P1-1

The boundaries and essence of anti-MOG syndrome

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Introduction: Myelin-oligodendrocyte glycoprotein (MOG) is a specific antigen on the outer surface of myelin sheaths. During recent years, MOG antibodies have been increasingly described in pediatric acute disseminated encephalomyelitis, optic neuritis, aquaporin-4 antibodies negative neuromyelitis optics spectrum disease (NMOSD) and even autoimmune encephalitis. However, the demographic and clinical boundaries of anti-MOG syndromes are ever changing. And its pathological alterations are also rarely described.(break)
Methods: Case reports and review of the literatures.(break)
*Results:*Case 1: Retrospective serum and CSF analyses confirmed MOG antibodies in a 63-year-old female patients with 17 clinical episodes (optic neuritis 13 times, brainstem involvement twice and myelitis twice) during 15 years. This case was compatible with aquaporin-4 antibodies negative NMOSD.(break)
Case 2: An 83-year-old male patient developed bilateral blurred visions, paresis of lower extremities and bladder dysfunction within a week. MRI showed multiple optic nerve, brain and spinal cord lesions. His clinical and radiological features also fulfilled clinical diagnostic criteria of aquaporin-4 antibodies negative NMOSD. Retrospective serum analysis confirmed MOG antibodies.(break)
Case 3: A 39-year-old female present in department of neurosurgery for a left parietal lesion with mass effect. Due to concerns of a neoplastic process, a biopsy was undertaken. Neuropathology showed active T cell dominant inflammatory demyelination with proliferation of astrocytes and relative preservation of axons.(break)
*Conclusions:*Anti-MOG syndrome can present with dozens of relapses and developed in elderly patients over 80 years old. Its associated demyelinating disorders pathologically mimic multiple sclerosis and distinct from aquaporin-4 antibodies positive NMOSD.

P1-2

MS lesion characteristics in Netherlands Brain Bank autopsy cohort: clinical and genetic correlates

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Introduction: We aim to better understand the pathogenic mechanisms underlying the substantial clinical heterogeneity seen in Multiple Sclerosis (MS), which currently remains largely unknown. Therefore we have studied the clinical and genetic correlates of MS lesion characteristics in the Netherlands Brain Bank MS autopsy cohort.
Methods: From 182 MS brain donors, 3188 tissue blocks containing 7562 MS lesions were dissected. Lesion demyelinating and inflammatory activity were visualized by immunohistochemistry for PLP and HLA-DR-DQ. Lesions were classified into active, mixed active/inactive, inactive or remyelinated, microglia/macrophage morphology was classified as ramified, amoeboid or foamy. The severity score was calculated from the time from first symptoms to EDSS-6. Donors were genotyped for 83 SNPs that were associated with clinical disease severity in GWAS studies and 22 SNPs in genes associated with MS lesion characteristics.
Results: We found that despite a relatively long mean disease duration of 28.6±13.3 years (mean±SD), active or mixed active/inactive lesions were present in 78% of all patients. Patients that had a more severe disease course showed a higher proportion of mixed active/inactive lesions (p=6e-06) and a higher lesion load (p=2e-04). Five SNPs showed a significant association with the proportion of active MS lesions or cortical grey matter lesion incidence.
Conclusion: MS lesion activity is substantial in progressive MS and correlates with clinical disease severity. Moreover, disease severity-linked genotypes correlate with higher proportions of active lesions. With these findings we begin to translate genotypic information into pathogenic mechanisms, which may facilitate the development of personalized therapeutic approaches in MS.

P1-3

Perivenous inflammatory demyelination is the prominent pathology in myelin oligodendrocyte glycoprotein antibody-associated disease

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Introduction:
Conformation-sensitive antibodies (Ab) against myelin oligodendrocyte glycoprotein (MOG) is detectable in a proportion of patients with inflammatory demyelinating diseases including optic neuritis, acute disseminated encephalomyelitis (ADEM) and neuromyelitis optica. Meanwhile typical multiple sclerosis (MS) is essentially negative for MOG-Ab. In several case reports on biopsied brain lesions in patients with MOG-Ab, the lesions were characterized by T-cell plus antibody-mediated demyelination (pattern II MS lesions). However, it is unclear whether MOG-Ab-associated demyelinating plaques show sharply demarcated confluent demyelination as seen in MS.
Methods:
We immunohistochemically analyzed biopsied brain tissues from five patients with MOG-Ab in our cohort.
Results:
The patients' median age at onset was 24 years-old (range 9-64) and the median interval from onset to biopsy was 1 (range 0.5-2) month. The clinically diagnoses were ADEM in two, multiple brain lesions without encephalopathy in two and leukoencephalopathy in one. All brain biopsies were performed before acute phase treatment. Pathologically, perivascular cuffings with T cells and macrophages were conspicuous in all cases. B cell infiltration was also observed in three. ADEM-like multiple perivenous demyelinating lesions were seen in all cases, and the case with leukoencephalopathy had confluent demyelinated lesions as well. Loss of MOG staining was relatively more remarkable compared to other myelin protein stainings. Varied deposits of complement and immunoglobulin were found around some blood vessels and myelin sheath.
Conclusions:
Our study suggests that ADEM-like perivenous inflammatory demyelination with variable cellular and humoral immune reactions is the prominent pathology in MOG-Ab-associated demyelinating disease.

P1-4

Multifocal central nervous system demyelination in a 40 year old: is it paraneoplastic?

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Introduction: Etiologies for central nervous system demyelination are diverse and diagnosing them can be challenging.

Clinical summary: A 40 year old male presented with gait ataxia and dysarthria of 3 months duration. In spite of steroid therapy for suspected demyelinating disorder, he worsened with lower limb weakness and urinary retention. MRI showed multiple non-enhancing T2/FLAIR hyperintensities in bilateral cerebellum and frontal lobes with a short enhancing lesion in spinal cord at T4-T5. CSF study showed lymphocyte predominant pleocytosis (15cells/ mm^3,90% lymphocytes), mildly elevated proteins (98mg/dl) and normal sugar. CSF and serum were positive for oligoclonal bands and serum negative for Aquaporin-4 antibody. Work-up for vasculitis, infection (fungal, tuberculosis, toxoplasmosis, etc) and malignancy was negative. Plasma exchange was initiated, however he developed sepsis and succumbed.

Pathological findings: At autopsy, cerebral hemispheres were mildly atrophic. Coronal sections showed softened white matter around bilateral occipital horns and in corpus callosum. Microscopically, multiple small, well-defined to confluent foci of demyelination were noted in frontal, occipital and cerebellar white matter. All the lesions appeared to be of similar age and were associated with mild perivascular CD8-predominant T-lymphocytic infiltration. Spinal cord white matter was focally rarefied. There was no evidence of metachromatic material, viral inclusion, vasculitis or neoplasm. Immunohistochemistry for JC virus, measles and toxoplasma were negative. Examination of other organs showed a latent papillary microcarcinoma in the thyroid gland.

Conclusion: CNS demyelination as a paraneoplastic phenomenon is uncommon and very rarely has been reported with papillary thyroid carcinoma. Could this case be a paraneoplastic phenomenon?

P1-5

The antidepressant effect of ketamine in a murine model of neuroinflammation involves the modulation of microglial activation

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Introduction: Depression is a severe condition that represents a major public health issue. Current therapies, targeting primarily monoaminergic neurotransmission systems, are partially ineffective due to their long response time and low remission rates. Studies have demonstrated a link between neuroinflammation and depression. Ketamine, an NMDA antagonist, has recently risen as a novel therapy to treat depression, notably in chemically resistant depressive patients. Recent studies suggest that ketamine might exert its effects through immunomodulating properties.

Methods: In a LPS-induced depressive-like behavior using a mutant mouse model ($CX3CR1^{GFP/+}$ mice with fluorescent microglial cells), we carried out a combination of two complementary approaches: clinical (behavioral tests) and functional associating morphological (histology/morphometry techniques combined with automatized 3D confocal microscopy allowing fine analysis of microglial cells morphology/reactivity), phenotypical and proteomic characteristics.

Results: We demonstrate that a single dose of ketamine attenuates and restores the LPS-induced depressive-like behavior at multiple levels: i/ by reversing anhedonia and anxiety at a behavioral level, ii/ by decreasing the levels of pro-inflammatory cytokines and by shifting the microglial immuno-phenotype to M2a in preference to M1 and M2b and iii/ by reducing the microglial morphological alterations induced by LPS injection.

Conclusion: Taken together, these data show that ketamine might have its antidepressant effect mediated by an anti-inflammatory action on microglia cells.

P1-6

Immunophenotype of lymphocytic primary angiitis of the central nervous system: a case study

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Introduction: The reports on immunohistochemical profiles about primary angiitis of the central nervous system (PACNS) are scant. Here we report a lymphocytic PACNS case. Clinical summary: A 31-years-old man without past medical history fell down suddenly and showed generalized seizure for a few minutes. Neurological examinations showed only amnesic aphasia. Brain MRI revealed multiple cortical and subcortical high intensity lesions in the left temporal and occipital lobes on FLAIR and T2-weighted images, many of which presented with small ring-enhancement. Cerebral angiography showed no significant regional stenosis. Blood investigations showed no findings with suspected neither inflammatory, infectious, nor collagen diseases. Cerebrospinal fluid analysis indicated mild increased protein concentrations with elevation of IL-6, anti-glutamate receptor antibodies, and granzyme B. Brain biopsy revealed lymphocytic vasculitis compatible with PACNS. Treatment with prednisolone and cyclophosphamide resolved both his clinical features and abnormal MRI findings. Pathological findings: Hematoxylin and eosin staining showed marked infiltration of lymphocytes without evidence of atypia and monoclonality, presenting with stenosis of arterioles in the cerebral parenchyma and meninges. Immunohistochemistry for lymphocytic markers revealed that CD3-positive T cells, which mainly consist of CD8-positive T cells, and CD20-positive B cells obviously infiltrated in the vessel wall and perivascular space, but randomly in the cerebral parenchyma. CD138-positive cells were not detected anywhere. Conclusion: Although the number of literatures showing the immunophenotypes of PACNS are limited, a mixed population of CD8-positive T cells and CD20-positive B cells in the affected vessels and brain tissue may be one of the common characteristics of lymphocytic PACNS.

P1-7

Brain biopsy findings in a patient with MOG antibody-associated encephalitis

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Introduction: Myelin oligodendrocyte glycoprotein (MOG) is a protein expressed on the surface of myelin sheath and oligodendrocyte. Pathological findings in patients with MOG antibody-associated encephalitis have, however, rarely been described to date. Clinical summary: A 44-year-old Japanese male developed fever and mild aphasia followed by impaired consciousness, agnosia, hiccup and urinary retention. Brain MRI revealed a Gd-enhancing mass lesion in the left frontal white matter. Cerebrospinal fluid analysis demonstrated lymphocytic pleocytosis on cytology and oligoclonal bands. Neoplastic conditions were unlikely on brain biopsy performed on Day 33 after onset. Clinico-radiological findings improved gradually after methyl-prednisolone pulse therapy followed by oral prednisolone. Thereafter, anti-MOG-antibodies turned out to be positive. Pathological findings: Microscopically, glioneuronal tissue showed microvacuolation with reactive gliosis in addition to perivascular and parenchymal lymphocytic inflammation, associated with histiocytic reaction predominantly composed of CD68-positive activated microglia in the parenchyma. Lymphocytes were predominantly composed of CD8-positive T-lymphocytes located in perivascular spaces. CD20-positive B-cells were confined to the perivascular spaces. Neither demyelinating lesions nor myelin laden macrophages were observed. Immunoreactivity for activated complement (C9neo antigen) was not detected. Conclusions: Pathological findings of MOG antibody-associated encephalitis were reported. A major findings were vacuolar change with T-cell dominant inflammation without typical demyelination, which were distinct from the previously reported findings such as T-cell-mediated inflammation with complements-associated demyelination. This case indicates the MOG antibody-related disease might be a heterogeneous in terms of pathophysiology.

P1-8

The pathological features of MOG antibody-positive cerebral cortical encephalitis as a new spectrum associated with MOG antibodies

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Introduction: Recently we experienced several adult patients with myelin oligodendrocyte glycoprotein (MOG) antibody-positive cerebral cortical encephalitis, whose clinical characteristics were different from the demyelinating disease associated with anti-MOG antibodies, including acute disseminated encephalomyelitis and aquaporin-4 seronegative neuromyelitis optica spectrum disorders. Here, we present the first pathology before immune therapy in an adult patient with MOG antibody-positive cerebral cortical encephalitis. *Clinical summary:* A 29-year-old healthy Japanese woman experienced generalized tonic seizure with an oedematous, FLAIR high-intensity lesion involving the right parietal cortex on the brain MRI. After a brain biopsy we found her serum anti-MOG antibodies positive. She underwent a full recovery with steroid therapy, and her anti-MOG antibody finally became negative. *Pathological findings:* A brain biopsy revealed mild inflammatory changes in the cortex and subcortex without distinct demyelination, although previous pathological reports with anti-MOG antibodies showed typical demyelination. There was the limited loss of MOG immunoreactivity accompanied by microglial proliferation in perivascular regions and the subcortical white matter in a patchy manner. *Conclusion:* From this case, we speculate that MOG antibody-positive cerebral cortical encephalitis may be clinicopathologically different from the well-known demyelinating disease. We propose that this disease will be a new spectrum associated with anti-MOG antibodies.

P1-9

Chronic leukoencephalopathy-like disease expansion and massive necrosis of the cerebral white matter in a patient with neuromyelitis optica

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Introduction: We describe an autopsy case of a patient with neuromyelitis optica (NMO) who exhibited a unique pattern of disease progression with regard to whit matter lesions. *Clinical summary:* We report the case of a woman with NMO who exhibited bilateral optic neuritis, longitudinally extensive myelitis, serum anti-aquaporin 4 (AQP4) antibodies. The disease duration was 26 years, and the patient died at the age of 65. Sequential magnetic resonance images revealed leukoencephalopathy-like lesions extending symmetrically and contiguously from the periventricular regions, which had begun to transform into multiple cavities with semi-annular partitions. *Pathological findings:* On autopsy, the patient's brain weighed 985g. The periventricular and cerebellar white matter were necrotic, with semi-annular partitions characterised by demyelination and fibrillary giosis. Severe loss of the ependymal linings adjacent to the lateral ventricles was observed, along with gliosis and AQP4-hyperreactivity, AQP4-immunoreactiviey was partially decreased in the remaining ependymal cells. AQP4-immunonegative, glial fibrillary acidic protein (GFAP)-immunonegative, and myelin basic protein (MBP)-immunopositive lesions were observed in the cerebral white matter surrounding the necrotic lesions. The cervical and thoracic regions of the spinal cord were severely atrophic, exhibiting longitudinal central necrosis and blood vessel hyalinisation. Lymphocyte infiltration was observed surrounding the vessels in the sacral cord. There were no vasculitic changes in the vessel walls of the general organs or central nervous system. *Conclusion:* These neuropathological abnormalities corresponded to those described in previous reports regarding NMO lesions. Our findings indicate that expansive, chronic leukoencephalopathy-like lesions can be observed in patients with NMO.

P1-10

Five cases of cerebral amyloid angiopathy related inflammation/angiitis diagnosed with brain biopsy

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Introduction: Cerebral amyloid angiopathy-related inflammation/angiitis (CAA-RI) is rare inflammatory disease of the central nervous system, associated with the clinical symptoms include subacute cognitive impairment or seizure. High diagnostic accuracy was reported with a small pathologic series, however, the pathological spectrum of CAA-RI is still unknown. We investigated the findings of brain biopsy of 5 patients with CAA-RI to evaluate the inflammatory response and the effect of treatment.Materials and methods: The average age of patients was 68.4 (53-80). All patients were men. Initial symptoms were subacute progressive dementia (3), seizure (1) and left sided motor dysfunction (1). Most patients had cerebral microbleeds, focal subarachnoid hemorrhage, asymptomatic small infarction and leptmeningeal enhancement on head MRI. We diagnosed all patients as CAA-RI with brain biopsy and treated them with corticosteroid 1mg/kg/day. Results: We investigated severity of inflammation and Alzheimer Disease (AD)-related pathology. All patients had severe CAA. Two patients had severe to moderate granulomatous angiitis of subarachnoid and parenchyma artery, but its AD-related pathology was minimum. Other 3 cases had mild inflammation around its subarachnoid and parenchyma arteries associated with moderate to severe AD related pathology. The effect of corticosteroid therapy was more prominent in 2 patients with severe to moderate granulomatous angiitis. Conclusion: Clinical symptom and pathologic severity of CAA-RI were various. The effect of corticosteroid therapy was related to pathologic findings. Severity of inflammation and concomitant AD related pathology appears associated with the responsiveness of treatment. CAA-RI could also influence the clinical course of AD.

P1-11

MOG antibody positive meningo-leukoencephalitis with demyelination

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Introduction: Myelin oligodendrocyte glycoprotein (MOG) antibodies are found in pediatric patients with demyelinating disease and patients with aquaporine 4 antibody-negative neuromyelitis optica spectrum disorders. Recently MOG antibodies have been identified in some patients with cerebral cortical encephalitis with epilepsy. In a report of similar case, brain biopsy revealed brain edema and perivascular cuffing. Myelin sheaths were preserved. The pathogenic roll of MOG antibody in this cortical involvement remains unclear. Clinical Summary: A 21 year-old man presented with repeated left-side motor seizures and progressive left hemiparesis. His brain MRI showed fluid attenuation inversion recovery (FLAIR) hyper-intensities involving the cortex and subcortical white matter of the right frontal, parietal and left medial parietal lobe, with gadolinium-enhancement along the sulci. After admission he developed bilateral optic neuritis. Brain biopsy was performed and pathological diagnosis during surgery was meningoencephalitis. Treatment with corticosteroids was started and he responded well. Retrospective analysis of the serum and cerebrospinal fluid confirmed to be positive for MOG antibodies. Pathological findings: Brain biopsy revealed inflammatory cell infiltration with lymphocytes and neutrophils of subarachnoid space and cerebral cortex. Myelin sheaths were preserved in some biopsy samples. The other sample of subcortical white matter showed a demyelinating lesion with foamy macrophages. Axons were relatively preserved in the same area. Conclusion: Demyelination was observed in our patient with MOG antibody-positive cerebral cortical encephalitis. This finding favors the hypothesis of direct pathogenicity of MOG antibodies.

