

## **Photobiomodulation following Traumatic Brain Injury**

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Photobiomodulation has been found to modulate various biological processes including traumatic brain injury (TBI). Following TBI in mice, in this study we assessed the use of several photobiomodulation protocols producing a beneficial effect on the long-term neurobehavioral outcome and brain lesions of these mice. TBI was induced by a weight-drop device, and neurobehavioral function was assessed from one hour and up to 56 days post-trauma using a neurological severity score (NSS). The extent of recovery is expressed as dNSS, the difference between the initial score, and that at any other, later, time point. An 808nm Ga-Al-As diode laser was employed transcranially 4, 6 or 8 hrs post trauma. Mice were divided into several groups. MRI was done prior to sacrifice. From 5 to 28 days post-TBI, the NSS of the laser-treated mice were significantly lower ( $p < 0.05$ ) than the control mice. The percentage of surviving mice that demonstrated full recovery 56 days post-TBI, namely NSS=0 (as in intact mice) was the highest (63%) in the group that had received photobiomodulation at 100 Hz. In addition, MRI analysis demonstrated significantly smaller infarct lesion volumes in laser treated mice as compared to control. Our data suggest that non-invasive photobiomodulation of mice post-TBI provides a significant long-term functional neurological benefit, and that 100 Hz is optimal for such treatment.

## **Oligodendroglioma, IDH-mutant and 1p/19q-codeleted with gangliocytic differentiation of a 31-year-old male: A case report and literature review**

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**Introduction:** Oligodendroglioma (OLG) is a diffusely infiltrating glial neoplasm. Sporadic case reports of neuronal differentiation of OLG and subset of neuronal gene expression of OLGs have been identified. Here, we report a rare case of OLG, IDH-mutant and 1p/19q-codeleted with gangliocytic differentiation in a 31-year-old male patient. **Clinical summary:** A 31-year-old male patient without specific medical history was admitted with a seizure. Brain computed tomography revealed 7cm-sized contrast enhancing cystic mass with internal necrosis and calcification, in the right frontal lobe. With suspicion of anaplastic OLG, gross total removal of the tumor was performed. Patient is alive well after subsequent radiotherapy. **Pathologic findings:** On microscopic examination, diffusely infiltrating tumor cells with clear cytoplasm were found in the cortex. Necrosis or endovascular proliferation was not found. Majority of tumor was composed of OLG-like clear tumor cells with chicken-wire pattern vasculatures. Throughout the tumor, atypical gangliocyte-like cells having hyperchromatic nuclei, prominent nucleoli and ample cytoplasm were observed. Differential diagnoses included ganglioneuronal tumors and OLG with gangliocytic differentiation. Tumor cells were diffusely positive for OLIG2 and IDH (R132H) immunohistochemical stainings (IHC). Scattered ganglion-like cells were highlighted by NeuN and synaptophysin IHC. Subsequent fluorescence in situ hybridization analysis revealed 1p/19q codeletion, confirmed the diagnosis of OLG, IDH-mutant and 1p/19q-codeleted with gangliocytic differentiation. **Conclusion:** Although rarely found, OLG can have neuronal differentiation and may present like long-term epilepsy associated tumor and lead to underdiagnosis. IDH analysis, preferentially IDH1 IHC would help to discriminate OLG from other glioneuronal tumors.

## **Histomorphological patterns of glioblastoma and its rare variant: a case series in the Indian subcontinent**

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the adult population, and about 75% of all the anaplastic gliomas. The prevalence of GBM is about 2-4 cases per 100,000. It is more common in men than in women, and its incidence increases with age. Variants of glioblastoma, poses both diagnostic and therapeutic challenges. Clinical summary: A reterospective case series included 11 cases of glioblastoma with its variant at the tertiary care centre. All of the patients presented with on and off headache, seizures, vomiting, and focal neurological deficit. The mean age was 44.6years. Radiological examination revealed as supratentorial mass, most common sites included temporal, frontal, followed by temporo-perital and occipital. Surgical craniotomy was done and tumor specimen was sent for histopathological diagnosis. Pathological findings: On histological analysis, sections shows infiltrating growth pattern, arranged in nests and sheets, with marked nuclear atypia, giant cell astrocytes, multinucleated tumor cells, epitheloid like cell,spindle cells, bizarre nuclei, areas of necrosis, microvascular proliferation and haemorrhage are also evident. Provisional diagnosis was glioblastoma. GFAP, CD99, CD56, Vimentin, myogenin,Synaptophysin, LCA, EMA, Ki67 immunohistochemical stains were done. Out of 11 cases, 2 cases of epitheloid GBM, 4cases of giant cell GBM, 3 cases of gliosarcoma, and 2 case of primitive neuronal component were reported after immunochemistry, which help us to arrive at the final diagnosis. Conclusion: Glioblastoma is the most common primary brain tumor in adults. The immunohistochemical stains make the diagnosis of GBM with its variants much easier and rule-out other differential diagnoses.

## Clinicopathologic features of an autopsied patient with epithelioid glioblastoma: experience of BRAF and MEK inhibitor treatment

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**Introduction:** Epithelioid glioblastoma (E-GBM) is a rare aggressive glioblastoma (GBM) variant. Approximately 50% of E-GBM harbors the *BRAFV600E* mutation. However, it has been unclear whether the *BRAF* and other molecular profiles might influence on clinicopathologic features of the patients. Recently, we experienced a patient with E-GBM, for whom we tried BRAF and MEK-targeted therapy. Here, we described clinical and autopsied features of this patient.

**Clinical and pathological summary:** The patient, a 57-year-old Japanese man, was admitted to a hospital because of headaches. A brain MRI study demonstrated a well-circumscribed mass in the left frontal lobe with gadolinium enhancement. Subtotal removal of the tumor was performed. Histopathologically, the tumor was composed of monotonous, discohesive patternless sheets of medium-sized rounded cells with abundant eosinophilic cytoplasm. Immunohistochemically, the cells were positive for S-100 protein and INI-1, but negative for IDH-1, GFAP or cytokeratin. A pathological diagnosis of E-GBM was made. A gene sequencing analysis revealed *BRAFV600E*, *TERT* (C250T) promotor mutation, and *CDKN2A/2B* loss. Postoperative radiotherapy and concomitant temozolomide therapy were performed, but the tumor disseminated into the subarachnoid space. BRAF and MEK-targeted therapy was introduced, but the effects appeared temporarily. The patient died 8 months after onset. At autopsy, massive leptomeningeal dissemination composed of E-GBM cells was evident. Surprisingly, tumor cells invading the brain parenchyma were rarely seen.

**Conclusion:** The clinicopathologic features and genetic profiles of this patient are distinct from those of GBM. Further analyses are needed for better understanding the pathomechanisms underlying this malignant brain tumor.

## Features of IDH- and H3F3A-mutated cerebellar high-grade gliomas of Japanese cases

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*Introduction:* Isocitrate dehydrogenase (*IDH*) -mutated or H3 K27M-mutated adult cerebellar high-grade gliomas (HGG) are rare. We analyzed two *IDH*- and two *H3F3A*-mutated adult cerebellar HGG cases histologically and genetically. *Methods:* For histological analyses, some primary antibodies including glial or neuronal markers were selected. The mutation statuses were assessed by direct sequencing. *Results:* The HGG case with *IDH1* R132H mutation was an 83-year-old man, whose tumor was mainly composed of densely packed round-to-polygonal tumor cells resembling epithelioid cells. High mitotic activity was observed, and vascular wall invasion was often detected. INI1 expression was retained in nuclei. The *IDH2* R172K-mutated 75-year-old woman's case was high-grade astrocytoma with an area of tumor cells forming a cord-like architecture or perivascular arrangement surrounded by a myxoid matrix. In both *IDH*-mutated cases, palisading necrosis and microvascular proliferation were absent, and ATRX expression was retained. One of *H3F3A* K27M-mutated HGG was occurred in 70-year-old woman, accompanied by a limited low-grade area showing the aggregation of plump tumor cells with an eosinophilic granular cytoplasm. Another *H3F3A* K27M-mutated case was a 68-year-old man, whose tumor was composed of diffusely proliferating atypical cells with high mitotic activity and hemorrhagic necrosis. DNA sequencing revealed that *HIST1H3B*, *BRAF*, and *TERT* promoter were wild type in all four cases. Literature reviews uncovered that infratentorial *IDH*-mutated gliomas are prone to show mutations other than *IDH1* R132H, and cerebellar H3 K27M-mutated cases were all adults. *Conclusion:* We presented rare adult cerebellar HGG with *IDH*- or *H3F3A*-mutations, and showed several clinicopathological features.

## **YAP/TAZ expression correlated with angiogenesis in astrocytoma**

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Recent studies reports YAP/TAZ act as a major regulator of physiological embryo angiogenesis. YAP/TAZ transmits the VEGF/VEGFR2 signaling into a specific transcriptional program, essential for vascular tip cell migration, blood vessel formation, and vascular barrier maturation in the sprouting angiogenesis of retina and brain during embryonic development. Glioblastoma multiform (GBM) is one of the most vascularized of all the human tumors. The presence of microvascular proliferation is a histopathological hallmark of glioblastoma. Therefore, the role of YAP/TAZ in pathological angiogenesis, especially in GBM blood vessel proliferation need to be verified. The large human astroglioma samples were used for detecting the expression of YAP/TAZ. The correlation between the vascular density and clinical blood perfusion in GBM were detected. In astrocytoma, the expressions of YAP/TAZ in both endothelial cells and tumor cells were increased with the malignant grade. In endothelial cells, the YAP/TAZ expression was positively correlated with the blood vessels density. In GBM, the YAP/TAZ positive staining was stronger in the glomerular type than that in the thin-walled type neovascularization. The YAP/TAZ expression also positively correlated with the VEGFR expression on the endothelial cells. Our studies indicated the critical role of VEGFR/TAZ signaling pathway involved in the endothelial proliferation in astrocytoma.

**P3-7**

## **mTORC2 regulates hypomethylator phenotype in glioblastoma**

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**Introduction:** Recent studies have demonstrated that glioblastoma (GBM) shows a decrease in DNA methylation on recurrence or malignant progression. From a therapeutic point of view, it is important to unravel how DNA hypomethylator phenotype is regulated in GBM. Here, we set out to determine the role of epidermal growth factor receptor (EGFR)-mammalian target of rapamycin (mTOR) pathway, which is hyper-activated in most GBM cases, in DNA hypomethylator phenotype. **Methods:** To uncover the regulatory mechanism of DNA hypomethylation and its functional consequences, we interrogated cell lines and clinical samples of GBM, the highly lethal brain cancer in human. **Results:** We discovered that in GBM, mTORC2, one of the mTOR complexes, induced DNA hypomethylation by suppressing the expression of DNA methyltransferase 3A (DNMT3A). Activation of mTORC2 enhanced TERT (telomerase reverse transcriptase) mRNA expression through demethylation of its promoter. Of note, GBM cells were addicted to overexpressed TERT for their survival. **Conclusion:** In GBM, mTORC2 regulates DNA hypomethylator phenotype and facilitates tumor cell survival through promoting the expression of specific oncogenes.

## **Glioblastoma, subependymoma and meningioangiomas; collision of three morphologically and genetically different entities in one patient**

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**Introduction:** Occurrence of multiple different primary brain tumors in one patient is rare. We report a patient with a subependymoma, meningioangiomas, and glioblastoma. **Clinical summary:** The patient was 61-year old man who presented with headaches; brain MRI showed a left intraventricular mass. Pathology demonstrated a subependymoma, WHO grade I. Four years later, routine MRI showed an enhancing right frontal lesion; pathology was meningioangiomas. Eighteen months later, he presented with new-onset seizures. Brain MRI showed a left frontal enhancing mass; pathology was glioblastoma, IDH-wildtype. One month later, he died, and underwent brain autopsy. **Pathological findings:** Surgical and autopsy tissue was examined, and molecular analysis with next generation sequencing was performed on each primary brain lesion using the Ion AmpliSeq Cancer Hotspot Panel v2, which targets clinically important regions of 50 cancer-related genes. Molecular analysis of each brain lesion showed the following results: glioblastoma-PTEN L295fs (C. 882delT). Notch1 V1578del was identified in meningioangiomas with very low allelic frequency (1%), pending confirmation. The subependymoma had no mutations. No variants in other genes on the panel were identified. **Conclusion:** PTEN mutation, present in this glioblastoma, and not mutated in the subependymoma or meningioangiomas, is reported to be mutated in 30% of glioblastomas. NOTCH1 gene mutation, detected in the meningioangiomas lesion, has not been reported in this entity, and was not present in the two tumors. Further studies to verify this finding are ongoing. These results support that these lesions are likely collision tumors/processes, occurring in a single individual without a known cancer predisposition syndrome.



## **Gliosarcoma with arterial invasion. Report of two cases**

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**BACKGROUND.** Ischemic strokes in patients with primary brain tumors are a postoperative complication or a complication of radiation therapy. Rarely, direct vessel occlusion by an adjacent primary brain tumor may cause a large vessel ischemic stroke. **CLINICAL CASES.** Case 1. A 68-year-old man. He started three months before his death with headache, dysarthria and hemiparesis. RMN reported a frontal tumor of 4.8 cm. He continued with drowsiness, left hemiparesis, cough and tachypnea. Surgery was not-accepted, and he died. Case 2. A 68-year-old man. He started fifteen months ago, with headache, disorientation and stupor. RMN reported tumor in right hemisphere brain with measures of 12x10x7 mm. Tumor was 90% resected and he received adjuvant radiotherapy. One year later, he was diagnosed with residual/recurrent tumor; he was treated with anti-edema management and he died at home. **HISTOPATHOLOGICAL FINDINGS.** Case 1. On autopsy, we observed a tumor of 5.5 cm on left hemisphere. At the periphery, there was a triangle injury with liquefy aspect. On microscopy, injury was due to gliosarcoma and ischemic changes in peripheral tissue; the lumen of middle cerebral artery was necrosis and few neoplastic cells. Case 2. On biopsy, there was a gliosarcoma, one artery had evidence of invasion into tunicas and lumen. **CONCLUSIONS.** Tumor-related ischemic strokes are most unusual in patients with malignant gliomas. This event is uncommon for gliosarcomas; authors have knowledge of an only report of a 46-year-old person with microscopic confirmation of invasion of tumour cells into the wall of a greater pre-existing blood vessel.

