal torpedoes within the Purkinje neurons. Genomic DNA extracted from blood revealed a hemizygous single base pair deletion in exon 17 of ATP7A gene located on chromosome X hence confirming the diagnosis of Menkes disease.

**Conclusion:** The index case illustrates the neuropathological features in a genetically proven case of Menkes disease at autopsy.

## Posters - Abstract 14

Free Neuropathol 4:9:33

Meeting Abstract

## Pituitary Macroadenoma with Apoplexy presented as Sudden bilateral vision loss

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**Background:** Pituitary apoplexy is true when there is clinical and radiological evidence of pituitary hemorrhage. A true apoplexy is an uncommon event occurring in 2 to 3 % of pituitary adenoma. In most cases, the event is spontaneous; however, a precipitating cause is identified in 25–30% of patients. Various precipitating causes reported in literature include hypertension, hypotension, major surgery, head trauma, radiation, drugs, endocrine anterior pituitary stimulation test, and thrombocytopenia. The two major mechanisms by which these factors cause apoplexy are either by causing acute fluctuations in blood pressure or by increasing the bleeding tendency. Pituitary apoplexy with sudden vision loss requires urgent trans endoscopic transsphenoidal surgical resection.

**Case Report:** A 35-year-old male presented with bilateral vision loss for 3 days and no other complaints. The patient was advised for MRI head and hormone test. LH- 3.98 m IU/ml, FSH 12.8 m IU/ml, Prolactin 2.36 ng/ml, Testosterone 416.14 ng/dl. The MRI head revealed a heterogenous sellar mass lesion with suprasellar extension measuring 45x32x22mm. The lesion uplifted the optic chiasma. The features were suggestive of Pituitary Macroadenoma with Apoplexy. The patient was operated, and the tumor was sent for histopathological examination. The tumor cells were arranged in sheets with small round nuclei and moderate amounts of granular eosinophilic cytoplasm. There was no significant mitotic activity and atypia. Many areas showed the presence of hemorrhagic infarction. Tumor cells were immunoreactive to synaptophysin, and Ki67 was 1%. Reticulin stain showed a distorted and fragmented staining pattern. Features were of Pituitary macroadenoma with apoplexy. Within a few days, the patient recovered from vision loss and now doing well on follow up.

**Conclusion:** Early surgical intervention is associated with a good prognosis in such cases.

## Posters - Abstract 15

Free Neuropathol 4:9:34

Meeting Abstract

## Polymorphous low-grade neuroepithelial tumor of the young (PLNTY): Rare but curable cause of refractory epilepsy

Aishwarya Karthikeyan<sup>1</sup>, Debajyoti Chatterjee<sup>1</sup>, Navneet Singla<sup>2</sup><sup>1</sup> Department of Histopathology, Postgraduate Institute of Medical Education and Research, Chandigarh, India<sup>2</sup> Department of Neurosurgery, Postgraduate Institute of Medical Education and Research, Chandigarh, India

**Background:** First described in 2016, Polymorphous low grade neuroepithelial tumor of the young (PLNTY) is an epileptogenic tumour of children and young adults. They present with seizures resistant to anti-epileptic drugs. Morphologically, they exhibit a diverse collection of neuro-epithelial neoplasms that, as a group, exhibit varying levels of glial with or without neuronal differentiation.

**Case Report:** In our case report, a 16-year male presented with a history of seizures since 9 months of age. MRI brain showed a well-defined expansile non enhancing multi-cystic cortex-based lesion involving the left medial temporal lobe with areas of mineralisation. Intra-operatively, the lesion was yellowish partly calcified, firm, and non suckable. Biopsy examined was in multiple fragments and showed grey and white matter fragments infiltrated by a moderately cellular tumour. The tumor was composed of uniform small round cells with bland vesicular chromatin and peri-nuclear halo having oligodendroglioma like appearance. Some areas showed spindling. There were areas of extensive calcification. There were no Rosenthal fibres or eosinophilic globular bodies. The tumor cells were positive for GFAP, CD34 (diffuse strong) and negative for IDH1, synaptophysin, P53 and OLIG2. NeuN highlighted entrapped neurons while tumour cells are negative. ATRX show retained nuclear expression. The final impression was PLNTY. MRI performed one year after surgery did not show any residual tumor, but he had intermittent episodes of seizures.