P1-12

DNA double-strand breaks in oligodendrocytes - the unifying step prior to myelin degeneration in Alzheimer's dementia and multiple sclerosis

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Introduction: Myelin degeneration is one of the earliest structural changes in the human ageing brain. Such pathology is obvious in frontal lobe and exacerbated in cognitive impairments. We have previously shown that DNA damage, but not amyloid deposition, is associated with oligodendrocyte loss in Alzheimer's dementia(AD). Here, we further hypothesize that genomic injury with DNA double-strand breaks(DSBs) in oligodendrocytes is the initiating cellular pathology prior to myelin loss in the canonical demyelinating disease, multiple sclerosis(MS). Methods: To test, oligodendrocytes and their DSBs burden in the frontal cortices were studied using immunohistochemistry. Three cohorts of postmortem specimens, including sporadic AD (n=29), familial AD (n=7), multiple sclerosis (n=12) and their age-matching controls were examined. To confirm, RNA-seq databases of oligodendrocyte differentiation and MS lesions(GEO-NCBI) were queried. The effects of DSBs on oligodendrocytes was experimentally tested at their distinct stages of differentiation using primary cell culture. Results: While histological quantifications are being completed, our preliminary results revealed the deposition of DSBs, marked by nuclear 53BP1 foci, in the oligodendrocyte in different frontal cortices. Our meta-analysis of oligodendrocytes RNA-seq datasets showed profound negative correlations between myelin and DNA repair gene expression. In cell culture, DNA damaging reagent, etoposide, attenuates proliferation and inhibits maturation of oligodendrocyte progenitor cells, while it induces aberrant cell cycle re-entry and apoptosis in myelin-forming post-mitotic oligodendrocytes. Conclusion: The present work is underway, but our preliminary data supports the hypothesis that oligodendrocytes are highly susceptible to DNA damage, and such DSBs could be a pathological marker in demyelinating conditions.

P1-13

Diaschisis in the experimental white matter stroke model: Histopathology and pathogenesis

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Introduction: Cerebral functional insufficiency in stroke might be due to pathologic changes of the primary focal lesion as well as metabolic depression in brain areas remote from initial ischemic lesion, i.e. diaschisis. Previously, we showed that the development of diaschisis lesions by FDG-microPET study in a rat model of experimental photothrombotic infarct of the internal capsule. In the present study we hypothesized that the reduced neuronal and synaptic activities in the diaschisis lesion can be caused by the inhibitory action of GABA. Methods: Tissue obtained from diaschisis lesions, focused by FDG-microPET image, studied by light and electron microscopy, especially immunostains for GFAP, neurofilament protein and GABA. Metabolic change of GABA synthesis checked using a reversible inhibitor of MAO-B, named KDS2010. Results: Experimental brain displays focal diaschisis lesions in the ipsilateral cortex at day 7 after ischemic insults. The lesions are sustained for more than 2 weeks, and evidenced by significantly increased cortical diaschisis volume. Tissue obtained from diaschisis in the motor cortex reveals atrogliosis and minimal pathologic changes of neuron; swollen dendrites and multi-vacuolar degeneration of neuropils. Significantly decreased volume of cortical diaschisis with recovery of glucose metabolism in the primary motor cortex observed by administration of KDS2010. No significant alteration of neuronal GABA present. Conclusion: The histopathologic change and hypometabolic state of diaschisis possibly caused by astrocytic GABA suppression. MAO-B could be the key enzyme for the pathogenesis of diaschisis.

P1-14

White matter neuropathology due to cerebral micro-hemorrhages in geriatric traumatic brain injury

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Introduction. The clinical significance of neuropathology associated with cerebral microbleeds (CMBs) due to mild traumatic brain injury (mTBI) remains unclear. Here we use magnetic resonance imaging (MRI), diffusion tensor imaging (DTI) and connectomic analysis to investigate the statistical association between mTBI-related CMBs, post-TBI changes to the human connectome and neurological/cognitive deficits. Methods. 26 (13 females) geriatric mTBI victims and 26 (13 females) age- and sex-matched healthy control (HC) volunteers were recruited. MRI and DWI volumes were acquired and, for each peri-lesional DTI streamline bundle, the null hypothesis implied no neurological or cognitive deficit associated with between-scan differences in the mean fractional anisotropy (FA) of DTI streamlines within each bundle. Results. In HC volunteers, the analysis failed to identify significant differences in the mean FA of DTI streamline bundles. In the mTBI group, significant differences were found in 21 out of 26 volunteers. In those volunteers where significant differences had been found, these differences were associated with an average of about 47% of all identified CMBs (sigma = 21%). In 12 out of the 21 volunters exhibiting significant FA changes, cognitive functions (memory acquisition and retrieval, top-down control of attention, planning, judgment, cognitive aspects of decision-making) were found to have deteriorated over the six months following injury ($r = -0.32$, $p < 0.001$). Conclusion. Our preliminary results suggest that acute mTBI vascular neuropathology may be associated with cognitive decline in some mTBI patients. Future research should attempt to identify mTBI patients at high risk for cognitive sequelae.

P1-15

Upregulation of annexin A1 in reactive astrocytes at the boundaries of human brain infarcts

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Introduction: Annexin A1 (ANXA1) is mainly expressed in astrocytes and ependymal cells of normal human brains. Regarding acute ischemic brain, increased expression of ANXA1 in microglia and vascular endothelium has been shown with rodent models; however, astrocytic expression of ANXA1 in infarcted brain tissues has been little focused on. Methods: We performed immunohistochemistry in autopsied human brain tissues from 15 cases with cerebral infarction, and the brain tissues of CB-17 mouse stroke model generated by occlusion of the middle cerebral artery. Result: Marked expression of ANXA1 was noted in the viable regions adjacent to necrosis. ANXA1 was mainly distributed in astrocytes rather than microglia at the viable boundary area, as well as in macrophages and endothelium at the necrotic area. Compared with the area of fibrillary gliosis revealed by GFAP, ANXA1-immunopositive area was restricted in the narrow band of viable periinfarct region. TMEM119-immunopositive resident microglia gathered in the periphery of necrosis, but this population was decreased in the ANXA1-immunopositive periinfarct areas. ANXA1 expression in microglia, macrophages and endothelium was also noted in the mouse ischemic brains, however, astrocytic ANXA1 was not observed regardless of the duration of ischemia. Conclusion: ANXA1 expression was elevated in reactive astrocytes around necrosis during acute ischemia of human brains. Astrocytic ANXA1 could affect the behavior of resident microglia through the strong anti-inflammatory properties. The act of ANXA1 during focal brain ischemia might be different between human and mouse species.

P1-16

A case of juvenile central nervous system venulitis mimicking multiple sclerosis

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Introduction: Central nervous system vasculitis is rare but could be a life-threatening disease. *Clinical summary:* The patient is a 17-year-old female with transient sudden weakness and dysesthesia on the right side, associated with headache and nausea. On examination, head MRI presented white matter lesions confined to the left hemisphere. Cerebrospinal fluid showed no specific findings, negative for oligoclonal bands. Screening bloodwork, including C-reactive protein and thyroid function, were normal. Extensive hematologic, infectious and autoimmune disease work-up were negative. Steroid pulse therapy was performed in suspect of multiple sclerosis. Fingolimod hydrochloride was administered 140 days after primary onset. At day 267, she again felt transient hypesthesia. Cranial MRI showed expansion of the high infiltrated areas of the left hemisphere on FLAIR and T2WI, accompanied with edema. Multiple contrasted areas were also observed. ECD-SPECT showed decreased accumulation in the left hemisphere. *Pathological findings and treatment:* Brain biopsy revealed lymphocytic, non-granulomatous inflammation in and around the vessels, especially in the venules of the subarachnoidal space. Lymphocytes were mostly T cells. Immune suppressive treatment including mPSL 1000 mg/day pulse therapy was induced. Her clinical symptoms and neuroradiologic abnormalities ameliorated. She is now followed by oral PSL 10 mg/day and azathioprine 100 mg/day. *Conclusion:* We experienced an extremely rare case of juvenile CNS isolated venulitis. Only a few cases are reported in this category. This case emphasizes the importance of brain biopsy in determining diagnosis and decision of treatment.

P1-17

Cerebral impact of muscle trauma

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Introduction: Mechanical trauma is the fifth cause of death on earth and the first cause of reduced life expectancy in young population, with many permanent sequelae. Among them, neurological impairments are the most serious and disabling. Well documented in sepsis and head trauma, the scientific literature remains poor regarding peripheral muscle trauma alone. Our aim is to characterize the immediate and long-term brain repercussion, on different aspects: clinical (behavorial and cognitive alterations), tissular (neuro-inflammation) and cellular (microglia reactivity).

Methods: Using a mutant mouse model ($CX3CR1^{GFP/+}$ mice with fluorescent microglia cells), we carried out a combination of two complementary approaches: clinical (behavioral tests) and morphological (histology/morphometry techniques combined with automatized 3D confocal microscopy allowing fine analysis of microglia cells morphology/reactivity).

Results: Peripheral muscle trauma has a major impact on central nervous system:
- at an early stage after muscle trauma: microglial cells demonstrate a reactivity in several brain areas, and more specifically in the hippocampus with an increase of microglial complexity within the first 24 hours
- at a late stage, after muscle regeneration: mice have an impaired memorization of a new object, despite no alteration of locomotion and anxiety.

Conclusion: Central nervous system-related sequelae have to be considered in any context of trauma, even when the brain is not directly involved. Thus, a muscle lesion can initiate durable cognitive disorders.

P1-18

Coexistence of transthyretin- and Aβ-type cerebral amyloid angiopathy in a patient with hereditary transthyretin V30M amyloidosis

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Introduction: We describe an autopsy case of late-onset systemic transthyretin (TTR) amyloidosis with a V30M mutation in the TTR gene showing coexistence of TTR- and amyloid β (Aβ) -type cerebral amyloid angiopathy (CAA). Clinical summary: An 84-year-old man with unremarkable family history developed lower and upper limb weakness, constipation, and anhydrosis at the age of 73. At the age of 77, he received a diagnosis of hereditary systemic TTR amyloidosis with TTR V30M mutation based on TTR-positive amyloid deposition in the sural nerve and genetic analysis. Oral administration of diflunisal was started; however, his symptoms related to neuropathy and cardiac dysfunction deteriorated. Diflunisal was replaced with tafamidis at the age of 83. He died of heart failure at the age of 84. The total clinical course was 11 years. Pathological findings: The brain and dura mater showed mild dilatation of the lateral ventricles and weighed 1,355 g before fixation. Microscopically, severe loss of myelinated fibers with TTR-positive amyloid deposition was demonstrated in the peripheral nerves. The dorsal root ganglia, sympathetic ganglia, skin, and pituitary also demonstrated considerable TTR-positive amyloid deposition. Leptomeningeal blood vessels throughout the central nervous system and the cerebral cortical blood vessels showed CAA comprising coexistence of TTR- and Aβ-positive amyloid deposition. Interestingly, most of the TTR and Aβ deposited independently on the vessel walls, as analyzed using the double labeling method. Conclusion: Independent deposition of the TTR and Aβ amyloid on the vessel walls indicate that cross-seeding of TTR and Aβ is less likely in humans.

P1-19

Expression of hepatocyte growth factor and c-Met receptor in the anterior horn cells of the spinal cord in the patients with spinal cord injury

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Introduction: To clarify the survival mechanism of the residual anterior horn cells for trauma, we investigated the immunohistochemical expression of hepatocyte growth factor (HGF), a novel neurotrophic factor, and its receptor, c-Met in the residual neurons of spinal cord injury (SCI) patients. Methods: We examined autopsy specimens of the spinal cords from 10 SCI patients and 10 neuropathologically normal individuals by routine staining and immunohistochemistry using anti-HGF and anti-c-Met antibodies. Results: In normal subjects, immunoreactivity to both anti-HGF and anti-c-Met antibodies was observed in almost all anterior horn cells of the spinal cords. As for SCI patients, we classified the injured lesions into "complete injury region" and "incomplete injury region" by damage level to spinal cord. In "complete injury region", no anterior horn cells were recognized in some cases, although some residual neurons were observed in the others. On the other hand, in "incomplete injury region", all cases had some residual neurons. Almost all residual anterior horn cells immunohistochemically co-expressed both HGF and c-Met. In both injured lesions, increasing the immunoreactive intensity of both proteins for residual neurons started by six days after injury in comparison to normal subjects and continued until one month. From one month to four years after injury, immunoreactivity was decreasing to the normal degree. Conclusion: These results suggest that the HGF-c-Met upregulate system by autocrine and/or paracrine is one of the self-protective systems of the residual anterior horn cells, and HGF-c-Met upregulate system in residual anterior horn cells is caused by trauma.

P1-20

Long-term interval from the spinal cord lesion to subsequent brain lesion in primary central nervous system vasculitis: a case report

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Introduction: Primary central nervous system vasculitis (PCNSV) is an uncommon vasculitis restricted to the small- and medium-size vessels in the brain and spinal cord. Previously, only 9 cases have been reported that initially manifested as an isolated spinal cord lesion with subsequent brain involvement, where the longest interval from onset to brain involvement was 1 year and 11 months. We present the case of an isolated spinal cord lesion with subsequent brain involvement appearing 7 years and 5 months later. Clinical Summary: A 50-year-old man presented with progressive walking difficulty and urinary retention. Neurological examination revealed lower legs muscle weakness and spasticity. Spinal MRI revealed high signal intensity on T2 weighted images of the cervical to thoracic cord, and no brain lesions were found. He was diagnosed as having myelitis and treated with steroid therapy, and his symptoms partially resolved. However, after discontinuation of steroid therapy, his leg weakness and spasticity worsened, and 7 years and 5 months later he presented with altered mental status, right temporal lobe lesion was found with brain MRI. A biopsy was performed from the lesion. Pathological findings: Inflammatory cells infiltrated within and around the vessel walls of leptomeninges and parenchyma, and the lumen of vessels were hypertrophic and stenotic. Immunohistochemically, amyloid β was negative in the vessel walls, and infiltrated inflammatory cells were mostly CD3-positive T-lymphocytes. The patient was diagnosed as having PCNSV. Conclusion: This case demonstrates that a brain lesion can develop after an extended interval from spinal onset in PCNSV.

P1-21

A case of congophilic amyloid angiopathy-related hemorrhages versus traumatic brain injury by car accident?

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Introduction: Congophilic amyloid angiopathy (CAA) is a known cause of cerebral lobar hemorrhages in the elderly. Precipitation of such hemorrhages may lead to confusion in forensic cases.
Clinical Summary: A 77-year-old female restrained driver was involved in a low speed (< 30 miles per hour) car crash. Her car was hit on the front driver's side bumper causing it to rotate and strike a snow bank deploying the airbags. She never lost consciousness, denied hitting her head and exited the car with minimal assistance. She initially refused medical attention and no injuries were appreciated. About 15 minutes later, emergency responders found her flaccid, non-verbal and leaning toward her left side. Her blood pressure was 180/100 mmHg. A computerized tomography of the head revealed two left cerebral hematomas and bilateral thin subarachnoid hemorrhage with a midline shift from left to right. She died after 6 days.
Pathologic Findings: At autopsy there was no external injury. Internally, there was a left frontal subscalpular hemorrhage. The 1350-gram-brain revealed two left frontal hematomas occupying the inferior and middle frontal sulci and neighboring subcortical white matter, showing continuities at bottoms of sulci. The Aβ-immunopositive severe CAA with microangiopathies was confirmed. No cortical contusions were noted.
Conclusion: The hemorrhagic stroke in this individual appeared to be secondary to CAA-associated hemorrhage initially in her cerebral cortex or sulcal subarachnoid space with extension into the underlying white matter. The excitement of the car crash appears to have provoked this hemorrhage, not any direct trauma to her head.

P1-22

A case of Aspergillus infection presenting as cerebral infarction and subarachnoid hemorrhage due to infectious aneurysm rupture

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Introduction:Central nervous system aspergillosis is a very poor prognostic disease. Clinical summary:A 71-year-old female, treating chemotherapy for ascending colon cancer stage IV, was admitted to our hospital due to high fever. Antibiotics treatment was started suspecting CV port infection. On the day of hospitalization, movement disorder of the right upper limb was observed. Head MRI showed cerebral infarction on the left side of the pons. MRA did not show any abnormalities including the basilar artery (BA). Thinking of perforating branch infarction, antithrombotic therapy was started. The course of cerebral infarction was good, however sudden consciousness disturbance occurred on the 7th day. Cranial CT and 3D-CT angiography showed subarachnoid hemorrhage (SAH) and newly developed aneurysm at the BA. Emergency endovascular surgery by coil embolization was performed. Extravasation was observed during the coil embolization. Hydrocephaly was recognized with head CT after embolic surgery, therefore, ventricular drainage surgery was also added. Her consciousness level did not recover and died on the 28th day. Aspergillus antibodies were confirmed from cerebrospinal fluid during treatment. Pathological finding: Invasion of Aspergillus into the vessel wall of the BA was recognized. Destruction of elastic fiber, smooth muscle layers and outer membrane of the BA was confirmed, resulting in the rapid growth and rupture of the BA aneurysm. Conclusion:It is a rare case of cerebral infarction and SAH caused by rupture of infectious aneurysm in Aspergillus.

P1-23

Pathology of hypertensive cerebral hemorrhage: Revisiting miliary aneurysm of Charcot-Bouchard using serial sections

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Introduction: It had been indicated that a hypertensive cerebral hemorrhage in the basal ganglia is accounted for by the rupture of microaneurysms of the small artery, referred to "miliary aneurysms (Charcot-Bouchard)". Nowadays, an abrupt rupture of penetrating branches of the lenticulostriate artery is thought to cause this condition, based on the atherosclerosis; however, this remains controversial. We pathologically examined culprit arterial lesions of hypertensive cerebral hemorrhages, and we present the pathology with persuasive photographic images. Methods: We analyzed culprit lesions of the lenticulostriate arteries including "bleeding globes" in cerebral hemorrhages of the basal ganglia of five sudden death cases at our institutions, using serial sections. Results: (1) The arteries ruptured abruptly, often at their bifurcations based on the atherosclerosis referred to as "lipohyalinosis," which is often associated with arterial wall dissection. (2) Bleeding globes consisted of extravasation and fresh thrombi, without any previously formed aneurysmal wall. (3) There were often organizing or organized lesions of arterial ruptures in hemorrhagic and contralateral basal ganglia, occasionally with microinfarctions. Conclusions: Hypertensive cerebral hemorrhage of the basal ganglion occurs as a result of an abrupt rupture of the lenticulostriate arteries based on atherosclerosis ("lipohyalinosis"). "Miliary aneurysm of Charcot-Bouchard" and "angionecrosis" are organized or organizing features of an incomplete rupture of small arteries, and are not the cause of the cerebral hemorrhage.