## **Temozolomide and Notch inhibitor MRK-003 induce cell protective autophagy in malignant gliomas**

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**Background:** Autophagy is a process in which intracellular proteins are sequestered, delivered to lysosomes and digested. Controversy remains whether autophagy induced by treatments in cancer are cell killing or protective. We set out to determine what type of autophagy is induced by temozolomide and Notch inhibitor MRK003 in gliomas. **Methods:** Two glioblastoma neurosphere lines (JHH520 and HSR-GBM1) were treated with DMSO, 0.5-5  $\mu$ M of MRK003, and/or 10  $\mu$ M chloroquine. Western blotting was performed to detect alterations in LC3B, p62 and cleaved PARP. Cell viability, proliferation, apoptosis, cell cycle and clonogenicity assays were performed to look at the combinatorial effects of MRK003 and the late stage autophagy inhibitor chloroquine. Similar experiments were performed to look at effects of temozolomide. Furthermore, 14 glioma patients who underwent surgical removal before and after treatment with temozolomide were stained for autophagy markers LC3B, LAMP1 and LAMP2A. **Results:** An LC3B-II band, suggesting induction of autophagy, was observed after Notch pathway blockade and temozolomide treatment. Decreased growth ( $p < 0.001$ ), proliferation ( $p < 0.05$ ), increased apoptosis (increased sub-G1  $p < 0.05$ ; increased Annexin V percentage:  $p < 0.05$ , increased cleaved PARP expression), and decreased clonogenicity were seen after combination MRK003 and CQ treatment compared to DMSO. Staining for autophagy markers was significantly increased in surgically obtained tissues after temozolomide treatment. **Conclusion:** Induction of cell protective autophagy occurs after Notch inhibition and temozolomide treatment in glioma cell lines. Inhibition of autophagy is a possible new treatment strategy to overcome resistance to such treatments in gliomas.

## **T-LAK cell-originating protein kinase (TOPK) in adult malignant glioma: Clinico-pathological and Immunohistochemical Study**

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**Introduction:** In order to investigate pathogenesis of T-lymphokine-activated killer cell-originating protein kinase (TOPK) in adult malignant glioma. **Methods:** The TOPK protein expression in glioma was examined by Western blot. Immunohistochemistry was performed to detect the TOPK, EGFR, TP53, c-myc, and Ki67 labeling index (LI) in 75 cases of adult malignant gliomas (grade II: III: IV = 1:1.05:1.7), the IDH1 status was determined immunohistochemically in 62 cases with IDH1-positive rate 33.9%. Semi-quantified expression levels were analyzed between low grade glioma (LGG, grade II) and high grade glioma (HGG, grade III/IV) groups. **Results:** The expression of TOPK protein in glioma was demonstrated by Western blot and immunohistochemistry. Strong nuclear staining of TOPK in HGG and moderate/focal nuclear staining in LGG were appreciated. The expression of TOPK and Ki67 LI were both significantly higher ( $P < 0.01$ ) in HGG than LGG. Expression of TOPK was significantly correlated with Ki67 LI ( $P < 0.01$ ) and TP53 expression level ( $P < 0.01$ ). Meanwhile, the TP53 expression level was also significantly correlated with the Ki67 LI ( $P < 0.01$ ). Moreover, EGFR expression in IDH1-positive group was significantly higher than in IDH1-negative group and significant correlation between TOPK and TP53 expression was found in HGG-IDH1+ group. However, in LGG, higher expression levels of c-myc ( $P < 0.05$ ) and Ki67 LI ( $P < 0.05$ ) were observed in IDH1+ group, than in IDH1-. **Conclusions:** Our results suggest that TOPK could be a novel and independent parameter, helpful to assess the behavior of adult malignant glioma, and may associated with TP53-related signal-pathways, but not IDH1 mutations. **Key Words:** glioma TOPK TP53 IDH1 immunohistochemistry pathology

**P3-12**

**Gliomas 1p/19q codeleted, p53 mutated and EGFR amplified. Are they mixed gliomas?**

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Introduction: Gliomas are the most frequent intrinsic brain tumors. The recurrent mutation in isocitrate dehydrogenase 1 and 2 genes (IDH1/IDH2) allowed to split gliomas into IDH mutant and IDH wild type mega-groups, the latter having less favorable course. Molecular markers were incorporated in the 2016 WHO update classification for diffuse gliomas. Accordingly, Oligodendroglioma (OD) is now defined by the simultaneous presence of IDH mutation and 1p-19q codeletion while Astrocytoma (A) is characterized by IDH mutation without the codeletion and usually harbors P53 and ATRX mutations. Methods: Molecular Institutional data base revealed 10 adult patients from a total of 105 IDH mutated tumors which presented 1p-19q codeletion together with EGFR trisomy and/or mutant TP53. Results: Histologically the honeycomb appearance was present in 8 cases (c), and 2c without perinuclear halos, had astrocytic like elements. Immunohistochemical study revealed ATRX retained label 5c, partially retained 3c and negative 1c reflecting mutation. Ki67 proliferation index showed mean value 9%. RT-PCR findings: codeletion 1p/ 19q, was detected in 10 c, 3x amplification EGFR in 8c, IDH1 mutation in 8c, IDH2 mutation in 2c and P53 mutation in 4c. A statistically significant difference in overall survival (OS) was detected when comparing this small group to OD (p=0.0115) but not to A ( p=0.2148) log-rank test. Discussion: According to the WHO classification the analyzed group should be defined as OD, but molecular aspects, OS, KI67 do not reflect the typical characteristics. These results raise the question about the existence of olygoastrocytoma.

## **Do gemistocytic astrocytomas really exist? the longstanding debate about gemistocytes present in diffuse gliomas may be solved**

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**INTRODUCTION:** The classification of diffuse gliomas established by the World Health Organization (WHO) has always been a matter of debate, with frequent inter observer disagreement. Recently, neuropathologists in charge of elaborating the 2016 classification have established criteria to make it more precise, incorporating molecular information, in particular the ATRX loss to differentiate astrocytomas from oligodendrogliomas. However, the practice shows that there are still controversial cases, including the fact that ATRX loss is not observed in gemistocytes present in diffuse gliomas. In addition, as already known, gemistocytes do not proliferate. Immunoreaction with KI67 is only seen in intermingled IDH1 positive cells with larger nuclei and scant cytoplasm. Considering the fact that gemistocytes are also negative or weakly positive with IDH1R132H, we postulate that the background rich in gemistocytes is reactive. To investigate this we performed double staining (ATRX/GFAP) in a series of gemistocytic astrocytomas. **METHODS:** We analyzed 120 diffuse gliomas from 2013 to 2018 of patients that at the time of diagnosis were older than 18 years. We selected 20 cases rich in gemistocytes and performed double stainings with immunohistochemistry, using GFAP (red chromogen) and ATRX (brown chromogen). **RESULTS:** In all cases most gemistocytes were ATRX positive and many involved ATRX negative neoplastic cells with bare nuclei. **CONCLUSION:** The gemistocytic astrocytoma, which is known to have a more aggressive behavior, probably shows in its gemistocytic component, a reactional pattern, serving as a framework of growth modulators for the proliferation of neoplastic glial cells.

## **A case of epithelioid glioblastoma; unusual presentation of a rare tumour with full biomarker assessment**

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*Introduction:* Epithelioid glioblastoma is a rare type of glioblastoma occurring in younger patients predominantly. We present an informative case presenting as an extra-axial tumour, in many respects mimicking meningioma, with molecular biomarker assessment.

*Clinical summary:* The patient was a 17-year-old female university student who was previously well. She presented with a few month history of headaches and intermittent “blackout spells” lasting 2-3 minutes each. There was no relevant family history. MRI investigation showed a left parieto-temporal dural based extra-axial enhancing tumour mass, thought to be most consistent with a meningioma. The patient underwent a “gross total type resection”.

*Pathological findings:* Neuropathologic examination showed a cellular neoplasm with areas of prominent epithelioid and rhabdoid type morphology. Tumour growth focally into the meninges and dura was evident. There was abundant mitotic activity as well as areas of palisading tumour necrosis and focal microvascular proliferation. A summary of the extensive immunohistochemical and biomarker profile showed epithelial membrane antigen, STAT6 and p53 to be negative. The tumour was positive for OLIG2 and focally positive for glial fibrillary acidic protein. Biomarker assessment showed the presence of BRAF V600E point mutation.

*Conclusion:* We present a rare case of an epithelioid glioblastoma presenting as an extra-axial dural based tumour. Given the superficial hemispheric growth of typical epithelioid glioblastomas, this presentation may be more common than realized and, with the rhabdoid type morphology, can easily be confused with rhabdoid meningioma. Immunohistochemistry for EMA, OLIG2, as well as BRAF V600 mutational testing, are useful for diagnostic assessment.

## **Adenocarcinoma arising in neurenteric cyst in the 4th ventricle mimicking choroid plexus carcinoma: A case report and literature review**

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**Introduction:** Neurenteric cysts are rare, and most commonly located in the subarachnoid space anterior to the cervical spinal cord. Malignant transformation of neurenteric cyst is an exceedingly rare complication. Here, we report a rare case of adenocarcinoma arising from the neurenteric cyst in the 4th ventricle, which clinically and radiologically mimicked choroid plexus carcinoma (CPC). **Clinical summary:** A 41-year-old female patient without specific medical history presented with persisting headache and nausea for a month. Brain magnetic resonance image (MRI) revealed a 3.7 cm-sized, enhancing cauliflower-like mass with cystic portion in right lateral ventricle with hydrocephalus with additional 2.2cm-sized non-enhancing mass in the left foramen magnum. Suspicion of choroid plexus papilloma with seeding tumor nodule, gross total removal of tumor was performed. Patient went into a coma with diffuse cerebral dysfunction and died 5 months after the surgery. **Pathologic findings:** At low power view, tumor had papillary growth pattern and brain invasion. Tumor cells were overtly malignant, consistent with carcinoma. In addition, cyst component composed of flat to stratified ciliated bland-looking epithelium was observed. Differential diagnoses included CPC, metastatic carcinoma from elsewhere, and malignant transformation of pre-existing neurenteric cyst. On immunohistochemistry, tumor cells were positive for CK and CDX2 (focal), and negative for TTF-1, PAX8, WT1, synaptophysin, GFAP. Taken together, diagnosis of adenocarcinoma arising from neurenteric cyst was rendered. **Conclusion:** Although rare, carcinoma arising from the neurenteric cyst within the ventricle can mimic CPC. Pre-existing benign cyst component and exclusion of metastatic carcinoma is important to make an accurate diagnosis.



**P3-16**

**Detection of alk and egfr gene mutation in non-small cell lung adenocarcinoma with brain metastases and its correlation with clinicopathological features**

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**Objective:** To analyze the pathological features of brain metastases in lung adenocarcinoma and the changes of ALK and EGFR genes, and to guide the treatment of patients with advanced lung cancer. **Methods:** From 2013 to 2016, a total of 74 patients with brain metastatic lung adenocarcinoma were enrolled in this study. Paraffin sections were stained with HE for pathological analysis, and using immunohistochemical method to detect Ki-67, ALK and EGFR gene. **Results:** All specimens were invasive adenocarcinoma, and were solid (59.46%), acinar (12.16%), papillary (19.7%), micropapillary (18.42%), there are significant differences between brain metastatic lung adenocarcinoma and primary lung adenocarcinoma ( $P < 0.01$ ). The average Ki-67 expression rate of solid, acinar, papillary, micropapillary was significantly different ( $P < 0.05$ ). Total expression of ALK gene and EGFR gene were detected in 7 cases (9.46%) and 39 cases (52.70%) respectively. Group of ALK gene high expression had the average tumor necrosis rate of  $7.14 \pm 2.75\%$ , while the low expression group was  $20.15 \pm 4.92\%$  ( $P < 0.01$ ), group of Ki-67 high expression of ALK gene was  $15.00 \pm 2.76\%$ , while the low expression group was  $26.31 \pm 4.70\%$  ( $P < 0.01$ ). **Conclusion:** There was a significant difference in pathologic subtype distribution between brain metastatic lung adenocarcinoma and primary lung adenocarcinoma. Tumor cell proliferation was closely related to pathologic subtype. The expression rates of ALK and EGFR genes in brain metastases were consistent with those of primary lung adenocarcinoma, and the expression levels of ALK and EGFR genes were mutually exclusive.



## **Intramedullary spinal cord angioliipoma**

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**Introduction:** Spinal cord angioliipomas are rare benign lesions accounting for approximately 0.1-0.5% of all spinal cord tumours and are represented in the literature as scattered, single case reports. Although most spinal angioliipomas are epidural tumours, a small proportion can be intramedullary. The usual clinical presentation includes back pain, and progressive numbness and weakness of the limbs. **Clinical Summary:** We report a case of a 47-year-old woman who presented with symptoms of decrease sensation of left arm and right leg, and difficulties in raising left shoulder. Patient has no evidence of spinal dysraphism. The MRI shows a small well-defined intense enhancing intramedullary nodule in the left sided posterior cord at C4 level and shows associated syringohydromyelia extending from medulla oblongata down to C4-C5 level. The pre-operative differential diagnoses included cystic astrocytoma, ependymoma and hemangioblastoma. The patient underwent surgery with total resection of the lesion. The gross section during intraoperative consultation shows a well-defined red brownish nodule. **Pathological findings:** The histopathological examination reveals mainly matured adipocytes with scattered intervening small vessels. There is no evidence of malignancy. The histopathological diagnosis is compatible with an intramedullary angioliipoma. Her clinical symptoms subsequently improved after surgery. **Conclusion:** Although, intramedullary angioliipoma is rare but it represents a potentially curable condition, and should therefore be considered in the differential diagnosis of primary intra-axial tumors in adults.

