Free Neuropathology 3:14 (2022)
doi: https://doi.org/10.17879/freeneuropathology-2022-4121

Meeting Summary

5th Asian Oceanian Congress of Neuropathology

along with the

5th Annual Conference of the Neuropathology Society of India

(AOCN-NPSICON)

Hosted by: Department of Neuropathology, NIMHANS, Bangalore, India

Meeting Abstracts

September 24–26, 2021

Submitted: 12 May 2022 · Accepted: 12 May 2022 · Published: 19 May 2022

The **5th Asian Oceanian Congress of Neuropathology along with the 5 th Annual Conference of the Neuropathology Society of India (AOCN-NPSICON)** was held in virtual mode on September 24–26, 2021, at National Institute of Mental Health and Neurosciences (NIMHANS), Bangalore, India, hosted by the Department of Neuropathology. It had 361 attendees from 20 countries from Asia and Oceania including India.

The event brought together pathologists, clinicians and neuroscientists from all over Asia and Oceania with invited speakers from the USA, Germany and Canada. The program was very comprehensive and covered advances in the fields of neurooncology with emphasis on the upcoming WHO 2021 classification of CNS tumors, neuromuscular disorders, epilepsy and neurodegenerative disorders through key note addresses and symposia that featured 78 distinguished international and national faculty sharing their expertise. In addition, there were case-based learning modules, opportunities for paper presentations and poster sessions for young faculty and postgraduates with several awards for young investigators, best papers and posters. A highlight of the conference was a unique debate on the hot topic of the decade: Methylation-based classification of CNS tumors and a panel discussion on COVID-19. The participants were highly appreciative of the academic content.

Abstract 1

Free Neuropathol 3:14:5

Meeting Abstract

Clinicopathologic analysis of diffuse midline gliomas: A single centre study

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Background: Diffuse midline gliomas are primary CNS tumors found in midline location of brain and spinal cord. These are WHO grade 4 tumors with characteristic H3K27M mutation and worse prognosis.
Objectives: To determine clinical, pathological, radiological, surgical outcome of patients diagnosed as DMGs.
Materials and methods: All patients diagnosed as DMG from January 2017 to July 2020 were included following ethical approval. Clinical presentation, radioimaging details were taken from medical records. Histopathologic features were noted. Immunohistochemistry (IHC) was performed with IDH1R132H (Dianova, dilution 1:200), ATRX (Sigma Aldrich, dilution1:500), H3K27M (Milipore, dilution 1:500), p53 (Sigma Aldrich, Ready to use) using poly HRP technique on fully-automated immunostainer (X Matrix, Biogenex).
Results: Study included a total 29 patients with mean age of 21±12.5years, M:F ratio of 2:1. Tumor distribution was thalamus (58.6%), brain stem (27.6%), cerebellum (20.7%), dorsal spine (10.3%) and cervical spine (6.9%). In 14 patients, tumor was biopsied and in the rest stereotactic or open excision was attempted. Morphology was variable in all cases. Gemistocytes, low cellularity, giant cells, PXA like pattern were some of the highlights in morphology. H3K27M showed dark nuclear expression in all with loss of ATRX in 21 cases. Twenty-two patients were treated with radiotherapy and 21 patients died on follow up at 6 months. High survival duration was seen in patients of >18 years age (p=0.02) who received RT (p=0.05).
Conclusion: DMGs are aggressive tumors. IHC with surrogate molecular marker helps in diagnosis. Prognosis is poor irrespective of surgery and radiotherapy.

Abstract 2

Free Neuropathol 3:14:6

Meeting Abstract

Low frequency of EZHIP overexpression in diffuse midline gliomas, H3 wildtype

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Background: Few Diffuse Midline Gliomas (DMGs) with H3K27me3 loss, lack H3K27M mutation. These H3 wildtype tumors have been shown to either overexpress EZHIP or harbour other mutations, thus categorised as DMG, H3K27 altered. However, studies on the frequency of EZHIP overexpression in DMG is sparse.
Objectives: The purpose of the present study was to analyse DMGs in paediatric and adult patients and study the frequency of EZHIP overexpression in DMG, H3 wildtype tumors.
Material and methods: Histological and immunohistochemical profiles of DMGs diagnosed between the years 2018 and 2020 (n=123) were reviewed and segregated into two groups; H3K27M mutant and H3 wildtype tumors. Immunohistochemistry was performed on the H3K27M wildtype tumors using rabbit monoclonal antibody to EZHIP(CXorf67).
Results: Of the 123 cases, 22 were in children and 101 in adults. 20/ 22 (91%) paediatric tumors and 64/101 (63.4%) adult tumors harboured H3K27M mutation. The common location of H3K27M mutant and H3wildtype tumours was thalamus in both age groups. Out of a total 39 H3wildtype tumours, only 2 showed EZHIP overexpression along with loss of H3K27me3. Both the tumours were located in the thalamus, with glioblastoma histology and occurred in young adults (30 and 36 years).
Conclusion: In our study, the majority of DMGs in paediatric age group and about two thirds in adults harboured H3K27M mutations. A very small subset of H3 wildtype tumours overexpressed EZHIP. This study highlights the low frequency of EZHIP overexpression in DMG H3 wildtype tumors.

Abstract 3

Free Neuropathol 3:14:7

Meeting Abstract

Location specific *KIAA1549::BRAF* fusion variants in pilocytic astrocytoma

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Background: Pilocytic Astrocytomas (PA) are characterized by constitutive activation of the RAS/MAPK signalling pathway. The most common underlying genetic alteration is *KIAA1549::BRAF* fusion, followed by *NF1*, BRAFV600E, *FGFR1* mutations, *BRAF* fusion with other proteins, *NTRK* family and *KRAS* mutation.
Objectives: To study the frequency of the most common *BRAF* genetic alterations, particularly *KIAA1549::BRAF* fusion variants and V600E mutation in PA and correlate with clinical features, and particular tumour site.
Material and methods: Retrospective analysis of 61 PA cases was undertaken, and they were tested for *KIAA1549::BRAF* fusion and V600E mutation by qPCR and IHC respectively. Whole RNA from FFPE tissues was reverse transcribed to cDNA. Using TaqMan assay, *KIAA1549::BRAF* fusion testing at 16-9, 15-9 and 16-11 exons was performed by qPCR. IHC was performed on tissue microarray sections.
Results: *BRAF* genetic alterations were seen in majority of PA (80.3%) *KIAA1549::BRAF* fusions accounting for 77% and V600E mutation for 3.3%. Fusion at exon junction 16-9 was the most common (68%) and majority were cerebellar tumors in children less than 15years age. Fusion at exon junction 16-11 (15%) was restricted to the cerebellum alone. We noted fusion at exon junction 15-9 (23%) frequently in midline location and few in cerebellum. Multiple fusions (16-9, 15-9) were seen in two. BRAFV600E mutations (2) were restricted to supratentorial location. *KIAA1549::BRAF* fusion and BRAFV600E mutation were mutually exclusive.
Conclusion: *BRAF* alterations are common in PA, especially in children. Different sites exhibit different *KIAA1549::BRAF* fusion transcripts in varying frequencies- 16-9 mainly in cerebellum, 15-9 mainly in midline, and 16-11 exclusively in cerebellum. Infrequent supratentorial PA show BRAFV600E mutation. These have prognostic and possible therapeutic implications.

Abstract 4

Free Neuropathol 3:14:8

Meeting Abstract

Epithelial to Mesenchymal Transition (EMT) in meningiomas

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Background: Epithelial-to-mesenchymal transition (EMT) is a process involved in invasion and metastasis of tumors. Its activation has been well documented in various malignancies and is associated with poor prognosis; however, data is limited in meningiomas.
Objectives: To analyse the expression of EMT related proteins and transcription factors in various grades of meningiomas and to correlate with clinical parameters.
Materials and methods: Seventy meningiomas of various histopathological subtypes and grades (WHO grade I=31, II=31, III=8) were analysed by immunohistochemistry for EMT related proteins (E-Cadherin, β-catenin, N-cadherin) and transcription factors (Snail-1, Slug).
Results: Downregulation (loss of expression) of E-cadherin, β-catenin and upregulation of Snail-1 was seen in higher frequency (82%, 72% and 69%) in WHO grade II/III meningiomas as compared to grade I meningiomas (6%, 3% and 13%) ($p<0.05$), thus indicating high frequency of EMT pathway activation in high grade meningiomas. N-cadherin and Slug expression was seen in only minority of cases. No difference in EMT phenotype existed between different histomorphological subtypes of grade I meningiomas. On survival analysis patients with EMT activation across all grades had shorter progression free and overall survival. Further, in four paired samples analysed, EMT activation was seen in all the principal tumors.
Conclusion: Meningiomas exhibiting EMT contribute to the aggressiveness and increased recurrence risk of these tumors. Hence EMT markers can be used for predicting the behaviour of meningiomas.

Abstract 5

Free Neuropathol 3:14:9

Meeting Abstract

Programmed death ligand 1(PD-L1) expression and tumor infiltrating immune cell subpopulations association with clinicopathological and prognostic parameters in diffuse gliomas

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Background: Recent discoveries have revealed that the glioma microenvironment includes a wide variety of immune markers that play an important role in the process of tumorigenesis.
Objectives: We aimed to analyze the utility of immune markers in prognostic stratification and understand the potential candidature of diffuse infiltrating gliomas for immune checkpoint blockade.
Material and methods: One hundred gliomas (WHO grade II–IV) were analyzed by immunohistochemistry for PD-L1 expressing tumor cells, tumor-infiltrating lymphocyte subsets (TILs; CD4, CD8, FOXP3, CTLA4) and tumor-associated macrophages (TAMs; CD68, CD163).
Results: Expression of PD-L1 was more frequent in adults, *IDH1* wild type gliomas (76%) and was significantly high in glioblastomas (GB, 74%) followed by grade III (50%) and II (27.5%) astrocytomas. Median CD8+ TILs, CD68+ and CD163+ TAMs density was higher among grade IV (5, 39 & 11/mm2) and grade III (4, 35 & 10/mm2) as compared to grade II tumors (1, 22 & 3/mm2). FOXP3 and CTLA-4 positive T cells were observed in minority of GBs only. Three-paired cases analyzed showed upregulation of PD-L1, TAMs, CTLA-4 and FOXP3 in recurrent tumors, indicating a role of the immune markers in recurrence. Further, positive correlation between PDL1 expression and CD8+ TILs and TAMs was noted. On survival analysis, increase in PDL1 expression, TILs and TAMs were associated with a shorter overall survival.
Conclusion: Immune markers are frequently expressed in gliomas in a grade-dependent pattern. Their analysis could aid in predicting the prognosis of patients and add potential value for immunotherapy treatments.