**Conclusion:** PLNTY is associated with drug resistant epilepsy. It can show extensive calcification and may resemble other low-grade gliomas. Diffuse CD34 expression can clinch the diagnosis.

## Posters - Abstract 16

Free Neuropathol 4:9:35

Meeting Abstract

## A rare case of cerebral cavernous malformation with concomitant intracranial mucormycosis infection

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**Background:** Cerebral cavernous malformation is angiographically detected occult solitary or multiple vascular anomalies. Intracranial mucormycosis is rare and represents one of the most severe manifestations, often determining the survival and functional outcome of patient with few case reports in literature in immunocompetent individuals. We, hereby report a case of cavernous malformation made rarer with concomitant mucormycosis.

**Case Report:** A 22-years old female presented with left sided facial seizures since age of 7 years and headache for past 3 years. Frequency of seizure was 1-2 episodes per day. There was no history of fever, headache, vomiting or head trauma. Past history was negative for tuberculosis, connective tissue disease or glucocorticoid use. Neurological examination also did not reveal any cranial nerves, motor, sensory or cerebellar abnormality. Magnetic resonance imaging revealed a contrast enhancing lesion with evidence of bleed in right posterior frontal lobe suggestive of cavernous malformation. Right frontal craniotomy with excision of cavernoma was done. Gross examination showed a 4x3 cm solid cystic mass with multiple mulberry protrusions. Histopathological examination revealed features of cavernous malformation with evidence of broad aseptate branching fungal hyphae conforming with the morphology of mucormycosis. Scant intervening brain parenchyma also revealed fungal infiltration along with reactive gliosis. Few foci of angioinvasion were seen. Final diagnosis of cavernous malformation with mucormycosis fungal infection was rendered and microbiological studies were advised.

**Conclusion:** To the best of our knowledge, this is the first case report of a cerebral cavernous malformation with mucormycosis in an immunocompetent patient without any risk factor.

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## Posters - Abstract 17

Free Neuropathol 4:9:36

Meeting Abstract

### Suprasellar masquerader: Chordoid glioma

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<sup>3</sup> Departments of Neurosurgery, Postgraduate Institute of Medical Education and Research, Chandigarh, India

**Background:** Chordoid glioma is a rare well-circumscribed glial neoplasm arising in adults and shows female predominance. Tanycytes of third ventricle are proposed as the cell of origin owing to its location. It is characterized by chordoid features with myxoid and inflammatory stroma. The specific molecular hallmark is recurrent PRKCA p.D463H missense mutation.

**Case Report:** We present 2 cases (30-year-old female and 45-year-old male) with similar complaints of behavioural change and headache. Midline suprasellar homogeneously enhancing mass was seen on contrast enhanced magnetic resonance imaging. Both the patients underwent craniotomy and subtotal tumor resection. Histopathology and immunohistochemistry was characteristic of chordoid glioma with cords and clusters of epithelioid cells arranged in a solid pattern. There was variable amount of myxoid stroma and lymphoplasmacytic infiltrate. No mitosis, necrosis or brain invasion was noted. The tumor cells expressed strong diffuse positivity for glial fibrillary acid protein (GFAP) and weak nuclear thyroid transcription factor (TTF-1). EMA and brachyury were negative. Subsequently, the lady underwent gross total excision and demised soon in the post-operative period. The male patient received radiotherapy and is currently doing well post 6 months of follow-up.