**P3-18**

**Diffuse leptomeningeal glioneuronal tumor exhibiting 1p/19q co-deletion and H3F3K27M mutation: A rare case with unique molecular profile**

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**Introduction:**Diffuse leptomeningeal glioneuronal tumour is a new entity in the recent WHO classification of CNS tumors (2016). It is a rare tumour characterised by predominant and widespread involvement of leptomeninges with oligodendroglial like cytology. Most are low grade, a small proportion show aggressive behaviour. Hence, a definite WHO grade is not yet assigned. **Clinical Summary:**A 13-year-old female child presented with complaints of diminution of vision in both the eyes and headache for 1 year and paraplegia with bladder and bowel dysfunction for 1 month. MRI revealed an intradural extramedullary mass in D1-D4 region of spinal cord and multiple T2 hyperintense lesions in sulcal spaces of cerebellum, choroid plexus of lateral ventricles, putamina and pons. **Pathological findings:**Biopsy from a mass in the conus region showed a tumour with oligodendroglia like cytology and glomeruloid vessels with moderately high MIB1 index. The tumour cells were immunopositive for GFAP, synaptophysin, NeuN while negative for IDH and showed retained ATRX expression. The tumor was found to harbour 1p/19q co-deletion by Fluorescence in-situ hybridisation and H3F3A mutation by Sanger-sequencing. IDH mutations and BRAF alterations were not found by sequencing and RT-PCR, respectively. Based on overall findings, a diagnosis of diffuse leptomeningeal glioneuronal tumour was rendered. **Conclusions:**Diffuse leptomeningeal glioneuronal tumors represent a distinct clinico-pathological entity. Even though histologically benign, they can show aggressive behavior due to involvement of wide area of leptomeninges, development around the brainstem and difficulty in surgical intervention. Hence, a knowledge of this new entity is imperative to arrive at the correct diagnosis.

## **Expression of collagen VI, laminin, MMP9, anticollagenase, claudins 1 and 5, N and E cadherins in choroid plexus tumors**

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**Introduction:** The Choroid plexus tumor(CPT) are an uncommon tumor derived from choroid plexus epithelial cells (CPECs), that are seen predominantly in children than adults. CPECs are closely connected to each other by tight junctions and establish the structural basis of the blood-CSF barrier. **Methods:** The immunohistochemical expression of Claudin 1, and 5, E and N cadherin, laminin, and anticollagenase, basement membrane component type IV collagen and proliferation of Ki67-li and MVD-li were investigated in 42 choroid plexus tumors. Clinical pathological, immunohistochemical and ultrastructure correlations. **Results:** 28(67%) were choroid plexus papillomas(CPP), 8(19%) were atypical choroid plexus papillomas(ACPP) and 6 (14%) choroid plexus carcinomas(CPC). 37 were female (62%9) and 23 males (42%). Tumor localization; supratentorial portion were 35(58%), and infratentorial region in 25(42%), 11(18%) were located in lateral ventricles, 6(10%) in III ventricle and 25(42%) in IV ventricle. The Ki67-li and MVD increased from CPC to ACPP, being the highest in malignant tumors as well as a strong immunoexpression of anticollagenase and were inverse correlation with claudin 5, E and N cadherin and collagen IV membrane basal immunohistochemical expression which added further significant information to the prognosis and varied according to the histologic classification. By ultrastructure the loss of membrane basal was observed in CPC. **Conclusions:** The loss of membrane basal and over expression of extracellular matrix could be considered as predictor factor in CPT as bad prognosis in CPT. Anticollagenase, MMP9 overexpression could be in relationship with basal membrane and BBB plasticity in CPTs.

## **A case of high-grade glioma simulating epithelioid glioblastoma**

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**【Introduction】** Epithelioid glioblastoma (EG) is a rare, recently recognized variant of glioblastoma composed of epithelioid and rhabdoid tumor cells. We herein reported a case of high-grade glioma simulating EG.

**【Case report】** A 47-year-old female visited a neurosurgical clinic, because of headache, which continued for 2 weeks and increased its intensity. She also complained of vomiting and misty vision. As a brain tumor was pointed out by MRI, she was referred to our hospital. No neurological symptoms other than headache and choked disc were present at admission. A tumor of 6cm in diameter, associated with cysts and calcification, was located in the right temporal lobe. DSA showed a light tumor shadow and the feeding arteries were the right posterior cerebral artery and the anterior and posterior temporal arteries. With the right subtemporal approach, the tumor was gross-totally excised, and the postoperative course was uneventful with radiation and temozolomide combination therapy.

**【Pathologic findings】** Microscopically, the tumor was composed of a sheet-like growth of epithelioid tumor cells with ovoid nuclei and eosinophilic cytoplasm, associated with calcification and hemorrhage. Mitotic figures, necrotic areas, and microvascular proliferation were noted. Immunohistochemically, tumor cells were positive for GFAP and p53, but negative for EMA, CD34, IDH1 R132H, and BRAF V600E. Ki-67 labeling index was 15%. 1p/19q codeletion was not detected by FISH.

**【Conclusion】** About a half of EG are known to have BRAF V600E mutation. Although the mutation was not present, the pathologic findings of the present tumor were similar to those of EG.

## **A poor prognostic case of pediatric glioblastoma with IDH1 mutation**

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**【Introduction】** Isocitrate dehydrogenase 1 (IDH1) mutation was found in 5-10 % of adult glioblastoma (GBM) patients. However, only few papers reported the cases of pediatric GBM with IDH mutation. Here, we report a rare case of pediatric glioblastoma with IDH1 mutation.

**【Case】** A-11-year-old female with a progressive right upper limb paralysis and motor aphasia admitted to our hospital. MR imaging revealed a ring-shaped contrast lesion in the left frontal lobe. The patient underwent surgery and post-operative MRI imaging showed subtotal resection of the tumor. Histopathological examination showed both microvascular proliferation and necrosis. Immunohistochemical staining revealed a negative of MGMT, and a positive of p53. The Ki-67 labeling index was 30%. The IDH1 (R132H) specific antibody was positive and it was confirmed by Sanger sequencing. The final diagnosis was GBM with IDH mutation. Following after surgery, she received radiation therapy concurrent with temozolomide. However, the tumor was recurred during radio-chemotherapy, then we performed 2nd surgery. Four months after 2nd surgery, the tumor enlarged again, she underwent 3rd surgery. Despite of bevacizumab treatment and intrathecal injection of methotrexate, it was difficult to control tumor growth. The patient was dead by disease 11 months after initial therapy. **【Discussion】** Korshunov et al. reported in 202 cases of pediatric GBM, IDH1 mutation was found in only 10 cases (4.9%). These cases had relatively good prognosis and 3 years overall survival rate was 90%. In contrast, our case was refractory to any treatment and showed poor prognosis.

## **An elderly case of anaplastic pleomorphic xanthoastrocytoma**

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Pleomorphic xanthoastrocytoma (PXA) is WHO grade II astrocytoma, mainly situated in the superficial regions of the temporal lobe in child and young adult. PXA with more than 5 mitoses per 10 high-power-fields was defined anaplastic pleomorphic xanthoastrocytoma (APXA) in 4th WHO classification, grade III. We report an elderly case of APXA. Case: A 77-year-old-man PH:HT, DM, Depression and renal cancerPI: The patient showed progressive hemiparesis in the right for 10 months before visiting our hospital. MRI revealed enhanced mass lesion in the left frontal lobe without cystic component. Subtotal tumor resection was performed. Pathological findings: In histopathological examination, tumor cells showed pleomorphism. Spindle cells, small round cells, giant cells were intermingled, proliferation of ganglion cells were found. Eosinophilic granular bodies were seen. Necrosis was not present. Microvascular proliferation was noted. Mitoses : 13/10HPF. Tumor cells were surrounded by reticulin fibers. In the immunohistochemical staining, tumor cells were positive in GFAP. Ki67 LI : 20%. BRAF V600E mutation was detected. IDH1, IDH2, H3F3A and TERT were wild type, We diagnosed APXA. Summary: Elderly patients with APXA are rare, although the age of onset in APXA is older than PXA. Only 17 APXA patients more than 60-year-old have been reported. Tumors were situated in the temporal lobe in 7cases of the 17 elderly onset APXA. The frequency of BRAF V600E mutation is lower among APXA than among WHO grade II PXA. We report a rare case of elderly APXA with BRAF V600E mutation.

**P3-23**

**Mitogen-activated protein kinase in gliosis and pilocytic astrocytoma**

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Pilocytic astrocytoma (PA), featuring activation of the mitogen-activated protein kinase (MAPK) pathway, is the most common tumor of the pediatric central nervous system. However, it remains unknown whether MAPK activation is present in the reactive gliosis of non-neoplastic lesions. Therefore, we investigated the expression of MAPK in reactive gliosis associated with cavernous angiomas. Immunohistochemical expression and the extent of BRAF, ERK, p38, and JNK were investigated in ten patients with gliosis surrounding cavernous angiomas (GS group) and ten patients with PA (PA group). Evaluation of these parameters was scored as 0, none; 1, scarce; 2, moderate; 3, global. In GS group, histopathologic features of PA included piloid cells, Rosenthal fibers, microcysts with eosinophilic granular bodies were identified. Expression of ERK, and p38 was shown in all patients in GS and PA groups. Expression of BRAF was identified in five patients (50%) in the GS group and in eight (80%) in the PA groups. The mean score of BRAF expression in the PA group was significantly higher than that in the GS group ( $p=0.019$ ). Reactive gliosis may resemble PA in histological findings and MAPK activation. Therefore, PA could be indistinguishable from reactive gliosis with classic histopathologic and/or immunohistochemical methods.

## **Efficacy of ICE plus Bevacizumab Therapy for Temozolomide-Resistant Anaplastic Astroblastoma: Case Report**

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We recently encountered a case of anaplastic astroblastoma with temozolomide (TMZ) resistance in which ICE plus bevacizumab (Bev) therapy was effective. This 41-year-old man presented with headache, nausea, speech difficulty, and complex partial seizures. MRI demonstrated an intraaxial mass in the left frontal lobe (about 7-cm diameter) with clear boundaries. Surgery was performed and postoperative MRI confirmed gross-total tumor resection. Postoperative histopathological examination revealed anaplastic astroblastoma. The patient underwent TMZ chemotherapy with 60 Gy radiation therapy and was discharged from our hospital. Seven months later, after five courses of TMZ maintenance therapy, he presented with systemic convulsion. MRI demonstrated multiple tumor masses on the dura mater of the clivus and the occipital lesion, and the whole spine. These findings were strongly suspected to indicate dural metastasis and CSF dissemination of the anaplastic astroblastoma. After a multidisciplinary discussion, ICE + Bev therapy was begun. After the second-line chemotherapy, the tumors remained well controlled for some months, but finally became uncontrollable and the patient died at 11 months after the diagnosis of tumor recurrence. Based on our experience, ICE plus Bev therapy is effective as second-line therapy for anaplastic astroblastoma.



## **A case of radiation-induced sarcomas 10 years after radiation therapy against glioblastoma**

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We report a case of radiation-induced sarcomas 10 years after radiation therapy against glioblastoma. A 61-year-old man was referred to our department because a brain tumor recurrence was suspected in the MR images. He had undergone left frontal tumor resection 10 years ago, and received radiotherapy (extended-local, 60Gy/30fr) and temozolomide chemotherapy. The tumor was recognized as enhancing nodules of the resected cavity wall on MR images. Some nodules taken by the resection surgery were diagnosed as osteosarcoma, and other nodules were recognized as rhabdomyosarcoma. There were no features of glioblastomas in all nodules. These two types of sarcomas were considered as radiation-induced tumors, even though such case is extremely rare.

**P3-26**

**Anti-tumor effects of metformin against malignant glioma**

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An antidiabetic drug metformin is known to have anti-tumor effects. We herein studied the mechanism of anti-tumor effects of metformin in glioma cells. We cultured a human glioma cell line U373MG in a medium with low-serum/low-glucose concentrations to optimize the effects of metformin. Then, we investigated the altered expression patterns of lipid metabolism-associated proteins after metformin treatment by immunoblotting and immunofluorescence. We also carried out microarray gene expression analysis after metformin treatment. We found that 1) metformin strongly inhibited proliferation of the glioma cells; 2) Metformin promoted phosphorylation of AMP-activated protein kinase (AMPK) and downregulated fatty acid synthase (FASN) and acetyl-CoA carboxylase  $\alpha$  (ACACA). In addition, ACACA was phosphorylated (inactivated), and translocated from the cytoplasm to the nucleus; 3) metformin upregulated 58 tumor suppressor genes. These findings suggest that in U373MG, metformin activates AMPK followed by phosphorylation and inactivation of ACACA as well as downregulation of FASN, resulting in inhibition of fatty acid synthesis and cell proliferation. Furthermore, metformin upregulated various tumor suppressor genes at the transcription levels. It is possible that metformin inhibits tumor growth through epigenetic modification of these tumor suppressor genes. We conclude that metformin exerts its anti-tumor effects in a multifaceted fashion.

## **Heterogeneous clinico-pathological features of diffuse midline glioma H3-K27M mutant**

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A specific lysin to methionine mutation (K27M) in histone variants H3.3 or H3.1 has been identified predominantly in diffuse infiltrative midline gliomas, and defined as a new glioma entity of grade IV malignancy in WHO Classification Criteria 2016 update. However, there remains a controversy whether harboring H3-K27M mutation is inevitably associated with a specific pathology showing unfavorable outcome or not. Here we present our recent experience of five patients with glial tumors diagnosed as DMG H3-K27M since 2016 in our institution. Representative cases: Case 1: 60 yo female, with a large non-enhancing thalamic mass; anaplastic astrocytic tumor with a high Ki-67 index (30%). She received radiotherapy (RT) and temozolomide (TMZ) but had recurrence 12.6 m later. Case 2: 29 yo female, with a non-enhancing pontine and enhancing cerebellar lesions. Glioblastoma-like tumor had a high Ki-67 index (40%). She received RT/TMZ followed by TMZ/bevacizumab (BEV), with PFS 10.4 m and OS 15.3 m. Case 3: 31 yo male, with a large enhancing mass with calcification and cysts in the cerebellum with EGFR amplification. He was treated with Stupp regimen without progression (15.1 m). Case 5: 36 yo male, with a huge non-enhancing mass involving bilateral cerebral hemisphere with a spot enhancing lesion. He was treated with RT/TMZ with response. These 5 cases illustrated glial tumors with common H3-K27M mutation without IDH mutation but associated with distinct spatial distribution, imaging characteristics, and response to treatment. The detailed features will be presented with potential classification of K27M tumors.