Abstract 6

Free Neuropathol 3:14:10

Meeting Abstract

Insights into molecular biology and immune micro-environment of pleomorphic xanthoastrocytoma

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Background: Pleomorphic xanthoastrocytomas (PXAs, grade II) are rare, accounting for less than 1% of astrocytomas and commonly occur in young patients. Some tumours which occur or recur with malignant change are known as anaplastic (APXA, grade III). There is limited data on their molecular characteristics and immune microenvironment.
Objectives: A comprehensive study highlighting the underlying molecular biology in PXAs for future development of a robust and cost-effective panel of biomarkers for risk stratification and discovery of novel drug targets.
Methods: Genome-wide expression profiling of 14 PXA and 6 APXAs was performed by microarray. Amongst differentially expressed genes (DEGs), Cyclin Dependent Kinase 14 (*CDK 14*) and Mitochondrial Fission Process 1 (*MTFP 1*) were validated by qRT-PCR. Immune profile was analysed using immunohistochemistry for PDL1 and CTLA4.
Results: Unsupervised hierarchical clustering revealed two distinct molecular clusters (Cluster 1: 10 PXA, 3 APXA and Cluster 2: 4 PXA, 3 APXA), indicating molecular heterogeneity within same grade. 10 differentially upregulated and 418 downregulated genes were identified between the clusters. qRT-PCR validation of *CDK 14* (upregulated in cluster 2) and *MTFP 1* (upregulated in cluster 1) showed strong concordance with expression array. There was no significant difference in age, sex, immunohistochemical profile, frequency of *BRAF* mutation or *CDKN2A* deletion between two clusters. Significantly worse progression-free survival was observed in cluster 2 (p=0.003). mRNA profiling-based prediction of recurrence was efficient, independent of histological grade and of *BRAF* mutation or *CDKN2A* deletion. PDL1 and CTLA4 expression was higher in PXA and APXAs than primary glioblastomas.
Conclusion: Study highlights distinct molecular subgroups of PXAs. DEGs between two clusters may be used for histology independent classification, prognostication, and prospective therapeutic targets. Higher up-regulation of PDL1 and CTLA4 suggests candidature for immunotherapy.

Abstract 7

Free Neuropathol 3:14:11

Meeting Abstract

Dynamics of cell-free DNA in predicting response in adult diffuse glioma on chemoradiotherapy

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Background: Adult diffuse glioma (ADG) is a heterogeneous primary brain tumor with a poor prognosis and treatment response. Tissue biomarkers are available for diagnostic and prognostic purposes. However, obtaining tissue is invasive and has limitations. Cell-free DNA (cfDNA) may help to meet these challenges in the management of ADG.
Objectives: The study aimed to quantify cfDNA in ADG on radiotherapy/chemotherapy and mutational profiling.
Material and methods: The study group comprised histopathologically confirmed ADG (n=50), including grade II, III and IV glioma, and controls (n=25). Serum cfDNA was extracted using Charge Switch gDNA 1ml Serum Kit (Invitrogen, USA) and quantified using SYBR based quantitative polymerase chain reaction (qPCR). Next-generation sequencing (NGS) was performed in 07 pre-operative and 05 post-operative cfDNA and tissue DNA on an Ion personal genome machine (Ion PGM) with an in-house designed NGS panel (including *TP53, ATRX*, and *IDH1* and *IDH2*).
Results: In patients with ADG, the Pre-Radiotherapy cfDNA level was significantly higher (Median; 113.46ng/ml), (IQR; 50.73-238.71) than normal controls (Median; 74.37ng/ml), (IQR; 49.67-120.00) (p=0.048). Non-responders had significantly higher cfDNA levels (Median; 184.4ng/ml), (IQR;73.84-631.10) than responders (Median; 68.12ng/ml), (IQR; 26.55-165.4**)**), (p=0.023). TP53 gene mutation was most common in both pre-operative and post-operative cfDNA samples.
Conclusion: Pre-radiotherapy cfDNA levels are associated with survival outcomes independent of other prognostic factors. Targeted NGS in pre-operative cfDNA matches the results of IHC analysis with high concordance, and it may be helpful in inoperable cases or have recurred.

Abstract 8

Free Neuropathol 3:14:12

Meeting Abstract

Regional heterogeneity in mitochondrial function in human brain ageing: Implications for region-specific vulnerability to neurodegeneration

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Background: Region specific vulnerability is implicated in neurodegenerative disorders. Mitochondrial dysfunction is implicated, while ageing is the greatest risk factor. It is unknown if age dependant variation in mitochondrial function exists across brain regions.
Objectives: This study investigates regional differences in mitochondrial function across different neuroanatomical regions in healthy ageing.
Material and methods: Five regions from post-mortem human brains (frontal cortex, cerebellum, striatum, hippocampus and medulla; age=0- 80yrs) was evaluated by mitochondrial complex assays. Enzyme histochemical staining and quantitative proteomics was performed in young (25±5 yrs) and old (≥65 yrs) ages.
Results: Mitochondrial enzyme assays revealed lowered activity of Complexes I & IV with age in all anatomical regions, Complex II showed increasing trend and Complex III remained unchanged. Medulla revealed highest activity, followed by cerebellum. On enzyme histochemistry, NADH labelled neuronal cytoplasm of frontal, striatum and cerebellar glomeruli and reduced with age. SDH showed increasing intensity with age, in neurons of striatum, cerebellum and medulla whereas COX showed reduced neuronal labelling intensity in hippocampus, cerebellum and medulla, with age. Mitochondrial protein expression profile in frontal, striatum and hippocampus was similar, compared to cerebellum and medulla. Medulla showed highest expression energy metabolism proteins and antioxidants irrespective of age, followed by cerebellum. Synaptic transmission & calcium transport pathways were enriched in frontal, striatum and hippocampus.
Conclusion: The study clearly demonstrates brain region specific mitochondrial metabolism, and redox homeostasis which could potentially contribute to region specific vulnerability to neurodegeneration.

Abstract 9

Free Neuropathol 3:14:13

Meeting Abstract

RYR1-related myopathies: A series of 5 patients from an Indian tertiary care centre

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Background: RYR1-related myopathies (RYR1-RM) are described as a rare, clinically and histopathologically heterogeneous, and slowly progressive neuromuscular disorders. They constitute the most common class of congenital myopathies. Clinical phenotypes are diverse and include King-Denborough syndrome, exercise-induced rhabdomyolysis, lethal multiple pterygium syndrome, adult-onset distal myopathy, atypical periodic paralysis, mild calf-predominant myopathy, and dusty core disease.
Objectives: To report clinicopathological features of a group of the patients diagnosed with ryanodinopathy in a tertiary care centre from India.
Material and methods: A retrospective study (2019-2020) was performed on the clinical, histopathological and genetic features of all pediatric and adult patients, in whom RYR1 mutation was detected using next generation sequencing.
Results: Five cases of RYR1-related myopathies were identified with age at onset varying from infancy to adulthood (2-39 years). A range of overlapping clinical phenotypes was noted: predominant proximal muscle involvement, facial weakness, external ophthalmoplegia, winging of scapula and mild tetraparesis associated with joint laxity. Two different histopathological patterns were recognized: centronuclear (n= 2) and central core (n = 3). Each case exhibited a different RYR1 mutation variant of which two novel genetic variants were revealed. Further one genetic variant was reported to be associated with malignant hyperthermia susceptibility.
Conclusion: There is a striking clinical and genetic heterogeneity among RYR1-related myopathies with identification of two new RYR1 variants. Its recognition is essential for genetic counselling and improving patient's safety during anaesthesia to avoid episodes of hyperthermia.

Abstract 10

Free Neuropathol 3:14:14

Meeting Abstract

Utility of respiratory chain complex assays in the diagnosis of mitochondrial disorders - A phenotype, histopathological and genotype correlation

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Background: Mitochondrial respiratory chain (MRC) enzyme complex assay play a crucial role in the diagnostic workup in a patient with suspected mitochondrial disorders. Determining the enzyme activities assist in defining isolated or multicomplex deficiency disorders and guide in identifying the molecular basis of the disease.
Objectives: To assess mitochondrial function in patients with suspected mitochondrial disorders.
Material and methods: This retrospective study (2014-2021) analysed a large cohort (n=1046) of cases with clinical diagnosis of mitochondrial disorders and /or other genetic and acquired skeletal muscle diseases. Fresh skeletal muscle tissue was subjected to MRC enzyme complex assay by spectrophotometry as a part of routine diagnostics.
Results: A total of 268/1046 cases (25.6%) revealed complex deficiencies. Amongst these, 208 cases [136 children (age range:10months-18years; M:F= 81:55) and 72 adults (age range:19-62 years; M:F= 39:33)] were primary mitochondrial disorders with syndromic and non-syndromic phenotypes. The syndromic phenotypes (n=65; 31.2%) include CPEO (n =15), mitochondrial myopathy (n=10), MELAS (n =9), Leigh syndrome (n=8), progressive myoclonic epilepsy (n=11), leukodystrophy (n=4), leukoencephalopathy (n=5), encephalomyopathy (n=1), sensory ataxia neuropathy (n=1) and NARP (n=1). Non-syndromic presentations constituted 143 cases (68.75%). Muscle histopathology findings was diagnostic in 33 (15.8%), while normal in 175 (84.13%). The deficiency included isolated complex I (n=127, 61%), isolated complex IV (n=31,14.9%), isolated complex III (n=5, 2.4%) and multiple complexes (n= 45, 21.6%). Complex I was the most common respiratory chain deficiency followed by multiple complex deficiencies, complex IV and complex III. Genetics done in over 100 cases revealed mutations across subunits of the complexes.
Conclusion: MRC enzyme complex assay enhanced the diagnostic yield in a large number of patients, in particular those with non-syndromic presentations as compared to conventional enzyme histochemical methods. Correlation of clinical, biochemical, pathological and genetics findings will be presented.

Abstract 11

Free Neuropathol 3:14:15

Meeting Abstract

Myelination changes in white matter following Severe Traumatic Brain Injury (Stbi): A neuropathological study

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Background: White matter injury after TBI involves both axonal injury and myelin pathology that evolves throughout the post-injury time course.
Objectives: To examine myelination changes in post sTBI patients.
Materials and methods: 64 Post mortem brain tissues (corpus callosum), 24 non-TBI and 12 control samples from the patients who died due to sTBI were collected. Patients with initial GCS score ≤ 8 and age above 18 years with positive CT findings were included. Routine H&E grading (3), myelin assay (LFB-PAS) and IHC for myelin basic protein (MBP) microscopic changes were graded on the basis of percentage of demyelinated area.
Results: Among sTBI group, H&E grading shows moderate demyelination in 39.06% patients and normal grade in 26.5% cases, whereas LFB-PAS & IHC –MBP grading, depicts severe demyelination in 29.8% patients and shows moderate demyelination in 26.5% patients.
Comparative to non-TBI group where 91.7% H&E grade and 83.3% LFB-PAS &IHC –MBP grade shows normal grade, control cases express 100% normal myelination grades. Both grading's found to be significant in sTBI compare to non-TBI and control groups.
Conclusion: Though H&E showed subtle demyelination changes, LFB-PAS & IHC –MBP grading depicted maximum changes following sTBI. Marked demyelination started in first week (3-10 days) after sTBI with reduced demyelination after 10 days which might suggest remyelination of demyelinated areas. Clinical evaluation of TBI will need to address the challenge of accurately detecting the extent and stage of myelin damage for identifying broader range of therapeutic opportunities to improve outcome after TBI.