P1-24

Intracranial internal carotid artery injury as a rare cause of traumatic subarachnoid hemorrhage in non-missile head injury: Clinicopathological analysis of nine forensic autopsy cases

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Introduction: Intracranial internal carotid artery (IICA) injury is a rare cause of traumatic subarachnoid hemorrhage (SAH) due to non-missile head trauma, and it has rarely been reported. We present nine forensic autopsy cases of IICA injury, and we discuss their clinicopathological characteristics. Methods: We analyzed nine autopsy cases (all males, ages 20s-70s) of IICA injury at our institutions. Results: The circumstances of the sustained injuries were traffic accidents (n=5), fights (n=2), a fall from a tree, and a fall on a road. The head CT images were indistinguishable from those of a non-traumatic SAH. Pathologically, the IICA injuries occurred before the bifurcation of the posterior communicating artery, showing a small laceration (less than several mm). Some arterial lacerations were covered with a fresh thrombus, making the lesions difficult to recognize macroscopically. The histological examination of the injured artery revealed an abrupt complete rupture, with a slight inward constriction of the internal and median layer. The adventitia extended outwards just a little. These morphological findings are quite different from those of a non-traumatic aneurysm or dissection of an IICA. The lacerated areas were covered with an injury-age-dependent thrombus. In some cases, there was an organized disruption of the internal elastic lamina apart from the injured site. Conclusion: In cases with a facial bruise, especially around the mandibular area, an IICA injury must be considered as a cause of a traumatic SAH. A detailed pathological evaluation is indispensable to distinguish traumatic from non-traumatic SAHs.

P1-25

"FAHR DISEASE" (symmetrical and selective cerebral calcification) is considered a kind of "ANGIOGENIC DISEASE" from the results of pathological and radiological studies

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Introduction: Fahr disease was named after Theodor Fahr who reported the autopsied case of cerebral calcification in 1930 and published the paper next year on the microscopic findings in the calcified cerebral microvessels. Methods: 2 autopsied cases were studied with various methods such as histological examination, soft X-ray roentgenography, contact microradiography(CMR), scanning electron microscopy (SEM), transmission electron microscopy(TEM). Results: Calcifications were observed almost symmetrically and selectively in the predilection sites such as basal ganglia, dentate nucleus in the cerebellum, the floor of cerebral cortex. With CMR, the spindle-shaped bodies of calcified entangled capillaries were found. With SEM, many calcified entangled capillaries were recognized on the surface of the brain stone. With TEM, electron dense psammoma-like bodies were observed at the interface between the basement membrane and astrocyte in the cross section of the calcified capillary. Discussion: From above results, we suppose that Ca and P extravasate through the endotherium of degenerated or damaged capillary wall probably due to the increased capillary permeability. This means that breakdown of blood brain barrier and accordingly neural system surrounded by capillaries lose its normal function secondarily both from insufficient supply of glucose & oxygen and from incompetent excretion of waste products. It is compatible with the clinical course that patients develop dementia gradually in proportion to severity of brain calcification. Conclusion: FAHR DISEASE considered a kind of ANGIOGENIC DISEASE which affects both vascular system primarily and neural system secondarily in the long course of disease process.

P1-26

Extensive calcifying CNS microangiopathy in a patient with scleroderma

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Introduction: Systemic sclerosis and associated syndromes may induce primary vascular changes in the brain mimicking various neurodegenerative diseases. Although cerebral hypoperfusion has been found in half of the patients with a scleroderma diagnosis, neuropathological alterations are scarcely reported. Here, we describe a case of extensive calcifying CNS microangiopathy in a patient with scleroderma. Clinical summary: We received a brain bank donation from a 59-year-old man initially diagnosed with CREST syndrome in his 30s. His neurological symptoms started 7 years ago and included progressive cognitive decline, tonic-clonic epilepsy, parkinsonism, swallowing difficulties and postural hypotension. MMSE was 20/30 and brain MRI described subtle generalised increase in deep white matter signal of doubtful significance. There was no family history of dementia. Pathological findings: Macroscopic examination revealed a moderately atrophic pons with mildly depigmented substantia nigra and locus coeruleus and mild cortical atrophy. Histology revealed prominent and widespread white matter pathology, also affecting the basis pontis. It consisted of multifocal, microinfarcts of varying duration associated with vascular abnormalities, such as vascular wall thickening, mineralisation, luminal obstruction and tortuosity. No other underlying cause for the vasculopathy or other neurodegenerative process was identified. The features were therefore in keeping with CNS microangiopathy secondary to scleroderma. Conclusion: It has been suggested that scleroderma may induce primary vascular changes in the brain, of which calcification of small arteries and arterioles may be a marker. In our case the observed multifocal white matter microinfarcts were probably secondary to a microangiopathy crisis rarely described in scleroderma.

P1-27

9-year old girl with Cerebellopontine angle mass

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Introduction: Neuromuscular choristoma (NMC) is a benign lesion mostly occurred in cranial and spinal nerves. It is a rare lesion which composed of fascicular and nodular assembled muscle, connective tissue and nerve fibers. In most cases, neuromuscular choristomas have initially been misdiagnosed as vestibular schwannomas, which are the most common tumors at cerebellopontine angle. Clinical summary: During surgery, a gray-white, well-demarcated mass was found at the left ponto-cerebellar angle. The tumor appeared rubbery, had a rich vascular supply and did not firmly adhere to the trigeminal nerve. The patient experienced left facial paralysis after the operation. Follow up study showed postoperative recurrence twelve months later. Pathological findings: Microscopically, the tumor predominantly consisted of strap-shaped cells arranged in fascicular orientation, intermingled with mature nerve fibers. The tumor cells had frequent cross-striations and peripherally located nuclei. Mitoses, atypia and necrosis were absent. Ki-67 proliferation index was very low (3%). The tumor cells exhibited immunoreactive for Desmin, Vimentin, Myoglobin and CD56, patchy staining for S-100, Actin (HHF35), CD34 and SMA. The tumor was negative for EMA and Myo-D1. Conclusion: NMC is fundamentally a benign lesion, but the risk of postoperative fibromatosis of this lesion is high. Resection is curative, although neurological deficits are a common consequence. No known characteristics in the clinical presentation or in imaging exist distinguishing these tumors from vestibular schwannomas. NMC should be included as a rare differential diagnosis in children patients with masses in the cerebellopontine angle.

P1-28

The specific accumulation of subunit c of mitochondria ATP synthase and curvilinear profile in neuronal cytoplasm of methylenetetrahydrofolate reductase deficiency

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Introduction: Methylenetetrahydrofolate reductase deficiency (MTHFR) is the most common inborn error of folate metabolism. Two general types of pathologic finding often have been described. In the first, intimal hyperplasia and fragmentation, subintimal fibrosis, disruption of elastic lamellae, and thromboembolism are the results of homocystinemia. In the second, neuronal loss, decreased myelination, fibrillary astrogliosis, and reduction of oligodendroglia have been attributed to decreased availability of methyl groups. We report new pathological findings; subunit c of mitochondria ATP synthase (SCMAS) accumulation and curvilinear profile (CVP) in neuronal cytoplasm of cerebral cortex.
Clinical summary: The patient was 15-year-old female who originally had mental retardation (IQ 70 degree). She developed walking disturbance, psychomotor retardation, transient psychogenic blindness, tremor, and mental excitement. After she entered to hospital because of seizure during bathing, her seizure was unstable and body temperature rose to 39 degree Celsius. She suffered cardiopulmonary arrest caused by using thiopental sodium 2mg/kg for sedation during MRI. Resuscitation was carried out but she died. FLAIR images of MRI scan showed high intensity subcortical white matter lesions located at occipital lobes. Genetic study disclosed MTHFR (compound heterozygous mutation: c.446GC>TT and c.976G>A).
Pathological findings: Postmortem examination revealed subcortical perivascular demyelination with reactive astrocytosis and infiltration of macrophages in cerebrum with SCMAS accumulation and CVP in neuronal cytoplasm of cerebral cortex.
Conclusion: The specific accumulation of SCMAS has been reported in neuronal ceroid lipofuscinosis, and other lysosomal disorders. Also in MTHFR, SCMAS accumulated and might be related to form CVP.

P1-29

Brain pathology of mucopolysaccharidosis type 2, mild form

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Introduction: Mucopolysaccharidosis type 2 (MPS2) is caused by insufficiency of iduronate-2-sulfatase enzyme, which results in accumulation of dermatan and heparan sulfates in tissues. Although brain pathology of severe MPS2 has been reported in detail, that of mild form is unknown. This is the first autopsy study of a patient with mild form of MPS2, who was treated with enzyme replacement therapy (ERT). Clinical summary: A 42-year-old male was emergently hospitalized due to confusion and seizure. He was diagnosed as having MPS2 at 4 years-old. He graduated from a junior college and could drive a car. The ERT was started at 41 years-old but was stopped at 8 times because of gait difficulty. Brain MRI showed no ventriculomegaly but honeycomb signals in the bilateral basal ganglia and thalami. The patient died of ventricular fibrillation 2 months after the admission. Pathological findings: The brain weighed 1595 g after fixation. There were many cavities in the subcortical white matter, basal ganglia and thalami. Neuronal loss and gliosis were present in the cerebral cortex and basal ganglia. The cerebral cortex was less injured. The remaining nerve cells did not show cytoplasmic ballooning. Perivascular spaces were dilated and filled with alcian blue and 10E4 (the antibody against heparan sulfate)-positive material.Conclusion: Our patient showed less neuronal loss and gliosis in the cerebral cortex than previously reported patients with severe MPS2. Ballooning neurons were less remarkable, and ventriculomegaly was absent. Brain pathology of MPS2 might be dependent on the clinical severity.

P1-30

Typical Type I lissencephaly in Miller-Dieker Syndrome: Report of an autopsy case

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Introduction: Type I lissencephaly or Miller-Dieker syndrome (MDS) is a rare disease, with a frequency of 1 per 100000 live births. MDS includes Type I lissencephaly and some other abnormalities. MDS is also known as a neuronal migration disorder, whose causative gene is LIS1 located in the short arm of chromosome 17 (17p13.3). An autopsied case with MDS is reported with a thorough review of English literatures.

Clinical summary: A female infant was delivered at 30 weeks of gestation by Caesarean section because of severe fetal growth restriction. She was diagnosed as MDS from the following findings: lissencepaly revealed by brain MRI, and other abnormalities such as small ventricular septal defect (VSD) and facial dysmorphology. Her chromosomal analysis showed a microdeletion on the 17p13.3. At two years old, she died of acute respiratory distress syndrome due to repeated pneumonia.

Pathological findings: Macroscopic findings showed facial abnormalities, including microcephaly, broad nasal bridge, an upturned nose, low set ears and prominent upper lip. The brain weighed 523 grams, showing complete agyria. Coronal section showed thickened cerebral cortex and thinned white matter, thinner corpus callosum, and enlarged ventricles. Microscopic examination showed a thick four-layered cerebral cortex, composed of molecular layer, a thin superficial neuronal layer, a sparsely populated cellular layer and a thick neuronal layer. Heterotopia of inferior olivary nucleus was noted. The cerebellum was of normal structure.

Conclusion: We reported an autopsy case of MDS with histological, immunohistochemical and genetic examinations.

P1-31

An autopsy case of late-infantile GM1 gangliosidosis survived long duration with artificial respiratory support

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Introduction: GM1 gangliosidosis is an autosomal recessive storage disorders caused by the deficiency of b-galactosidase (GLB1), a lysosomal hydrolase. GM1 gangliosidosis is divided to three main clinical forms, infantile, late-infantile and adult. We report an autopsy case of GM1 gangliosidosis who have received artificial respiratory support (ARS) and survived long duration. Clinical summary: The patient was a 40-year-old woman, who was born after a normal pregnancy and delivery. She had difficulty in walking at the age of two and started having seizures at the age of nine. At the age of 21, she became bed-ridden. At the age of 36, she had pneumoniae necessitating the introduction of ARS. She died of pneumoniae at age 40. Molecular study revealed c.152T>C (p.I51T), a common mutation for Japanese adult GM1 gangliosidosis, and c.1348-2A>G mutations in GLB1. Autopsy was performed 3hour post mortem. Results: The brain weighted 419g with severe atrophy predominantly observed in the frontal cortex. In the cerebral cortex and putamen, severe gliosis and loss of neurons were observed. A number of neurons of spinal cord, thalamus and hippocampal formation was relatively preserved. Severe neuronal swelling was seen in the amygdala, hippocampal formation, and the stored material in these neurons was negative with PAS. Neuronal cytoplasmic inclusions similar to membranous cytoplasmic bodies (MCB) were observed in the amygdala. Conclusion: Clinical features and neuropathological findings were consistent with late-infantile form although this patient had a common mutation for Japanese adult GM1 gangliosidosis. Despite of long duration, the limbic region was relatively preserved.

P1-32

Chronic consequences of neonatal exposure to common organic solvents on behavior, motoric functions and brain morphology in young rats

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Introduction: Dimethyl sulfoxide (DMSO), propylene glycol (PG) and miglyol (MG) are common organic solvents often used to dissolve neuro-pharmacological agents for in vivo assays in animal models of various pediatric brain disorders. Nonetheless, these compounds were reported to exhibit pharmacological and pathological effects on the central nervous system of their own. Here we report chronic effects of these solvents on behavior, motoric functions and brain morphology in young rats (P35-37), following neonatal exposure to one of the compounds (P6). Methods: Compounds were administered intraperitoneally (DMSO, 2 or 4 ml/kg; MG, 2 ml/kg) or per os (PG, 2.5 ml/kg) at concentrations considered safe and non-interfering with neuroscience research. Age/sex matched controls received phosphate-buffered saline (PBS). Animals were sacrificed following behavioral and locomotor assays (P40) and their brains were subjected to pathological analyses. Results: Rats exposed to DMSO (n=10; 4 ml/kg only), spent significantly more time in the open field center and traveled shorter distance ($p<0.05$) vs. controls (n=10). Rats exposed to DMSO and MG exhibited shorter social interactions vs. controls ($p<0.05$). CatWalk gait analysis showed various disturbances ($p<0.05$) in rats exposed to any of the three compounds (DMSO, 4 ml/kg only). Brain pathological analyses revealed increased expression of microglia (Iba-1+) and reactive astrocytes (GFAP+) in rats exposed to DMSO ($p<0.05$). Conclusion: Observed chronic behavioral, motoric and morphologic sequelae of neonatal exposure to DMSO, PG or MG at concentrations that are generally considered safe raise concerns about under-appreciated neuro-toxicity of these common organic solvents, which warrants further exploration in larger translational studies.

P1-33

Poorly differentiated chordoma with loss of SMARCB1/INI1 expression in a pediatric patient: a case report

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Introduction:Chordoma is a rare tumor (0.2% of brain tumors in children) involving the clivus and spine. Poorly differentiated chordoma is characterized by SMARCB1/INI1 deletion that is also seen in malignant rhabdoid tumors and atypical teratoma/rhabdoid tumors (AT/RTs). Therefore, for differential diagnosis between poorly differentiated chordoma and other diseases, pathological evaluation may be necessary for pediatric cases with a clivus lesion. Clinical summary: A 2-year-old girl with an atrioventricular septal defect and pulmonary hypertension since birth had cervical pain for 2 months and left upper limb paralysis for 2 weeks. Magnetic resonance imaging (MRI) showed an extradural mass arising from the clivus, causing significant compression of the pons. Osteoblastic metastatic lesions were found in the left upper arm and right iliac bone. A tumor biopsy was performed through the oropharynx, which revealed an INI1-negative small round cell tumor diagnosed as poorly differentiated chordoma. After four courses of combinatorial chemotherapy, a partial response was confirmed by MRI. Pathological findings: Sections showed proliferation of small round cells and short spindle cells with distinct nucleoli and a high nuclear-cytoplasmic ratio. Mitotic figures were occasionally seen (3/10 HPFs). Immunohistochemically, tumor cells were diffusely positive for AE1/AE3, vimentin, EMA, CD99, and Brachyury, but negative for LCA, S100P, desmin, synaptophysin, chromogranin A, NSE, myogenin, Myo D1, and CD1a. SMARCB1/INI1 immunoexpression was completely absent.Conclusion:Combination of INI1 and Brachyury are useful to diagnose poorly differentiated chordoma.

P1-34

Severe mental retardation associated to central nervous system developmental disorders. Report of two cases in Mexico (postmortem pathology)

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Introduction: The World Health Organization defines mental retardation as the subnormal function of inteligente, originates during development and is associated with learning and social adaptation deficits.
Methods: Two autopsies were performed at the Fray Bernardino Álvarez psychiatric hospital for further analysis.
Clinical summary: #1: Woman, 31 years old, with severe mental retardation, poor comprehension and cognition from birth; responsive to verbal stimuli, emitted guttural sounds and few phone mes. She was admitted for postprandial emesis. During her hospitalization she presented respiratory symptoms, subsequently dying of respiratory failure.
#2: Male, 13 years old, with profound mental retardation. He made guttural sounds, had scattered attention. The electroencephalogram reported cortical neurons diffuse deficit. During his hospitalization presented undefined respiratory and enteral symptoms.
Results: #1: Microcephaly of 850 g, left cerebral hemisphere asymmetry and both temporal lobes hypoplasia. Microscopically, neuronal laminación loss, cortical dysplasia, heterotopias, globoid neurons, meganeurons with wavy axons; irregular fibers (length and thickness) massive fragmentation, arranged in whorls and decreased myelin. Cerebellum showed different size and thickness foliae, failed neuronal migration with hypoplasia.
#2: Microcephaly of 950 g, left cerebral hemisphere asymmetry, uncal hypoplasia, temporal lobes hypoplasia with focal lissencephaly, bilateral pachygyria in frontal and occipital lobes; loss of neuronal lamination, heterotopias, globular neurons, meganeurons with wavy axons, irregular fibers in length and thickness and some fragmented. The cerebellum development and neuronal migración alterations.
Conclusion: The nervous system development disorder was confirmed in both cases; with microcephaly, neuronal distortion, cortical dysplasia, failed neuronal migration, and severe alterations of myelination.

P1-35

Clasmatodendrosis in Influenza-Associated Encephalopathy is associated with dendritic spines and does not represent autophagic astrocyte death

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Introduction: Influenza-associated encephalopathy (IAE) is one of the most serious CNS complications of an influenza virus infection, with unclear pathophysiology. Clasmatodendrosis is a complex of morphological changes in astrocytes characterized by fragmentation of the distal processes and swollen cell bodies. Although pathologists in Japan have long been aware of the presence of clasmatodendrosis in IAE brains, few studies have been reported to date. We aimed to confirm the existence, and characterize the spatial distribution of clasmatodendrosis in postmortem IAE brains.
Methods: Autopsied brains from 7 patients with IAE and 8 non-IAE subjects were examined immunohistochemically. In addition, immunofluorescent staining and electron microscopy were performed.
Results: Clasmatodendrosis was present in all examined regions of the IAE brains, but none of the control brains. Fragmented processes of astrocytes in IAE brains were closely adjacent to synapses on the dendritic spines, with the fragmentation especially prominent in the cerebellar molecular layer. In addition, the clasmatodendrotic astrocytes were negative for autophagy markers. Furthermore, whereas aquaporin 4 was predominantly detected in the perivascular endfeet of astrocytes in the control brains, its primary localization site shifted to the fragmented perisynaptic processes in the IAE brains.
Conclusion: Clasmatodendrosis was distributed diffusely in the IAE brains in close association with synapses, and was not caused by astrocyte autophagy. Clasmatodendrosis may be a suggestive pathological feature of IAE.