## **An autopsy case of diffuse midline glioma around the foramen of Monro**

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**【Introduction】** Diffuse midline glioma with histone H3-K27M mutation is a new tumor entity defined by the 2016 WHO Classification of Tumors of the Central Nervous System. Several studies using biopsy or surgical specimens reported that the pathological features of diffuse midline glioma are highly variable, ranging from WHO grade I -like to Grade IV-like. We herein report an autopsy case of diffuse midline glioma. **【Case】** A 43-year-old woman presented with headache and cognitive decline. Head CT revealed a tumor around the right foramen of Monro. Histologically, this tumor diagnosed as a high grade glioma based on high Ki-67 expression and the presence of the histone H3 K27M mutation, despite low grade glioma-like morphology. The patient was treated with combination therapy of radiotherapy and chemotherapy, but died three years after the initial presentation. An autopsy revealed a right basal ganglia glioma with subarachnoid spread and invasion in the corpus callosum. Histologically, the tumor showed high grade morphological features with necrosis and microvascular proliferation. In a small area, low grade morphological features were found similar to the initial biopsy. **【Conclusion】** This autopsy case revealed marked histologic intratumoral heterogeneity of diffuse midline glioma. For accurate pathological diagnosis, it is important to perform biopsy from the appropriate site and to keep in mind that most of diffuse midline glioma show marked intratumoral heterogeneity.

## **Imaging and immunohistochemical characteristics of H3 G34R-mutant gliomas -a report of three cases-**

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The K27M mutation in histone H3.3 (H3F3A) and H3.1 (HIST1H3B/C) are defined as a new entity and named "diffuse midline glioma, H3 K27M-mutant" in WHO 2016 update. The G34 mutations, on the other hand, are found predominantly in supratentorial non-midline tumors and are not categorized as a new entity yet. We report the immunohistochemical and imaging characteristics of this rare tumor. Case 1: A 13-year-old. MRI showed non-enhancing left frontal tumor with intratumoral hemorrhage and was hyper-intense on diffusion-weighted imaging (DWI). The tumor was excised in toto and was histologically diagnosed as glioblastoma based on 2007 WHO classification. Case 2: A 19-year-old female. MRI revealed a right parietal tumor with partial enhancement and slight hyper-intensity on DWI. The tumor was completely excised and was histologically diagnosed as anaplastic astrocytoma based on 2007 WHO classification. Case 3: 15 year-old female. MRI revealed a right fronto-parietal tumor with partial enhancement and hyper-intensity on DWI. The tumor was partially excised and was histologically diagnosed as PNET based on 2007 WHO classification. In these cases, the tumor cells were immunoreactive to H3 G34R-mutant and p53 antibodies, and non-reactive to H3 K27M-mutant, IDH1-R132H, ATRX, and olig2. Immunohistochemical characteristics are valuable for predicting the mutation of H3 G34R in pediatric, adolescents and young adult gliomas. Negativity to olig2 may be the characteristic of H3 G34R-mutant gliomas. DWI hyper-intensity reflects the tumor cellularity and may be associated with malignant grade of H3 G34R-mutant gliomas.

## **Histopathological analysis of the new mouse glioma model which shows perineural invasion**

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The treatment to diffuse invasion of glioma is difficult. Now, there is little effective treatment to diffuse invasion of glioma. We produced the new mouse glioma model which shows perineural invasion. We compared the feature of both histopathological for the mouse glioma model used conventionally. We investigated the proliferation potency of a mouse glial cell line with Histone 3.3 K27M mutation. We transfected Histone 3.3 K27M mutant into the mouse glial cell (K27M cell). The expression level of the cell line was confirmed by real-time RT-PCR and immunofluorescence with antibodies. In vitro, we performed co-culture, K27M mutant mouse glioma cell and primary neuronal cells. We demonstrated the active tumor cell motion by time lapse photography. In vivo, we transplanted K27M cell or GL261 cell to the nude mouse brain(N=5). Cells were injected ( $5.0 \times 10^5$  cells/ $\mu$ l) into the right striatum. GL261 model proliferated in distensibility. Furthermore the border of this model was clear. By contrast, K27M cell model proliferated diffuse invasion. The border of this model wasn't clear. Furthermore we demonstrated much perineural invasion. We established the new mouse glioma model which shows perineural invasion. This model leads to elucidation of the mechanism of the perineuronal invasion for diffuse glioma.

## **A case of anaplastic astrocytoma with appearance of IDH-mutant astrocytic cells at recurrence**

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We report a 57-year-old man who had a brain tumor in right front-temporal lobe. MRI showed a high intensity area in T2WI without contrast-enhanced lesion. Then the tumor was slowly growing and appeared with contrast-enhanced lesion. This patient underwent craniotomy and gross-total resection was done. This tumor was diagnosed histologically anaplastic astrocytoma, WHO grade III and immunohistochemically showed IDH1R132H-negative, ATRX-loss, p53-mutant. The patient received TMZ-based chemoradiotherapy postoperatively. 8-months later, MRI showed a local recurrence with contrast-enhanced lesion. The patient received second craniotomy and removed the lesion. The resected lesion showed necrotic brain tissue by radiotherapy. However small amount of atypical astrocytic cells were seen and they showed IDH1R132H-positivity immunohistochemically. After that, the lesion tended to growing, we think this was residual/recurrent tumor. This is so problematic case, because status of IDH-mutation doesn't change according to current WHO 2016. We want to discuss this case.

## Cerebellar radiation-induced glioma after complete remission of pineal tumor

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**【Background】** Histopathological diagnosis of radiation-induced glioma (RIG) is difficult in many cases as there remains a lack of reliable biomarkers. **【Case Description】** A 10 year-old boy was diagnosed as a pineal tumor based on the neuro-imaging and achieved complete remission after radiation therapy with 49 Gy (whole brain: 21 Gy, focal: 28 Gy). Follow-up MR imaging showed no recurrence during more than 30 years. He presented with gait disturbance due to progressive right cerebellar ataxia 31 years after the irradiation (at age 41 years). MR imaging demonstrated ring-like enhanced lesion without perifocal edema in the left superior cerebellum, rapidly growing over 5 months. The tumor was gross totally removed via occipital transtentorial approach. Histological examinations showed diffuse proliferation of atypical tumor cells and invasion into the cerebellar parenchyma, however apparent pseudopalisading necrosis and microvascular proliferation could not be identified. Immunohistochemical examinations revealed phenotypes of the tumor cells as follows; GFAP (+), INI-1 loss (-), ATRX (nuclear alpha thalassemia/mental retardation syndrome X-linked) loss (-), isocitrate dehydrogenase1 (IDH1)-R132H (-). The MIB-1 labeling index was up to 59%. Direct DNA sequencing analysis showed no mutations of IDH1, IDH2, telomerase reverse transcriptase (TERT) promoter, H3F3A, HIST1H3B and BRAF. **【Conclusion】** Negative findings of the molecular biomarkers for conventional gliomas might provide important and helpful information on pathological diagnosis of RIG, especially in cases with unknown histological diagnosis of the primary lesions.



## **Consideration of integrated diagnosis of gliomas**

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Genetic status of *IDH*, *ATRX*, *BRAF*, *H3K27M* and 1p/19q should be incorporated to make integrated diagnosis according to the revised WHO classification in 2016. Here, we compared between histological and integrated diagnosis of astrocytomas (A), oligodendrogliomas (O), oligoastrocytomas (OA) and glioblastomas (GBM) operated at our hospital since 2016. As a result, histological diagnosis and integrated diagnosis were largely correlated. All cases of histological A were proven to be integrated diagnosis of A. Some cases of histological O were changed to integrated diagnosis of A. Histological OA were proven to be A or diffuse midline glioma with *H3K27M*. There were small number of cases with *IDH*-mut which could not be detected immunohistochemically. Although there were cases in which 1p/19q co-deletion was observed with FISH, some of them showed partial deletion of 1p or/and 19q by MLPA and *IDH*-wt by sequencing. There might be some relationship between partial deletion pattern of 1p/19q detected by the MLPA and histological findings.

## **A case of malignant transformation of NF1-associated spinal astrocytoma**

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The most common glioma occurring in patients with neurofibromatosis type 1 (NF1) is a pilocytic astrocytoma, although other types of gliomas such as diffuse astrocytoma and glioblastoma are also known to occur. NF-1 associated gliomas follow an atypical clinical course and show peculiar histopathologies, and few cases of malignant transformation were described. We present a rare case of malignant transformation of NF1-associated spinal astrocytoma in a course of 7 years. A 27-year-old man with NF1 presented with weakness of lower extremities, and MRI revealed an intramedullary spinal cord tumor involving Th11-Th12 levels. The tumor was resected and histologically demonstrated a nodular proliferation of atypical spindled cells with relatively thick cytoplasmic processes. Multipolar tumor cells were also seen between these nodules. No necrosis or microvascular proliferation was observed. Immunohistochemically, the tumor cells were positive for GFAP and negative for IDH1 R132H. The MIB-1 labeling index was approximately 5%. The diagnosis of NF1-associated astrocytoma, grade II, was rendered. Seven years after the surgery, he developed leg paralysis and was found to have a recurrent tumor, involving the spinal cord from Th5-L3 levels. Since the spinal cord was completely replaced by tumor below the level of Th8, spinal cordectomy was undertaken. The histopathological examination revealed pleomorphic glial tumor cells infiltrating diffusely into the spinal cord parenchyma, with prominent subarachnoid spreading and nerve root involvement. Both necrosis and microvascular proliferation were observed. The MIB-1 labeling index was about 20% and the recurrent tumor was diagnosed as a high-grade infiltrating astrocytoma (malignant transformation).

## **A case of primary diffuse leptomeningeal gliomatosis with multi-nodular lesions**

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Primary diffuse leptomeningeal gliomatosis (PDLG) is a rare and fatal tumor, arises from heterotopic neuroglial tissue in the leptomeninges and spreads widely throughout subarachnoidal space. We report a 72-year-old man with PDLG presenting gait disturbance. MRI showed leptomeningeal multi-nodular mass lesions with gadolinium enhancement. CSF cytology was class 2. Preoperative diagnosis was meningeal carcinomatosis of unknown origin. Open biopsy revealed that the tumor was elastic hard with clear margin. Pathological examination demonstrated composed fascicles of spindle cells with atypical nuclei. Immunohistochemically, the spindle cells were positive for GFAP, oligo2, EMA, S100 and ATRX, but negative for neurofilament. IDH1 was wild type and Ki-67 labeling index was 30%. Pathological diagnosis was high grade glioma (grade 3). He underwent whole brain radiotherapy and stereotactic radiosurgery boost followed by bevacizumab therapy. He died 5 months after initial presentation. Autopsy was performed, and our diagnosis was PDLG (grade4). We emphasize that PDLG with multi-nodular lesions must be included in differential diagnosis in cases with MRI suggesting nodular leptomeningeal carcinomatosis of unknown origin, and a biopsy should be performed in the early stages.

## A case of diffuse leptomeningeal glioneuronal tumor

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Diffuse leptomeningeal glioneuronal tumor (DLGNT) is an extremely rare tumor, which was recently recognized as a new glioneuronal tumor entity. DLGNT usually occurs in children and young adults and is characterized by prominent and widespread leptomeningeal growth of oligodendroglia-like tumor cells. Their clinicopathologic features and biological behavior are still unclear. Here, we report an adult case of DLGNT, which showed the aggressive clinical course. The patient was a 42-year-old male who visited a hospital, suffering from fever and disturbance of consciousness. Based on signs of meningeal irritation and abnormalities in CNS fluid, meningitis was clinically suspected. Despite antibiotics and steroids treatment, his condition deteriorated, associated with hydrocephalus, paralysis, and incontinence. MRI, which was taken a half year later, demonstrated swelling of spinal cord and diffuse enhancement of leptomeninges throughout the CNS. As neoplastic process was suspected, biopsy was performed from the cauda equina. In the biopsy specimens, there was proliferation of uniform round tumor cells, surrounding spinal nerve fascicles. Tumor cells, arranged in small nests, possessed round nuclei and clear cytoplasm, simulating oligodendroglia. Immunohistochemically, tumor cells were variedly positive for GFAP, Olig2, and synaptophysin. Ki-67 labeling index was 5-10%. Based on the pathologic findings, the tumor was diagnosed as DLGNT. Chemo-radiotherapy was refused and the patient died one month after the diagnosis. Clinical progression of DLGNT is usually slow, but some examples may show the aggressive course. For the appropriate and early diagnosis of this challenging tumor, the acquaintance of DLGNT is mandatory.

## Glioblastoma suspected association with Lynch syndrome

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**【Background】** Lynch syndrome is an autosomal dominant disease caused by aberrations in DNA mismatch-repairing genes, which present colon cancer and various gastroenterological cancers, urological cancers or brain tumors. Little is known about clinical characteristics of glioblastoma associated with Lynch syndrome. **【Case Presentation】** The patient is a 50 year-old male with past history of rectal cancer at the age of 38, and familial history of multiple cancer including renal pelvis cancer, prostate cancer, bladder cancer, colon cancer and skin cancer in his brother. A brain tumor in right parietal lobe was detected due to loss of consciousness, and pathological diagnosis of glioblastoma was provided after surgical resection. Although he underwent local 60Gy of irradiation concomitant with oral administration of temozolomide, additional resection was required due to growth of residual tumor. During maintenance treatment with temozolomide, he underwent several times of polypectomy for a number of colon polyps and ileocecal resection for cecal cancer, which suggested a familial colorectal cancer syndrome. He underwent 24 courses of temozolomide treatment without recurrence. At 40 months after initial operation, he underwent resection surgery for newly detected gadolinium-enhanced lesion around resection cavity but tumor cells were not confirmed pathologically. However, he eventually experienced recurrence at 47 months and died at 52 months after initial surgery. **【Conclusion】** Although genetic examinations have not been performed for present case, Lynch syndrome was strongly suspected by clinical course and familial history. This case suggested the efficacy of standardized treatment with temozolomide.