Abstract 12

Free Neuropathol 3:14:16

Meeting Abstract

Is cerebral malaria an astrocytopathy? A post mortem study of BBB dysfunction

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Background: Pathogenesis of edema and seizures in cerebral malaria (CM) leading to mortality is unresolved. Microvascular pathology with sequestration of parasitized RBCs, endothelial activation, inflammatory mediator release and disruption of blood brain barrier (BBB) is a central pathogenetic event. However, role of astrocytes, major regulators of BBB, that protect from vasogenic edema via AQP4 channels in their end feet is unexplored.
Objectives: To evaluate histomorphological alterations in astrocytes and their role in pathogenesis of cerebral malaria.
Materials and methods: Clinical, demographic and neuropathological changes of six patients who succumbed to cerebral malaria were reviewed. Immunohistochemistry was performed for glial (GFAP, S100b) BBB (AQP4, IgG) and immune (p65 (NFκB)) markers.
Results: Patients [age range:14-40yrs; Male:Female=2:1; duration of illness (DOI):2-21days] were arbitrarily divided into Group1 (DOI <10days-hyperacute) and Group 2 (>/= 10days, acute). Brain showed marked cerebral edema with slate-grey discoloration. Histopathologically, all showed sequestration of parasitized RBCs in microcirculation, fresh ring and/or ball haemorrhages (6), resolving haemorrhages (4), and Durck granulomas (DG) (1). Astrocytic alterations were striking. In hyperacute stage (Group1), astrocytes were markedly stunted with attenuated processes, prominent dystrophic beading and retraction of processes, with reduced ensheathing of vessels. Progressive reduction in GFAP, S100b and AQP4 expression occurred with increasing DOI. Loss of AQP4 expression demonstrable around haemorrhages and DG, with leakage of IgG from vessels in acute stage. p65 (NFkB) expression was limited to resolving haemorrhages and DG.
Conclusion: Astrocytopathy results in BBB dysfunction in CM. Understanding the pathogenetic events at microvascular interface could aid design effective therapy to prevent mortality and morbidity in CM.

Abstract 13

Free Neuropathol 3:14:17

Meeting Abstract

Does mitochondrial dysfunction play a role in pathogenesis of mesial temporal lobe epilepsy secondary to hippocampal sclerosis?

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Background: Studies in animal models of temporal lobe epilepsy suggest a pathogenetic role for mitochondrial dysfunction, although validation studies in humans are scarce.
Objectives: We chose to evaluate the mitochondrial status in the hippocampus resected from patients with mesial temporal lobe epilepsy (MTLE) through proteomic approaches.
Material and methods: Crude mitochondrial preparations from human hippocampus samples, resected from patients with MTLE, who underwent amygdalohippocampectomy (Early-onset <10years of age, n=9 and late-onset >11years of age, n=9), compared with age matched normal controls (n = 9) were subjected to quantitative proteomics using high-resolution mass spectrometry (MS). MS data was validated by mitochondrial respiratory chain complex assays (CI- CIV).
Results: The MS identified 7,961 proteins among which, 190 proteins and 60 mitochondrial proteins differentially over expressed in early and late onset respectively ($p<0.05$). Proteins associated with biological processes such as mitochondrial electron transport chain, mitochondrial translation and branched-chain amino acid catabolic process were differentially overexpressed in cases with early onset MTLE, suggesting a pathogenetic role. Fatty acid beta-oxidation and glutathione metabolic processes were common to both early and late onset MTLE. Mitochondrial respiratory complex Iactivity was higher in early onset compared to late onset MTLE and controls, validating the proteomics data. The activities of mitochondrial complexes II-IV remained unaltered.
Conclusion: Mitochondrial dysfunction in hippocampus appears to have a role in the pathogenesis of early onset MTLE, in particular, mitochondrial complex I subunits. Evidence for role of mitochondrial dysfunction may aid in development of novel therapeutic strategies for treatment of MTLE.

Abstract 14

Free Neuropathol 3:14:18

Meeting Abstract

Diffuse midline gliomas with H3K27 mutation – clinico-pathological correlates

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Background: H3K27M mutant diffuse midline gliomas are infiltrative, midline high-grade gliomas with a K27M mutation in either *H3F3A* or *HISTIH3B/HIST1H3C* and have been reported to have a poor prognosis.
Objectives: To assess the morphology, the H3K27M status and clinical outcomes in H3K27M positive and negative diffuse midline gliomas.
Material and methods: Seventy-three cases of diffuse midline gliomas of WHO grades II-IV from 2012 to 2020, underwent immunohistochemical evaluation using H3K27M mutation specific antibody and H3K27me3 trimethylation antibody. Morphological parameters, clinical details and outcome were correlated with mutational status.
Results: Forty four of the 73 tumours were positive for the H3K27M mutation.H3K27M mutant diffuse midline gliomas occurred more commonly in adults and in the thalamus. They corresponded most often to a WHO Grade III. The MIB-1% was significantly higher in the mutant group of tumours. When considering the entire cohort, the H3K27M mutant group showed better overall survival and recurrence free survival compared to the wild group. However, RFS in the mutant group was worse in the supratentorial tumours compared to the infratentorial tumours and spinal cord H3K27M mutant tumours showed shorter OS and RFS compared to wild type tumours. In the cohort of H3K27M mutant tumours, children showed worse OS when compared to adults.
Conclusion: Contrary to reported literature H3K27M mutant diffuse midline gliomas occurred more commonly in adults and in the thalamus. H3K27M mutant tumours had a better RFS and OS than the wild-type cases. However, amongst H3K27M mutant tumours, children had worse OS than adults. Spinal cord H3K27M mutant tumours had a shorter RFS and OS when compared to brainstem and thalamus.

Abstract 15

Free Neuropathol 3:14:19

Meeting Abstract

Significance of nestin and CD133 as cancer stem cell markers in diffuse gliomas and its association with *IDH-1* status and p53 expression

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Background: Based on the cancer stem cell (CSC) theory, they have self-renewal, uncontrolled proliferation, multi-directional differentiation properties. We have studied CD133 and Nestin, which are the most commonly used two CSC markers with consistent expression in diffuse gliomas.
Objectives: To assess of the level of expression of CSC markers; Nestin and CD133 and identify the correlation among various grades of diffuse glioma, *IDH* status and p53.
Material and methods: A cross-sectional retrospective study conducted in department of pathology and neuro-surgery with 102 subjects on expression of CSCs and correlation with that of p53 and *IDH1* status in adult diffuse gliomas by immunohistochemistry on FFPE sections. The scoring of expression of CD 133 and nestin was adopted from Z*hang et al* and p53 from *Aruna et al.* The data was further analysed.
Results: The diffuse gliomas were graded based on WHO into grade II, III and IV. The expression of CD133 and nestin was compared with the increasing grades of diffuse gliomas and plotted on ROC curves with AUC of 0.6806 and 0.6119 respectively. This expression also showed a positive correlation with the *IDH* status of tumor.
Conclusion: CSC markers are expressed in diffuse gliomas and have higher expression with increasing in WHO grade and have significant association with *IDH-1* mutant status. Hence, it can be inferred that diffuse gliomas with the higher expression of CSC markers have poorer prognosis. Further, they have the potential to be used as therapeutic targets in the future.

Abstract 16

Free Neuropathol 3:14:20

Meeting Abstract

Immunophenotypic profile of pediatric brain tumors reflecting molecular alterations

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Background: Pediatric brain tumors are the most common solid pediatric tumors. Currently, there has been a drive towards "Personalised medicine" or "Precision medicine," where chemotherapy is targeted against specific driver mutations. The revised 4th edition and the yet-to-be-released 5th edition of WHO has considered this and included genetic information into the classification for a combined phenotypic-genotypic approach. As molecular analyses are not available in many centres in India, surrogate immunohistochemistry (IHC) markers corresponding to genetic alterations have been developed.

Objectives: To study the immunophenotypic profile of pediatric brain tumors corresponding to molecular alterations

Material and methods: This is a cross-sectional descriptive study of immunophenotyping of 51 patients with pediatric brain tumors reflecting molecular alterations on FFPE sections. Immunohistochemistry for beta-catenin, GAB-1, YAP-1, INI-1, p53 and LIN28A was done for 22 embryonal tumors. ATRX, BRAFV600E and H3K27M was done on 27 glial tumors and IDH-1 wherever necessary. BRAFV600E was done on 2 gangliogliomas.

Results: Using beta-catenin, GAB-1 and YAP-1, 19 medulloblastomas were classified into non-WNT/SHH pathway activated (16/19), SHH pathway activated (3/19) and) WNT pathway activated (0/19). Out of the 2 ETMRs diagnosed morphologically, one showed LIN28A expression, the other ETMR showed INI-1 loss and hence reclassified as ATRT. Out of 9 pilocytic astrocytomas, 2/9 showed ATRX loss, 4/9 showed BRAFV600E expression. H3K27M was positive in 2/2 diffuse midline gliomas. Of the 3 anaplastic astrocytomas and 6 glioblastomas, 1/3 anaplastic astrocytoma was IDH positive with ATRX loss. Hence it was reclassified as *IDH* mutant grade 3 astrocytoma. Rest all were IDH negative. 1/3 anaplastic astrocytoma and 4/6 glioblastomas showed loss of ATRX; hence they were assumed to be H3G34 altered diffuse hemispheric gliomas. The remaining 1/3 anaplastic astrocytoma and 2/6 glioblastomas showed retained ATRX expression and hence considered diffuse pediatric high-grade glioma, H3-wildtype and IDH-wildtype.

Conclusion: For embryonal tumors, currently, many clinical trials are underway based on this molecular classification. For example, for WNT-activated medulloblastomas, the dose of radiation has been reduced. For SHH medulloblastomas, SMO inhibitors have been introduced. BRAFV600E and H3K27M mutated tumors can also be given targeted therapies. Hence, in a resource-limited setup, these surrogate IHC markers can help fine-tune the diagnosis so that appropriate treatment can be given.

Abstract 17

Free Neuropathol 3:14:21

Meeting Abstract

PDL1 expression in CNS tumours

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Background: Immune checkpoints like PDL-1 regulates tumour microenvironment. PD-1 is expressed on activated T cells while PDL-1 is expressed on antigen presenting tumor cells. PDL-1 inhibits T cell activation; decreases proliferation and cause T cell apoptosis. Tumour survival is a balance between immune surveillance and cancer cell proliferation. It may be immunomodulated by PD-L1. Anti PD-L1 have be emerged in the treatment for multiple cancers in advanced stage

Objectives: Detection of PDL-1 expression in CNS tumour.

Material and methods: Cross Sectional study was conducted on 99 cases of CNS tumour (50 Diffuse Astrocytoma; 6 pilocytic astrocytoma; 7 Ependymoma; 2 oligodendroglioma; 27 meningioma; 07 embryonal tumour) between January 2014 to August 2020 in Department of Pathology and Lab Medicine, All India Institute of Medical Sciences, Bhopal.

Results: Diffuse Astrocytoma total 50 cases of which 1/9 of grade II, 1/6 of grade III (1/1 TIL), 7/19 of grade IV (2/3 TIL) and 10/16 of recurrent glioma (4/4 TIL). Pilocytic Astrocytoma (3/6 cases with 1/1TIL); Ependymoma 7 cases (0/ 1 supratentorial, 3/3 posterior fossa and 2/3 spinal cord (0/1 TIL); Oligodendroglioma (0/2); Meningioma 27 cases (6/18 grade I (2/3 TIL); 8/8 grade II (2/2 TIL), 1/1 grade III (1/1 TIL)); Medulloblastoma 0/6 cases; Atypical teratoid/rhabdoid tumour 1/1 were PDL1 positive. (43/99 with TIL 13/16)

Conclusion: 43.3% CNS tumour showed PDL-1 positivity with higher percentage in high grade. 16.16 % tumour showed TIL with 81.25% PDL-1 expression.