**Conclusions:** The rare occurrence, radiological and morphological overlaps in chordoid gliomas make them a true masquerader. Combination of GFAP and TTF-1 in the immunohistochemical panel can be useful in differential diagnosis. Mainstay of treatment is complete surgical excision, with evolving role of adjuvant radiotherapy.

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## Posters - Abstract 18

Free Neuropathol 4:9:37

Meeting Abstract

## Paediatric high-grade glioma' in association with constitutional mismatch repair deficiency syndrome (CMMRD)

Shalini Suman<sup>1</sup>, Sumanta Das<sup>1</sup>, Kavneet Kaur<sup>1</sup>, Shweta Kedia<sup>2</sup>, M C Sharma<sup>3</sup>, Vaishali Suri<sup>3</sup><sup>1</sup> Department of Pathology, All India Institute of Medical Sciences, New Delhi<sup>2</sup> Department of Neurosurgery, All India Institute of Medical Sciences, New Delhi<sup>3</sup> Department of Neuropathology lab (NSC) All India Institute of Medical Sciences, New Delhi

**Background:** Paediatric high-grade gliomas (pHGGs), H3- wildtype, IDH- wildtype are aggressive tumors considered as WHO grade 4. A small proportion of pHGGs are reported to be associated with cancer predisposition syndromes like Li Fraumeni syndrome, CMMRD and Neurofibromatosis type 1 (NF1). Glioblastoma arising in setting of CMMRD has unfavorable prognosis.

**Case Report:** A 2.5-year-old female born of consanguineous marriage, presented with left parietal-occipital lobe SOL with T2- weighted MRI suggestive of an enhancing tumor.

The Histomorphological, and immunohistochemical analysis showed features of paediatric type high-grade glioma with MIB-1 labelling index of 35-40%, absence of IDH1 R132H mutation, loss of ATRX expression, p53 mutation, H3 wildtype, (absence of H3 K27 mutation; loss of nuclear expression of H3 K27 me3; absence of H3 G34 R and H3 G34 V mutation), loss of ALK and N-MYC expression. Further immunohistochemistry for mismatch repair genes demonstrated loss of MLH1 and PMS2 expression in tumour and vascular endothelial cells while MSH2 and MSH6 expression were retained. Based on clinical, morphological and immunohistochemistry findings a final diagnosis of constitutional mismatch deficiency syndrome was rendered.

**Conclusion:** Early diagnosis can guide genetic testing, family screening and surveillance, as well as directly impact treatment decisions like avoiding temozolomide and using PD-1 immune checkpoint inhibitors at progression.

## Posters - Abstract 19

Free Neuropathol 4:9:38

Meeting Abstract

## Dumbell spinal tumor with INI-1 loss in an infant- A potential diagnostic pitfall

Anjali Chimnani<sup>1</sup>, Neha Bhardwaj<sup>2</sup>, Kirti Gupta<sup>2</sup>, Amita Trehan<sup>3</sup>, Prashant Chhabra<sup>3</sup>, Gargi Kapatia<sup>4</sup><sup>1</sup> *Departments of Pathology, Postgraduate Institute of Medical Education and Research, Chandigarh*<sup>2</sup> *Departments of Histopathology, Postgraduate Institute of Medical Education and Research, Chandigarh*<sup>3</sup> *Departments of Pediatrics, Postgraduate Institute of Medical Education and Research, Chandigarh*<sup>4</sup> *Department of Pathology, All India Institute of Medical Sciences, Bathinda, India*

**Background:** Atypical teratoid/rhabdoid tumour (AT/RT) is a high-grade malignant neoplasm (CNS WHO Grade 4) composed of variable numbers of poorly differentiated and rhabdoid cells. Spinal AT/RT are extremely rare, belong to AT/RT-MYC molecular subgroup and carry a dismal prognosis. These are characterized by biallelic inactivation of *SMARCB1* corresponding to loss of nuclear expression of INI-1. At this location, while other small blue round cell tumors are commoner differentials, poorly differentiated chordoma is another rare possibility, which needs exclusion with appropriate immunohistochemistry.