## **An operative case of brain stem glioma with IDH1 mutation**

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**【Introduction】** The isocitrate dehydrogenase (IDH) mutation in glioma has been studied with regard to the clinical feature and biological significance. However, the IDH mutation in the brainstem glioma is rare; there are only seven cases in our knowledge. Now, we report the adult brain stem glioma case with IDH mutation who showed secondary malignant change. **【Case】** 49 years old male. In August 2011, he developed diplopia, and the brainstem tumor was suspected by the image. During the first visit, perceived decrease of sensation in right upper/lower extremities, left abducent palsy, and left facial palsy were recognized. MRI showed T2WI/FLAIR high-intensity lesion on the left side of pons. Obvious contrast enhancement was not observed. We had underwent biopsy. Pathologically, the tumor showed findings of low-grade glioma. After surgery, the initial treatment by local irradiation with 54Gy and temozolomide had performed. Then he was carried out temozolomide maintenance therapy in outpatient. However, since January 2017, he developed ataxia and headache. MRI showed the contrast enhanced lesion in the left cerebellar hemisphere. The surgery was performed again. Pathological search showed findings of glioblastoma with IDH mutation. He had died after SRT and conservative treatment in terminal stage. **【Consideration】** the report on the brainstem glioma with IDH mutation is rare; it is about to be seen in case report and a few cases of multi-case analysis. This case is also a rare case as an adult brainstem glioma with IDH mutation and malignant transformation. We report the the clinical course with literature examinations.

## **The anti-tumor effects of COX-2 inhibitor against malignant astrocytic tumor cells *in vitro* and *in vivo***

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**【Purpose】** We examined an anti-tumor effect of celecoxib (CXB), a COX-2 inhibitor, combined with temozolomide (TMZ) and irradiation *in vitro*. CXB exerted an anti-tumor effects in dose dependent manner, and the viability of C6 cell line was reduced more effectively by CXB when combined with TMZ and irradiation. The present study aimed to define the anti-tumor effects of CXB alone or combined with TMZ and/or irradiation, against C6 cell line *in vivo*.

**【Methods】** With the use of C6 cell line, we analyzed the anti-tumor effect of CXB *in vivo*. C6 cells ( $1 \times 10^5$  cells) were implanted into mice by stereotactically guided injection into the fore brain. After 7 days, mice were treated with CXB (100mg/kg/day IP), TMZ 7.5mg/kg/day IP, irradiation (15Gy), CXB and TMZ, CXB and irradiation, TMZ and irradiation, or CXB and irradiation and TMZ for a week. The tumor volume, invasion and dissemination were analyzed histopathologically.

**【Result】** CXB exerted an anti-tumor effects more effectively by CXB when combined with TMZ and irradiation *in vitro*. Here we report the anti-tumor effect of CXB *in vivo*.

## **Stratification of IDH wild-type WHO grade II / III gliomas by molecular marker**

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**【Background】** According to the revision of 2016 WHO Classification of Brain and Central Nervous System Tumors, grade II / III gliomas were classified into astrocytoma and oligodendroglioma with the presence of 1 p / 19 q co-deletion and IDH mutation. On the other hand, IDH wild-type grade II / III gliomas are thought to be an of various tumors, but the detail has not been reported. In this report, we indicate the correlation among genetic characteristics about IDH wild-type grade II / III gliomas and their prognosis. **【Methods】** Our study included 37 patients of IDH wild-type grade II / III gliomas. Their first surgery was performed at our hospital from April 2004 to April 2018. We investigated the correlation among Overall Survival (OS) and genetic characteristics, including BRAF V600E, hTERT promoter, p53, ATRX mutation and DNA copy number. **【Results】** Median OS was 30 months and median PFS was 10 months. DNA copy number at + 7 ( $p = 0.0004$ ) and - 10 q ( $p = 0.03$ ) characteristically in glioblastoma, ATRX mutation ( $p = 0.02$ ) was related with shorter OS significantly. Multivariate analysis for +7, -10 q and ATRX mutation, which were a significant factor in univariate analysis, showed that - 10 q significantly contributed to shorter OS. **【Conclusions】** Our genetic analysis of this study suggested that IDH wild-type grade II / III gliomas were an aggregate of various tumors, including glioblastoma. We will report additional genetic characteristics of IDH wild-type grade II / III gliomas.



## **Three cases of unclassified low-grade gliomas with presence of numerous CD34-positive cells**

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We report here three cases of low-grade gliomas, mainly composed of oligodendroglia-like cells (OLC) along with numerous CD34-positive multipolar cells. Two patients were under 10 years old and had chronic epilepsy. Astrocytic tumor cells were also intermingled in the lesion. Dysplastic neurons or glioneuronal elements of DNT were not observed in any of them. Immunostainings revealed OLCs were positive for Olig2 but negative for GFAP or neuronal cell markers. Ki-67 LIs were less than 3% in all cases. Genetic analysis identified BRAFV600E mutation in two cases. None of them showed IDH1 or 2 mutations. Considering the presence of numerous CD34-positive cells in the lesion, these tumors might arise based on focal maldevelopmental processes of the brain.

## **Adult gliomas concurrently harboring 1p/19q codeletion and TP53 mutation: molecular analysis of two cases**

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The diagnosis of "Oligoastrocytoma" is discouraged in the current diagnostic system based on the CNS WHO 2016 because virtually all IDH mutated tumors harbor either 1p/19q codeletion or TP53 mutation, that is a hall mark of oligodendroglioma or astrocytoma, respectively. However, a small portion of 1p/19q codeleted tumors exhibit TP53 mutations. In this study, we reviewed the clinical and genetic features of two cases of "Oligodendroglioma, IDH mutant, 1p/19q codeleted, and TP 53 mutant". The first case (Case 1) had a history of craniotomy for left frontal tumor 7 years before, and underwent the second surgery for tumor removal in our hospital. The second case (Case 2) underwent repeated surgeries for right frontal tumor recurring locally. Both cases exhibit partial calcification in computed tomographic images. Genetic analysis revealed IDH1 R132H mutation, 1p/19q codeletion, TERT promoter mutation, and missense point mutation in the exon of TP53 in the specimens of the second surgery of the Case 1 and the first and second surgery of Case 2. Loss of heterozygosity (LOH) analysis using microarray technique showed the normal copy number of 17p in all specimens. Our cases lacked copy number neutral LOH of TP53, which are typically observed in IDH-mutated astrocytomas while having TERT promoter mutations. Although further pathological analysis of intratumoral heterogeneity is needed, our results suggest that low grade gliomas with 1p/19q codeletion and TP53 mutation may have strong features of oligodendrogliomas rather than astrocytomas.

## **A case of adult supratentorial anaplastic pilocytic astrocytoma**

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Pilocytic Astrocytoma (PA) is most commonly occurs in children, and classified in WHO grade I. However, PA is infrequently seen in adult population and about 1.5% of PA present histologically anaplastic feature. We report a case of adult anaplastic PA (APA).

A 39-year-old-man presented with progressive headache for one week. Clinical examinations revealed no apparent neurological deficit. Brain MRI revealed a mass lesion within the right temporal lobe with a diameter of 28 mm. It demonstrated isointensity on a T1-weighted image and hyperintensity on a T2-weighted image with contrast enhancement and severe perifocal edema.

We performed gross total removal of tumor. Tumor was slightly hard and greyish, we used carmustine wafers. Histologically, tumor showed typical biphasic pattern, but with brisk mitotic activity and hypercellularity. There was no necrotic component. As a result of immunohistochemical stains, GFAR, Nestin, Olig2, p53 were positive, IDH1 was negative. MIB1 labeling index was 8.1%. This tumor was diagnosed APA, considering progressive clinical course. We started adjuvant radiotherapy (60Gy) and temozolomide (75mg/m<sup>2</sup>/day) administration. However, 3 weeks later, MRI revealed enhancement of removal cavity and pial dissemination was suspected. Therefore, we added bevacizumab (10mg/m<sup>2</sup>/2weeks). Now, follow up MRI after 9 months did not reveal any tumor progression.

We reported a case of adult supratentorial APA. This case was diagnosed as 'Anaplastic' PA depending on its progressive course, even though it did not show necrotic component histologically, Overall survival of APA is reported about 2 years. In this case, bevacizumab seems effective, better prognosis can be expected.

## **Two cases of pilocytic astrocytomas with challenging diagnosis**

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Pilocytic astrocytoma (PA) is tumor in young people, the common locations of which were cerebellum, the optic pathway and the fourth ventricle. We report the cases with challenging diagnosis due to their atypical location, imaging and pathology.

Case 1: A 7-year-old boy with right hemiparesis onset. The imaging showed the enhanced multi-cystic tumor with calcification located in left basal ganglia. Craniotomy was used to perform the tumor resection. Pathological findings: Astrocyte-like tumor cells increased in myxoid change-background with microcalcification. While mitosis and microvascular proliferation were not seen, the invasive feature was observed. Immunohistochemical staining (IHC) was positive for GFAP, Olig2, ATRX, and p53, but negative for IDH1-R132H and BRAF-V600E. MIB1-LI was 10%. Although one of the preoperative diagnoses was diffuse midline glioma, the final diagnosis was PA from the results of H3K27 wild type and of BRAF-V600E mutation by direct sequence.

Case 2: A 25-year-old woman with epilepsy onset. The imaging showed non-enhanced tumor located in right lateral ventricle. Endoscopic biopsy was performed. Pathological findings: Astrocyte-like tumor cells increased in compact and spongy background. Microvascular proliferation and eosinophilic granular bodies were seen. IHC showed positive for GFAP, Olig2, ATRX, and p53, but negative for IDH1-R132H and BRAF-V600E. MIB1-LI was 2%. While preoperative diagnosis was subependymoma, the final one was PA.

Although most PA cases can be diagnosed from imaging findings alone, atypical locations and a non-enhancing feature sometimes make accurate diagnosis difficult. Moreover, since there are cases with high MIB1-LI and invasive features, we suggest the indispensability of comprehensive diagnosis.

## **Three case reports of radiation-induced glioblastoma after complete remission of acute lymphoblastic leukemia**

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Radiation therapy is sometimes performed to control intracranial acute lymphoblastic leukemia (ALL), but may lead to radiation-induced malignant glioma. The clinical, radiological, histological, and molecular findings are described of three cases of radiation-induced glioblastoma after treatment for ALL. They received radiation therapy at age 6- 8 years. The latency from radiation therapy to the onset of radiation-induced glioblastoma was 5- 10 years. Magnetic resonance imaging demonstrated diffuse lesions with multiple nodular small enhanced lesions in all cases. Histological examination showed that the tumors consisted of mainly small round astrocytic atypical cells in one case, and astrocytic atypical cells with elongated cytoplasm and nuclear pleomorphism with small cell component in two cases. Microvascular proliferation was present in all cases. Immunohistochemical analysis for isocitrate dehydrogenase 1 R132H and B-Raf V600E, and mutational analysis for the isocitrate dehydrogenase (IDH) 1, IDH2, and H3F3A gene revealed the wild-type alleles in all three cases. The integrated diagnoses were isocitrate dehydrogenaseIDH wild-type glioblastoma, and local irradiation and concomitant temozolomide were performed. After initial treatment, significant shrinkage of the diffuse lesion and enhanced lesion was found in all cases. Radiation-induced glioblastoma occurring after treatment for ALL had unique clinical, radiological, histological, and molecular characteristics in our 3 cases.

**P3-46**

**A cerebellopontine angle tumor mimicking an extra-axial mass**

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A 70 years old woman suffering right hearing disturbance for 5 years and dizziness for 8 months. Head magnetic resonance imaging (MRI) revealed a large cerebellopontine angle (CPA) tumor. Because this tumor was well demarcated and was thought as an extra-axial mass. This tumor was hypo-intensity on T1-weighted image, hyper-intensity on T2 weighted image, and was homogeneously enhanced by Gd-DTPA. This tumor seemed to relate with root exit zone of right trigeminal nerve, thus, we preoperatively diagnosed root type trigeminal schwannoma. We performed tumor resection by right retro-sigmoid approach. Operative view revealed that this tumor did not have a relationship with the trigeminal nerve, but tightly attached to the ventrolateral portion of pons. This tumor was arose from pons and exophytically grew toward CPA. Histological diagnosis was glioma.

## **A case of extraventricular subependymal giant cell astrocytoma in an infant**

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**【Introduction】** Subependymal giant cell astrocytoma (SEGA) and subependymal nodules (SEN) are the most common central nervous system tumors in patients with tuberous sclerosis complex (TSC). We report a case of extraventricular SEGA in an infant.

**【Case report】** A 2-month-old infant had bilateral eyelid- and tongue spasms after feeding. Computed tomography (CT) scan revealed multiple lesions in the right frontal lobe and bilateral basal ganglia. Magnetic resonance imaging (MRI) of those lesions showed hyperintense T1-weighted images, and hypointense T2-weighted images. He was diagnosed with TSC because he had white, leaf-shaped macules. Electroencephalographic examination showed the epileptic focus to be located in the right frontal lobe, for which he underwent a lesionectomy of the frontal area. After surgery, the seizure was well controlled. The specimen showed gangliocyte- and gemistocyte-like giant cells with eosinophilic cytoplasm, and neurocytes with Nissl granules. The pathologic diagnosis was SEGA.

**【Discussion】** SEGA is often located near the foramen of Monro, and develops from the lateral ventricular walls. Most patients with SEGA present with symptoms of hydrocephalus. Extraventricular SEGA is rare compared with intraventricular SEGA.

**【Conclusion】** We present here a case of extraventricular SEGA in an infant, who should be carefully followed up because he may require additional treatment such as secondary surgery or molecular-targeted therapy.