P1-36

Classification systems in surgical pathology of drug resistant epilepsy: the old versus new

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Introduction: Drug resistant epilepsy (DRE) is a major cause of morbidity and about two-thirds of DRE are amenable to surgery. Over four decades, several classifications have been introduced for the surgical pathology of DRE, particularly hippocampal sclerosis (HS) and focal cortical dysplasia (FCD). This study reviewed effect of ILAE classification on histopathological diagnosis.

Methods: 322 surgically treated DRE (2005-2016) reviewed. For HS, Wyler grading and Blumcke classification were compared with ILAE 2013 classification. In FCD, Palmini classification was compared with ILAE 2011 classification.

Results: 88 cases (27.3%) underwent major revision with reallocation to a different diagnostic category. 5% were reclassified within the same category.

Of 30 mesial temporal sclerosis (MTS) diagnosed using Wyler grading system (2005-2008), 92.3% of grade 4 and all grade 3 were classified as HS 1. Of 105 MTS diagnosed using Blumcke classification (2009-2014), only 9.5% required resubtyping and the category of Probable HS was applied to nine.

Of 33 FCD (isolated-10, associated-23) as per Palmini classification system, 24 (72.7%) needed revision, 22 of which were FCD I and one each of FCD IIa and IIb. Although ILAE 2011 classification was used to characterize FCDs between 2011-2016, interobserver discordance was noted in 64.9%, highest with FCD I (isolated-50%, associated-80%) and least with FCD IIb (6.3%).

Conclusion: With its more stringent criteria, ILAE classifications help define various pathologies more precisely. However, diagnosis of FCD I (isolated or associated) is still prone to high interobserver discordances and will await discovery of specific biomarkers.

P1-37

A case of mild malformation of cortical development with oligodendroglial hyperplasia (MOGHE): a new pathological entity of frontal lobe epilepsy

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Introduction: To analyze the clinical and histology characteristics of a patient with frontal lobe epilepsy diagnosed with mild malformation of cortical development with oligodendroglial hyperplasia, and to recognize the new neuropathological entity. Clinical Summary: It was a female patient aged 16 y/o with 12 years history of epilepsy. The seizures manifested as episodes of conscious loss with automatism including grope and voice lasting for seconds. About 10 episodes a day were found and sometimes with secondary GTCS. MRI showed blurring of grey-white matter interface in left orbital frontal cortex. VEEG revealed left frontal lobe origin of seizures. So left prefrontal lobe was removed. Pathological findings: Histology showed almost normal of cortex neuropil and neurons. Blurring of grey-white interface in some area with patches of proliferation of oligodendrocytes in the corresponding sub-cortical white matter was found. The density of oligodendrocytes was significantly higher in sub-cortical than deep white matter both shown in H&E and Oligo-2 stain. Obvious oligodendrocytes increase and satellite phenomenon in deep cortical layer as well as increased ectopic neurons in sub-cortical white matter was found in the lesion. In proliferation area, there were some nuclei stained with Ki-67, but not as high as tumor. Subsequent follow up for 2 years proved the operation and benign prognosis. Conclusion: There are special and undiscovered histopathological entities in epilepsy etiology. Although known as grey matter disease, white matter pathology plays an important role in epilepsy pathophysiology which will need further research.

P1-38

Meningioangiomatosis: an incidental find during epilepsy surgery

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Introduction:

Meningioangiomatosis is a rare malformative lesion usually affecting the leptomeninges and underlying cortex. Little over 120 cases have been reported yet incidence may be higher since clinical diagnosis alone may be very difficult.

Sporadic cases are usually solitary and manifest through epileptic seizures and headaches. Neurofibromatosis type II patients however may have multiple lesions and are asymptomatic.

Methods:

A 32 years old male was diagnosed with drug resistant epilepsy at the age of 15. He presented two types of seizures of different intensity, both accompanied by headaches which severely affected his quality of life. Neuroimaging revealed an enlarged, edematous right temporal lobe which was interpreted as cortical dysplasia.

Neurosurgical resection of the affected region was decided.

Results:

Grossly, the surgical specimen appeared unremarkable but was however thoroughly sectioned and embedded into paraffin blocks.

Microscopic evaluation of the resulted hematoxilin-eosin slides revealed a thickening of the leptomeninges with meningothelial cells distributed intracortically, surrounding vascular structures throughout the cortical layer and sometimes adopting a more fibroblastic aspect. The lesion was accompanied by several psamomma bodies. A certain degree of cortical dysplasia was also observed but interpreted as reactive.

Conclusion:

Out case represents the typical presentation of sporadic meningioangiomatosis. Despite the 17 years history of pharmacoresistant epilepsy, the diagnosis was not suspected before being confirmed by histopathological examination. Neurological improvement is to be expected but the case will require close follow-up.

P1-39

Eosinophilic astrocytic inclusions of the white matter in patient with epilepsy

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Introduction: Glial and neuronal protein aggregations are known in neuropathological conditions such as neurodegenerative diseases, viral inclusions, low grade tumours and inclusions in clinical setting of epilepsy. Rarely, astrocytic inclusions are associated with seizure disorders but there are cortically located. Clinical summary: This 39-year-old man has a long standing history of epilepsy. His imaging shows a focal right frontal cortical lesion. Cerebral biopsy is done. Pathological findings: The histological examination shows small pieces of unoriented gray matter and white matter. The cerebral cortex shows focal neuronal clustering. Dysmorphic and balloon neurons are not seen. Numerous bright, eosinophilic astrocytic inclusions are seen throughout the white matter and they are located predominantly in the processes of the astrocytes. They are GFAP-positive and they are negative for neurofilament, Alpha beta crystalin, PAS, Congo red, Alcian blue and Ziehl Neelsen. GFAP stain highlights gliosis in both grey and white matter. Neither neuronophagia nor well-formed microglial nodules are identified. There is no evidence of malignancy. IDH-1(R132H) is negative. Conclusion: We report a case of unique astrocytic inclusions predominantly in the white matter in patient with long standing epilepsy. These inclusions are not similar to the previously reported inclusions in patient with epilepsy such as inclusions with filaminopathy. These inclusions could be the cause or the result of the long standing seizure. Further studies are needed to determine the exact nature of the inclusions for better understanding of the pathology.

P1-40

Comprehensive analysis of protein expression profiles in sclerotic hippocampus from patients with mesial temporal lobe epilepsy

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Introduction: Hippocampal sclerosis (HS) is the most common neuropathological condition observed in adults with drug-resistant epilepsy and represents a critical feature in mesial temporal lobe epilepsy (MTLE) syndrome. Many MTLE patients show HS, but some patients do not. The role of the sclerotic hippocampus in the causation and maintenance of MTLE has remained mostly unresolved. In order to elucidate the difference in protein expression profiles between hippocampal tissue of MTLE patients with and without HS, we performed 2-Dimensional Fluorescence Difference Gel Electrophoresis (2D-DIGE).

Methods: Surgically resected tissues of hippocampus and neocortex from drug-resistant MTLE patients with (n = 10) or without HS (n = 10) were homoginized using lysis buffer (7 M urea, 2 M thiourea, 30mM Tris-HCl, 4% CHAPS). Proteins were separated by 2D-DIGE and identified by mass spectrometric amino acid sequencing.

Results: We identified 16 proteins at 18 spots in which the protein expression levels differed between sclerotic and non-sclerotic hippocampi. Most of the identified proteins that underwent an increase or decrease in the expression level were known to be associated with synaptic loss due to neuronal death and gliosis. In addition, a decreased level of 3-phosphoglycerate dehydrogenase (PHGDH), a protein expressed by astrocytes and an increased level of stathmin 1, a protein expressed by neurons were specific to sclerotic hippocampi.

Conclusion: Although the protein expression profile of HS was mostly expected from neuronal loss and gliosis, the decreased astrocytic PHGDH and increased neuronal stathmin 1 expression may represent pathognomonic changes of HS among MTLE patients.

P1-41

Histopathological Findings in Brain Tissue of an anti-NMDAR Encephalitis Patient Obtained during Epilepsy Surgery

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Introduction: An up-to-date multi-centered research on neuropathology finding after epilepsy surgery suggested 1.5% patients were encephalitis. Autoimmune encephalitis is the recently recognized subtype of encephalitis during last decade and mainly mediated by autoantibodies. As the most common autoimmune encephalitis and only diagnosed by serology testing, neuropathological features of anti-NMDAR encephalitis has been rarely described. *Methods:* Case report. *Results:* A 28-year-old man was presented for admission after 10 days of headache, nausea and episode of seizures. His past medical history was unremarkable and headache without fever had been attributed to non-specific viral infection. MRI showed T2 FLAIR hyperintensity and focal gadolinium enhancement of the right temporal lobe. In MRS, choline peak was high, NAA peak was low and accompanied with lactate peak. His NAA/Cr ratio was 1.17 and Cho/Cr 2.67. An operation was performed for suspicious glioma. Histopathological examination revealed the lymphocytic infiltration of the leptomeninges and adjacent cortex, with scattered plasma cells and eosinophils. Perivascular lymphocytic cuffing, activated microglia, neuronal loss and degeneration were also noticed. But there was no necrosis, viral inclusions and microglial nodules, which may suggest infections. The inflammatory microscopic findings made autoimmune etiologies should be rule out. Later, autoimmune encephalitis antibody panels showed his serum and CSF were both anti-NMDAR-IgG positive. The diagnosis of anti-NMDAR encephalitis was made. *Conclusions:* Recent onset encephalitis without histological features of infection should raise the concern of autoimmune encephalitis. And the serology testing of specific autoantibodies may help to make the final diagnosis.

P1-42

Pathological examination of transmantle sign of FCD exhibiting T1-high-intensity on magnetic resonance imaging

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Introduction: Transmantle sign is a characteristic radiological finding of FCD observed on magnetic resonance imaging (MRI). It generally exhibits high signal intensity on T2-weighted and FLAIR images, and shows low signals on T1-weighted images. However, in some cases, it showed high signal intensity on T1-weighted images. Here, we examined the pathology in patients undergoing surgical resection in whom transmantle sign showed T1-high signals. Methods: There were 20 FCD patients who had transmantle sign on MRI. All of them underwent surgery for intractable epilepsy at our hospital. Patients were grouped based on T1-intensity signal of the transmantle sign; high intensity, group H (n=8) and low intensity, group L (n=12)]. The pathological diagnosis was done according the ILAE classification. In addition, the density of the balloon cells was evaluated at a site where they could be observed in high number and the presence of the calcification was assessed in all cases. Results: The age at surgery was 7.4 ± 5.9 and 26.7 ± 15.8 years in groups H and L, respectively. Based on pathological findings and ILAE classification, the diagnosis in all cases was FCD type IIb. Interestingly, the density of balloon cells tended to be higher in group H than in group L. Microcalcification was observed in 3 cases in group H, but was absent in group L. Conclusion: The high density of balloon cells may contribute to the change in signal on MRI. Further studies are required to validate this information.

P1-43

Epileptogenesis of the subiculum associated with hippocampal sclerosis in patients with MTLE

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[Introduction] Mesial temporal lobe epilepsy (MTLE) is the most frequent focal epileptic syndrome in adults, and the majority of seizures originate primarily from the hippocampus. The resected hippocampal tissue often shows severe neuronal loss as that referred to hippocampal sclerosis (HS). Accordingly, there is a paradox between the clinical and pathological features: why should epilepsy be derived from such degenerated tissue? Here we investigated epileptiform activities ex vivo using living hippocampal tissue taken from patients with MTLE. [Methods] We prepared acute brain slices from patients with MTLE within 45 min after resection, and optical imaging or local field potential recordings (LFP) was performed ex vivo. We also used a brain block corresponding to the mirror surface of each slice and performed histopathological examination. [Results] We revealed that epileptiform activities developed from the subiculum, regardless of the existence of HS. We found spontaneous rhythmic activities in the subiculum and detected discrete component of high frequency oscillations (HFO), a clinical biomarker of the ECoG suggesting the epileptogenic regions. Immunohistochemistry of the HS tissue revealed loss of inwardly rectifying K+ channel 4.1 (Kir 4.1) in astrocytes in the subiculum, indicating failure of the extracellular K+ buffering and possible association with neuronal hyperexcitability. [Conclusion] These results indicate that pathophysiological alterations involving the subiculum could be responsible for epileptogenesis in patients with MTLE.

P1-44

Reversible enlargment of amygdala without definite pathological abnormality

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Introduction: Amygdala enlargement (AE) occurs in patients with temporal lobe epilepsy (TLE), however its underlying pathophysiology is unclear. Proposed pathology includes tumors, autoimmune mechanism and focal cortical dysplasia. Recent reports informed us that at follow-up, 50% of TLE patients with AE became seizure-free and 60% of them had partial or full remission of AE on brain MRI. Clinical summary: A 66-year-old right- handed man visited the memory clinic of our hospital with chief complaint of memory skip. His Mini-Mental State Examination score was normal (29/30) but CDR disclosed loss of distant memory with well preserved recent memory. Brain MRI showed enlargement of the left amygdala but EEG could not detect abnormality. Therapeutic trial of zonisamide 100mg per day completely ameliorated symptoms. From 68 years of age, zonisamide was tapered down to zero for three years. At age 73, a follow- up MRI showed full remission of initial AE. Just after the MRI, he died unexpectedly at home. Pathological findings: No definite pathological findings were present in his central nervous system, including amygdala. Conclusion: This case may indicate that the reversible AE with TLE may require different approach to prove it pathogenesis. The cause of death may be classified into unexpected death of epilepsy, warning cession of anti- epileptic drugs even without clinical symptoms of this syndrome.

P1-45

Hippocampal morphometry in sudden and unexpected death in epilepsy (SUDEP)

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INTRODUCTION. Hippocampal developmental abnormalities, including granule cell dispersion (GCD) of the dentate gyrus (DG), DG invaginations (DGI) and subiculum/ hippocampal malrotation (SM) have been reported in sudden unexpected death in childhood, and proposed as risk biomarkers. GCD is a common finding in temporal lobe epilepsy with hippocampal sclerosis (HS). Our aim was to investigate morphological hippocampal alterations in SUDEP. METHODS. In 186 post-mortems from three groups [SUDEP (67; 13 with HS), non-SUDEP epilepsy controls (EC =66; 23 with HS) and non-epilepsy controls (NEC= 53)] Nissl/H&E stained sections from left and right hippocampus at several coronal levels were digitised. Image analysis for mean GCD (inner and outer DG), DGI, SM and hippocampal dimensions (HD) for shape [width (HD1), height (HD2)] and medial positioning [(HD4) in relation to parahippocampal gyrus (PHG) length (HD3)] were measured, with multivariate statistical comparisons between groups. RESULTS. Findings included significant GCD in all cases with HS than those without ($p<0.001$). In non-HS cases a trend for increased GCD in EC compared to NEC ($p<0.05$) but not between SUDEP and NEC was noted. There was no significant difference in the presence of DGI, SM, HD1 and HD2 lengths between SUDEP, EC and NEC groups, when factoring for HS and coronal level. HD3 was significantly greater in SUDEP than NEC and EC ($p<0.01$) when factoring for presence of HS and coronal level; however multivariate analysis considering age at death showed no significant differences in HD3 between the three groups. CONCLUSIONS. No signature histological hippocampal morphometric alterations were identified in SUDEP.

P1-46

Focal cortical dysplasia associated with CNS injury in early childhood

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Introduction: Intrauterine or perinatal hypoxic-ischemic injury causes encephaloclastic lesions associated with morphological alterations of focal cortical dysplasia (FCD) in the better preserved cortex. To determine if FCD occurred following injury later in infancy or childhood, we examined surgical resection specimens from patients being treated for intractable epilepsy with a history of an injurious event in early life, beyond the perinatal period. *Methods*: Twelve cases, from the archives of the Department of Clinical Neuropathology, Kings College Hospital, London, were reviewed. *Results*: Patients ranged from 8 to 39 years at surgery, with seizure onset from 1 month to 8 years. The precipitating events were infections, head injury due to falls and shaking, neonatal hypoglycemia and cerebrovascular accident related to congenital heart malformation, occurring mostly within the neonatal period to the first year of life. Principal lesions were porencephaly in the multilobar resections and ulegyria; in three, marbled cortex was seen. Adjacent cortex showed nodules and clusters of neurons, which were frequently hypertrophic. In four specimens, there was thin unlayered cortex, in two, microcolumnar arrangement of neurons and scattered dysmorphic neurons in two. *Conclusion*: Changes of FCD do result from disturbed postnatal development and reorganization of less damaged cortex, and may be responsible for the epilepsy.

P1-47

Male of 19 years with superefractory genetic epilepsy associated to bilateral porencephaly. Case report in Mexico

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Introduction. Some epileptic seizures come from punctual genetic defects, which can be confirmed by established molecular tests, or genetic component evidence derived from familiar and genetic studies.

Methods: Autopsy was performed at the Fray Bernardino Álvarez psychiatric hospital for further anatomopathologic and molecular analysis.

Clinical summary. A 19-year-old male presents epilepsy since childhood. Family history of consanguinity (grandparents, parents), brother with epilepsy and carrier of mutation in a heterozygous state composed of TBC1D24 gene, CPA6 (c.799G> A, P. Gly267Arg and c.619C> G, P. Gln207Glu). Product of full-term pregnancy, eutocic delivery, birth weight 3060 g. Emited first word at 24 months. At 3 years old he presented absence crisis, behavior arrest and abnormal crying. At 16 years with episodes of dystonia, blinking, right upper limb clonic seizures, secondarily generalized. Treatment with regular crisis control. In 2016, associated with a reduction in CBZ, he presented mood alterations, clonic movements in the right hand, progressing to hemibody, lasting 1 hour. He presented multiple generalized clonic tonic crises (up to 40 daily), with an average duration of 5 minutes, returning partially to baseline.

Results. Autopsy findings: brain weighed 1250 g, with left cerebral hemisphere asymmetry, extensive frontal lobe lissencephaly, incomplete corpus callosum, extensive ventricular and cisternal communication, and two porencephalic cysts at the middle brain, resembling accessory ventricles, both had internal choroid plexuses, identified as extensions from the lateral ventricles.

Conclusion. This case showcases the relationship between familial epilepsy, TBC1D24 mutations and bilateral porencephaly.