Abstract 18

Free Neuropathol 3:14:22

Meeting Abstract

Droplet Digital PCR: A robust technique for detection of IDH1 R132H mutation in formalin fixed tissue samples

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Background: Mutations involving isocitrate dehydrogenase 1 (*IDH-1*) occur in a high proportion of diffuse gliomas (≈90%), with implications on clinicopathologic diagnosis and prognosis. IHC is an easy and quick method of detecting IDH1-R132H mutations, but sometimes there may be some discrepancies. Traditional approaches, such as Sanger sequencing is laborious and lack sensitivity due to tumor heterogeneity and low tumor purity of glioma samples. The recently developed droplet digital PCR (ddPCR) technique generates a large amount of nanoliter-sized droplets, each of which carries out a PCR reaction on one template. Therefore, ddPCR provides high precision and absolute quantification of the nucleic acid target.
Objectives: The present study compares results of IHC with ddPCR in diffuse gliomas.
Material and methods: 50 diffuse infiltrating IDH1 immunopositive gliomas and 25 control samples (meningiomas) were included in the study. All cases were assessed for *IDH1* mutations by ddPCR. A cut off criteria which includes Mutant Allele Fraction was standardized. The detection limit was calculated using serially diluted positive mutant DNA in a background of wild-type DNA.
Results: There was 100% concordance of results between IHC and ddPCR. All control samples detected negative for *IDH1* mutation by ddPCR. Further compared with sanger sequencing, ddPCR was less time consuming (≈3 hours) and less laborious.
Conclusion: DDPCR is a reliable, rapid, robust,100 % sensitive and specific method for screening the *IDH1* mutation. It can be used to detect even low-frequency mutation burden.

Abstract 19

Free Neuropathol 3:14:23

Meeting Abstract

TERT promoter mutations in meningiomas: A clinicopathological correlation

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Background: Mutations in the non-coding promoter region of *TERT* gene has now been clearly established as one of the most dominant non-histological biomarker for aggressiveness in meningiomas.
Objectives: To study the pattern of *TERT* promoter (*pTERT*) mutations across different histological grades of meningiomas.
Materials and methods: Diagnosed cases of meningiomas, which had been evaluated and interpretable for *pTERT* mutations by direct target (C228 and C250) sequencing were analysed for their correlation for clinicopathological features.
Results: 155 cases (with age-range: 18-75 years & male to female ratio: 0.98 [males=58, females= 59]) formed the study cohort. Commonest location was cerebral convexity. Histologically, 63 were grade 1 (angiomatous:1; transitional:38; meningothelial: 14, fibroblastic:2 and NOS:8) , of these 28 had subtle atypical features (≥1 and ≤ 3 atypical histological findings i.e. high cellularity, small cell change, prominent nucleoli, necrosis, mitotic activity <4/10 high power fields (HPF) and necrosis). 79 were grade 2 (clear cell:1; chordoid: 1, 77: atypical) and 13 (papillary:2; rhabdoid:1) were grade 3. 8/155 (5.2%) showed *TERT* promoter mutation (C228T: 5, and C250T: 3). 2 (of 13; 15.4%) were grade 3, 3 (of 79; 3.8%) were grade 2 and 3 (of 63; 4.8%) were grade 1. All three *pTERT* mutant histologically grade 1 meningiomas, showed subtle atypical features, none (n=35) of the typically grade 1 showed *pTERT* mutations.
Conclusion: *pTERT* mutations are uncommon in meningiomas and are seen only in cases with presence of histologically aggressive features.

Abstract 20

Free Neuropathol 3:14:24

Meeting Abstract

Evaluation of *TERT* promoter mutation status in meningiomas

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Background: Meningiomas are the most common benign intracranial tumours. Approximately 20% of the patients show aggressive phenotype with significant patient morbidity and mortality. *TERT* promoter (*pTERT*) mutations have been associated with upregulation of telomerase activity and TERT mRNA expression in diverse cancer types including glioblastomas and oligodendrogliomas. Few studies on meningiomas have documented that presence of *pTERT* mutations is associated with higher tumour grade, enhanced risk for recurrence and progression.
Objectives: To analyse the frequency of *pTERT* mutation and assessed its prognostic significance in meningiomas.
Material and methods: A total of 125 cases (57 males and 68 females) of Grade 1 (n=60), 2 (n=42), 3 (n=13) and control (n=10) were included in the study (2012 to 2020). They were assessed for C228T and C250T hotspot mutation in the *pTERT* region by using Sanger Sequencing. Samples were stratified into two groups *TERT* mutated vs *TERT* wild type.
Results: There were 111 adult and 4 paediatric cases. The mean age of the patients was 38.8 years (range 10–70 years). *pTERT* C228T mutation was found in only **1.7% (2 of 115)** meningiomas. Both were grade 2 and adults. On follow up, both the patients died of tumour recurrence.
Conclusion: *pTERT* mutations are infrequent in meningiomas and associated with aggressive biology. Further, the predictive power of *pTERT* status essentially allow the clinician to identify aggressive meningiomas, patients at risk for early recurrence and provides biomarker for new therapeutic interventions.

Abstract 21

Free Neuropathol 3:14:25

Meeting Abstract

Pitfalls in diagnosis of oligodendrogliomas on squash cytology

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Background: Oligodendrogliomas (ODG) are one of the less common gliomas. ODG presents with a broad morphological spectrum and may mimic a variety of glial and non-glial neoplasms. The diagnostic peri-nuclear halo on histopathology is not seen in squash smears at all, thereby posing diagnostic difficulties in squash smears.
Objectives: To evaluate the diagnostic accuracy, limitations and pitfalls of intraoperative cytology in Oligodendrogliomas.
Materials and methods: Intraoperative squash smears of CNS tumours stained with haematoxylin and eosin stain were evaluated followed by corresponding histopathology sections. Appropriate immunostains were utilised where they were relevant. The findings were reviewed to determine the diagnostic pitfalls in twelve cases of ODG from our institution in the last two years.
Results: Amongst the 12 cases of histomorphologically proven ODG, 5 were correctly diagnosed as ODG grade 2 on squash smears. Amongst four cases diagnosed as astrocytoma on squash, three were ODG grade 2 and one was anaplastic ODG (grade 3) in HPE. One case diagnosed as low grade glioma (ODG) on squash cytology showed mini-gemistocytes. This was diagnosed as an anaplastic ODG on HPE. Two cases were incorrectly diagnosed as central neurocytoma and lymphoma respectively on squash.
Conclusion: The absence of properly defined intra-operative squash cytological features and sparse literature, leads to inter-observer variability during diagnosis of ODGs on squash smear alone. The discerning nuclear features of an ODG on squash smear are also lost with increase in grade and thus, further pose a diagnostic dilemma. Mini-gemistocytes are a helpful clue for anaplasia on squash smear.

Abstract 22

Free Neuropathol 3:14:26

Meeting Abstract

Low prevalence of *BRAF* V600E mutations in pleomorphic xanthoastrocytoma

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Background: The prevalence of *BRAF* V600E mutations in pleomorphic xanthoastrocytomas (PXA) and anaplastic PXAs (APXA) varies from 60 to 80%. There are conflicting reports on the prognostic relevance of this mutation in PXAs.
Objectives: To study the prevalence of *BRAF* V600E mutation in patients with pleomorphic xanthoastrocytoma (PXA) and correlate this with the outcome.
Materials and methods: This retrospective study included 33 patients with a diagnosis of PXA/APXA operated between 2007 and 2020. The demographic and clinico-radiological data were obtained retrospectively from the electronic database. The biopsies were reviewed and the samples were assessed for the presence of *BRAF* V600E mutation, using droplet-digital polymerase chain reaction. The histological grade and *BRAF* V600E mutational status were correlated with progression-free survival (PFS) and overall survival (OS).
Results: There were 20 patients in the PXA group and 13 patients in the APXA group. *BRAF* V600E mutation was seen in 40 % (8/20) of the PXA and 15 % (2/13) of the APXA cases. Recurrence was seen in 7/13 (55%) APXAs but none in the PXA group recurred at a mean follow-up of 45months. The overall survival was significantly better in PXAs compared to the APXAs (p=0.02). *BRAF* V600E mutated tumours had a better OS as compared to wild type tumours but this did not reach statistical significance. (p=0.364).
Conclusion: *BRAF* V600E mutations were seen in only 30% of PXA/APXAs limiting its usefulness as a diagnostic marker. *BRAF* V600E mutant tumours had a better overall survival, however, this was not statistically significant.

Abstract 23

Free Neuropathol 3:14:27

Meeting Abstract

Unusual primary intracranial sarcomas – Ewing's sarcoma and synovial sarcoma

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Background: Primary Sarcomas of brain are rare – hence two cases of primary intracranial sarcomas of brain are being presented.
1. Synovial sarcoma is an aggressive soft tissue sarcoma and intracranial occurrence is rare. It is characterized by a unique chromosomal translocation t(X;18) (p11.2; q11.2).
2. Primary Intracranial Ewing Sarcoma is also rare. It is characterized by chromosomal translocation t(11;22) (q24;q12) .
Very few cases, of primary intracranial synovial sarcoma and primary intracranial Ewing's sarcoma have been reported in the literature.
Objectives: To present two unusual sarcomas of brain and emphasize on the diagnostic challenges.
Material and methods: Case reports of two primary intracranial sarcomas
Results: Case 1 – 31 years old male on imaging was found to have left frontal SOL. Histopathological examination with immune stains, suggested a synovial sarcoma. FISH studies done at two laboratories were negative for *SYT-SSX2*. Later the translocation was detected by RTPCR, confirming the histological diagnosis.
Case 2 –Twenty-year male came with complaints of headache since 3 months. MRI – revealed heterogeneously enhancing left tentorium based Sol. Histopathological examination with immune stains showed features of primitive neuroectodermal tumor. FISH studies revealed *EWSR 1* gene re-arrangement with the final diagnosis of pPNET.
Conclusion: Sarcomas though rare can be seen as primary intracranial tumors, hence awareness of these entities with appropriate molecular studies is important for making the correct diagnosis.

Abstract 24

Free Neuropathol 3:14:28

Meeting Abstract

Relevance of the 4-variable risk stratification model in CNS solitary fibrous tumours

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Background: Solitary fibrous tumour/Hemangiopericytomas (SFT/HPC) of the CNS are graded based on their morphological phenotype and mitotic activity. In contrast, SFTs arising in the non-meningeal sites are prognosticated using the 4-variable risk stratification model (described in WHO classification of soft tissue and bone tumours, 2020) which has been observed to be an improvement over the traditional benign/malignant distinction.
Objectives: To determine pertinence of the 4-variable risk stratification model in meningeal SFT/HPCs.
Materials and methods: This retrospective study identified 53 patients operated between 2014 and 2021 and diagnosed as SFT/HPC on histopathology. Follow up data was available for 27/53 patients. The cases were sorted into low, intermediate and high risk groups as per the 4-variable risk stratification model. The results were correlated with the follow-up data, including the presence or absence of distance metastasis.
Results: One tumour was diagnosed as SFT, WHO grade I, while 6 tumours and 20 tumours were diagnosed as HPC, WHO grade II and III, respectively. All 27 tumours were immunopositive for STAT6. In accordance with the 4-variable risk stratification model, 19 (70.4%) patients fell in to the low risk group, while 8 (29.6%) fell into the intermediate risk group. Local recurrence was observed in 3 patients, while distant metastasis was seen in 3 patients (lung (1/3), L5-S1 spine (1/3) and submental soft tissue (1/3)). All patients with local recurrence or distant metastasis were diagnosed with HPC, WHO CNS grade III. Among the patients with metastasis, two belonged to low risk group and one to intermediate risk group (as per the 4-variable risk stratification model).
Conclusion: Despite the limited sample size, it is observed that the 4-variable risk stratification model validated in non-meningeal SFTs did not prognosticate the meningeal counterparts appropriately. It is therefore unlikely that this model might replace the original grading described in WHO classification of CNS tumours, 2016.