**Case Report:** A 11-month-old boy presented with quadriparesis. Magnetic resonance imaging (MRI) of the spine showed an intradural extramedullary dumbell tumor in the cervical region extending from C3-C5 causing cord compression. A radiological diagnosis of neurofibroma was kept. MRI brain and ultrasonography abdomen revealed normal study. Biopsy from the cervical mass revealed a tumor arranged in cords and singly scattered cells in a basophilic mucopolysaccharide-rich matrix. The tumor cells had eccentric nuclei with abundant homogeneously eosinophilic cytoplasm giving a rhabdoid appearance. Few cells showed cytoplasmic vacuolations. Mitoses were frequent. Immunohistochemistry performed showed loss of INI-1 expression along with negativity for synaptophysin, NKX2.2, desmin, WT1 and SATB2 excluding neuroblastoma, Ewing sarcoma, rhabdomyosarcoma, Wilms tumor and osteosarcoma, respectively. Poorly differentiated chordoma was also considered, as it features INI-1 loss similar to AT/RT; however, immunonegativity for brachyury excluded the former.

**Conclusion:** AT/RT demonstrates broad spectrum of morphology, and a panel of immunohistochemistry is mandated for an accurate diagnosis.

## E-Posters - Abstract 1

Free Neuropathol 4:9:39

Meeting Abstract

## ***BRAF* and *KRAS* mutations analysis in Rosai-Dorfman disease involving central nervous system: an observational study**

Mayur Parkhi<sup>1</sup>, Debajyoti Chatterjee<sup>1</sup>, Dharambir Kashyap<sup>1</sup>, Ashish Aggarwal<sup>2</sup>, Bishan Radotra<sup>1</sup>

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**Background:** Rosai-Dorfman disease (RDD) is characterized by clonal proliferation of S-100 positive histiocytes, variable emperipolesis, and commonly affecting cervical lymph nodes. The central nervous system (CNS) involvement is extremely rare.

**Objectives:** We attempted to evaluate the Cyclin D1 expression and frequency of *KRAS* and *BRAF* mutations in the RDD involving the CNS.

**Material and methods:** All patients with histopathologically diagnosed RDD involving CNS were recruited from year 2011 to 2022. All cases were subjected to immunohistochemistry for CD68, CD163, S100, CD1a, GFAP, CD207, EMA, IgG4, and CyclinD1. The real-time polymerase chain reaction (RT-PCR) for hotspot mutation analysis of *KRAS* (exons 2, 3 and 4) and *BRAF* (V600E) was done on formalin-fixed paraffin-embedded tissue using commercial kit (EntroGen).

**Results:** A total of seven cases were included. The median age was 31 years with 6 male and 1 female. It showed spinal cord (n=4) and intracranial (n=3) involvement. Histologically, all cases showed histiocyte rich inflammation with evidence of emperipolesis. These histiocytes are positive for S100, CD68, CD163, and Cyclin D1, whereas negative for CD1a, CD207 and EMA. None of the control cases with histiocytic infiltrate (5 cases each of demyelination and infarct) showed CyclinD1 expression. Four cases showed increase in IgG4 positive plasma cells (>10/HPF). *BRAF* V600E mutation was detected in one case (14.28%), while none showed *KRAS* mutation.

**Conclusion:** RDD involving CNS is an extremely rare and diagnostically challenging. Nuclear Cyclin D1 expression is a strong diagnostic clue. *BRAF* and *KRAS* mutations are rare in CNS RDD.

## E-Posters - Abstract 2

Free Neuropathol 4:9:40

Meeting Abstract

### Role of inflammation in muscle atrophy of Limb Girdle Muscular Dystrophy 2A/R1 (LGMD 2A/R1)

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**Background:** Muscle atrophy is one of the major characteristic features of Limb Girdle Muscular Dystrophy 2A/R1 (LGMD 2A/R1) patients. The ubiquitin proteasome system (UPS) is known to play an important role in muscle protein degradation. Inflammation is also observed in these patients, which may further activate the UPS.