## **A case of astroblastoma**

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**【Introduction】** Astroblastoma is a rare, mostly supratentorial glial tumor, occurring predominantly in children and young adults. Due to the rarity, treatment strategies are still to be discussed. **【Case】** A six year old male presented with headache and nausea. MRI revealed a left frontal cystic mass lesion with bubbly contrast enhancement and macrocalcifications. After gross total tumor resection histological examination showed the tumor contained neoplastic cells with astroblastic arrangements. A striking perivascular array of pseudorosettes was also found. In the end, the diagnosis of high grade astroblastoma was rendered. Eighteen months later, the patient was suggested a local recurrence and received stereotactic radiotherapy. The last MRI follow-up 12 months after irradiation showed no further recurrence. Classification and histogenesis of this tumor is still debated. Lack of clinicopathological correlation makes the prognosis of this tumor unpredictable.



## **A case of anaplastic astroblastoma in the elderly**

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Although astroblastoma is a rare variant of gliomas, the anaplastic type and/or the elderly case were especially rare. We report a case of anaplastic astroblastoma in the elderly. A 72-year-old female presented with progressive dementia was admitted to our hospital. Brain MRIs showed multinodular and multicystic masses with ring-like enhancement in the right temporal lobe. Partial resection was performed and pathological examination showed a high-grade glioma. Postoperatively, she was treated with a combination of radiation therapy and temozolomide chemotherapy. However, gradually progressive consciousness disturbance appeared during postoperative treatment, MRIs revealed the rapid and massive regrowth of the residual tumor. Therefore re-subtotal resection was additionally performed. In the histopathological examination of the first and second surgical specimens, highly proliferation of round eosinophilic tumor cells with mitotic figure and pleomorphism were observed. Astroblastic pseudorosette and perivascular hyalinization were confirmed. In immunohistochemical staining, the tumor cells were positive for GFAP, ATRX and BRAF V600E, negative for EMA, CAM5.2, IDH1 and H3K 27M. The staining index of MIB-1 was 20%.

## **Sellar ependymoma with sinus invasion: the ninth case report and review of literature**

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### **Introduction:**

Ependymoma is a common type of glioma which can rarely develop outside of the ventricular system. Within the pituitary region however only eight cases have been encountered to date. We report the ninth.

### **Methods:**

Our patient, a 64 years old female was referred for neurosurgical evaluation after complaining of visual disturbance and headaches, accompanied by signs of panhypopituitarism. Neuroimaging revealed a large sellar mass extending to the cavernous as well as sphenoid sinuses which was interpreted as a nonfunctional pituitary macroadenoma. Transsphenoidal resection was decided and both sinus and sellar components were removed.

### **Results:**

Histopathological evaluation of classical hematoxylin-eosin slides revealed the typical features of an ependymoma. Due to the presence of a high mitotic index and large areas of necrosis in the sellar component, our case was ultimately considered anaplastic though prognostic significance is debatable here. Immunohistochemically, the tumor showed strong, diffuse positivity for GFAP and S100 as well as a Ki67 index of 28%.

### **Conclusion:**

The first sellar ependymoma was reported in 1956 and only seven others have been described afterwards. The origin of this neoplasm has been theorized as either from a small population of "ependymal pituicytes" or a defect of migration during embryogenesis. All reported cases presented typical histology and only two were subjected to long term follow up. While data about the older cases is limited, it appears our case is the first showing anaplastic features as well as extension to the sinus mucosa. Further clinical significance is to be established as this unusual case is being followed up.

## **Anaplastic ependymoma with ganglioneuronal differentiation**

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6-year-old Japanese boy without previous medical problem presented with recurrent vomiting and gradually deteriorated headache for 3 weeks. Computed tomography and magnetic resonance imaging of the brain revealed a multicystic heterogenous ring enhancing mass in left occipital lobe. He underwent drainage for intracranial pressure control and the lesion was biopsied. Microscopically, the tumor was composed of areas with small round cells and areas with large polygonal cells. In the former area, tumor cells formed perivascular rosettes and true rosettes. Necrosis and microvascular proliferation and mitoses were noted. Immunohistochemically, L1CAM was diffusely positive. Thus the tumor was diagnosed as ependymoma, RELA-fusion positive. In the latter area the polygonal cells, which are with round nuclei and prominent nucleoli and abundant eosinophilic cytoplasm, reminiscent to ganglion cells. Mitoses were also noted. Immunohistochemical study of GFAP, neurofilament and synaptophysin and NeuN clarified neuronal differentiation in addition to glial differentiation. Finally the tumor was diagnosed as anaplastic ependymoma with ganglioneuronal differentiation.

## **Upregulation of Programmed Cell Death Ligand 1 (PDL1) expression in RELA fusion positive ependymomas suggests a role for immunotherapy in these aggressive tumors**

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**Introduction:** RELA-fusion positive supratentorial (ST-RELA) ependymomas are an aggressive subset associated with poor prognosis. The oncogenic C11orf95-RELA fusions result in constitutive NF- $\kappa$ B pathway activation, with the latter known to play important roles in inflammation and innate immunity. Recent advances in cancer immunotherapy has seen the development of treatments targeting immune check point interactions such as Programmed Cell Death Ligand 1 (PDL1/CD274) and its receptor, Programmed Death-1 (PD-1). PDL1/PD-1 inhibitors are now in clinical use for advanced lung and urothelial carcinomas expressing PDL1, while clinical trials are ongoing in several brain tumors. We analyzed the expression of PDL1 in ST-RELA ependymomas to study the applicability of anti-PDL1 immunotherapy in this aggressive subset. **Methods:** Quantitative-Real time PCR for Type I and II C11orf95-RELA fusions was performed followed by Sanger sequencing. Gene expression analysis was performed for PDL1. ChIP-qPCR was performed to study the interaction of RelA protein with PDL1 gene. **Results:** 41 supratentorial ependymomas were included, of which 25 cases harboured RELA fusions (60%). ST-RELA ependymomas predominated in children (80%) and were frequently of Grade III histology (76%). PDL1 was significantly overexpressed in ST-RELA ependymomas. ChIP-qPCR demonstrated enrichment of RelA on PDL1 promoter. **Conclusion:** The present study reports significant over-expression of PDL1 in supratentorial ependymomas harbouring RELA fusions and demonstrates a physical cross-talk between RelA and PDL1 gene. In addition to suggesting a role for anti-PDL1/PD1 immunotherapy, this study raises the need to delve into the immune microenvironment and various immune networking signals to better understand the pathogenesis of RELA fusions.

## **Improved risk-stratification for posterior fossa ependymoma of childhood considering clinical, histological and genetic features**

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*Introduction:* Currently, treatment protocols for children with posterior fossa ependymomas are risk-adapted by clinical features (age, extent of resection). We aimed to identify independent histological and molecular outcome predictors to develop improved stratification models. *Methods:* Tumor samples of 134 patients (0.2 - 15.9 years) enrolled between 1999 and 2010 and treated according to the risk-adapted German GPOH-HIT protocols were analyzed for histological and immunohistological features including mitotic activity, necrosis, vascular proliferation and H3-K27me3 expression as well as genomic alterations by SNP and methylation array hybridization and molecular inversion probe analysis (MIP). Survival analysis was performed by Kaplan-Meier method with log rank test and Cox regression. *Results:* The majority of the samples were anaplastic corresponding to WHO grade III tumors and PFA posterior fossa ependymomas; 7 PFB tumors were identified (5.2%). Residual tumor, chromosome 1q gain and structural genomic alterations were identified as predictors of significantly shorter event-free (EFS) and overall survival (OS). Furthermore, vascular proliferation, necrosis and high mitotic activity were predictive for shorter OS. PFB assignment was not significantly associated to outcome. Multivariate Cox regression revealed residual tumor, chromosome 1q gain, vascular proliferation and high mitotic activity as independent predictors of OS; for EFS, chromosome 1q gain, residual tumor and mitotic activity were predictive. The independent predictors for outcome were used to develop an improved 3-tiered risk-stratification model. *Conclusion:* The independent outcome predictors residual tumor, chromosome 1q gain and mitotic activity could be integrated in an improved risk-stratification model for posterior fossa ependymoma of childhood that outperforms current stratification procedures.

## CNS high-grade neuroepithelial tumor with BCOR internal tandem duplication: a histopathological and molecular genetic analyses of six cases

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*Introduction:* Central nervous system high-grade neuroepithelial tumors with *BCOR* alteration (CNS HGNET-*BCOR*) are a recently reported rare entity, identified as a small fraction of tumors previously institutionally diagnosed as so-called CNS primitive neuroectodermal tumors. Their genetic characteristic is a somatic internal tandem duplication in the 3' end of *BCOR* (*BCOR* ITD), which has also been found in clear cell sarcomas of the kidney (CCSK) and soft tissue undifferentiated round cell sarcomas/primitive myxoid mesenchymal tumors of infancy (URCS/PMMTI), and these *BCOR* ITD-positive tumors have been reported to share similar pathological features. *Methods:* We performed a clinicopathological and molecular analysis of six cases of CNS HGNET-*BCOR*, and compared them with their counterparts in the kidney and soft tissue. *Results:* Although these tumors had histologically similar structural patterns and characteristic monotonous nuclei with fine chromatin, CNS HGNET-*BCOR* exhibited glial cell morphology, ependymoma-like perivascular pseudorosettes and palisading necrosis, whereas these features were not evident in CCSK or URCS/PMMTI. Immunohistochemically, diffuse staining of Olig2 with a mixture of varying degrees of intensity, and only focal staining of GFAP, S-100 protein and synaptophysin were observed in CNS HGNET-*BCOR*, whereas these common neuroepithelial markers were negative in CCSK and URCS/PMMTI. *Conclusion:* Although CNS HGNET-*BCOR*, CCSK and URCS/PMMTI may constitute a group of *BCOR* ITD-positive tumors, only CNS HGNET-*BCOR* has histological features suggestive of glial differentiation. In conclusion, we think CNS HGNET-*BCOR* are a certain type of neuroepithelial tumor relatively close to glioma, not CCSK or URCS/PMMTI occurring in the CNS.

## Integrated histo-radio and molecular study of high-grade gliomas in teenagers

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**Introduction:** We performed a multicentric retrospective study of teenager patients from both adult and pediatric Ile-de-France neurosurgical units, between 1998 and 2013 with a histologically proven high-grade glioma (HGG) to determine their histo-radio-molecular profile. **Methods:** We included 85 teenager patients with a grade III or IV glioma according to the following inclusion criteria: age at diagnosis between 15 and 25 year-old, pathological diagnosis of HGG, available clinical data, pre-surgical and follow-up MRI. All MRI and tumoral samples have been centrally reviewed, while blind to initial diagnosis and follow-up data. We performed a direct sequencing for Histone, IDH and BRAF mutations. A consensus and integrated neuropathological diagnosis was reached by 3 neuropathologists, according to the 2016 World Health Organization classification of tumors of the Central Nervous System. **Findings:** The most frequent histomolecular subtype is a pediatric-like HGG profile with Histone H3 mutation (33/85: 38.8%): 22 H3K27M-mutants (25.9%) and 11 H3G34R-mutants (12.9%). Compared to the exclusively pediatric HGG series, the percentage of IDH-mutant gliomas appears to be more important, reaching 29.4% with only 2 IDH-mutant 1p19q co-deleted oligodendrogliomas. Concerning the rarest mutations, we found 2 (2.4%) Mismatch repair cancer syndrome (MMR), 1 BRAF-mutant (1.2%), and 1 NF1-mutant (1.2%). The histone and IDH wildtype tumors (27%) will benefit from whole exome or RNA sequencings. **Conclusion :** HGG in teenagers comprise a clinicopathological and biological heterogeneous groups of tumours, with a high proportion of pediatric-subtypes: Histone mutated or MMR. Whole exome sequencing will eventually help refining the Histone or IDH wild type tumors to emerging subgroups



## **H3K9 methyltransferase inhibitor BIX01294 inhibits tumorigenicity in diffuse intrinsic pontine glioma and glioblastoma**

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**Introduction:** Diffuse intrinsic pontine glioma (DIPG) is an invasive and treatment-refractory pediatric brain tumor. It is well known that 70-80% of DIPG has mutation of H3K27, which acts as one of the major chromatin repressors. Recent studies revealed the H3K27 mutation caused inactivation of H3K27me3 and activation of several oncogenes, but the role of other chromatin repressor including H3K9 methylation in DIPG is still unclear. **Methods:** We used 3 DIPG lines with H3K27 mutation (JHH-DIPG1, SF7761 and SU-DIPG-XIII) and 2 glioblastoma (GBM) lines without H3K27 mutation (JHH520 and HSR-GBM1), and assessed the therapeutic effects of BIX01294 in these cell lines. **Results:** DIPG lines showed high expression of H3K9me2 and H3K9me3 compared to GBM lines. Micromolar levels of H3K9 methyltransferase inhibitor BIX01294 suppressed the growth of all cell lines. And 2  $\mu$ M BIX01294 reduced expression of H3K9me2 in all cell lines, but H3K9me3 in only JHH-DIPG1, SF7761 and HSR-GBM1. Proliferation capacity was suppressed after treatment with 2  $\mu$ M BIX01294 in DIPG lines but not in GBM lines. Moreover, 2  $\mu$ M BIX01294 induced apoptosis and enhanced radiotoxicity in JHH-DIPG1, SF7761 and HSR-GBM1. Clonogenicity was markedly suppressed after treatment with 1  $\mu$ M BIX01294 in SU-DIPG-XIII, JHH520 and HSR-GBM1. **Conclusion:** We conclude that H3K9 methyltransferase inhibition is a promising potential candidate for DIPG and GBM treatment.