Abstract 25

Free Neuropathol 3:14:29

Meeting Abstract

Oropharyngeal psammomatous melanotic schwannoma, non-syndromic - An unusual tumour at an unusual site

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Background: Psammomatous melanotic schwannoma is a rare tumour of uncertain histogenesis and indeterminate biologic behaviour with known association with Carney's syndrome.
Objectives: To present a rare case of an oropharyngeal psammomatous melanotic schwannoma which has no syndromic association presently.
Material and methods: Case report of oropharyngeal sammomatous melanotic schwannoma
Results: A 25-year-old female presented with complaints of a swelling in her oral cavity for about ten years, gradually increasing in size and causing difficulty in swallowing. A clinical diagnosis of hemangioma was given. The swelling was excised and sent for histopathological evaluation. A circumscribed reddish to brownish black mass measuring 5x4x3.5cms was received. The cut surface showed reddish-brown to haemorrhagic areas and foci of calcification. On microscopic examination, a diagnosis of psammomatous melanotic schwannoma was given. The patient was not found to have any associated feature of Carney's syndrome on clinical examination. She had no significant personal or family history. The patient is on regular follow up and is doing well three years post-surgery.
Conclusion: Psammomatous melanotic schwannoma is a rare tumour of uncertain biologic potential. A knowledge of this entity is helpful for correct diagnosis and appropriate patient management with long-term follow-up in view of potential malignant transformation.

Abstract 26

Free Neuropathol 3:14:30

Meeting Abstract

Silent Corticogonadotroph Adenoma (SCGA): A silent monster

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Introduction: Pituitary adenomas are usually benign tumors which are classified based on differentiated cell type origin. Silent corticogonadotroph adenoma are rare, benign but aggressively growing biochemically silent adenoma subtype showing rare characteristics of bilineage differentiation of both corticotroph and gonadotroph. Till now there is only a single study published in literature about this entity and further studies need to be done.
Objectives: To report a case of silent corticogonadotroph adenoma
Material and methods: Case report of silent corticogonadotroph adenoma
Results: A 25year old male presented with complaints of multiple episodes of headache and vomiting since 3 weeks and bilateral loss of vision since 5-6 years**.** NCCT brain showed large, well developed, extra-axial sellar and supra sellar predominantly solid lesion with peripheral cystic component measuring 6.3x2.7x5.3cm. Histomorphological analysis showed a tumor with features of pituitary adenoma. Immunohistochemistry for the hormonal profile showed diffuse positivity for ACTH, whereas tumor cells were negative for LH, FSH, PRL, GH and TSH. In addition, the tumor cells were diffusely positive for LMWCK with MIB1 labelling index of 2%. Hormonal profile suggested a corticotroph adenoma. However, IHC for transcription factors showed contradictory results with tumors cells positive for SF1 and GATA3 while negative for Tpit and PIT1. Integrating clinical, morphological and immunohistochemistry findings a finally diagnosis of silent corticogonadotroph adenoma was rendered.
Conclusion: Due to the rarity of this lesion, SCGA may not be considered as a differentials while working up the case. The diagnosis of this subtype emphasizes increased postoperative surveillance for earlier detection of recurrences and hypopituitarism thereby reducing morbidity and improving quality of life in these patients.

Abstract 27

Free Neuropathol 3:14:31

Meeting Abstract

Molecular profiling: A key to clinical and histological enigma in an ambiguous case

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Background: The upcoming 2021 WHO Classification of CNS tumors highlights the importance of molecular diagnostics.
Objectives: Molecular characterization of a tumor showing ambiguous histology and clinico-radiological picture.
Material and methods: A 27-year-old female presented with history of headache, vomiting and vision deterioration for a month with no motor/sensory deficits. On CECT, there was a well-defined lobulated, solid-cystic lesion with calcification involving anterior corpus callosum and bilateral anterior frontal lobe. Craniotomy and tumor excision were done. Intraoperatively, it was soft and vascular tumor extending to the left lobe. A radio-clinical diagnosis of oligodendroglioma or high-grade glioma was rendered.
Results: H&E-stained sections showed a tumor comprising of round monomorphic cells with clear cytoplasm forming small nests and rosettes with extensive neuropil in the background. Hyalinized blood vessels, Rosenthal fibres and eosinophilic granular bodies were seen. There was an occasional focus of endothelial cell proliferation. No mitotic activity or necrosis was noted. Immunohistochemically, the tumor cells were positive for OLIG2, MAP2, β-tubulin while negative for GFAP, Neu-N, NF, CD34, EMA and EBP-50. Neuropil was highlighted by synaptophysin. The tumor cells were negative for IDHR132H, p53 and LICAM and showed retained ATRX expression. Based on these findings, a diagnosis of glioneuronal tumor, NEC, WHO Grade 1 was suggested. Molecular analysis by FISH, RT-PCR and Sanger sequencing exhibited MAPK pathway activation.
Conclusion: A cryptic case with deregulation of MAPK pathway is highlighted. Molecular characterization is essential in such unusual cases owing to availability of targeted therapy.

Abstract 28

Free Neuropathol 3:14:32

Meeting Abstract

Pseudotumoral hemicerebellitis masquerading as Lhermitte–Duclos disease – A case report

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Background: Pseudotumoral hemicerebellitis is an exceptionally rare presentation in which unilateral cerebellar involvement mimics a tumour. The aetiology is diverse including post vaccination and post infection.
Objectives: To report a rare case of pseudotumoral hemicerebellitis masquerading as Lhermitte–Duclos disease
Material and methods: Case report of pseudotumoral hemicerebellitis masquerading as Lhermitte–Duclos disease.
Results: A 11 year old girl presented with headache and vomiting for 1 month, associated with right cerebellar signs. MRI revealed a T2 hyperintense contrast enhancing right cerebellar lesion with diffusion restriction, and features of tiger stripe pattern suggestive of Lhermitte–Duclos disease. There were no neurocutaneous markers. She underwent craniotomy with biopsy of right cerebellar tissue which revealed an irregularly expanded cerebellar folia with florid lymphoplasmacytic infiltration admixed with histiocytes in the meninges and parenchyma. This was associated with marked reduction in the granule cell layer neurons and polyfocal destruction of folial architecture. There were no granulomas, parasites, viral inclusions, or collection of dysplastic neurons or neoplastic cells. Special stains for fungi, acid fast tubercle bacilli and bacteria were negative. The patient did not have recent history of fever, vaccination or drug ingestion. Extensive work up for infectious aetiology in both serum and CSF proved to be negative. Serum and CSF panel for autoimmune encephalitis, paraneoplastic neuronal and NMO–MOGSD antibodies were also negative.
Conclusion: Pseudotumoral hemicerebellitis is the close differential diagnosis for Lhermitte–Duclos disease radiologically. It typically has a benign course, the main management comprising supportive measures, steroids or antivirals. Better understanding and awareness of this rare entity would help in accurate presurgical diagnosis and patient management.

Abstract 29

Free Neuropathol 3:14:33

Meeting Abstract

Anoctamin-5 muscular dystrophy: Report of 2 cases with different phenotypes and genotypes from Indian subcontinent

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Background: Anoctaminopathies are a group of autosomal recessive skeletal muscle disorders with various clinical phenotypes, caused byanoctamin 5 (*ANO5*) gene mutations and the abnormal expression of ANO5 protein. Patients with recessive mutations in *ANO5* present with variable symptoms ranging from asymptomatic hyperCKemia and exercise-induced myalgia to proximal and/or distal muscle weakness.
Objectives: We describe the clinical, pathological, and molecular findings of two unrelated patients with ANO5-related muscular dystrophy.
Material and methods: 96 histologically identified muscular dystrophy cases were subjected to next generation sequencing using a customized panel of 54 genes (IIlumina Design Studio).
Results: Two patients were diagnosed with ANO5-related muscular dystrophy. One patient had a pathogenic homozygous mutation of c.1406G>A in exon 14 while the other patient had a novel heterozygous mutation of c.2141C>G in exon 19 of *ANO5* gene. Both showed two different phenotypes (Limb girdle Muscular dystrophy 2L and miyoshi myopathy) and histomorphological pattern. Muscle biopsy of one patient in addition showed amyloid deposition in the blood vessels walls. Neurologic examination was unremarkable with insignificant family history. Serum creatine kinase (CK) was elevated in both.
Conclusion: *ANO5*-related muscular dystrophy is a heterogeneous disease with different clinical phenotypes as well as genotypes. All muscle biopsies with unclassified muscular dystrophies should be subjected to congo-red stain to look for amyloidosis. The results of this study further suggests that screening for *ANO5* gene should represent an early step in the diagnostic work-up of the patients with undiagnosed muscular dystrophy and persistent asymptomatic hyperCKemia even when muscle biopsy is normal.

Abstract 30

Free Neuropathol 3:14:34

Meeting Abstract

Dysferlinopathy in a cohort of North Indian patients: Clinical histopathological and mutational spectrum

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Background: Dysferlinopathy is a group of autosomal recessive muscular dystrophy caused by mutations in the dysferlin gene (*DYSF*). It is the second most commonly reported LGMD subtype (27%) in India after GNE myopathy (31%). Phenotypic variants includes Miyoshi myopathy (MM), limb-girdle muscular dystrophy (LGMD2B), and other atypical phenotypes, such as the proximo-distal phenotype and distal anterior compartment myopathy.
Objectives: To describe the clinical, histopathological and mutational spectrum of dysferlinopathy in a cohort of patients from northern India
Material and methods: 96 patients (2018-19) suspected of LGMD from non-related families underwent thorough phenotypic characterization followed by muscle histopathological analysis. These cases were subjected to next generation sequencing using a customized panel of 54 genes.
Results: Eleven patients (6 male and 5 females) were diagnosed as dysferlinopathy amounting to a prevalence of 11.4% of LGMD in north Indian population. Eight patients presented with proximal LGMD2B, 2 with distal MM and 1 with proximo-distal phenotype. Mean age of onset and diagnosis was 24.4 years and 36 years respectively. CPK was elevated in all and ranged from 540 to 13000 U/L. Histomorphological analysis showed predominant dystrophic changes with necrotic-regeneration pattern and inflammation. Immunohistochemistry revealed partial to complete loss of dysferlin in all except one case. Sequencing reveal 9 novel and 6 known mutations including exonic (frameshift, stop gain and SNVs) and splice variants.
Conclusion: A high proportion of novel mutations were identified in the *DYSF* gene thus broadening the genetic spectrum of dysferlinopathy. No genotype-phenotype correlation existed suggesting that the clinical phenotype is determined not only by *DYSF* variants but also likely through a complex interplay of environmental, epigenetic, and genetic factors.