**Objectives:** The study aimed to explore the role of inflammation in muscle atrophy of LGMDR1 patients.

**Materials and methods:** Expression of atrophy markers, MuRF-1 and atrogin-1 was analyzed in muscle biopsies of fifteen LGMDR1 patients by qRT-PCR and Western blotting. Expression of cytokines, TNF- $\alpha$ , IL-1 $\beta$ , and IL-6 was analyzed by qRT-PCR from muscle biopsies, and by ELISA from serum samples. Expression of NF $\kappa$ B, FoxO1 and FoxO3 genes was analyzed by qRT-PCR and Western blotting from muscle biopsies. The expression of genes and proteins of the UPS pathway under inflammatory conditions was studied in calpain-3 silenced C2C12 cell line (using calpain-3 siRNA transfection) and further confirmed using a proteasome inhibitor (MG132).

**Results:** The present study showed significantly increased level of pro-inflammatory cytokine TNF- $\alpha$  in LGMDR1 patients, which activated the UPS pathway by two transcription factors, i.e., NF $\kappa$ B and FoxO. Increased and decreased phosphorylation of NF $\kappa$ B and FoxO respectively, resulted in activation of atrogin-1 and MuRF-1 proteins. The calpain-3 silencing of myoblasts simulated the patient data, and treatment with MG132 showed reversal of catabolic signaling of TNF- $\alpha$  by targeting the UPS pathway mediators.

**Conclusion:** The study suggested that MG132 may prevent degradation of muscle protein breakdown by inhibiting the proteins related to the UPS pathway.

## E-Posters - Abstract 3

Free Neuropathol 4:9:41

Meeting Abstract

## Gene expression signature of meningioma identifies potential prognostic biomarker for tumor progression

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**Background:** Meningioma are common intracranial tumors categorized into three WHO grades I, II and III based on histological characteristics. These WHO grades fail to reliably predict their biological behavior of frequent recurrences & progression. Recently, Immune checkpoint inhibitor, *PD-L1* and NF- $\kappa$ B pathway have been implicated in the progression and recurrence of meningioma. Also, *PD-L1* expression is associated with up-regulation of genes of NF- $\kappa$ B pathway.

**Objectives:** We aimed to evaluate the expression of *PD-L1* and pathways associated with it and genes related to tumor progression in 3 grades of meningioma.

**Material and methods:** Transcriptomic sequencing was performed in 6 meningiomas (2 of each WHO grade). Differential expression was assessed using DESeq2 to shortlist differentially expressed genes. Gene Set Enrichment Analysis (GSEA) was performed to identify their association with various pathways.

**Results:** Transcriptomic profiling revealed gene expression signatures, which are distinct to each WHO grade. *CD274* (*PD-L1*) Immune check-point inhibitor, *NFKB2* and *RELB* genes belonging to NF- $\kappa$ B pathway were found to be significantly upregulated in grade II and III compared with grade I meningioma. While *DSC2* and *DSC3* genes belongs to cell-cell adhesion pathway were significantly downregulated in higher grades (II and III) compared to grade I meningioma.

**Conclusions:** Genes related to *PDL1* and NF- $\kappa$ B pathway are found to be upregulated while those of cell-cell adhesion pathway are downregulated in higher grades of meningioma, which can be used as potential therapeutic target to check tumor progression and recurrence.

## E-Posters - Abstract 4

Free Neuropathol 4:9:42

Meeting Abstract

### Detection of BRAF fusion expression patterns in Pilocytic Astrocytoma of the paediatric age group

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**Background:** Pilocytic astrocytomas (PA) are among the most common primary tumors found in children and adolescents. Majority (>70%) of PA cases demonstrate the presence of an oncogenic tandem duplication at 7q34. This duplication results in a KIAA1549::BRAF fusion gene with constitutive BRAF kinase activity and MAPK pathway activation. The second most the BRAF V600E mutation.