P1-48

Pathological characteristics of peripheral neuropathy in eosinophilic granulomatosis with polyangitis

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Introduction: Eosinophilic granulomatosis with polyangiitis (EGPA) is a multisystemic disorder, defined pathologically as the combination of extravascular granulomas, small and medium-sized vessel vasculitis and the eosinophilic infiltrates. Anti-neutrophil cytoplasmic antibody (ANCA) have been demonstrated in 30-40% of EGPA patients. We have the hypothesis that pathogenic mechanism of neuropathy in EGPA is distinct between ANCA-positive and negative patients. Method: We retrospectively examined histological features of sural nerve biopsy specimen in 16 EGPA patients (4 ANCA-positive and 12 ANCA-negative). Results: Necrotizing vasculitis were shown in 25% (1/4) of ANCA-positive patients and in 8% (1/12) of ANCA -negative patients. Ischemic pattern of axon loss was shown in 50% (2/4) of the ANCA-positive patients and in 17% (2/12) of ANCA -negative patients. Eosinophilic infiltrations in the epineurium and degranulations of eosinophilias were shown in 33% (4/12) of ANCA-negative patients, while no ANCA-positive patients showed these changes. Conclusion: There were two pathogenesis in EGPA with neuropathy, ischemia with vasculitis and toxic eosinophilic effect. Necrotizing vasculitis and ischemic pattern of axon loss were observed more frequently in ANCA-positive EGPA patients than in ANCA-negative patients. Eosinophilic infiltrations in the epineurium and degranulations of eosinophiles were found only in ANCA-negative patients. These findings suggest that, in ANCA-negative EGPA patients, a toxic effect on nerve fibers associated with eosinophilic infiltrations is the cardinal feature to cause peripheral neuropathy, not vasculitic occlusion due to small vessel vasculitis.

P1-49

Label-free visualization of abnormal lipid accumulation in tissues from Fabry disease patients using Raman spectroscopic marker of globotriaosylceramide

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Introduction: Fabry disease is a genetic disorder resulting from deficient activity of alpha-galactosidase A. It causes systemic accumulation of globotriaoslyceramide (Gb3) in plasma and cellular lysosomes of tissues throughout the body. In routine histopathological studies, toluidine blue staining usually demonstrates Gb3 accumulation, but it is not molecular specific and the other lipids are potentially stained at the same time. In this study, we measured molecular vibrational spectra of Gb3 using Raman spectroscopy. They provide vibrational information characteristic of chemical groups or bonds in a molecule without any labeling procedures. Tracing spectral fingerprints enables us to locate and quantitate Gb3 within tissues in a molecular specific manner.

Methods: Vibrational spectra of a 10μm-thick frozen sections of peripheral nerves biopsied or autopsied from three Fabry disease patients were obtained using spontaneous Raman microspectroscopy and compared with the spectra of Gb3, phosphatidylcholine (PC) and sphingomyelin (SM) *in vitro*.

Results: The Raman shift in 1064cm^{-1} was more prominent in PC and SM than in Gb3, whereas the Raman shift in 1088cm^{-1} only existed in Gb3. The ratio of them (1088cm^{-1} to 1064cm^{-1}) enabled us to visualize Gb3 in the perineurium around PC- and SM-rich nerve fibers in Fabry disease patients. This ratio was not elevated in the sections from the disease control (vasculitis) cases.

Conclusions: The Raman shifts worked as a molecular specific marker of Gb3 within the tissues from the patients. This is a label-free and lipid-specific visualization technique of Gb3 and is potentially useful even within the tissues other than peripheral nerves.

P1-50

Vasculopathy in hereditary transthyretin amyloidosis: an electron microscopic study

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Introduction: Peripheral neuropathy is the cardinal feature of hereditary transthyretin (ATTRm) amyloidosis, but its mechanism has not been fully elucidated. Methods: We used electron microscopy to examine sural nerve biopsy specimens from 49 ATTRm amyloidosis patients with Val30Met mutation. Patients were consisted of 11 early onset cases from endemic foci and 38 late onset cases from non-endemic areas. Results: Loss of nerve fibers with or without neighboring amyloid deposition was a common feature. The amount of amyloid deposition was greater relative to the extent of nerve fiber loss in early onset cases than in late onset cases. The atrophy of Schwann cells, particularly nonmyelinating cells, that were apposed to amyloid fibrils was more conspicuous in early onset cases than in late onset cases. The numbers of endothelial cell nuclei, endothelial cell profiles, and occluded microvessels were significantly increased in the ATTRm amyloidosis patients compared with 37 patients with nutritional/alcoholic neuropathies ($p < 0.05$, 0.01, and 0.01, respectively). Findings suggestive of the disruption of blood-nerve barriers, such as the loss of tight junctions and the fenestration of endothelial cells, were also more frequently found in the ATTRm amyloidosis patients ($p < 0.001$), irrespective of the presence or absence of amyloid deposition. Conclusions: These findings suggest that direct insult of amyloid fibrils causes Schwann cell damage resulting in the predominant loss of small-fiber axons characteristic of early onset cases. In addition, vasculopathy may also participate in the pathogenesis of neuropathy, particularly in late onset cases.

P1-51

An autopsy case of acute autonomic and sensory neuropathy

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Introduction: Patients with acute autonomic and sensory neuropathy (AASN) often present with psychosis; however, the pathomechanisms underlying the psychiatric symptoms have remained unclear so far.
Clinical summary: A 46-year-old man developed spontaneous pain of his trunk and four limbs with stomach ache. Neurological examination revealed character changes, mydriasis, and impairment of superficial sensations with spontaneous pain over the entire body. Deep sensation was normal in his four limbs. The autonomic dysfunctions including orthostatic hypotension, bladder and bowel dysfunction, and hypohidrosis were shown. Mild muscle weakness was observed in his four limbs. Nerve conduction studies revealed sensory-dominant axonal neuropathy. Cervical MRI demonstrated hyperintense lesions on the T2-weighted images in the dorsal area of the spinal cord at the C3-7 vertebral levels. Sural nerve biopsy revealed severe loss of the myelinated fibers (2,462/mm^2).
Pathological findings: The cerebrum showed mild atrophy of the bilateral frontal lobes. On histopathologic examination, no abnormalities were demonstrated in the cerebrum, cerebellum, or brain stem. In the dorsal column of the spinal cord, severe loss of the myelinated fibers with infiltration of macrophages and perivascular lymphocytes comprising of CD8-positive T lymphocytes was observed. The number of the myelinated fibers in the dorsal roots were severely decreased; however, the anterior roots were preserved. Obvious loss of the ganglion cells with formation of the Nageotte's nodules in the sympathetic and dorsal root ganglia were seen. The intermediolateral nucleus of the thoracic cord was intact.
Conclusion: The pathological changes responsible for the character changes in our patient could not be detected.

P1-52

Peripheral polyneuropathy associated with leptomeningeal carcinomatosis and lymphomatosis: diseases simulating Guillain Barre syndrome. Report of two postmortem cases

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Introduction: Lymphomatosis and leptomeningeal carcinomatosis are a dissemination through the subarachnoid space, affecting cranial nerves, medullary roots and/or cerebral and medullary parenchyma. It is subacute, with headache and deficit of the cranial and spinal nerves. Clinical summary: Case 1: a 51 year old woman with pain in the right hypochondrium who returned with treatment in 2015, later diplopia and paresis of the pelvic limbs, remaining bedridden with a diminished tone and reflexes of absent muscle stretching and diagnosis of Guillain-Barre syndrome, later she died. Case 2: a 58 year old man with a diagnosis of chronic polyneuropathy in 2015 managed with immunoglobulin therapy without improvement. In 2016 he showed prostate enlargement by ultrasound. Later, he presented an infection in the left pelvic limb and a torpid evolution with absence of vital signs, declaring his death. Pathological findings: Case1: adenocarcinoma of the gallbladder, with extension to the liver bed and metastasis to multiple organs. The histology shows neoplastic cells in the subarachnoid space, wrapping the anterior medullary roots and conditioning central chromatolysis of the motor neurons. Case 2: enlarged prostate, whitish and solid. The histology shows diffuse infiltration by small cells with hyperchromatic nuclei, increased nucleus-cytoplasm ratio and involvement of multiple organs. Positive immunohistochemistry for CD20, bcl-2 and CD10, diagnosed as grade I diffuse follicular lymphoma. Conclusion: Because treatment in Guillain Barre syndrome is more effective when administered earlier, patients should be treated after the exclusion of possible imitators such as leptomeningeal dissemination due to neoplasm.

P1-53

B cell activating factor (BAFF) expression in active phase of vasculitic neuropathies

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Introduction Various factors including proinflammatory cytokines which affect humoral and cellular immunity, have been related to the onset of vasculitic neuropathies. Recently, the presence of ectopic B cell follicular-like structures has been reported in many autoimmune disorders and the importance of B cell in the pathogenesis of immune mediated neurologic disorders. BAFF recently has been identified as one key molecule in the pathogenesis of autoimmune disorders and regulates B cell proliferation and survival. To clarify the role of BAFF in peripheral nerve with vascular inflammation, we examined the expression of BAFF and its receptor using immunohistochemistry. Material and Methods Sural nerve biopsy specimens from patients with RA (n=5), MPA (n=5), EGPA (n=5) were studied by immunohistochemistry. Each patient provided informed consent. Consecutive paraffin sections were each immunostained with primary antibodies (antiBAFF, antiBAFF-R, CD3, CD20, CD68). Results In 11 of 15 cases, BAFF immunoreactivity showed at perivascular infiltrates in the epineurium. Most of them were CD68 positive macrophages. In cases of highly expression of T cell, BAFF expression seems to be scarce. In the active phase of vasculitis with accumulation of B lymphocytes, perivascular infiltrates showed highly immunoreactivity for BAFF. Conclusion BAFF immunoreactivity for the active phase of vasculitic neuropathies was identified at perivascular infiltrates in epineurium. It may reflect a breakdown of B cell tolerance and an increase in autoantibody production due to autoreactive B cell induced by a BAFF stimulation.

P1-54

Anti-HMGCR antibody shows bcl-2-positive lymphocyte infiltration and follicles

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Introduction Idiopathic inflammatory myopathies (IIM) are classified in five categories including polymyositis (PM), dermatomyositis (DM), immune-mediated necrotizing myopathy (IMNM), inclusion body myositis (IBM), and non-specific myositis by their muscle pathologies findings. In addition, more than 15 autoantibodies specific for myositis including anti-HMGCoA reductase (HMGCR) antibody are already recognized. HMGCR affects the supression of low grade lymphoma by regulating mevalonate pathway. In this study, we aimed to determine the association between anti-HMGCR antibody positive IMNM and a specific morphological phenotype. Materials and methods We studied patients with anti-HMGCR antibody positive IMNM (n=10), other IMNM (n=20), PM (n=12), DM (n=12), and IBM (n=14). Their muscle biopsy specimens were subjected to routine histochemistry and immunohistochemistry. Results In anti-HMGCR antibody positive patients, perivascular bcl-2 positive lymphocyte infiltrations were frequently observed. About 50% of all inflammatory cells were positive for bcl-2. In addition, extranodal lymphocytic follicles are scatterd in cases with anti-HMGCR antibody and higher serum LDL-cholesterol levels. In these follicles, lymophcytes were positive for bcl-2, CD4, CD8, and CD79a, but not for CD20. Abnormal lymphocytes were not observed in all cases. In IIM except for anti-HMGCR antibody positive IMNM, bcl-2 positive lymphocytes were less than 5% of all inflammatory cells. Ki-67 positive lymphocytes were less than 5% of inflammatory cells in all cases. Conclusion Our data showed that bcl-2-positive lymphocyte infiltration are specific for anti-HMGCR antibody positive myopathy. These findings suggested that effects of anti-HMGCR antibody might be contrary to those of statins.

P1-55

Fatal disseminated Annacaliia algerae myositis mimicking polymyositis in an immunocompromised patient

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Introduction: Anncaliia algerae myositis is a rare, life-threatening, microsporidiosis among immunocompromised hosts which can be potentially cured if treatment is instituted prior to clinical deterioration. We report a case of A algerae myositis in a man who was on long term immunosuppression for treatment of psoriatic arthritis. Clinical summary: A 55 year old man with a long history of treatment with immunosuppressive agents including methotrexate, leflunomide and corticosteroids for psoriatic arthropathy was investigated for an unexplained myositis. A vastus lateralis muscle biopsy performed led to a diagnosis of A. algerae microsporidial myositis. Immunosuppressive drugs were stopped and patient was treated with cholestyramine wash and albendazole. He also developed Pneumocystis jirovecii pneumonia which was treated with IV. Despite therapy, patient deteriorated with involvement of bulbar and respiratory muscles requiring intensive care and ventilation. He died 3 weeks after diagnosis. Pathological findings: Light microscopy demonstrated a necrotizing myositis with scattered clusters of ovoid spores within the myocyte cytoplasm resembling microsporidia. DNA was extracted from the muscle biopsy specimen, amplified by PCR and subsequent sequence analysis was consistent with A. algerae. Electron microscopy confirmed microsporidial myositis with features characteristic of A. algerae. Post mortem examination of skeletal muscle from tongue and intercostal muscles also revealed numerous organisms confirming disseminated disease. Conclusion: A high index of suspicion is required for the diagnosis of this rare, but often fatal microsporidial myositis in immunocompromised patients. A timely muscle biopsy can lead to diagnosis and directed therapy.

P1-56

Pathological finding of the first autopsy case with adenylosuccinate synthetase-like 1 (ADSSL1) gene mutation myopathy

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Introduction: ADSSL1 myopathy is one of the myopathy inherited in an autosomal recessive fashion. ADSSL1 gene is also known as one of the beta-amyloid(Aβ) toxicity modifier genes. We report a 66-year-old man with ADSSL1 myopathy in the course of 30 years, the first autopsy case.

Clinical summary: He could not run well since student. He had no family history of neuromuscular disease. In the late thirties, he could not step stairs with his own feet. At the age of 56, he could not walk without support. Next year, he admitted to the hospital with dyspnea, diagnosed Brugada syndrome and implanted a cardioverter defibrillator. At the same time, he referred to the neurology division and presented dysphagia and muscle weakness in face, respiratory muscles and distal limbs. Cognitive function was normal. Serum creatine kinase was 45 mU/ml. Electromyography showed myogenic change. At the age of 66, He died of respiratory failure seven months after tracheotomy. Genetic examination revealed heterozygous c.910G>A ADSSL1 gene mutation.

Pathological findings: Muscle necropsy showed chronic myopathic features with a few nemaline rods, some rimmed vacuoles and type 1 fiber predominance. Fixed brain weighed 1460g. Senile plaque Braak stage A, Neurofibrillary tangle Braak stage 2. Alpha synuclein and TDP-43 were negative. The spinal cord was unremarkable.

Conclusion: Muscle pathology findings were similar to the past reports, suggesting the specific findings with ADSSL1 gene mutation. Mild Aβ deposition was found in the brain, but further investigation is needed to clarify the relation to ADSSL1 gene mutation.

P1-57

Clinical and pathological features in patients with Nakajo-Nishimura syndrome and inclusion body myositis

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Introduction: Nakajo-Nishimura syndrome (NNS) is an autosomal recessive disease characterized by remittent fever, skin rash, emaciation of the face and upper body, and long gnarled fingers with contractures. Mutation of the gene encoding the β5i subunit of the immunoproteasome causes the accumulation of ubiquitinated or oxidated protein due to proteasomal dysfunction. Inclusion body myositis (IBM) is a form of inflammatory myositis characterized by weakness and atrophy of the quadriceps femoris (QF) and flexor digitorum profundus (FDP). Although the pathogenesis of IBM is unknown, inflammation, degeneration, proteasomal dysfunction are thought to be its underlying mechanisms. In this study, we investigated the clinical and pathological features of NNS and IBM. *Methods:* We examined the clinical symptoms (e.g., region of weakness, muscle magnetic resonance imaging (MRI), and laboratory data) of 4 NNS patients. Immunohistological studies of muscle biopsy specimens from NNS and IBM patients were also performed. *Results:* Weakness of the QF and FDP and high-signal intensity in T2WI were observed in IBM and NNS patients. One NNS patient with dysphagia had impaired relaxation of the cricopharyngeal muscle, which was also characteristic of IBM patients. We found p62-positive cytoplasmic deposits and Lys63- and Ly48-linked polyubiquitin-positive deposits in muscle specimens from NNS and IBM patients. *Conclusion:* NNS and IBM patients share many common clinical findings. Furthermore, both groups of patients have similar pathological findings, which involve the ubiquitin-proteasome system and selective autophagy. Our study suggests that dysfunction of these pathways plays an important role in the pathogenesis of both diseases.

P1-58

Myopathological features of cancer-free myositis with anti-TIF1-γ-Ab positive

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Objective: Cancer is not detected in juvenile myositis patients with anti-transcriptional intermediary factor 1 γ autoantibody (anti-TIF1-γ-Ab), but is common in those adult patients. We aimed to characterize myopathological features associated with anti-TIF1-γ-Ab itself by excluding the background of cancer-associated myositis (CAM).Methods: We reviewed the database of 945 adult patients with idiopathic inflammatory myopathies between May 2000 and November 2017. Anti-TIF1-γ-Ab was analyzed by immunoprecipitation assays. Among anti-TIF1-γ-Ab(+) patients, the cancer-free patients, who were not detected cancer over three years after myositis diagnosis and did not include cancer history, were compared with those with CAM who had cancer within three years of myositis onset.Results: A total of 80 patients with anti-TIF1-γ-Ab(+) were included (DM 77). Among them, in comparison to 57 with CAM, 13 cancer-free patients were identified with long-term follow-up (6.0 ± 2.4 years, range 3.0 to 10.5 years from myositis onset). Those patients were not younger (58.9 ± 19.0 years) with longer duration (8.0 ± 10.3 months, $p < 0.05$), and showed lower serum CK levels (349 ± 339 IU/L, $p < 0.05$). In myopathology, vacuolated fibers were less frequent (31% vs 61%, $p < 0.05$), but perifascicular atrophy (38% vs 35%) and C5b-9 deposits on capillaries (46% vs 67%) were in a similar proportion.Conclusion: The CAM can induce vasculopathy of vacuolated fibers with higher CK levels. Myopathological findings of cancer-free myositis patients with anti-TIF1-γ-Ab(+) are associated with PFA or C5b-9 deposits. Our findings can give a new insight into the pathogenesis of those juvenile patients.

P1-59

Juvenile dermatomyositis in a 1-year-and-9-months-old boy

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Introduction: Juvenile dermatomyositis is a subtype of inflammatory myopathies with affected patients below 18 years of age. The average age onset is 5 to 14 years with the median age at 7 years. The authors report the very young case of juvenile dermatomyositis.
Clinical summary: A 1-year-and-9-months-old boy presented with progressive proximal muscle weakness of upper and lower extremities for 4 months. The patient developed Gottron's papule and heliotrope on of both hands, feet and upper eyelids since 1 year old. He had difficulty rising from the sitting position or raising his arms over his head. He could not walk unassisted, nor could he turn his body or lift his neck. No dysphagia or aspiration was noted. Physical examination showed the heliotrope rash on both upper eyelids and malar rash without nasal sparing. His neurologic examination showed normal extraocular muscles movement and no neurological deficit/localizing signs. Motor power revealed proximal muscle weakness with normal muscle tone. Deep tendon reflexes were normal throughout. He was the second child of the family. No history of the neuromuscular disorder in his family. He had average growth and development before this episode of disease.
Pathological findings: The muscle biopsy reveals perifascicle atrophy and findings which compatible with juvenile dermatomyositis. Immunohistochemistry(MAC and MHC-I) supports the diagnosis.
Conclusion: To our knowledge, this is the youngest case of juvenile dermatomyositis in Thailand.