Abstract 31

Free Neuropathol 3:14:35

Meeting Abstract

Role of mitochondrial respiratory chain complexes in pathogenesis of temporal lobe epilepsy

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Background: Role of mitochondrial dysfunction in seizure generation comes from frequent occurrence of epilepsy in inherited mitochondrial disorders. Less is known about its role in acquired epilepsies such as temporal lobe epilepsy (TLE). Targeting mitochondrial oxidative stress with antioxidant treatment may prove a useful adjuvant in the management of epilepsy.
Objective: To determine the role of mitochondrial dysfunction in the pathophysiology of TLE by assessing mitochondrial function in the Temporal Lobe.
Materials and methods: Mitochondria isolated from human temporal lobe samples, resected from patients with TLE who underwent anterior temporal lobectomy (Early-onset <10years of age, n=9 and late-onset >11years of age, n=9), compared with age matched normal controls (n=9) subjected to assays for Malate dehydrogenase, Succinate dehydrogenase, Mitochondrial Complexes I to IV and ADP/ATP ratio.
Results: Mitochondrial respiratory complex assay data analysis revealed significant increase in complex I and III activity in early and late onset TLE compared to controls. The mitochondrial complex II activity was higher in controls compared to early and late onset TLE whereas complex IV had higher activity in controls compared to early onset. The ATP/ADP ratio was decreased indicating reduced bioenergetics. An elevated activity of Malate Dehydrogenase and Succinate Dehydrogenase was also observed.
Conclusion: The specific targeting of mitochondrial oxidative stress, dysfunction, and bioenergetics may have significant role in inducing epileptogenesis with respect to respiratory chain complexes and antioxidant treatment may prove to be a useful adjuvant in the epilepsy management.

Abstract 32

Free Neuropathol 3:14:36

Meeting Abstract

Gliotic and destructive brain lesions associated with drug resistant epilepsy - A clinicopathological study

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Background: Destructive insults during brain development result in various radiologically-defined lesions which may lead to drug resistant epilepsy (DRE). Their histomorphology is rarely described.
Objectives: To describe the histopathological features of lesions resulting from destructive brain injuries/insults with DRE.
Materials and methods: Histopathological evaluation of surgical specimens of lesions attributable to destructive brain insults over 4 years' period.
Results: Study included 58 cases (32 males and 26 females) with 93.1% presenting with complex partial seizures and 67.2% having early life adverse events. Age of onset ranged from Day 12 to 18.6 years (mean=5.6 years) with mean age at surgery of 14.7 years (2-39 years). Lesions frequently involved occipital lobe (51.7%) and often had multilobar involvement. Histopathological abnormalities were categorised as: ***(1)*** Gliosis and atrophy (n= 25) of cortex and/or white matter showing a combination of cortical abnormalities ranging from unlayered, 4-layered and nodular architecture to complete neuronal loss. ***(2)*** Exclusive layer 4 neuronal loss and gliosis (n=6) without other cortical abnormalities. ***(3)*** FCD type IIId (n=9) in which there was cortical dyslamination (microcolumnar architecture in 8 and cortical layer 2 loss in 1) adjacent to gliotic and atrophic parenchyma. ***(4)*** Non-specific changes (n=18).
Conclusions: Histomorphological changes include a combination of cortical and white matter gliosis and multiple patterns of cortical dyslamination. Exclusive layer 4 neuronal loss and gliosis may represent a specific subtype. FCD type IIId often takes the form of microcolumnar architecture in the adjacent uninvolved cortex.

Abstract 33

Free Neuropathol 3:14:37

Meeting Abstract

Cytopathic changes of herpes zoster encephalitis in CSF mimicking malignant cells

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Background: Herpes zoster is the reactivation of Varicella Zoster virus which remained latent in the dorsal root ganglia after the primary infection. Only 0.1%–0.2% of patients with disseminated Varicella-zoster have been reported to have manifest with encephalitis, that too in severely immune-compromised individuals. We are presenting a cytological challenging case of zoster meningitis mimicking malignancy.
Objectives: To substantiate large worrisome cells in CSF due to cytopathic change masquerading as neoplastic cells.
Material and methods: Case Presentation of herpes zoster encephalitis
Results: A 72-year-old male presented with chest wall swelling and CSF evaluation performed for his neurological symptoms viz. fever and episodes of focal clonic seizures of right upper limb and impaired awareness. MRI brain with contrast was normal. CSF was evaluated for cytology and biochemical parameters, displaying worrisome large pleomorphic singly scattered cells with few lymphocytes, plasma cells and neutrophils. Further clinical workup was performed to substantiate large cells. On re-examining the patient, the chest lesions were multiple, painful vesicles with surrounding erythema. On review, CSF cytology shows mature and transformed lymphocytes with viral cytopathic change. Nucleomegaly, cytomegaly and bi/trinucleation were noted. The enlarge nuclei shows Cowdry type A nuclear inclusion. CSF proteins were 57mg/dl and glucose were 63mg/dl. CSF PCR was positive for Varicella Zoster.
Conclusion: Large worrisome cells in CSF need proper substantiation as management of neoplastic vs infective etiology are significantly different. In our case we substantiate viral etiology by several tests and treated appropriately.

Abstract 34

Free Neuropathol 3:14:38

Meeting Abstract

Resolving the diagnosis of HMSN with nerve histopathology and genetics

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Background: Atypical presentations of hereditary motor and sensory neuropathies (HMSN) pose a great diagnostic challenge and delay diagnosis by several years.
Objectives: To describe the diagnostic odyssey of three patients with HMSN.
Material and methods: Case reports of HMSN with atypical presentations
Results: *Case 1*: A 71-years-old gentleman developed progressive paraesthesias and weakness of distal limbs, and imbalance while walking, from 54 years of age. Examination showed distal wasting, pes cavus, global hyporeflexia, and foot drop. Nerve conduction studies (NCS) showed demyelinating neuropathy. Nerve biopsy showed thinly myelinated fibers, regenerating clusters, ill-formed onion-bulbs and epineurial perivascular inflammation. He was treated on lines of chronic inflammatory demyelinating polyneuropathy (CIDP) with multiple courses of intravenous immunoglobulin and steroids. His deficits progressively worsened. Targeted sequencing revealed a novel heterozygous missense variation in *MPZ* (c.223G>T, p.Asp75Tyr).
Case 2: A 54-years-old gentleman manifested with progressive hearing impairment, cramps, and asymmetric weakness and wasting of lower extremities from 34 years of age. He had pes cavus, bifacial weakness, bilateral sensory neural hearing impairment, global hyporeflexia and foot drop. Nerve biopsy showed hypertrophic demyelinating neuropathy. The patient was treated with plasmapheresis, steroids, cyclophosphamide and azathioprine, despite which he continued to develop progressive deficits. Targeted sequencing revealed a heterozygous six-base pair deletion in *MPZ* (c.207_212delGCCCGA, p.Pro70_Glu71del) and a heterozygous missense variation in *DNMT1* (c.1018G>A, p.A340T).
Case 3: A 38-years-old lady presented with paresthesias, weakness and wasting of both lower limbs and poorly controlled diabetes mellitus. Onion bulbs of variable sizes were seen on the nerve biopsy. She was treated on lines of CIDP. Genetic testing revealed *PMP22* duplication.
Conclusion: In view of heterogeneous onset, progression and severity, the diagnosis of HMSN may be delayed. Nerve biopsy coupled with genetic testing can help in avoiding misdiagnosis and inadvertent treatment.

Abstract 35

Free Neuropathol 3:14:39

Meeting Abstract

Understanding the ER stress response to predict clinical outcome in focal cortical dysplasia patients

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Background: Focal cortical dysplasia (FCD) is a significant cause of drug-resistant epilepsy (DRE). Complete seizure-free outcomes are not observed even after surgery in some patients, but the reasons are still unclear. The epileptic patients were found to have severe endoplasmic (ER) stress that led to cellular damage and even cell death.
Objectives: This study focused on understanding ER stress in predicting the post-surgical seizure-free outcome in FCD patients.
Material and methods: Magnetic Resonance Imaging (MRI) and Fluoro Deoxy Glucose Positron Emission Tomography (FDG-PET) tests were used to find the lesion location. After surgery, the samples were snap-frozen with liquid nitrogen and stored at -80 0C. Double immunofluorescence, Hematoxylin & Eosin staining, western blot, Thioflavin-T, and H2O2 neutralization assays were performed. The post-surgical follow-up data was observed for more than three years to determine the clinical outcome.
Results: 10 (34.6%) patients were females in our patient cohort, and 16 (59%) were males. 14, 8, and 4 patients were FCD I, FCD IIa, and FCD IIb, respectively. The follow-up study was performed for more than three years to find the post-operative seizures reoccurrence. Then we categorized the patients according to International League Against Epilepsy (ILAE) guidelines. Ten (38.4%), nine (34.6%) and seven (26.9%) patients were classified into class 1 (complete seizure-free), class 2 (less frequent seizures or auras) and class 3 (frequent seizures) categories. Severe ER stress was observed in class 2 and 3 patients, which further caused the accumulation of reactive oxygen species (ROS) and protein aggregates. In addition to this, we observed upregulation of an apoptosis initiation marker CHOP/GADD54 in the brain samples of ILAE classes 2 and 3 patient samples.
Conclusion: Our data suggest that FCD patients belonging to ILAE class 1 showed reduced protein aggregates and limited ROS had better seizure-free outcomes than the rest. Understanding the ER stress response severity in resected clinical samples can help predict the possibility of post-surgical seizure-free outcomes and hint at the post-surgical anti-epileptic drug (AED) therapy.

Abstract 36

Free Neuropathol 3:14:40

Meeting Abstract

Candida meningitis mimicking tuberculous meningitis in an immunocompetent patient - Diagnostic conundrum

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Background: Fungal meningitis is often associated with immunocompromise due to primary/secondary immunodeficiency, HIV, prolonged antibiotic usage, indwelling catheters, intracranial shunts etc. Candida is the fourth most common cause of nosocomial infections, and the most frequent cause of systemic opportunistic fungal infections, though CNS involvement is rare, representing disseminated infection in severely immunocompromised patients.
Objectives: We present a rare case of Candida meningitis occurring in a middle aged immunocompetent host diagnosed at autopsy.
Material and methods: Case report of candida meningitis in an immunocompetent patient.
Results: A 43-year-old man without co-morbidities (diabetic/hypertension, HIV seronegative), presented with a history of altered sensorium and fever for 6 day. Cranial MRI revealed multiple ring enhancing lesions in putamen, caudate, medial basifrontal and cerebellum. Repeated CSF examination showed no bacterial/fungal growth. He was managed with anti-toxoplasma and anti-tubercular regimen, along with steroids. After seven days of admission patient succumbed. Autopsy revealed thick yellowish white basal exudates in interpeduncular cisterns resembling tuberculous meningitis. Several hemorrhagic necrotizing lesions were seen in left medial frontal, bilateral putamen, thalamus, right insula, bilateral hippocampus and cerebellum. Histopathology revealed multiple necrotizing lesions, with dense vasculitis and clusters of pseudohyphal forms area with angio-invasion closely mimicking Aspergillus *spp* on PAS and GMS stains. However, Gram positivity of “hyphal” forms suggested Candida and cultures from CSF grew *Candida albicans*.
Conclusion: *Candida albicans* is a very rare cause of chronic meningitis, unsuspected in immunocompetent hosts. An antecedent bacterial meningitis, treated with broad-spectrum high dose antibiotics, anemia are high-risk factors. Although rare, this has to be considered in the differential diagnosis of all atypical meningitis even in immunocompetent individuals and serological/PCR tests for fungal etiology should be included in panel of diagnostic tests.