**Objectives:** To determine the frequency of KIAA1549-BRAF fusions in posterior fossa pilocytic astrocytomas of the pediatric age group.

**Material and methods:** Formalin-fixed paraffin-embedded tissues of 60 consecutive pilocytic astrocytomas (PAs) from the posterior cranial fossa were evaluated for KIAA1549::BRAF fusion transcripts (KIAA1549::BRAF 16-9, KIAA1549::BRAF 15-9, and KIAA1549::BRAF 16-11) by reverse transcriptase polymerase chain reaction and 38 PAs were evaluated for BRAFV600E. The sample was amplified by ddPCR using the QX100 ddPCR system (BioRad, USA).

**Results and conclusions:** Twenty two (22/60, 36.6%) cases showed fusion transcripts of which twenty (33.3%) showed KIAA1549-BRAF 16-9 transcripts and 2 (3.3%) the KIAA 1549::BRAF 15-9 fusion transcript. KIAA1549::BRAF 16-11 fusions were not detected in any of the cases. All the KIAA1549::BRAF fusion negative cases (38) were tested for BRAFV600E mutation via ddPCR and only 1 (1.6%) case was positive for BRAF V600E mutation. The frequency of molecular alterations (38%) seen in this cohort was lower than that reported in other parts of the world (60-70%), emphasizing the need to expand the panel of testing to make it more comprehensive. Finally, the data will be more meaningful when these findings are correlated to outcome.

## E-Posters - Abstract 5

Free Neuropathol 4:9:43

Meeting Abstract

## Comparative differential gene analysis in Supratentorial Ependymoma

Aastha Saraswati<sup>1</sup>, Kirti Gupta<sup>1</sup>, Prateek Bhatia<sup>2</sup>, Pravin Salunke<sup>3</sup> and BD Radotra<sup>1</sup><sup>1</sup> Department of Histopathology, Post Graduate Institute of Medical Education and Research, Chandigarh<sup>2</sup> Department of Pediatric (onco division), Post Graduate Institute of Medical Education and Research, Chandigarh<sup>3</sup> Department of Neurosurgery, Post Graduate Institute of Medical Education and Research, Chandigarh

**Background:** Supratentorial Ependymoma (ST-EPN) is segregated into two molecular subgroups denoted as ST-EPN-RELA and ST-EPN-YAP1; the former subgroup accounts for 70% of ST-EPN. While activation of NF- $\kappa$ B pathway through C11orf95-RELA fusion is known to drive the oncogenesis of RELA fusion EPN, not much is known about RELA fusion negative EPN.

**Objective:** Transcriptomic profiling of fusion positive and negative EPN for comparative analysis of gene expression and their association with cellular pathways.

**Material and methods:** Transcriptomic sequencing was performed on 5 cases of ST-EPN negative, 3 cases of ST-EPN Positive and 2 normal brain as control using Ion amplicon sequencing platform. Differential expression analysis between sample groups (positive and negative EPN) was performed using module from bioconductor from R package. Further analysis was carried out using Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways and Gene Ontology (GO).

**Results:** Transcriptomic sequencing identified 2366 significant genes that are abundantly expressed in ST EPN. Genes (*NFKB1L1*, *NFKB2*, *IL1B*, *PTGS*, *TNFRSF1B*) of NF- $\kappa$ B and TNF signalling pathways were highly expressed in ST positive and downregulated in ST negative whereas genes (*FOXJ1*, *PARD6B*, *FGF19*) of Hippo signalling pathway and pathways of neurodegeneration were upregulated in ST negative and downregulated in ST positive. These genes play an important role in cell proliferation and distinguishing between ST positive and negative EPNs.

**Conclusion:** Our results revealed intertumoral heterogeneity of EPN seen on gene expression level. The prognostic significance and further validation of these gene expression signatures needs to be determined on in-vivo models.