P1-60

Granulomatous myositis associated with anti-PD-1 antibody

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Introduction: Immune-related adverse events (irAEs) are harmful effects associated with immune checkpoint blockers typified by anti-programmed death-1 (PD-1) and -programmed death ligand 1 (PD-L1) monoclonal antibodies (Abs). The skeletal muscle is a target tissue of irAEs, but the immunopathogenesis of muscle destruction remains unclarified. Here, we report two cases of granulomatous myositis following anti-PD-1 therapy.
Clinical summary: Case 1. A 79-year-old woman with lung adenocarcinoma developed proximal limb weakness following nivolumab treatment. Her creatine kinase (CK) level was 1,638 IU/L. Myositis-specific autoantibodies (MSAs) and anti-acetylcholine receptor (AChR) Ab were negative. Needle electromyography showed spontaneous activities. Case 2. A 70-year-old man who received pembrolizumab and axitinib for renal cell carcinoma developed left ptosis, diplopia, and weakness with myalgia in his neck and left shoulder. Laboratory tests showed a CK level of 1,832 IU/L, positivity for anti-AChR Ab, and negativity for MSAs. Needle electromyography and repetitive nerve stimulation were normal.
Pathological findings: Case 1's muscle biopsy showed patchy mononuclear cell infiltrates and granuloma formation in muscle fascicles. In the granulomas, both M1 and M2 macrophages were abundant. PD-1+ cells were scattered in the granulomas and PD-L1 was upregulated on the non-necrotic fibers around the granulomas. CD8+ T-cells invading non-necrotic fibers were also observed. Case 2 showed findings similar to those of Case 1 and giant cells in the granulomas.
Conclusion: Granulomatous myositis is one characteristic phenotype of irAE with anti-PD-1 antibody. The PD-1 immune checkpoint pathway may be involved in the aberrant macrophage activation.

P1-61

Macrophage and chronic Graft-versus-host-disease myositis. A clinicohistopathologic study

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Introduction:The pathology of chronic graft versus host disease (cGVHD) myositis is not well understood, but infiltration of CD8+ cells has been reported. In recent years, involvement of macrophages has been reported in cGVHD. Macrophages are roughly classified into M1-like acting on inflammation and M2 like anti-inflammatory. The involvement of macrophages in the chronic GVHD myositis is unknown. Methods:From our myositis biopsy database from January 2000 to March 2018, we identified 9 patients with cGVHD. We collected clinical information by reviewing the patients' clinical records. For pathological analysis, frozen muscle specimens were processed for immunohistochemistry including staining for CD11c (M1 macrophage) and CD163 (M2 macrophage). We assessed the amount of CD11c + or CD163 + cells semi-quantitatively. Results:Patients were 7 women and 2 men. The serum CK was normal in 3 patients and elevated in 6 patients (239 to 9194 IU/L). Myositis specific antibodies were negative in all patients. The amount of necrotic fibers and inflammatory cells was various; no to mild (n=6) and severe (n=3). All patients showed over expression of MHC-1 on muscle fibers. In three patients with severe inflammation, CD11c+ cells but not CD8+ lymphocytes, were surrounding and/or invading non-necrotic fibers. On the other hand, CD163+ cells were diffusely distributed in perimysium and endomysium. Conclusions:The clinical and pathological features of cGVHD myositis were heterogeneous. The three patients with elevated very high serum CK and frequent CD11c macrophages infiltration in endomysium suggests a subtype of cGVHD myositis.

P1-62

Abundant cytoplasmic bodies in myotendinous junctions

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Introduction: Nemaline and cytoplasmic bodies are found in normal myotendinous junctions. However, abundant cytoplasmic bodies in myotendinous junctions might be abnormal. Methods: Retrospective study in cases with cytoplasmic bodies, which were not assumed diagnostic at first, because of existence of myotendinous junctions in the section. Results: Two cases were found. Case 1. A 77-year-old man presented with distal neuropathic leg muscle atrophy and lumbar paraspinal muscle atrophy. Anti-GalNAc GD1a IgG antibody was positive (++). IVIg was not effective. Needle EMG showed single fiber spontaneous abnormalities and decreased motor units. Nerve conduction studies showed markedly low amplitude of M waves and mildly slow motor nerve velocity in the tibial and peroneal nerves, but sural nerve was normal. Peroneus muscle was biopsied with sural nerve. There was grouped atrophy, but myopathic changes with disorganization of intermyofibrillar networks was prominent. Cytoplasmic bodies and nemaline bodies were found beyond myotendinous junction. Sural nerve was within normal. BAG3 mutation was found. It was difficult to detect myopathic changes by neurophysiological methods. Case 2. Semitendinosus was biopsied in a 32-year-old man with distal myopathy. Rimmed vacuoles were frequent. Muscle fibers with cytoplasmic bodies were mostly hypertrophic and scattered. TTN mutation was found. Conclusion: Abundant cytoplasmic bodies found in muscle fibers can be abnormal even if there are myotendinous junctions in the sections.

P1-63

An autopsy case of myotonic dystrophy combined with idiopathic normal pressure hydrocephalus

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Introduction: Myotonic dystrophy is a hereditary neuromuscular disorder with multisystem involvement. Hydrocephalus is detected uncommonly in adult form of myotonic dystrophy, but idiopathic normal pressure hydrocephalus is rare as a late complication of the disease. We report an autopsied case of myotonic dystrophy combined with idiopathic normal pressure hydrocephalus. Clinical summary: She was not good at physical exercise, since she was adolescence. In her forties, she felt difficulties in walking and became fall down easily. At the age of 51, she was diagnosed as myotonic dystrophy. She began to use a wheelchair for about 60 years old. At the age of 64, an enlargement of the ventricle was pointed out by CT. At the age of 65, a decline in cognitive function and daily activities was noted, and progressive ventricular enlargement and narrowing of the subarachnoid space of the supratentorial convexity were detected by MRI. Tap test was performed and the activities of daily living and cognitive function were improved. Shunt operation was not performed, as she did not accept it. At the age of 66, she died of respiratory failure. Pathological findings: Fixed brain weighed 1190g. Mild demyelination was noted in the frontal lobes. Arteriolosclerosis accompanied by gliosis in the white matter were seen. Neurofibrillary tangles and AT-8 positive neurons were scattered in the limbic system, striatum, substantia nigra. Amyloid beta was not detected immunohistochemically. Conclusion: We assume that age-related pathomechanism of myotonic dystrophy might play a role in the development of NPH.

P1-64

Phosphorylated TDP-43 (pTDP-43) aggregates in the axial skeletal muscle of patients with sporadic and familial amyotrophic lateral sclerosis

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Introduction: Muscle atrophy and weakness are core features of amyotrophic lateral sclerosis (ALS). Studies in ALS patients and animal models have provided evidence that muscle plays an active role in the disease.

Methods: We studied 148 muscle specimens from 57 ALS patients for phospho-TDP-43 (pTDP-43) inclusions in appendicular (quadriceps, deltoid) and axial (diaphragm, paraspinous) groups. p62/ sequestosome-1 and FUS inclusion pathologies were also examined and in a subset of samples electron microscopy was performed. These samples were contrasted with 25 non-ALS samples with neurogenic atrophy, including samples of inclusion body myositis (IBM). SQSTM1 and TARDBP gene expression was examined in ALS, IBM, and atrophy samples. Pathologic findings were associated with salient disease characteristics in ALS, such as disease duration and genetic status.

Results: pTDP-43 myofiber inclusions were identified in 19 ALS patients (33.3%) in 24 samples (16.2% of blocks screened). pTDP-43 pathology was significantly more common in axial than appendicular muscles in ALS ($P = 0.0087$) and was not associated with pertinent clinical, genetic, or nervous system TDP-43 pathologic data. Among non-ALS samples, pTDP-43 inclusions were seen only in IBM, where they were more diffuse than in ALS ($P = 0.007$). p62/ sequestosome-1, but not FUS, labeling was seen in pTDP-43-positive foci in ALS and IBM and both groups showed significant up-regulation of TARDBP and SQSTM1 expression.

Conclusions: These findings suggest that the impaired clearance of misfolded proteins in ALS, recognized in motor neuron degeneration, may play an important role in pTDP-43 pathology in ALS muscle.

P1-65

Anaplastic medulloblastoma with multilineage differentiation in Indian subcontinents: a case report

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Introduction:Medulloblastoma with multilineage differentiation is a rare variant with poor prognosis. Medulloblastoma is the most common malignant brain tumor of childhood with predilection for cerebellar vermis. Peak age is 7 years and metastasizes via CSF. Medulloblastoma may have the potential to differentiate into neuronal, astrocytic, myogenic, lipomatous or melanotic types. Very few cases of simultaneous multipotent differentiation are known. Here we present a case of anaplastic medulloblastoma showing multilineage differentiation. This case suggests multipotent stem cells origin of medulloblastoma. Clinical summary:21 years male presented with nausea, vomiting and on&off schizures. No previous medical and surgical history. Haemogram was unremarkable. MRI revealed heterogeneously enhancing posterior fossa tumor arising from fourth ventricle. Pathological findings:Light microscopy demonstrated cellular neoplasm with morphologically distinct components. There was admixture of closely packed anaplastic cells with round to oval hyperchromatic nuclei, scant cytoplasm, occasional rosettes along with large pleomorphic rhabdoid cells having eccentric nuclei and brightly eosinophilic cytoplasm. The third component consisted of cells with small, hyperchromatic nuclei and scant cytoplasm in a fibrillary background. Mature ganglion cells, melanotic tumor cells and frequent mitoses were also present. Immunohistochemistry revealed diffuse expression of GFAP with focal expression of Synaptophysin, NSE, Desmin and HMB45. Thus a final diagnosis of medulloblastoma with myogenic, neuronal, astrocytic, and melanotic differentiation was given. Unfortunately the patient died within 2 months of radiotherapy. Conclusion:Histopathology and Immunohistochemistry play important role in diagnosis and subtyping. Their exact histogenesis is unclear. Definitive characterization of each medulloblastoma subtype may improve prognosis.

P1-66

Genomic Alterations and Molecular Subgroups in Atypical Teratoid/ Rhabdoid Tumors: The Medical University of Vienna (MUV) Experience

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Background: Atypical teratoid/rhabdoid tumors are characterized by biallelic inactivation of the SMARCB1/INI1 gene, and may occur sporadically or within the setting of a rhabdoid predisposition syndrome. Three distinct molecular subgroups (ATRT-TYR, ATRT-MYC, ATRT-SHH) have been defined. Patient outcome is in general poor, however, improved patient outcome could be achieved with an intensive multimodal therapy developed at the MUV. Methods: Tumor tissues and constitutional DNA from 16 patients treated at the MUV for primary or recurrent tumors were analyzed using immunohistochemistry, MLPA, Sanger sequencing and 850K methylation arrays. Patient age at diagnosis ranged between 3 months and 22 years. 5 were females, 11 males. Tumor location was in 10 patients supratentorial (ST) and in 6 posterior fossa (PF). Results and conclusion: In 8 patients, homozygous deletions of the SMARCB1/INI1 gene were observed. In 3 patients, the combination of a coding sequence mutation and a deletion was found. In 5 tumors only one hit was detectable within the tumor tissue (4 deletions, 1 mutation). Molecular subgroups could be determined in 13 patients and revealed 6 ATRT-SHH (5 ST/1 PF), 4 ATRT-TYR (all PF) and 3 ATRT-MYC (all ST). In 3 patients, 1 ATRT-MYC, -SHH and -TYR respectively, a germline alteration was found, including 2 deletions and 1 coding sequence mutation. 11 patients, including 1 patient with germline mutation are alive, 3 patients died of disease, 1 patient died of secondary glioblastoma and 1 patient from sepsis. The documentation of genotype/phenotype correlations is important to detect patients who might have an improved survival.

P1-67

Congenital central nervous system tumors: a mono-institutional series of 51 consecutive patients

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Congenital central nervous system (CNS) tumors are rare and histologically heterogeneous. Their incidence is 1.1-3.4 per million live births depending on the definition of congenital used. We present a mono-institutional series of 51 consecutive CNS tumors diagnosed within the first year of age. The predominant age and gender were ≤ 4 months (23, 45%) and male (35, 69%). Thirty-eight (74%) tumors were supratentorial. The encountered tumors were astrocytomas (18, 37%), embryonal tumors (12, 24%), neuronal-glial tumors (8, 16%), choroid plexus tumors (8, 16%), teratomas (2, 4%) and ependimomas (3, 4%). Two of 2 (100%) teratomas and 9 of 12 (75%) embryonal tumors were diagnosed within 4 months of age. Three of 3 (100%) ependymomas, 6 of 8 (75%) mixed neuronal-glial tumors, 5 of 8 (62%) choroid plexus tumors and 11 of 18 (61%) astrocytomas affected children ≤ 4 months old. Eighteen (35%) patients were died (median survival 18 months, range 1-98 months), 17 (33%) were alive and well (median survival 68 months, range 24-114 months), 14 (27%) were alive with disease (median survival 31 months, range 7-76 months), 2 (4%) was lost at the follow-up. Most frequent tumor among died, alive and well or alive with disease patients were respectively embryonal tumor (7, 39%), choroid plexus papilloma (6, 35%) and low grade astrocytoma (6, 40%). Congenital CNS tumors frequently affect male and are supratentorial. They encompass numerous histotypes with different frequency depending on the age. Embryonal tumors predominate in short survivors patients.

P1-68

A clinical diagnostic challenge: cranial nerve and leptomeningeal involvement by Atypical Teratoid/Rhabdoid Tumor (AT/RT) in a 15-month-old male infant presenting with lip swelling

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Introduction: Atypical Teratoid/Rhabdoid Tumor (AT/RT) is an aggressive embryonal CNS tumor characterized by loss of SMARCB1 or SMARCA4 genes. AT/RT occur most frequently in the posterior fossa of young children with signs and symptoms of increased intracranial pressure. In this report, we describe a male infant with orofacial swelling associated with cranial nerve and leptomeningeal AT/RT. Clinical summary: An otherwise healthy 15-month-old male infant presented with 2 months history of lip swelling. The swelling occurred suddenly in the left side of the upper lip. Parents reported on and off fever as well as facial asymmetry. Infectious workup ruled out herpes which prompted a tissue biopsy from the lip lesion. Microscopically there is only an ulcer and granulation tissue. Multidisciplinary team approach was initiated to rule out infectious, inflammatory, or neoplastic processes. While in hospital, the baby became lethargic and brain MRI demonstrated a hydrocephalus with extensive leptomeningeal and cranial nerve enhancement. There was also a dural based enhancement in the left cerebellopontine angle. An urgent ventricular shunt was performed. Cerebrospinal fluid cytology analysis showed no malignant cells. Decision was made to target the meningeal enhancement for tissue biopsy. Pathological findings: Biopsy from cerebral cortex revealed expanded subarachnoid space by sheets of small round blue cells. The neoplastic cells immunoreact positively for vimentin, smooth muscle actin and CD99 with lost nuclear staining for INI1. Therefore the diagnosis of AT/RT was confirmed. Conclusion: We hereby describe a very unusual manifestation of AT/RT with an isolated cranial nerve paresis/paralysis in a very young child.

P1-69

Grading of Meningeal Solitary Fibrous Tumors/Hemangiopericytomas: Prognostic Value of the Marseille Grading System in a Cohort of 132 Patients in correlation with molecular data

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Introduction: The finding that meningeal Solitary Fibrous Tumors (SFTs) and meningeal Hemangiopericytomas (HPCs) are both characterized by NAB2-STAT6 gene fusion pushed their inclusion in the WHO 2016 Classification of tumors of the central nervous system (CNS) as different manifestations of the same entity. However, it is presently unclear whether the grading criteria are still adequate. Also, the prognostic value of molecular characteristics of CNS SFTs/HPCs is presently unclear. Methods: We investigated the prognostic value of an updated version of the Marseille Grading System (MGS), of different NAB2-STAT6 fusion variants and of Telomerase Reverse Transcriptase (TERT) promoter mutation in a retrospectively collected cohort of 132 primary meningeal SFTs/HPCs. Results: 73 cases (55%) were MGS I, 50 cases (38%) MGS II, and 9 cases (7%) were MGS III. In multivariate analysis, extent of surgery, mitotic activity ≥5/10 High Power Fields (HPFs), MGS I, and MGS III were independent prognostic factors for progression free survival, while necrosis, MGS III, and radiotherapy were independent prognostic factors for disease specific survival. Although the NAB2ex6-STAT6ex16/17 type of fusion was significantly more frequent in MGS II and III tumors (p=0.004), there was only a trend for worse prognosis in cases with this fusion type (p=0.172). TERT promoter mutation had no prognostic value. Conclusion: This study shows that the combination of histologic criteria used in the updated MGS (mitotic activity ≥ 5/10 HPF and necrosis) is valuable for grading meningeal SFTs/HPCs. No clear prognostic value was found for NAB2-STAT6 fusion type nor for TERT promoter mutation.

P1-70

Lack of H3K27 hypomethylation in pediatric meningiomas

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Modifications of histone H3 at lysine K27 are of interest in oncology due to their prognostic and potential therapeutic implications. Since hypomethylation has been associated with a worse overall (OS) and recurrence-free survival (RFS) in adult meningiomas, we sought to determine if this association exists for pediatric tumors as well. Clinical data from patients aged ≤17 with a pathologic diagnosis of primary meningioma between the years 1989-2017 was collected. Tumors were graded based on WHO 2016 criteria. Immunohistochemical staining for H3K27 trimethylation (H3K27me3) was interpreted as positive (endothelial and tumor cell staining) or negative (endothelial staining only). The Kaplan-Meier log-rank method and Fisher exact test were used to determine relationships to OS, RFS, sex, NF2, methylation status, and grade. Clinical data from 35 patients was collected. Median patient age was 12 years (range 2-17). Fourteen patients had a clinical diagnosis of neurofibromatosis type 2 (NF2). There were 18 Grade I (51.4%), 13 Grade II (37.1%), and 4 Grade III (11.4%) tumors. Tissue was available for 29 patients. There were no significant differences in OS or RFS for grade, NF2, or sex. Complete loss of H3K27me3 staining was not observed in any of the tumors. Though H3K27 hypomethylation has been associated with reduced OS and RFS in an adult population, our study did not demonstrate hypomethylation in 29 pediatric meningiomas. This may suggest a distinct tumor biology for pediatric and adult tumors. However, larger studies are necessary to confirm these findings and further elaborate the role of epigenetics in pediatric meningiomas.

P1-71

Large dural based mass with bony remodeling in a 16 year old: An IgG4 related pseudotumor mimicking lymphoplasmacyte-rich meningioma

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Introduction: IgG4 related disease is an autoimmune process that presents with tumefactive lesions characterized by storiform fibrosis, a dense lympho-plasmacytic infiltrate rich in IgG4 positive plasma cells, obliterative phlebitis, and often elevated serum IgG4 levels. CNS IgG4 related disease occurs as hypophysitis, hypertropic pachymeningitis or rarely as intraparenchymal lesions. We present a rare instance of IgG4 related hypertrophic pachymeningitis presenting as a dural pseudotumor mimicking meningioma.