Abstract 37

Free Neuropathol 3:14:41

Meeting Abstract

Rare case of dorsally located multiple neurenteric-cyst without spinal dysraphism – Neuropathology insights and systematic review

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Background: Neurenteric-spinal-cysts (NC) are rare. Most are isolated-ventral, and intradural-extramedullary. Cervical location is commonest. Reports of NC which are multiple, dorsally located, intramedullary and without spinal dysraphism are extremely rare. Are they different embryologically/pathologically?
Objectives: We present a case (less than five are reported till now) of multiple dorsally located NC without spinal dysraphism, one of which was IDEM and the other was intramedullary. We also present a systematic review of all such cases with focus on neuropathology, IHC, and clinic-radiological-pathological correlation.
Material and methods: Case: A 40 years old gentleman with back pain and lower limb weakness for three years underwent gross-total-resection of D10-D11 lesion and partial-resection of conus medullaris lesion with detethering.
Systematic review: As per PRISMA 2009 literature searched in PUBMED, MEDLINE, Web of Science, Scopus, Cochrane, Google Scholar, SCiELO. Neuropathology, surgery, demographics, and outcome extracted. Quality of studies and descriptive statistics applied.
Results: Gross: thick glistening white capsule with cheesy material. Cytopathology: Occasional cell clusters with cilia. Histopathology: Columnar ciliated and mucinous cells, PAS+. IHC: EMA+, CK7+, GFAP-focal+. Search yielded 1,788 citations. Most were male. Lumbar location was common for intramedullary and complete resection was not possible. Most were EMA+, CK7+, and focal-+-GFAP.
Conclusions: Multiple IDEM and intramedullary dorsally located NC without spinal dysraphism are extremely rare. Most of these lesions have characteristic histopathology and IHC findings. It is important to differentiate it from arachnoid cyst for appropriate management. These lesions are distinct from the NC with spinal-dysraphism.

Abstract 38

Free Neuropathol 3:14:42

Meeting Abstract

Efficacy of dimethyl fumarate in chronic constriction injury induced neuropathic pain in rats

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Background: Dimethyl fumarate (DMF) has shown beneficial effects in multiple sclerosis. Further, DMF has demonstrated promising results in experimental models of autoimmune neuropathy and chemotherapy induced peripheral neuropathy.
Objectives: To study the effect and mechanism of DMF in Chronic Constriction Injury (CCI) model of neuropathic pain in rats.
Material and methods:30 male Wistar rats were divided into 5 groups of six rats each as follows: Group I: Sham + Carboxymethyl cellulose (CMC) 0.5%, Group II: CCI + CMC 0.5%, Group III: CCI +Gabapentin (75 mg/kg): Group IV: CCI + DMF (25 mg/kg). Group V: CCI + DMF (50 mg/kg). Animals were anesthetized before surgery. CCI was induced by silk ligature, applied 2 mm apart on sciatic nerve. DMF and Gabapentin were administered daily from day 0 to day 28. Pain threshold was assessed using thermal hyperalgesia, mechanical allodynia and cold allodynia responses on days 0, 7, 14 and 28. Animals were sacrificed on day 28, using high dose of anaesthesia, and sciatic nerve was dissected for histopathological analysis (Hematoxylin & eosin and Luxul fast blue). Plasma proinflammatory cytokine estimation was done for IL-1β, IL-6 and TNF-α. Levels of p38 MAPK and BDNF were quantified by elisa in the dorsal horn of the spinal cord.
Results: A significant increase in the pain threshold parameters was observed. Histopathological analysis demonstrated that DMF significantly reduced the macrophage infiltration and myelin loss in the injured nerve. A significant decrease in proinflammatory cytokines, p38 MAPK and BDNF were observed in the DMF treated animals.
Conclusion: The present study suggested that DMF reduces CCI neuropathic pain by protecting the peripheral nerves and preventing the central sensitization.

Abstract 39

Free Neuropathol 3:14:43

Meeting Abstract

Moya Moya Disease: An autopsy case study

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Background: Moya Moya disease is a rare chronic cerebrovascular disorder characterized by progressive narrowing of distal ICA and proximal components of MCA and ACA leading to formation of collateral vessels which resembles a 'puff of smoke' on angiography. It is an uncommon cause of stroke in adults and children.
Objective: To illustrate the pathologic features of Moya Moya Disease with the help of autopsy findings.
Material and methods: A 31 year diabetic patient presented with slurring of speech since 20 days associated with headache, moderate, non-throbbing type. This was followed by sudden onset weakness of right upper and lower limb. Examination revealed right UMN facial palsy with right hemiplegia. MRI Brain showed infarcts in left frontal white matter region with right supraclinoid ICA and right ACA narrowing. Patient was diagnosed as stroke with possible CNS vasculitis. He was treated with IV steroids, cyclophsophamide and antibiotics. His condition did not improve. He developed pneumonia and succumbed on day 18 of admission.
Results: A complete body autopsy was performed after informed consent. The brain showed extensive subarachnoid hemorrhage. The sections from bilateral ICA and MCA showed intimal prolifetaion of smooth muscle cells with reduplication of IEL, irregular undulation of the internal elastic lamina and duplication. There was no evidence of vasculitis. Bilateral lobar pneumonia was seen in lungs.
Discussion: Sporadic MMD is common in East Asian countries. Intracerebral or ventricular hemorrhage is the catastrophic events leading to mortality. However, SAH has been described rarely. The vascular morphology of this disease is also well characterized in this autopsy study which helps to rule out fibromuscular dysplasia, atherosclerosis and vasculitis.
Conclusion: MMD is an uncommon cause of stroke in adults. It needs to be differentiated from moya moya syndrome which can occur due to secondary causes. Subarachnoid hemorrhage is an uncommon complication.

Abstract 40

Free Neuropathol 3:14:44

Meeting Abstract

Hematolymphoid malignancies presenting with neurological manifestations and hand-mirror cells in peripheral blood: Report of two cases

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Background: Hematolymphoid malignancies involve myeloid and lymphoid cell lineages and affect blood, bone marrow, lymph nodes and lymphatic system. Clinically they may present with features suggestive of systemic involvement. CNS involvement is not uncommon. These malignancies may present with hand- mirror cells in peripheral blood which can be the initial findings of such malignancies.
Objectives: This study aims to emphasize that the presence of hand-mirror cells should prompt appropriate investigations, workup, and management.
Material and methods: This study includes two patients, first, an adolescent male and second, a middle-aged female patient who separately presented with back pain and bilateral lower limb weakness. T
Results: The peripheral blood smears of both patients revealed atypical cells, hand-mirror cells and thrombocytopenia. Imaging studies showed extradural spinal lesions in both cases. Flow cytometric immunophenotyping of the first patient showed features suggestive of acute myeloid leukaemia. Both underwent laminectomy. The histopathological study of the laminectomy specimen of the first patient showed features of myeloid sarcoma and that of the second patient showed diffuse B cell lymphoma.
Conclusions: Hand-mirror cells can be seen in both malignant and non-malignant conditions. However, their presence may be the initial finding in peripheral blood that indicates underlying malignancy with or without symptomatology and leucocytosis. Their presence should prompt the pathologist to recommend further evaluation for the diagnosis and management of hematolymphoid malignancies.

Abstract 41

Free Neuropathol 3:14:45

Meeting Abstract

Mullerian choristoma as a cause of tethered cord syndrome: A case report in a 13-year-old worsening after the onset of menarche

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Background: Mullerian choristoma as a cause for tethered cord syndrome is exceedingly rare with very few cases being reported in the literature.
Objectives: To document a rare cause of tethered cord syndrome
Material and methods: Case report of a 13-year-old girl with spinal dysraphism who was operated in 2013 for lipomeningomyelocele and tethered cord.
Results: The patient now presented to us with back pain and leg pain for 6 months duration. MRI of lumbosacral spine revealed an intra medullary cystic mass in the conus medullaris associated with haemorrhage in association with the residual lipoma. Intraoperatively following excision of intramural lipoma, a hemorrhagic cystic intramedullary mass was encountered and excised. Histopathology of the mass revealed a uterus like structure with endometrial lining and associated structure resembling fallopian tube. A diagnosis of Mullerian choristoma was made.
Conclusion: Mullerian choristoma is a rare cause of tethered cord syndrome.

Abstract 42

Free Neuropathol 3:14:46

Meeting Abstract

Plurihormonal Pit-1-positive adenoma: A short series

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Background: Plurihormonal Pit-1-positive adenoma is a newly described entity in the 2017 WHO classification of tumors of endocrine organs with an aggressive behaviour.
Objectives: A histopathological study of plurihormonal Pit-1-positive adenomas diagnosed at our Institute in last 5 years.
Materials and methods: This is a retrospective study. Routine Haematoxylin and Eosin (H & E), immunohistochemistry for pituitary hormones, pituitary transcription factors (Pit-1, Tpit), MIB-1 and p53 were performed in all cases.
Results: Seven cases of plurihormonal Pit-1-positive adenomas were diagnosed. The patient age ranged from 10-51 years (median: 35 years) with 4 males and 3 females. Four adenomas presented with acromegaly and 3 with decreased vision. All adenomas, with the exception of one were primary. Four adenomas were invasive and 3 were non
invasive. On immunohistochemistry, the most extensively expressed hormones were GH and PRL, followed by TSH-beta and alpha-subunit. ACTH was negative in all, except in one adenoma. Pit-1 was diffusely expressed in all adenomas and Tpit was negative. The MIB-1 labelling index ranged from 1%-7% (median: 3%). All patients were treated with surgery and one patient received radiotherapy for residual disease. The follow-up period was 5-24 months (median: 13 months) and all patients were alive and free of disease at last follow-up.
Conclusions:

1. GH, PRL, TSH-beta and alpha-subunit were co-expressed in all adenomas, with one adenoma also expressing ACTH.
2. Pit-1 was diffusely expressed in all tumors.
3. There was almost equal distribution of invasive and non-invasive adenomas and median MIB-1 labelling index was 3%.

Abstract 43

Free Neuropathol 3:14:47

Meeting Abstract

An interesting case of extradural tumour in a pediatric patient

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Background: Ewing's Sarcoma is a highly malignant bone tumour, belonging to a family of small round blue cell tumors, derived from primordial bone marrow- derived mesenchymal stem cell which typically affects the pelvis and the long bones of the lower extremities. It's primary involvement of the skull is encountered in only 1% cases.
Objectives: To describe a rare extradural sarcoma in paediatric patient.
Material and methods: Case report of a pediatric case with extradural tumour.
Results: We present a pediatric case with rapidly growing, painless swelling over the left temporal region, not compressible and fixed to the scalp and underlying bone.
Patient underwent gross total resection of the tumour with adjuvant chemotherapy and radiation. He had a favourable outcome without any neurological deficit. No local or systemic recurrence was found at 12 months postoperatively.
Conclusion: Intracranial Ewing Sarcoma/pPNET is a rare tumor with nonspecific clinical presentation and radiological findings. They are locally invasive. Gross Total Excision with adjuvant chemoradiation is the mainstay of treatment.