## E-Posters - Abstract 6

Free Neuropathol 4:9:44

Meeting Abstract

## Surgical spectrum of parasitic infections of nervous system - an audit from neuropathology archives

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**Background:** Parasitic infections of the nervous system can be caused by a wide array of organisms from protozoans to metazoa. They may affect both children and adults, and are more prevalent in immunosuppressed individuals. Spectrum of parasitic infections involving the central and peripheral nervous system as well as neuromuscular system is not widely described, with no reports from India.

**Objectives:** To determine the spectrum of parasitic infections in the neuromuscular and central nervous system.

**Material and methods:** All cases histopathologically diagnosed as parasitic infections between 2017 to 2022 were reviewed. The clinical, demographic and neuropathological details were retrieved from records.

**Results:** Over the past 6 years, parasitic infections were reported in 96/42,913(0.2%) of patients [age range: 6-61 yrs; M;F=47:49]. Neurocysticercosis (NCC) was most frequent (53 cases, lobar-23, intraventricular-21, spinal-1) followed by cerebral toxoplasmosis (22 cases, multifocal lobar; HIV seropositivity status available in 68%), hydatidosis (14 cases; lobar-6, bone-1, spinal-5). Less frequent were acanthamoeba meningoencephalitis (3 cases, 18-49 years; all lobar), toxocara (1 case, 64 yr/F, spinal), sparganosis (1 case, 40yr/M, multifocal lobar). In skeletal muscle, one case each of NCC, microsporidiosis in a HIV positive (40yr/F), and trichinosis (34yr/M) was diagnosed.

**Conclusions:** The most common infection amongst surgical biopsies was neurocysticercosis followed by toxoplasmosis. This spectrum pertains to surgical biopsies and does not reflect community prevalence. High index of clinical suspicion in appropriate clinical settings is essential for early diagnosis and optimum patient management.

## E-Posters - Abstract 7

Free Neuropathol 4:9:45

Meeting Abstract

## O6 methylguanine-DNA methyltransferase (MGMT) promoter methylation in adult type diffuse high grade gliomas, CNS WHO grade 4 by droplet digital PCR

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**Background:** Alkylating chemotherapy for adult type diffuse high-grade gliomas, CNS WHO grade 4 with epigenetic silencing of MGMT gene has been associated with a better prognosis. We designed a droplet digital PCR (ddPCR) assay, to determine MGMT promoter methylation and determined its utility in terms of ease and cost of analysis in comparison to methylation-specific PCR (MS PCR).

**Objectives:** To determine the O6-methylguanine-DNA methyltransferase (MGMT) promoter methylation in adult type diffuse high grade gliomas using ddPCR. To ascertain if CG16 dinucleotide methylation can be a stand-alone marker for MGMT promoter methylation. To determine the ease of performance and cost in comparison with MS PCR.

**Material and methods:** To determine the O6-methylguanine-DNA methyltransferase (MGMT) promoter methylation in adult type diffuse high grade gliomas using ddPCR. To ascertain if CG16 dinucleotide methylation can be a stand-alone marker for MGMT promoter methylation. To determine the ease of performance and cost in comparison with MS PCR.

**Results:** When compared with MS-PCR, MGMT gene promoter methylation by ddPCR had a sensitivity of 88.4% and a specificity of 81.3% and CG16 dinucleotide methylation by ddPCR had a sensitivity of 90.7% and specificity of 62.5%. Discrepant cases were sequenced by bisulphite sequencing and sensitivity and specificity were reassessed. The cost per test for MGMT promoter methylation by MS-PCR was much higher than ddPCR.

**Conclusion:** Although ddPCR and MSPCR had equal sensitivity for detection of MGMT promoter methylation, ddPCR had a higher specificity. Droplet digital PCR being an easier and cost-effective testing platform could replace the existing standard MS-PCR. CG16 dinucleotide methylation by ddPCR had a low specificity and hence cannot be used as a stand-alone marker to ascertain MGMT promoter methylation status.