Clinical summary: A 16 year old male presented with focal seizures for last 5 months. Imaging revealed a large extra-axial contrast enhancing mass lesion in left frontoparietal region with focal calvarial thickening.

Pathological findings: Histopathology revealed a fibrosclerotic lesion involving dura with polymorphic infiltrate of plasma cells, mature lymphocytes, histiocytes, occasional eosinophils and few meningothelial whorls. Immunohistochemical work up excluded the possibilities of meningioma, lymphoproliferative neoplasms and histiocytic lesions. Majority of plasma cells were IgG4 positive with IgG:IgG4 ratio of more than 50%. Based on overall features final diagnosis of IgG4 related inflammatory pseudo-tumor was rendered.

Conclusion: IgG4 related tumefactive lesions of the CNS are under-recognized. Identification requires appropriate work up to exclude commoner mimics. They show excellent response to steroids and steroid sparing drugs. Documentation of such cases is essential to improve understanding.

P1-72

A case of Xanthomatous meningioma

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Introduction: Xanthomatous meningioma is a very rare subtype of Grade 1 metaplastic meningioma, in 2016 WHO classification of Central nervous system. We present this case, along with a literature review. Clinical summary: A 70-year-old Japanese female, admitted for generalized seizure. Magnetic resonance imaging demonstrated a well-demarcated, homogeneously and brightly contrast enhancing mass, measuring 3x2.5x2.2 cm located in the fornix of left frontal lobe. It showed a dural tail sign. Cerebral artery embolization was performed before tumorectomy. Tumor revealed demarcated yellow-tan colored, attached to the dura. Pathological findings: Tumor was consisted of meningothelial cell proliferation and numerous xanthomatous changed cells. Scattered Psammomatous bodies and many hyalinous vessels were excisted. Mitosis was rare and necrosis was absent. The xanthomatous tumor cells showed immunoreactivity for epithelial membrane antigen and vimentin. MIB-1 stained less than approximately 1% of the tumor cells. Conclusion: We diagnosed this case as Xanthomatous meningioma, WHO Grade I. The patient was followed for 14 months without any evidence of recurrence.

P1-73

Hypertrophic pachymeningitis accompanying lymphoplasmocyte-rich meningioma-a case report

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Introduction: Hypertrophic pachymeningitis is a rare chronic fibrosing inflammatory process involves cerebral and/or spinal dura mater. Its underlying cause varies, including neoplasm. Lymphoplasmocyte-rich meningioma is also a rare histological subtype of meningioma with relatively good prognosis. The combination of both entities has seldom been reported. (break)
*Methods:*Case report.(break)
*Results:*A 41-year-old woman was present for admission after 3 years of bilateral hearing loss and 1 year of bilateral vision loss.Brain MRI reveal thickened and contrast-enhanced dura of tentorium cerebelli, bilateral internal acoustic meatus,cavernous sinus and optic nerve sheath. Her CSF showed elevated white blood cells uo to 504 per microliter and protein 166mg per deciliter. Her serum interferon γ release assay was also positive. Other laboratory tests were normal. A biopsy was performed for suspicious chronic tuberculosis meningitis. Pathologically, the specimen showed fibrous tissue hyperplasia,lymphoplasmacytic infiltration, scattered Russell bodies and meningothelial nests. Immunohistochemistry showed CD3,CD20,CD38,CD138 and EMA were all positive.Ki67 index was less than 5 percent.IgG was positive but IgG4 negative. The diagnosis of hypertrophic pachymeningitis accompanying lymphoplasmocyte-rich meningioma was made.(break)
Conclusion: Hypertrophic pahcymeningitis is a chronic inflammatory disorder of the dura matter that may cause multiple neurological deficits. When the laboratory evaluation for its underlying cause is uncertain,a prompt biopsy should be considered.

P1-74

Tumour metastasis to meningioma: report of a challenging case

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Tumour metastasis to meningioma : report of a challenging case Introduction The occurrence of tumour to tumour metastasis is generally uncommon. In the central nervous system, the most common recipient tumour is meningioma. In a recent review of the literature, 144 cases of tumour to meningioma were reported. Clinical Summary A 63 year old Chinese lady presented with visual blurring in the right eye. There was no other significant history noted. Radiology showed extra-axial T2 hypointense and enhancing mass centered over the right anterior clinoid, extending superiorly into the right frontal lobe. Pathological Findings At frozen section, the lesion demonstrated predominantly papillary features and myxoid areas. There are also areas composed of spindled cells with whorl formations, in keeping with a meningothelial neoplasm. Paraffin section of frozen remnant and additional tissue submitted revealed glandular formation with cribriform nests and papillary tufts, associated with a myxoid background and areas resembling conventional meningioma. Both components were immunoreactive for EMA. A papillary meningioma was considered, with differential of metastasis involving a meningioma. A subsequent postoperative scan of the thorax showed multiple lung nodules. Additional immunohistochemistry confirmed metastatic adenocarcinoma elements positive for CK7, TTF1 and NapsinA, while the meningioma component was negative. The final diagnosis is that of a metastatic adenocarcinoma of the lung involving a WHO Grade I meningioma. Conclusion In summary, we present a case report of a metastatic lung adenocarcinoma involving a low grade meningioma. Pathologists, radiologists and neurosurgeons should be aware of this diagnostic pitfall.

P1-75

Intracranial angioleiomyomas: report of 4 rare cases

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Introduction: Angioleiomyomas are benign, mesenchymal soft tissue tumours. Intracranial angioleiomyomas are extremely rare. We report 4 Chinese cases of intracranial angioleiomyomas. Clinical Summary: The lesions of present 4 cases located in the skull base, parasagittal and parafalcine. The neuroradiologic features of these lesions were indistinctive, and they were all misdiagnosed before surgery. Pathological findings: Histopathologically, these lesions consisted of thick-walled vessels blending with spindle cells, which were positive for vimentin, desmin and smooth muscle actin, while negative for cytokeratin and HMB45. Cytological atypia and necrosis were hardly observed. And, the Ki-67 labelling index were less than 2%. Conclusion: Although rare, angioleiomyomas should be considered as a differential diagnosis of meningioma and other mesenchymal, non-meningothelial tumours of the central nervous system.

P1-76

Central nervous system marginal zone B-cell lymphomas involving brain or spinal parenchyma: clinicopathological study of eight cases

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Introduction:Marginal zone B-cell lymphomas (MZBCL) are non-Hodgkin lymphomas arising from postgerminal center marginal zone B-cells. MZBCL are subclassified into extranodal-, nodal-, and splenic MZBCL. Intracranial MZBCL, one of the extranodal examples, typically present as a solitary dural mass. MZBCL involving the central nervous system parenchyma (MZBCL-CNSP) are, however, extremely rare, and their clinicopathological features are not well characterized.*Methods*:We assessed clinocopathological feature of 8 MZBCL-CNSP cases (86, 53, 46, 49, 43, 68, 58, 60 years old, 6 males and 2 females). MRIs showed a solitary lesion in 2 patients and multiple lesions in the brain or spinal cord in 6. Aggressive and indolent clinical courses were recorded in 2 and 4 cases, respectively, and 2 patients remained in remission. Histological and immunohistochemical as well as genetic studies were performed using formalin-fixed and paraffin-embedded tissue samples obtained form brain biopsy.*Results*:Biopsy specimens of all cases revealed atypical small lymphocytic infiltrates with plasma cells in a predominantly perivascular growth pattern. Atypical cells were positive for CD20, but negative for CD3. In addition, tumor-infiltrating T cells were prominent. It was, therefore, extremely difficult to differentiate the MZBCL-CNSP from inflammatory or demyelinating diseases or lymphomatoid glanulomatosis in all cases. However, an analysis of immunoglobulin heavy chain variable region (IgVH) genes was valuable in confirming the diagnosis of MZBCL-CNSP in all cases.*Conclusion*:The results indicate that the MZBCL-CNSP may not always be clinically indolent. Detection of IgVH gene rearrangement is necessary for the definite diagnosis of MZBCL-CNSP.

P1-77

Epstein-Barr virus-associated diffuse large B-cell lymphoma in the patient with temozolomide-treated glioblastoma: A case report

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Introduction: Temozolomide is a DNA-alkylating agent fort treatment of glioblastoma (GM). So far, around 10 cases of non-Hodgkin lymphoma have been reported in glioma patients after temozolomide treatment. Here, we reported a rare case of Epstein-Barr virus(EBV)-associated diffuse large B-cell lymphoma (DLBCL) subsequently developed after glioblastoma treated with temozolomide. Clinical summary: A 57-year-old female patient received gross total removal of GM of left parietal lobe and underwent subsequent concurrent chemoradiation and temozolomide for maintenance. Seven months later, aphasia was developed after 4th cycle of temozolomide. Brain magnetic resonance image (MRI) revealed a newly appeared rim-enhancing mass in left parietal lobe. As tumor recurrence was suspected, the lesion was surgically removed and diagnosed with EBV-associated DLBCL. Patient treated with high-dose methotrexate combined with vincristine and dexamethasone. Six month later from diagnosis of DLBCL, follow up brain MRI revealed T2-intense lesion in right temporal lobe, and recurrent GM was suspected. Patient is still alive, being treated with salvage radiotherapy. Pathologic findings: The firstly removed tumor was typical glioblastoma, IDH-wildtype, harboring palisading necrosis and endovascular proliferation. The secondly developed lesion showed radionecrosis and multiple patchy lymphocytic proliferation. In addition, coagulative necrosis and angiodestructive growth pattern of monotonous lymphocytes were suspicious findings. The lymphocytes were diffusely positive for CD20 and EBV in situ hybridization. Taken together, a diagnosis of EBV-associated DLBCL was made. Conclusion: Although rare, secondary lymphoma could be developed during or after temozolomide treatment, might be derived by drug toxicity or induced immunosuppression and EBV infection.

P1-78

Histopathological features of an autopsied patient with lymphomatoid granulomatosis in the central nervous system

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Introduction: Lymphomatoid granulomatosis (LYG) is one of the Epstein-Barr virus (EBV) -associated lymphoproliferative disorders, rarely involving the central nervous system (CNS). Clinical summary: A 68-year-old male developed gait disturbance with falling. Parkinsonism was observed. Levodopa was ineffective against his symptoms. He was clinically diagnosed as multiple system atrophy. Then, he deteriorated and one year after the onset, he suddenly fell into coma followed by status epilepticus. MRI revealed Gd-enhancing lesions in the left cerebral subcortical white matter, corpus callosum and middle cerebellar peduncles. Approximately 20 months after the onset, he died. Pathological findings: At autopsy, the brain weighted 1,500 g. Macroscopically, the left cerebral hemisphere was severely swollen. Coronal sections of the cerebrum demonstrated ill-demarcated grayish and softening lesions mainly in the left cerebral subcortical white matter, corpus callosum, and middle cerebellar peduncle. Microscopically, marked perivascular and parenchymal lymphocytic inflammations with necrosis were noted. Granuloma like-mass lesions consisting of numerous CD68-positive macrophages, CD3- or CD20-positive T- or B-lymphocytes and plasma cells with necrosis were also observed. Neither prominent mitotic changes nor viral inclusions were demonstrated. Epstein-Barr encoding region (EBER) in situ hybridization disclosed positive nuclei of the infiltrating cells. Conclusions: We reported the autopsy findings of LYG. LYG could be classified as a T-cell rich, EBV-associated, B-cell lymphoproliferative disorder. However, it remained controversial that CNS-LYG may be a disorder derived from T-cell monoclonal lymphoproliferation. Further histopathological studies are needed to clarify the histogenesis and prognostic variability on the CNS-LYG.

P1-79

An autopsy-proven case of paraneoplastic lower motor neuron disease due to Waldenstrom's macroglobulinemi

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Introduction:Waldenstrom's macroglobulinemia(WM) is defined as a lymphoplasmacytic lymphoma that develops in the bone marrow and is characterized by immunoglobulin M paraproteinemia. A few reports have evaluated the association with motor neuron disease(MND) and definitively diagnosed monoclonal paraproteinemia due to WM during an autopsy. Clinical summary:We report a case of a 77-year-old man who developed WM with sensorimotor neuropathy who was pathologically confirmed to have lower MND by autopsy. Pathological findings:After informed consent for family, Autopsy was done. Whole brain, brain stem, spinal cord, and peripheral nerve were fixed with 4% formalin. Routine hematoxylin and eosin staining and Luxol fast blue were done. Moreover, immunostain by anti-CD20 antibody, anti-CD38, and anti-pTDP-43 antibody was carried out. Autopsy findings showed degeneration of the hypoglossal nuclei, prominent neuronal loss and atrophy in the anterior horn of the whole spinal cord despite the presence of mild astrocytosis, degeneration of the gracilis on one side, and infiltration of inflammatory cells which included B cells and plasma cells in the lumbar anterior and posterior roots, iliopsoas muscle, and perivascular area of the cervical cord. On immunostaining, pTDP-43 antibody positive cytoplasmic inclusions were observed in the motor neurons and astrocytes of hypoglossal nuclei and whole spinal cord. Conclusion:Although the relationship between WM and lower MND is obscure, we speculate that the paraneoplastic effect or immunological factors due to WM might enhance motor neuron death and degeneration of the posterior funiculus.

P1-80

Castlemans disease plasma cells type intraspinal and unicentric: report of a case and review of the literature

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Introduction: Castlemans disease is a rare lymphoproliferative disorder. The unicentric disease, typical of the hyaline-vascular type, however, the type of plasma cells can present as a localized mass, approximately 10%, with resolution of symptoms after surgical resection. Clinical summary: A 51 year old woman who started in 2012 with low back pain, limitation of movements and loss of strength in pelvic limbs. After surgery recovered strength, remitting in August 2016, with paresthesias, making it impossible to walk, decreased thermal sensitivity and pain in both extremities. The physical examination revealed a decrease in thermoalgesic sensitivity of T7 towards caudal. Magnetic resonance imaging shows an intraspinal, extraaxial lesion that compresses the spinal cord at the level of T4-T5. Pathological findings: Multiple fragments of light brown tissue and rubbery consistency. The histology shows multiple reactive lymphoid follicles and germinal centers with stainable body macrophages. The interfollicular, paracortical and medullary space are full of monotonous and non-atypical plasma cells. Immunohistochemistry with reactive pattern for CD20 and CD3 in the germinal centers and the paracortical compartment respectively, CD138 positive in plasma cells, with polyclonal expression for the Kappa and Lambda light chains and negative for HHV8. Conclusion: Castlemans disease is uncommon and clinically it can be unicentric or multicentric. The plasma cell type is most often multicentric. Histologically, it can have hyperplastic lymphoid follicles and plasma cell mantles without atypia that dilate the sinusoids and that can be found in the paracortical and interfollicular zone. The intraspinal presentation is extremely rare.

P1-81

Extranodal Rosai Dorfman disease: case with primary involvement in the central nervous system

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Introduction: Rosai Dorfman disease is a clinicopathological entity of unknown nature and scarce frequency. It occurs as massive lymphadenopathy with sinus histiocytosis and systemic symptoms such as fever. Exceptionally, it presents as an extranodal entity without lymphatic involvement. Clinical summary: A 35 year old man who started in 2016 with a slight decrease in the strength of the left thoracic limb, ipsilateral peripheral facial paralysis and a tonic-clonic seizure episode. The physical examination showed facial asymmetry to the gesticulation with deviation of the mouth corner to the right. Magnetic resonance imaging shows a solid lesion in the right temporoparietal plate dependent on the dura mater. No neck ganglion growths were observed. Patological findings: Fragment of thickened dura mater and fine granular surface, grayish white color and rubbery consistency. The histology shows substitution of the meningeal parenchyma for mixed inflammatory infiltrate, with formation of lymphoid follicles, eosinophils and abundant clear cytoplasm histiocytes, oval nuclei and fine granular chromatin. In some areas the phenomenon of emperipolesis is observed, without atypical mitoses, necrosis or neoplastic cells. Positive immunohistochemistry for PS-100 and negative for CD1a. Conclusion: Rosai Dorfman disease with meningeal disease is a rare entity. In imaging studies, it is usually diagnosed as plaque meningioma. Clinically it presents with focal motor deficits, seizures and headache. The diagnosis is morphological and immunohistochemistry can help rule out neoplastic lesions of lymphoid strain. In most cases surgery is indicated, but in patients with extensive lymph node involvement, corticosteroids and radiotherapy are used as adjuvants.

P1-82

Chondroblastoma-like tumor of the skull in a patient with cardio-facio-cutaneous syndrome

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Introduction: Cardio-facio-cutaneous syndrome (CFCS) is a rare genetic disorder characterized by craniofacial deformities and heterogenous cardiac and cutaneous manifestations. The condition is caused by de novo activating mutations in the RAS/MAPK signaling pathway, including BRAF, MEK1, MEK2, and KRAS. Urothelial carcinoma, embryonal rhabdomyosarcoma and neuroblastoma have been reported in the setting of CFCS. Clinical summary: Herein we report a chondroblastoma-like lesion of the skull in a 20-year-old man with a clinical diagnosis of CFCS and a long standing history of medically intractable epilepsy. The patient presented with altered mental status, lethargy and vomiting. Imaging studies demonstrated expansion of the left mastoid temporal bone along with a large left temporal intracerebral hematoma. He underwent left temporoparietal craniectomy and debulking of the hemorrhagic tumor. Pathologic findings: Histologic examination revealed a mixed solid and cystic lesion. The more solid areas exhibited sheets of mononuclear cells, many with nuclear grooves, variably sized multinucleated giant cells and fibrochondroid islands. The latter consisted of blood-filled cystic spaces lack of endothelial lining and focal unmineralized bone along the cyst walls. FISH analysis for USP6 gene rearrangement was negative. While these features are mostly consistent a chondroblastoma with secondary aneurysmal bone cyst formation, next generation sequencing studies revealed no mutations in H3F3A or H3F3B gene, respectively. However, a p.Q257R mutation located on exon 6 of the BRAF gene characteristic of CFCS was identified. Conclusion: Patients with CFCS have prevoiusly been noted to have poorly-defined giant cell-rich lesions and this may be one such example.