## Molecular neuropathological classification of pediatric diffuse gliomas WHO-grade II -Annotation to biologically different disease entities

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*Objective:* We investigated the frequency of distinct histologically and molecularly defined tumor entities in pediatric diffuse gliomas WHO grade II (DG2) and their outcome. *Patients & Methods:* 100 DG2 among 1645 pediatric low-grade gliomas of the SIOP-LGG-2004 cohort were identified by central neuropathological review (median age, 9.44 years (0.8-17.8); NF1 4%). Localization: cerebral hemispheres 42, supratentorial midline 27, focal pontine-medullary 11, cerebellar 10, spinal 10 cases. FFPE material was available from 64 DG2 for molecular evaluation combining immunohistochemistry, pyrosequencing, DNA methylation array and RNA-fusion analysis including BRAF fusions (Nanostring). *Results:* In these 64 cases, we identified 10 IDH-, 4 Histone3-K27M-, 12 BRAF-V600E-mutated DG2, 6 with KIAA1549-BRAF-fusion, and 32 DG2 wild-type for IDH/H3/BRAF. Further rare aberrations were revealed by Nanostring RNA-analysis and methylation profiling. All H3-mutated DG2 were located in the midline und all IDH-mutated DG2 in the cerebral hemispheres. Treatment included surgical resections without (n=68/100) or with subsequent non-surgical therapy (chemotherapy, irradiation, or multiple salvage treatments). 5-year-OS in the whole DG2 cohort (n=100) was 89.6% ( $\pm 3.1\%$ ). 13 patients died with tumors located in the thalamus (6), caudal brain-stem (4) or elsewhere (3). Molecular classification showed, that 4/4 patients with Histone3-K27M-, 1/10 IDH-, 1/12 BRAFV600E-mutated, 0/6 BRAF fusion positive, 3/32 IDH/H3/BRAF wild-type tumors died. *Conclusions:* Pediatric DG2 represents a heterogeneous group of genetically defined, biologically different tumors. Histone3-K27M-mutation was associated with tumor progression and death, while other genetic features lacked prognostic impact. Therefore, even in histologically low-grade diffuse gliomas a histone3-K27M mutated midline glioma should be ruled out.

## **Giant cell glioblastoma in a 7-year-old Japanese girl: a case report**

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**Introduction:** Giant cell glioblastoma (GCG) is a rare variant of glioblastoma multiforme (GBM). Although it occurs at a younger age than ordinary GBM, its occurrence in childhood is very rare. **Clinical summary:** A 7-year-old Japanese girl presented with headache and restlessness. Magnetic resonance imaging revealed a massive tumor 7 centimeters in diameter in her left frontal lobe with dissemination into the basal cistern. The tumor extended to the lateral ventricles causing acute hydrocephalus due to obstruction of the foramen of Monro. At first, she underwent ventricular drainage and neuro-endoscopic biopsy from the posterior horn of the left lateral ventricles. The initial pathological diagnosis indicated an atypical teratoid/rhabdoid tumor. After the dissemination subsided due to the first chemotherapy including dacarbazine, carboplatin, and vincristine, she underwent the first tumor resection via a left frontal transcortical approach. Then she received a second chemotherapy including ifosfamide, cisplatin, and etoposide; however, the residual tumor showed no change. A near total resection was achieved by a second, transcallosal approach, leading to improvement of the hydrocephalus. Receiving again chemotherapy, her symptoms improve now. **Pathological findings:** Hematoxylin-eosin (HE) staining of the resected tumor revealed diffuse proliferation of large-sized pleomorphic cells with abundant cytoplasm and multiple bizarre nuclei, which were sometimes eccentrically located. Additionally, numerous mitoses and pseudopalisading surrounding necrotic foci were found. Immunohistochemistry disclosed a diffuse positivity for SMARCB1 (INI-1) and a limited positivity for glial fibrillary acidic protein resulting in the final diagnosis of GCG. **Conclusion:** Pediatric GCG presenting dissemination at initial diagnosis is rare.

## **A novel case of recurrent intraventricular atypical central neurocytoma with prominent gangliogliomatous differentiation in a 10 year-old boy with 10 years of follow-up**

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**Introduction:** Central neurocytoma (CN) is a rare neuronal tumor that typically occurs in young adults. Infrequently, these tumors exhibit advanced neuronal maturation and glial differentiation, giving rise to a histologically diverse tumor, in contrast to a typical CN. **Clinical summary:** The patient was a 10 year-old boy who presented with gait changes, headache and vomiting. MRI brain showed a large, 5cm, irregular, partially cystic enhancing lesion centered in the left lateral ventricle and extending into the basal ganglia and thalamus. He underwent subtotal resection. His disease was stable for roughly 4 years, then demonstrated slow, steady growth and he developed right sided weakness. MRI brain performed 10 years after the first resection again showed massive recurrence in the left lateral ventricle. He underwent a second subtotal resection. Adjuvant therapy was recommended after the second resection. **Pathological findings:** Both resection specimens showed a dimorphic population of tumor cells. One population exhibited hypercellular sheets of uniform neurocytic cells, constituting the CN component; the second population showed large, dysplastic ganglionic cells in fibrillary background, constituting the area with gangliogliomatous differentiation. Atypical features, including microvascular proliferation and elevated mitotic activity were identified in the recurrent specimen. **Conclusion:** Our case demonstrated a rare CN in a pediatric patient with prominent gangliogliomatous differentiation that developed atypical features in the recurrent specimen. This case may provide insight into the divergent differentiation capability of a neurocytic tumor and illustrates diverse histological features of this rare entity.

## **Central neurocytoma of the third ventricle in Indian subcontinent - a rare case report**

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**Introduction:** Central neurocytomas are slow-growing primary brain tumors of neuronal origin, grows from foramen of Monro or septum pellucidum into lateral or third ventricle. Most common neoplasm in young adults but still < 1% of all CNS tumors. We present this case in 13 years old male because of its rarity, especially in this age and its location. **Clinical summary:** A 13year old male boy presented with headache, nausea and vomiting for 1month duration. On &off seizures and weakness in both lower limbs are also present for the past 15 days. On magnetic resonance imaging of the brain shows heterogeneous enhancing lesion in intraventricular area of left choroid plexus. Intraoperatively, tumor was soft, succable, greyish white with ill defined margins. Clinical and MRI finding was left choroid plexus carcinoma. CT scan findings are suggestive of central neurocytoma. The patient was operated, and craniotomy was done. Tumor tissue sent for histopathology for the confirmation of diagnosis. **Pathological findings:** Tumor tissue received as multiple gray brown to greyish white, soft tissue pieces collectively measuring 2x2cm in size. Whole embedded, sections cut, stains with hematoxylin & eosin. On histopathology, monomorphic, small sheets of atypical cells, round to oval to hyperchromatic nuclei with occasional nucleoli and mitotic activity was noted. On immunohistochemistry, GFAP & EMA were negative, both synaptophysin and NSE were positive helping us to arrive at the diagnosis of central neurocytoma. **Conclusion:** The immunohistochemical stains make the diagnosis central neurocytoma much easier and rule-out other differential diagnoses such as choroid plexus carcinoma.

## **Disseminated atypical extraventricular neurocytoma without mitosis or necrosis**

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**Introduction:** Extraventricular neurocytoma is a rare tumor and only a small number of case series have been reported. The WHO brain tumor classifications include extraventricular and central neurocytoma as neuronal and mixed neuronal-glial tumors. **Clinical summary:** The patient was a 57-year-old man who visited a general hospital complaining of headache of 3 months in duration. MRI demonstrated multiple spreading lesions. Over a two-month period, the patient was examined for various infectious diseases at the outpatient clinic of the department of infectious diseases. However, no abnormalities were detected. MRI performed at this time showed the progression of the tumor. MRI showed extra-axial and intra-axial tumor with right temporal cyst and seeding. All tumors showed heterogeneous contrast enhancement. Partial right temporal tumor removal was performed for a histological examination. The extra-axial tumor margin was clear, while the intraaxial tumor margin was not clear. **Pathological findings:** The tumor had an enlarged round nucleus, granulated chromatin, and clear cytoplasm. Atypical tumor cells grew in dense honeycomb-like pattern. No necrosis or mitosis was observed. Immunostaining revealed the following findings: PAS (-), S-100(+), synaptophysin(+), Olig2(+), GFAP(-), pancytokeratin(-), EMA(-), CD10(-), HMB45(-), c-kit(-), PLAP(-), hCGbeta(-), CD3(-), CD20(-), CD30(-), IDH1(-), ATRX(+), NeuN(-); the MIB-1 labelling index was 13.9%. We diagnosed the tumor as extraventricular neurocytoma. **Conclusion:** The preoperative clinical and radiological findings and the atypical tumor cells and high MIB-1 index were malignant findings. However, neither mitosis nor necrosis was found, and tumor shrinkage was observed after surgery.

## Molecular and histologic characterization of 40 cases of dysembryoplastic neuroepithelial tumors: a multi-institutional study from the United States of America and Italy

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*Introduction:* Dysembryoplastic neuroepithelial tumors (DNT) are identified by their hallmark specific glioneuronal elements with mucin-matrix floating neurons; however, a proportion preclude confident classification. We explored histology and molecular alterations of DNTs to identify signature profiles.

*Methods:* A retrospective review of 40 patients with DNT and low grade glial-neuronal tumors (GNT) from the Childrens Hospital of Philadelphia (n=33) and Meyer Childrens Hospital of Florence (n=7) was performed (classic ganglioglioma excluded). Tumor histology was examined and genomic data was collected. Genomic methodology included fusions by anchored multiplex PCR, *BRAF* by Sanger sequencing, 237 cancer gene panel by next generation sequencing (NGS), and copy number variants (CNVs) by genome wide array or NGS.

*Results:* The average age was 10 years with 2:1 M:F. Two-thirds represented primary tumors. Some genomic data was available for 33 tumors. DNT morphology represented 80% (23/32 with specific glial-neuronal component) with generic features of GNT in 20%. Fusions with *FGFR2*, *NTRK2*, and *BRAF* were identified in 5/19 and were mutually exclusive with *BRAF* V600E (5/29). Additional mutations were identified in *FGFR1* (n=2), *KDM5C*, and *PDGFRA*. 9/28 contained CNVs. Germline cancer predisposition syndromes were identified in 17% (*ATM* twice, *NFI*).

*Conclusion:* Our data show various genetic alterations affecting the MAPK signaling pathway in DNTs, including a 26% rate of gene fusions. Additionally, we identified a potential association with ataxia-telangiectasia. Given the spectrum of genetic abnormalities and small size a definitive genetic profile distinguishing classic DNT was not identified.

## Epigenetic, genomic, histopathological and imaging integrative work on pediatric dysembryoplastic neuroepithelial tumors

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**Introduction.** Dysembryoplastic neuroepithelial tumor (DNT) belongs to low-grade neuroepithelial tumors, which encompasses a large spectrum of tumors including recently genetically described entities. DNTs include three histopathologic subtypes described before the molecular biology era (simple/complex specific DNT [spe-DNT], non-specific DNT [ns-DNT]). Rare progressive DNTs have been reported. The classification scheme for these tumors still needs to be clarified using the recent molecular advances. **Methods.** We searched for BRAFV600E, FGFR1 mutations and FGFR1 tyrosine-kinase domain internal tandem duplication (FGFR1-ITD) by digital PCR in 82 DNTs, including 22 progressive spe-DNTs confirmed by imaging review. Negative cases were further analyzed by RNAsequencing and whole-exome sequencing. The tumors were classified by DNA-methylation profiling. A correlation to the histopathology and imaging was performed. **Results.** 35 tumors (45%) showed FGFR1 disruption (mutation/structural variants [SV]), including two FGFR1-TACC1 fusions. No BRAF mutation was observed in spe-DNT. Among ns-DNT, BRAF (mutation/SV) and MYBL (SV) were the most frequently altered genes. Two cases harbored a novel fusion, FGFR2-INA. By DNA-methylation profiling, 92% of spe-DNTs and 19% of ns-DNTs clustered in the LGG-DNT subgroup. At relapse, specific-DNTs continued to cluster in the LGG-DNT subgroup but harbored numerous copy number changes. These tumors showed contrast enhancement either at diagnosis or throughout disease progression. **Conclusion.** Spe-DNTs, with or without FGFR1 disruption, can be progressive and the genomic alterations that cause these DNTs to grow must be elucidated to adapt current therapeutic strategies. The ns-DNT histopathologic subtype corresponds to a biologically heterogeneous group of tumours including the newly genetically identified entities.



## **A clinicopathological study of desmoplastic infantile gangliogliomas with analysis of BRAF and H3F3A gene alterations**

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**ORIGINAL STUDY** Nambirajan A, Malgulwar PB, Suri V, Sarkar C, Sharma MC Department of Pathology, All India Institute of Medical Sciences, New Delhi 110029 A clinicopathological study of desmoplastic infantile gangliogliomas with analysis of BRAF and H3F3A gene alterations Introduction: Desmoplastic infantile gangliogliomas (DIG) are benign glioneuronal tumors characterised by a desmoplastic stroma. Despite Grade I histology, nearly 40% patients have complicated clinical course. Recently BRAF alterations have been described in other glioneuronal tumors. Limited data is available in DIGs due to its rarity. Methods: Retrospective analysis (7 years) during which all DIGs were retrieved. Sequencing for BRAF and H3F3A gene mutations and real time PCR for BRAF fusions and gain were performed. Results: A total of 4 DIGs were diagnosed over a 7 year period (0.001% of all brain tumors). All were male infants with age ranging from 8-12 months. Histopathology showed desmoplastic leptomeningeal component in all cases with an appreciable small round cell component in one cases. MIB-1 labelling indices ranged from 1% to 4%. On sequencing, BRAF gain was identified in one case, while BRAFV600E mutation, KIAA1549-BRAF fusions or H3F3A mutations were absent. Two cases, including one with BRAF gain showed diffuse positivity for pS6kinase, indicating mTOR pathway activation. Conclusion: Our study for the first time demonstrates the occurrence of BRAF copy number gain in DIG, suggesting BRAF gain in the absence of BRAFV600E mutation in DIGs may lead to aberrant m TOR signalling. These tumors may be potential candidates for BRAF therapy.