Abstract 44

Free Neuropathol 3:14:48

Meeting Abstract

Case report of rare extra axial cerebellopontine angle medulloblastoma, a meningioma mimicker: Caution advised

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Background: Medulloblastoma, the most common malignant paediatric brain tumour, presents as a posterior fossa intra-axial mass. It infrequently affects adults forming less than 1% of intracranial tumours. Very rarely, it is found in extra-axial locations. To the best of our knowledge, less than 50 cases of extra-axial medulloblastomas have been reported in literature, majority in cerebellopontine (CP) angle, affecting mainly adults and very few with dural attachment.
Objectives: To present a rare case of extra-axial tentorial medulloblastoma in an adult with radiological features of a meningioma expanding the differential diagnoses of lesions with dural attachment in the CP angle
Materials and methods: Case report of a CP angle tumour
Results: A 40-year-old man presented with headache, imbalance and recent onset vomiting. MRI revealed an extra-axial lesion in left CP angle arising from the inferior tentorium cerebellum, with dural tail, radiologically considered as meningioma. The patient underwent excision of lesion, and dural attachment was noted intraoperatively with no cerebellar involvement. Histopathology revealed a classic medulloblastoma with stromal desmoplasia, and immunoprofile consistent with SHH-activated, p53 wildtype molecular subtype: Beta catenin (-), GAB1(+), YAP1 focal (+), p53 negative, OTX2(-)
Conclusion: Medulloblastoma rarely presents in the CP angle with tentorial attachment leading to its omission in the differential diagnoses. Available literature cites that WNT- and SHH-activated subtypes are seen in extra axial medulloblastoma. This report highlights the importance of its consideration in atypical posterior fossa extra-axial lesions. Strong suspicion can lead to early detection, prognostication and appropriate management.

Abstract 45

Free Neuropathol 3:14:49

Meeting Abstract

Potpourri of five cases of rare central nervous system tumors with review of literature

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Background: The overall annual incidence rate of all brain tumours are 7 per 100 000 population. Meningioma is the most common brain tumor, accounting for about 30 percent of them. Here we are presenting 5 unusual & rare cases of CNS tumours.
Objectives: To study the clinicomorphological & radiological features of unusual Central nervous tumors (CNS) & its association with any systemic diseases.
Materials and methods: Case reports of 5 cases
Results: 1. A 5 years old female child presented with a swelling in the Frontal region. 2. 35-year-old woman was presented with leg weakness, numbness, seizures and headache for 18 months. 3. 41 years old male who presented with a 9 months history of headache, double vision & leg weakness. 4. A 50 years old Male presented with headache & visual disturbances of 6 months. 5. 11 years old child was presented with bilateral nasal obstruction & discharge for one year. H/o Headache for 7 months. Radiological imaging was done & Patients were underwent tumor resection & submitted for histopathological examination.
Conclusion: Herewith discussing one case of Langerhans cell histiocytosis (LCH), one case of Chordoid meningioma, one case of Chordoma, one case of Primary lymphoma & one case of Pituitary tumor. Hence, we have to correlate with clinical, radiological, histopathological & Immunohistochemical markers for final diagnosis and thereby providing therapeutic implication. Follow up & further treatment is needed to prevent recurrence.

Abstract 46

Free Neuropathol 3:14:50

Meeting Abstract

Primary yolk sac tumor of cerebellar vermis: A case report

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Background: Extragonadal germ cell tumors are rare and usually occur along midline of body. Primary yolk sac tumor (YST) of brain is rare, however occurs usually in pineal and suprasellar regions. We present a rare case of primary cerebellar vermis YST.
Objectives: To report a rare case of cerebellar yolk sac tumour.
Material and methods: Case report of biopsy proven yolk sac tumour of the cerebellum.
Results: A 3-year old male presented with ataxia, vomiting and decreased feeding which the parents noted around 15-20 days back. Contrast-enhanced MRI revealed a left cerebellar lesion involving vermis, with perilesional edema which was isointense on T1 and T2 hyperintense. Intense contrast enhancement was noted. Radiological possibilities suggested were medulloblastoma and atypical teratoid/rhabdoid tumor. Intra-operative frozen section was sent and the smears showed markedly pleomorphic cells in small glands, papillae and dispersed singly. A diagnosis of germ cell tumor was rendered. Definitive sections showed a tumor with cells arranged in a myriad of histological patterns, including reticular microcystic pattern, glands and solid areas. Other classical features seen were presence of PAS positive intracytoplasmic hyaline globules and numerous Schiller Duval bodies. A diagnosis of yolk sac tumor was rendered and the child was started on chemotherapy 2 weeks back. No mediastinal or testicular lesions were identified.
Conclusion: Primary YST of cerebellar vermis is a rare entity. A knowledge of such entities is helpful in timely diagnosis and appropriate patient management.

Abstract 47

Free Neuropathol 3:14:51

Meeting Abstract

A diagnostic dilemma - Astroblastoma

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Background: Astroblastoma is an extremely rare CNS tumor, accounting for 0.45 to 2.8% of all neuroglial tumors. It was first described by Bailey and Cushing in 1926 and further characterized by Bailey and Bucy in 1930.According to published data there is slight female preponderance and bimodal age distribution with one peak between 5-10 years and other between 21-30 years.
Objectives: To study a rare case of Astroblastoma.
Material and methods: After diagnosing on H&E correlation with the radiological investigation was done. Subsequently Immunomarker study and Molecular workup by FISH was done.
Results: On H&E Differential diagnosis of i) Well differentiated Astroblastoma ii) Papillary ependymoma iii) Atypical choroid plexus papilloma /CA was given and further workup was advised. IHC marker and Molecular information by FISH assay confirms the diagnosis of Well differentiated Astroblastoma.
Conclusion: Astroblastoma is a very rare primary brain tumor. Its diagnosis is often challenging because of the astroblastic aspects that can be found in astrocytic tumors in ependymoma and in non-neuroepithelial tumors. The low incidence rate makes it difficult to conduct studies to examine tumor characteristics. The exact histogenesis of Astroblastoma is controversial. Patient with astroblastoma should be treated with curative intent.

Abstract 48

Free Neuropathol 3:14:52

Meeting Abstract

Meningioangiomatosis: A rare cause of refractory temporal lobe epilepsy

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Background: Meningioangiomatosis is a rare meningovascular malformation or hamartomatous lesion responsible for refractory seizures. Radiographic appearance can be highly variable and histopathology is necessary for confirmed diagnosis.
Objectives: To describe a case of Meningioangiomatosis
Materials & methods: A 27-year male, with no co morbidities presented with seizures since 15 years. He was treated with antiepileptic agents however there was no change in seizure pattern. The frequency of seizures increased from 4-5 episodes/month to 8 -10 episodes/month. The EEG showed abnormal record with diffuse slowing of left temporal epileptiform focus. MRI Brain – Focal fairly smooth expansion of left squamous temporal bone with slight sclerosis of inner cortical region. He underwent left temporal lobectomy and hippocampectomy
Results: The temporal neocortex showed a well circumscribed mass of 3X2cm with white fibrous appearance on cut section. The histopathology of the mass showed a lesion comprised of multiple vascular channels surrounded by bland spindle cells. These cells have oval to elongated nuclei with intranuclear inclusions. Multiple psammoma bodies were identified. There was no atypia. The cells showed immunoexpression for EMA and vimentin. Hippocampus showed loss of neurons in CA1, CA3 and CA4 regions with dispersion and bilayering of granular neurons of dentate gyrus.
Conclusion: Meningioangiomatosis is a very rare hamartomatous lesion associated with epilepsy. The preoperative consideration is important as prognosis with surgical resection is good.

Abstract 49

Free Neuropathol 3:14:53

Meeting Abstract

Isolated cerebral Rosai Dorfman disease with granulomatous angiitis

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Background: Rosai Dorfman is a non-dendritic, non-Langerhans histiocytic disorder. Isolated intracranial involvement without lymphadenopathy is uncommon. Only one report in brain and lung respectively documented a coexistent granulomatous angiitis.
Objectives: Case report of an uncommon association between two rare cerebral entities.
Material and methods: A 30-year-old male presented with seizures, limb weakness and violent behaviour since 3 months. There was no fever, lymphadenopathy or hepatosplenomegaly. Complete hemogram, ESR, hepatic and renal function tests were normal. Serology was negative for retrovirus and autoantibodies. On radioimaging, parietotemporal lobe showed a large mass 8.6 x 7.4 x 3.2 cm. It was hypointense on T1W1, hypointense on T2W1/ FLAIR and heterogenously contrast enhancing. MR Spectroscopy showed reversed NAA/Cr and increased Cho/Cr ratio suggestive of primary CNS lymphoma, glioblastoma and tumefactive demyelination. Subtotal resection was done.
Results: Histopathology revealed sheets of mature lymphocytes, plasma cells, foamy histiocytes showing emperipolesis, Touton giant cells and florid granulomatous angiitis with resultant coagulative necrosis. There was absence of eosinophils, Langerhans cells or atypical lymphoid cells. The differentials included lymphomatoid granulomatosis, tuberculosis, tumefactive demyelination and Wegener's granulomatosis.
Tumor cells were positive for CD68 and S100, while negative for CD1a, EBER and IgG4. Fungal and mycobacterial stains were negative. Thus, Rosai Dorfman disease with coexistent granulomatous angiitis was diagnosed. On follow up for six months, there was no recurrence or new lesions.
Conclusion: Only two cases in literature (cerebral and pulmonary) show granulomatous angiitis associated with emperipoletic histiocytic tumefaction. An overlap between IgG4 related disease and Rosai Dorfman is also postulated.

Abstract 50

Free Neuropathol 3:14:54

Meeting Abstract

Twin tales of anaplastic ependymoma with extensive vacuolation/signet cell change and lipomatous differentiation

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Background: Ependymomas are circumscribed glial tumours with unique morphology. The diagnosis is relatively straightforward in the majority of the cases. However, there are scenarios where the morphology is obscured leading to diagnostic difficulty. We present two such cases of supratentorial anaplastic ependymoma in pediatric age group with one showing large areas of vacuolated/ signet-ring change and another showing lipomatous differentiation.
Objectives: To describe uncommon histological features in ependymoma
Material and methods: Case reports of two cases with histopathological description.
Results: *Case 1* is a 9-year-old male child with a well-defined intra-axial, lobulated solid cystic lesion (4.5x3.6cm) in the right parieto-temporal region. Biopsy showed monomorphic tumour cells interspersed with large areas of vacuolated cytoplasm/signet ring change in large areas posing a diagnostic challenge. These cells showed strong and diffuse perinuclear cytoplasmic dot-like positivity for EMA along with diffusely positive GFAP. However, the tumour recurred within 11 months showing anaplastic morphology lacking the previous features. *Case 2* is a 3-year-old male child with similar presentation except in this case there was lipomatous change mimicking adipocytes in large areas posing diagnostic difficulty.
Conclusion: Lipomatous change, vacuolation and signet ring change has been reported in ependymoma in few reports. The origin of vacuolar change is still debated. Some reports state it as dilation of intracytoplasmic membrane and some as metaplasia. These changes have been observed in other tumours like neurocytomas, medulloblastomas, cerebellar and spinal cord astrocytomas. There can be confusion between clear cell ependymoma and areas showing oligdendroglial proliferation as both show cytoplasmic clearing. In tumours with extensive change, search for classical areas and immunohistochemistry can facilitate the diagnosis.