P1-83

Sellar atypical teratoid/rhabdoid tumor (AT/RT): a clinicopathologically and genetically distinct variant of AT/RT

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Introduction: Atypical teratoid/rhabdoid tumors (AT/RT) are rare, aggressive tumors of the central nervous system that predominantly affect infants. Although adult AT/RT is rare, accumulated cases have revealed adult-specific AT/RT in the sellar region. Eighteen previously reported cases of sellar AT/RT exclusively occurred in adults, suggesting biological differences from conventional infant AT/RT. We herein investigated a series of seven sellar AT/RT to clarify the clinicopathological and genetic outlines of this tumor. Methods: Seven cases of sellar AT/RT were histologically and immunohistochemically assessed. Fluorescence in situ hybridization, direct sequencing, and multiplex ligation-dependent probe amplification analyses for the INI1/SMARCB1 gene were performed. Results: All seven cases were adult females, ranging in age from 21-69 years old. Tumors were histologically characterized by a hemangiopericytoma-like stag-horn vasculature within a dense, diffuse proliferation of jumbled cells and a few scattered rhabdoid cells. This vascular pattern is not a common finding in AT/RT and appears to be characteristic histology of sellar AT/RT. Biallelic alterations in the INI1 gene were identified in five out of the six cases analyzed. Four out of the five cases harbored two different mutations, presumably on different alleles (compound heterozygous mutations), and one case of which had a splice-site mutation. Combined with previous findings, the prevalence of compound heterozygous mutations and splice-site mutations was significantly higher in sellar AT/RT than in pediatric AT/RT. Conclusion: Sellar AT/RT represent a clinicopathologically and possibly genetically distinct variant of AT/RT showing characteristic demography, different patterns of INI1 alterations, and histology featured by a unique vasculature.

P1-84

Thirty Years Experience with Pituitary Adenomas

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Introduction:The immunohistochemistry results of resected pituitary adenomas in 1989,1999 and 2008 were compared from a database of 4800 cases (1984-2017) Methods: The extent of immunohistochemical reaction to prolactin, human growth hormone, beta sub-units of FSH, LH,and TSH ,alpha sub-unit, ACTH, Mib-1Cam5.2 and p53 for all pituitary adenomas at MGH since 1987 were recorded on a scale of zero to 3+ (none, scarce, some and many or most). The data from the years 1989. 1999,and 2008 were compared for trends in types of tumors and immunohistochemical investigations. Results: The numbers of adenomas increased from 65 per year in 1989-1999 to about 140 per year through 2017. 73, 115 and 124 cases were recorded in 1989, 1999 and 2008. 1989 73 tumors including 12 Cushing (16%),prolactinoma 10(14%),14 acromegaly(19%,). 1999 115 tumors including 23 Cushing(20%,18F),6 prolactinomas(5%),12 acromegaly(10%,4F). and in 2008 124 tumors including 23 Cushing(20%,22F), 9 prolactinomas(7%), 21 acromegaly (17%,12F). In the three time periods there were no Mib1, p53 or Cam5.2 performed in 1989. Only 8 Mib1 was performed in 1999. In 2008 86 Mib1, 28 p53 and 17 Cam5.2. Five of the latter with a dot-like pattern. Conclusion: Construction of this database has enabled recognition of changing patterns of immuno-histochemical analysis of pituitary adenomas. The most noticeable change was the adoption of Mib1 proliferation index, Cam5.2 between 1999 and 2008. and enabled clinical pathological exploration of adenoma behavior. This database has contributed to many publications.

P1-85

Histological, MRI and clinical characteristics in patients with IgG4-related pathology in pituitary gland

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Introduction: IgG4-related disease is a multiorgan disease histologically characterised by lymphoplasmacytic infiltration with a high proportion of IgG4-reactive plasma cells, fibrosis and occasional obliterative phlebitis. IgG4-related hypophysitis has been increasingly reported. However, diagnostic criteria and whole spectrum of histological changes are still unclear due to limited number of biopsy-proven cases. Methods: We have reexamined specimens obtained by pituitary surgery performed at Uppsala University Hospital in the period 2010-2017 that were originally reported to represent inflammatory changes. An additional specimen was available from dura from a patient who presented with clinical signs of hypophysitis followed by chronic meningitis. Patients with IgG4-related changes in tissue specimens were selected and their MRI, clinical and histopathological characteristics correlated. Results: Five pituitary specimens fulfilled histological criteria for IgG4-related hypophysitis. IgG4-related pathology has also been confirmed in the dural biopsy. Additional histological changes that are not traditionally related to IgG4 process were identified in all the biopsies. Specific MRI changes suggestive for IgG4-related pituitary pathology could not be identified. One of the patients had slightly elevated serum IgG4 and extracranial manifestations potentially related to IgG4 process. Conclusion: Preoperative diagnosis of IgG4-related hypophysitis is difficult due to lack of specific clinical and MRI features. Patients with IgG4-related hypophysitis rarely show disease manifestations in other organs. The presence of the histopathological changes not strictly related to IgG4 process suggests the role of organ specific mechanisms that potentially trigger IgG4 cell proliferation and fibrosis. Possibility of the intracranial propagation of the IgG4 process cannot be excluded.

P1-86

Craniopharyngioma recurrent with extended necrosis (craniopharyngioma apoplexy): two cases reports

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Introduction: The term pituitary apoplexy is a less common condition when a pituitary tumor outgrows its blood supply a stroke, describes larger bleeds leading to the sudden onset of symptoms. Little is known about the Craniopharyngioma apoplexy. We presented 2 cases of apoplexy CP. Clinical Summary: 30-year-old woman who for 18 years old has been diagnosed a CP. Until now she has recurred in 6 different times, last one, she was admitted to our hospital with sudden headache, drowsiness and hyponatremia, as a large infiltrating tumor across the skull base and extends through the nose. 60-year-old man, with visual disturbance, RMI showed a selar tumor. Total removal was performed. After surgery the patients presented a thalamic infarct and dead. Histological findings: adamantinomatous craniopharyngioma with extensive necrosis, thrombosis, fibrin, and reactive changes of the epithelium were observed in both cases. These changes should take into consideration when we have a highly aggressive tumor. 2th case report illustrates the possible occurrence of intracranial thalamic infarct after surgery induced vasculopathy after CP resection. Lipid thrombosis and thalamic infarct that was considered as complication post-surgery of CP. Conclusions. We present two cases with extensive hemorrhage and necrosis, fibrin thrombi and tumor rupture. The first with reactive epithelial changes and the second with thalamic infarction. Unusual conditions of the CP. It is striking that despite being a benign tumor with necrosis shows changes that suggested an interrogation, and histologically and/or being considered as apoplexy.

P1-87

The Glut family members in association with heat shock proteins in the boundary of craniopharyngiomas. Clinical, histopathological and immunohistochemical correlation

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Introduction. Craniopharyngioma is a rare brain tumor. These lesions have a tendency to recurrence and invade surrounding structures and to recur after an apparently total resection. The Glut family members expressed and controls glucose uptake and metabolism necessary for motility and maturation. Methods. We examined GLUT (GLUT1, 2, 3, and 4) in correlation with HSP proteins (27, 70, 90 and 94) and lactate dehydrogenase in craniopharyngiomas and to test the hypothesis that recurrent hypoglycemia changes the brain's capacity to utilize different energy substrates and HSPs activation. Clinical, histopathological and immunohistochemistry correlation. Results. 28 CPs were included in this paper. 12 (43%) were females and 16 (57%) were males, the ranged aged was from 17 to 55 yrs (median 31.43± 10.057) Recurrence in 12 (46%) cases. Glut 1, 3 and IGF immunoexpression was in wet keratin and dystrophic calcification, more observed in recurrence than no recurrence tumors. HSP27 and 70 were positive in astrocytes and Rosenthal Fibers. However, HSP 90, and 94 were higher immunoreaction in wet keratins and dystrophic calcifications. The patients who presented more WK, and DC features showed metabolic syndrome, and glucose dysfunction. Conclusion. WK and DC correspond to histological structures that remain metabolically active and that stimulate the presence of HSP proteins. This is observed more in recurrent than in non-recurrent tumors as well as in patients those presented metabolic syndrome. IGF-I as well as HSP90 and 94 as a glial rescue agent. Glucose metabolism is implicated in brain infiltration and recurrence.

P1-88

Brain normal adjacent tissue to Craniopharyngioma boundary and oxidative stress expression

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Introduction. Craniopharyngioma is an epithelial tumor of the sellar region with a high survival rate but a high rate of recurrence. Methods. We analyzed different antibodies involved in oxidative stress and inflammation process in CP, ultrastructure of brain invasion and chemically analyzing of oily content cystic were performed. Clinical, pathological, immunohistochemical correlation. Results. 28 patients were included, 13 (46%) with recurrence and 15 (54%) presented adjacent brain tissue invasion. Note that cystic contents contained high levels of lipids, cholesterol, glucose, protein, bilirubin, transaminases and low hemoglobin content. Adjacent brain tissue invasion correlated with gender ($p = 0.044$), OR from 222 to 6730 (1.222), inflammation ($p = 0.048$), Rosenthal fibers ($p = .000$), and epithelial rupture ($p = .000$). Dystrophic calcification form in invasion was positive for recoverin, lactate dehydrogenase, TNF, IFI16, and NFE2L2 and was negative for perilipin and TNFα, nitrotiroxin, e-NOS, Hif-1α, GSK3 and negative for GLUT-4 and NFE2L2. The way to encroach upon wet keratin was positive for recoverin, lactate dehydrogenase, KF-κB, TNF, IFI16, and NFE2L2 and was negative for perilipin and TNF, nitrotiroxin, e-NOS, Hif-1α, GSK3 and nitrotiroxin. Conclusion. The way to infiltrate as single cells was positive for lactate dehydrogenase, TxrR1, TNFα, IFNγ, nitrotiroxin, Hif1α, e-NOS, GSK3, Glut-4, NFE2L2, CD71 and perilipin. Conclusions. When tumor cells invade the brain tissue that is performed by the active factors oxidative stress pathway by rupture of basal membrane and oil fluid exit or runoff.

P1-89

ACTH-producing pituitary carcinoma. A case report

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Introduction: Pituitary carcinoma is extremely rare and strictly defined as a tumor of adenohypophyseal cells with craniospinal dissemination or systemic metastasis. Here, we report an autopsy case of pituitary carcinoma which produced ACTH, with the review of literatures. Clinical summary: A 79-year-old man presented with diplopia and oculomotor nerve palsy. Sellar tumorous lesion was detected by MRI and was clinically diagnosed as meningioma. His neurological symptoms were worsened after gamma knife therapy, and MRI showed the tumor invasion to the cavernous sinus. Transsphenoidal surgery was perfomed and neuroendocrine carcinoma of the sellar region was histologically suspected. Despite the additional chemoradiation, the tumor was enlarged with extensive meningeal dissemination, and he died 2 years after the first symptoms. An autopsy was performed to search for the primary lesion of the tumor. Autopsy findings: In the sellar region, atypical cells with eosinophilic cytoplasm proliferated in an alveolar pattern. These atypical cells were widely disseminated to the meninges and metastasized to the liver, lung and peripancreatic lymph node. Immunohistochemically, the atypical cells were positive for synaptophysin, CD56 and CK(AE1/AE3), focally positive for ACTH, and negative for GH, PRL, TSH, FSH and LH. Conclusion: The previous surgical specimen had showed the same immunophenotype as the autopsied one. From the histopathological findings and clinical course, we diagnosed the case as ACTH-producing pituitary carcinoma.

P1-90

Agressive behavior of Spindle cell oncocytoma: a case report

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Introduction: Spindle cell oncocytoma, a non-neuroendocrine neoplasm of the pituitary gland showing nuclear expression of TTF1, is a rare entity that despite being defined as grade I WHO, may assume malignant and aggressive behavior with multiple relapses and a high proliferative index. Clinical Summary: A 34-year-old man was admitted in March 2017 with unilateral right headache for a year with worsening in recent weeks, progressive ptosis, right III, IV and VI cranial nerves palsy and hypoesthesia of the V. MRI revealed a massive sellar and suprasellar lesion extending into the right cavernous sinus, which was approached via transsphenoidal. A solid and bleeding tumor was partially resected. The lesion, initially treated with radiotherapy, recurred 3 months later and the new CT scan revealed tumor expansion compressing the floor of the third ventricle and remodeling the sellar floor. The patient was re-operated in December 2017 via frontal craniotomy. Pathological Findings: Proliferation of cells with predominant fusiform appearance, arranged in bundles, with moderate nuclear pleomorphism. Mitoses were frequent and there were areas of necrosis. Tumor cells were immunopositive for EMA, TTF-1, GFAP and INI-1. CAM5.2 and progesterone receptor were negative and Ki67 was 20%. The diagnosis was spindle cell oncocytoma. In the second resection the histology was similar, except for and increased number of polygonal cells and anaplasia, as well as focal chordoid appearances and a ki67 of 40%. Conclusion: Although this neoplasia has usually a good prognosis, this case, as few others previously reported, showed aggressive histology and clinical course.

P1-91

Differential diagnostic impact of DNA methylation profiling on brain tumor classification

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Introduction: Genome-wide DNA methylation profiling is a new promising approach for improved brain tumor diagnostics. The potential of this approach has recently been successfully explored by the German Cancer Research Center. We report the diagnostic impact of a DNA methylation-based classifier tool tested in a clinico-pathological setting. Methods:We collected tumor tissue from 135 patients, where the initial diagnoses were inconclusive or where a more precise classification was needed. DNA methylation profiling was performed using the EPIC BeadChip (850K). Data files were generated and uploaded to a DNA methylation-based classifier tool and matched to a brain tumor reference cohort with more than 2800 CNS tumors covering more than 80 tumor methylation classes. Reports were generated including a classifier score and a DNA copy-number variation (CNV) profile. Results: Eighty eight tumors (65%) significantly matched a methylation class. The initial histopathological diagnoses were changed in 24 out of 88 tumors representing a reclassification rate of 27%. This was based on methylation profiling scores representing a match to a specific DNA methylation class as well as CNV changes, immunohistochemical findings and next-generation sequencing results. A change in WHO tumor grade among the reclassified tumors was observed in 67% of the tumors, with downgrading of 25% and upgrading of 42%.Conclusion: DNA methylation profiling is a valuable diagnostic tool for tumor classification, especially in cases, where morphological and genetic features are inconclusive. The use of DNA methylation profiling initiated re-evaluation and incorporation of additional tools leading to more precise brain tumor diagnostics.

P1-92

A targeted NGS-based overall solution to support diagnostics and therapy prediction in neurooncology: Considerations for a flexible and cost-efficient platform choice and panel design

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Introduction: The new WHO classification still poses challenges to many neuropathology labs. Some of the relevant alterations (e.g. C11orf95-RELA) are hard to assess or complex subclassifications (e.g. for medulloblastomas) are required. Some labs rely on a two-tiered approach: i) methylation arrays for tumor classification and ii) targeted NGS panel sequencing for identifying actionable mutations. However, high initial investment and annual costs for running two platforms in parallel hinder a fast expansion of the new techniques in the breadth of neuropathology. Methods/Results: We decided to focus on the sole use of the relatively cost-efficient Mini-Seq NGS platform (Illumina). First, we designed a DNA panel (FFPE, HaloPlex, Agilent; no Covaris required) that is suited for detection of DNA mutations, copy number alterations and chromosomal alterations (459 kbp, 58 genes, 4082 SNPs, 98.83% coverage). We successfully used this platform to support tumor classification in astrocytomas, oligodendrogliomas, meningiomas and medulloblastomas and identified actionable targets of clinical use. We then designed a RNA panel (FFPE, Sure Select, Agilent) that detects gene fusions and covers a broad range of alterations particularly relevant to pediatric tumors (e.g. pediatric glioblastomas, ependymomas, CNS PNETs) (148 kbp, coding sequence of 31 genes, 99.88% coverage). Conclusion: With these two panels we cover the most relevant molecular alterations in the field of neurooncology. The cost-efficient and flexible single platform approach enables state-of-the-art molecular diagnostics in virtually every neuropathology lab. Functionality is guaranteed for future revisions of the WHO classification as novel biomarkers can be easily included in an adapted panel design.

P1-93

Molecular subgrouping of gliomatosis cerebri according to the 2016 World Health Organization classification of tumors of the central nervous system

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Gliomatosis cerebri (GC) is a diffuse neoplastic glial cell tumor infiltrating at least three lobes of brain and preserving the local parenchymal architecture. The entity of GC was deleted from the 2016 WHO classification of the CNS tumors. However, GCs still remain curious in both phenotype and genotype. This study is to stratify GCs into molecular categorization on the basis of genetic parameters of new integrated diagnosis and to investigate whether this molecular classification provide specific information. Methods: We performed direct sequencing and PNA-mediated real-time PCR clamping for IDH1/2 and FISH or LOH for 1p/19q codeletion, immunohistochemistry using 90 paraffin-embedded tissues. Results: IDH1 and ATRX mutations and 1p/19q codeletion were detected in 35/90 patients (38.9%), 23/83 patients (27.7%), and 4/90 patients (4.4%). 90 GCs were subcategorized into astrocytic tumors (n=89) and oligodendroglial tumors (n=1). Among the 89 astrocytic tumors, 73.0% were IDH-wildtype astrocytomas, grade II (n=27), III (n=35), and IV (n=3) and 27.0% were IDH-mutant astrocytomas, grade II (n=9), III (n=13), and IV (n=2). There was a case of oligodendroglioma,IDH-mutant&1p/19q-codeleted (1.1%). There was no statistical difference between overall or progression-free survivals and molecular subtypes within GCs. 30 patients showed disease progression during follow-up. A half of these patients were diagnosed with glioblastoma at second biopsy and they were initially IDH-wildtype (n=13) or IDH-mutant tumors (n=2). Conclusion: GCs largely comprised IDH-wildtype astrocytic tumors as a genotype, and the majority of these tumors progressed to glioblastoma, IDH-wildtype. New classification could not make it perfectly possible to stratify GC into prognostic relevant categorization.

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Gliosarcoma in the IDH era: Imaging characteristics of 25 patients with correlative immunostaining

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Background: In the 2016 World Health Organizations Classification of Tumors of the Central Nervous System, gliosarcoma (GSC) is considered a variant of IDH-wild type glioblastoma (GBM) characterized by a biphasic pattern with alternating areas exhibiting glial and mesenchymal differentiation. GSC can be primary or radiation-induced and is an intra-axial brain lesion which often abuts a dural surface. While some GSC have indistinguishable imaging characteristics from glioblastoma, aggressive lesions can erode through the dura and skull and involve the extra-cranial soft tissues. We present the largest known imaging series of GSC with immunohistochemical and histologic correlation, documenting them as IDH(-) and delineating their imaging spectrum.Methods: Pathology proved GSC cases were collected from our quaternary care center spanning the last 16 years. IDH status was either documented or obtained by staining tissue blocks. When available, p53, PTEN, MIB-1, EGFR amplification status, and MGMT methylation status were recorded and imaging findings tabulated.Results: 25 cases were identified, 21 were de novo, and 4 were radiation-induced. All lesions contacted a dural or pial surface. All cases were negative for an IDH R132H mutation, including post-radiation GSC. 16/16 cases showed non-amplification of EGFR/CEP7. MGMT methylation was present in 2/17. Imaging features included areas of nodular thickening in necrotic lesions which appeared to abut the site of pial or dural contact.Conclusion: We present the largest reported imaging collection of GSC cases with correlative molecular and histologic testing.