**P3-65**

**Chordoid glioma: a case at an uncommon location**

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CASE REPORT Kan A1 1 Department of Pathology, Tuen Mun Hospital, Hong Kong SAR  
Chordoid glioma: a case at an uncommon location  
Introduction: Chordoid glioma is mostly described in the literature as a low grade glioma in the third ventricle. We encountered a myxoid neoplasm in the fourth ventricle resembling chordoid glioma. Clinical summary: A 51-year-old lady complaint of 3 year history of unsteady gait and the MRI revealed a 3cm partially cystic enhancing lesion within the fourth ventricle associated with prominent hydrocephalus. Pathological findings: Histology shows a myxoid neoplasm containing isolated or cords of eosinophilic tumour cells with occasional intracytoplasmic vacuoles and mild lymphocytic infiltrate. The tumour cells are diffusely immunopositive for vimentin, S100 and olig 2 while focally positive for EMA while negative for GFAP, CD34, TTF1, PR, brachyury, IDH1, D2-40 and SSTR2. Conclusion: We report a myxoid neoplasm most in keeping with chordoid glioma in an uncommon site.

## **MYB-QKI rearrangement in Angiocentric glioma: a study in Chinese population**

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**Introduction:** To evaluate the diagnostic value of MYB-QKI in Angiocentric glioma (AG) by immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH). **Methods:** Twenty-six AG samples were collected from five hospitals, and MYB protein expression was detected by IHC, MYB-QKI rearrangement was detected by FISH, then MYB-QKI status and clinicopathological association were analyzed. **Results:** All 26 patients had a history of refractory epilepsy with a mean history of 12 years and a median age at surgery of 18 years. The AG lesions were located in superficial cerebrocortical locations. Except for the classical histological features, the involvement of superficial cortex extending to the leptomeninges, microcalcification, and the cystic pattern with microcystic formations were observed in 42.3% (11/26), 11.5% (3/26) and 15.4% (4/26), respectively. In all 26 cases, the IHC positive rate of GFAP, Vimentin, NeuN, EMA, D2-40, MYB, IDH1R132H, BRAF V600E, L1CAM, H3K27M were 100% (26/26), 100% (26/26), 0% (0/26), 84.6% (22/26), 76.9% (20/26), 50% (13/26), 0% (0/26), 0% (0/26), 0% (0/26), 0% (0/26), respectively. The Ki-67 labeling index was 1-5% in 24 cases, the other 2 cases was 10% and 20%. The positive rate of MYB-QKI rearrangement with FISH was 95.7% (22/23) in AGs. **Conclusions:** The study showed that FISH was more appropriate for MYB-QKI rearrangement detection. MYB-QKI rearrangement was confirmed in majority of AGs, which may act as potential diagnostic biomarker for AGs.

## **Rosette-Forming Glioneuronal Tumors: A Small Case Series**

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**Introduction:** Rosette-forming glioneuronal tumor (RGNT) is a rare, WHO grade I tumor originally included in the 4th edition of the World Health Organization (WHO) classification of tumors of the CNS and included in the revised editions (2007, 2016). Thought to arise exclusively in the 4th ventricle, it has been described in the pineal gland, septum pellucidum, lateral ventricle and thalamus. **Methods:** A retrospective review of the neurosurgical files at The University of Kansas Medical Center from 2011 to 2018 using the following search items was performed: "rosette" and "glioneuronal" in the "final diagnosis" and/or the "diagnosis comment". Cases that met the current WHO 2016 criteria were included. Radiographic findings and long-term follow up were correlated for each case. **Results:** Five cases were retrieved. Clinically, all were female, age ranging from 18 - 56 (average 36.6). Tumor locations included left posterior cerebellum, 3rd ventricular mass, cerebellar vermis, and two 4th ventricular masses. Clinical presentations included hydrocephalus, incidental lesions discovered on imaging, and dizziness and headaches. Clinical follow up ranged from 2 to 66 months and all lesions are stable and have caused no further concern. Radiographically, two of the lesions showed T2 hyperintense, T1 hypointense and nonenhancing lesions, as described in the WHO 2016. Two lesions were cystic with patchy enhancement, and another was cystic and non-enhancing. **Conclusion:** Rosette-forming glioneuronal tumors are rare WHO grade I lesions with bland histology and excellent long-term follow up. Originally described in the 4th ventricle, the unique histology may also be seen in other locations.

## **A case of rosette-forming glioneuronal tumor with an increased MIB-1 labeling index and mitotic figures in glial component**

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Rosette-forming glioneuronal tumors (RGNT) is a rare tumor of WHO grade I commonly arising in the fourth ventricle or cerebellum of young adults. Histologically they are characterized by a biphasic pattern consisting of well-differentiated neurocytic rosettes and pilocytic astrocytoma-like areas. This tumor behaves indolently, though postoperative deficits may occur. Here we report a case of RGNT, which showed an increased MIB-1 labeling index and mitotic figures in glial component. The patient is a 19-year-old male who visited a doctor for a head trauma in June 2015. CT scan incidentally demonstrated a 15 mm tumor in the midbrain and ventricular enlargement. The biopsy revealed proliferation of astrocytic cells with fibrillary matrix and neurocytic cells often arranged in rosettes. The latter were positive for synaptophysin. MIB-1 index was an extremely low (0.3%). These pathologic findings led to the diagnosis of RGNT. One and a half years later, tumor growth (30 mm) and hydrocephalus appeared and rebiopsy was performed. Microscopic features were almost identical to those of the first biopsy specimen; however, mitotic figures was observed at maximum 2/10 HPF and a MIB-1 index was 30% in the glial component. At present (May 2018), the tumor did not show significant growth (33 mm). Although RGNT is considered to be benign, glial cells of this tumor occasionally may exhibit an increased proliferative activity like our case. It is necessary to carefully follow up the clinical course of those RGNT.

## **A case of spinal rosette-forming glioneuronal tumor**

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Rosette-forming glioneuronal tumor (RGNT) is a rare tumor which was first reported as the fourth ventricle tumor by Komori, et al. and is classified as a distinct clinicopathological entity by the WHO Classification of Tumors of the Central Nervous System as of 2007. Although RGNTs were reported to occur in both supratentorial and infratentorial sites, only four case reports of spinal RGNT have been demonstrated. This case report describes an RGNT arising from the cervical spinal cord with unique pathological features including the results of molecular analysis, which occurred in a 37-year-old female. Magnetic resonance imaging revealed an intramedullary mass at C1 to C5, which was totally resected. Pathological analysis showed a unique biphasic cellular architecture consisting of perivascular pseudorosettes dominantly with few neurocytic rosettes and diffuse astrocytoma component. The tumor cells composed of perivascular pseudorosettes showed positivity for both synaptophysin and olig2. In the genetic analysis, neither IDH1/2, FGFR1, BRAF, PIK3CA mutations nor 1p19q codeletion were found. We review the relevant literature and summarized the clinical course including the treatment and prognosis, pathological features and molecular features of spinal RGNT.

## **A glioneuronal tumor with intermediate feature between rosette-forming glioneuronal tumor (RGNT) and pilocytic astrocytoma (PA) harboring FGFR1 mutation: consideration of "RGNT-PA sequence"**

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**【Introduction】** Rosette-forming glioneuronal tumor (RGNT) is a rare glioneuronal tumor that preferentially arises in the fourth ventricle in young adults. Although the tumor has many similarities to pilocytic astrocytoma (PA) both histologically and genetically, its histogenesis is largely still unknown. We report a case of PA-like glioneuronal tumor including a tiny amount of glioneuronal rosette-like component harboring FGFR1 mutation. **【Clinical Summary】** A 16-year-old female presenting with absence seizures. MRI revealed a right temporal lobe mass with low T1 and high T2/FLAIR signals and a multinodular enhancing by gadolinium administration. A macroscopic total tumor resection was performed. **【Histological Findings】** Most of the tumor was composed of round to oval oligodendrocyte-like cell (OLC) with variable perinuclear haloes. Abundant Rosenthal fibers and eosinophilic granular bodies were identified. Mitoses and necroses were absent. Focal neurocytic rosette feature, which exhibits ring-like arrays of OLC around delicate eosinophilic neuropil cores, were observed. Massive hemosiderin depositions were seen in the superficial layer of the cortex, which were consistent with superficial siderosis. **【Mutational Findings】** Direct sequencing revealed a missense mutation in FGFR1 exon 14 (K656F), whereas FGFR1 exon 14 (N546K), PIK3CA exon 9 (E542K), PIK3CA exon 20 (H1047R), BRAF codon 600 were intact. A KIAA1549-BRAF fusion was not detected by FISH analysis. **【Discussion】** This tumor possessed intermediate characteristics between RGNT and PA both histopathologically and genetically. These similarities might suggest consideration of "RGNT-PA sequence" as a concept.

## Clinical and molecular features of two cases of rosette-forming glioneuronal tumor at midbrain

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**【Background】** We experienced two cases of rosette-forming glioneuronal tumor (RFGT) at midbrain. In this study, we discussed the clinical, histological, and molecular features of RFGT at midbrain. **【Cases】** One case was 18 year-old male presented with right upper limb hemiparesis, and the other case was 23 year-old female presented with left hemisensory disturbance. Tumors were located at midbrain and showed ring-enhancement by gadolinium-enhanced T1-weighted magnetic resonance imaging. A partial removal was conducted through the occipital transtentorial approach in each case. Histologically, HE staining demonstrated biphasic pattern of neurocytic and glial architecture. The former structure consists of neurocytic rosettes and perivascular pseudorosettes with positivity for synaptophysin. The other immunohistochemical staining demonstrated GFAP-positive, IDH1R132H-negative, and 2-3% of MIB-1 labeling index, thus the diagnosis with RFGT was made. **【Discussion】** RFGT is categorized in WHO grade I, and its incidence is reported to be very rare. RFGT usually arise in the fourth ventricle. Several reports also demonstrated RFGT at brain stem. Histologically, RFGT resembles ependymoma and pilocytic astrocytoma, and the key for the diagnosis is the presence of neurocytic architecture. Genetically, the involvement of PI3KCA and FGFR1 gene mutations are reported. Molecular analysis of the current two cases is under investigation. **【Conclusion】** Brain tumor at midbrain is rare, and RFGT needs to be considered as a differential diagnosis.

## **A case of atypical central neurocytoma with Rosettes and relatively rapid growth**

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Central neurocytoma is a rare tumor and is considered to be 0.25-0.5% of the intracranial tumor. Although the growth is slow, there are reports that some cases show anaplastic property and some cases have high proliferative potential. Also, normally rosette is not observed. We report a case of Atypical central neurocytoma which had increased relatively rapidly before surgery and was observed Rosette. A 21-year-old man was introduced to examine mass lesions adhering to the left lateral ventricle sidewall, which was discovered in headache scrutiny. The lesion was not accompanied by calcification, MRI showed high signal in T2 weighted image, ADC was low, contrast effect was poor. As a distinction on images, Subependymoma, Central neurocytoma was considered. Since the diameter increased from 12 mm to 19 mm in the course of six months, it was a surgical plan. The tumor was soft and easy to bleed. Adhesion / infiltration findings with the ventricular wall were observed. Total tumor was removed. In intraoperative consultation, Ependymoma was thought to be due to the increase of compact circular nucleus and acidophilic body and Rosettes. Immunohistochemical study showed positive Synaptophysin. EMA, Chromogranin A, NFP and OLG 2 were negative. Although we could not point out angiogenesis or necrotic image, three or more nuclear fission images were recognized per High-Power Field. And the Ki - 67 labeling index was 6.5%. Because it was a diagnosis of Atypical central neurocytoma, it is considered as radiation irradiation at the time of recurrence.



## **Growing papillary glioneuronal tumor (PGNT) with solid components: A case report**

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Papillary glioneuronal tumor (PGNT) is classified as one of mixed neuronal-glia tumors, WHO grade I. Most PGNT is accompanied with cystic formation in the cerebral hemisphere, mainly in youth. Here we report a 38-year-old man with growing papillary glioneuronal tumor without cyst formation and epilepsy for 11 years after the first diagnosis. In his past history, he had undergone surgery for arachnoid cyst. MRI at the initial visit showed that it was 14mm in the major axis in precentral gyrus and hypointense in T1W1 and hypointense in T2W1 with a gadolinium-enhanced spot. Subsequent MRI studies showed the slow growth of tumor and its enhancement associated with surrounding brain edema for 11 years. He underwent tumor resection to identify its pathology. The histopathological study revealed that the tumor was composed of neuronal and glial tumor cells showing pseudopapillary architecture with hyalinized blood vessels. Neuronal and glial tumor cells have oval nucleus with acidophilic cytosol. Rosenthal fibers and acidophilic granules were also observed. Immunohistochemical analysis showed that the neuronal component was positive for synaptophysin and NeuN, and that the glial was positive for Olig2 and GFAP. Based on these findings, it was diagnosed as papillary glioneuronal tumor.

## **High-grade glioneuronal tumor with NTRK fusion: a case report**

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Here, we present a rare case of high-grade glioneuronal tumor with Neurotrophic Tyrosine Kinase Receptor (NTRK) fusion. A 13-year-old girl presented with headache and vomiting. Computed tomography showed a left frontal cystic lesion and hydrocephalus, with calcified cystic lesions in the contralateral hemisphere. Magnetic resonance images detected a solid lesion and enhanced cystic components. We performed a left frontal craniotomy to remove the tumor and provide ventricular drainage. She was initially treated with temozolomide as anaplastic oligodendroglioma. During follow up, this tumor recurred and was resected again. Moreover, we added radiation therapy. Histological findings showed small, hypervascular, spindle-shaped astrocytic components, but no endothelial proliferation or necrosis. The specimen also included round cells with perinuclear halos. These round cells and the ganglioid cells were found in the recurrent area. Immunohistochemistry showed the cells to be partially GFAP+, Olig2+, NeuN-, synaptophysin+, mIDH1-, and ATRX. The MIB-1 labelling index was approximately 20% in initial lesion, and 54 % in recurrent area. In both specimens, direct sequencing showed IDH1/2, H3F3A (K27 and G34), and BRAFV600E were not mutated; however, FISH and MLPA showed a 1p19q codeletion. In central pathology review this case was finally diagnosed as high grade glioneuronal tumor. RNA sequencing identified a fusion gene, ARHGEF2 (encoding Rho/Rac guanine nucleotide exchange factor 2)-NTRK1. From these genomic findings, we diagnosed a glioneuronal tumor with NTRK fusion. Detecting this fusion gene may become important in stratifying subjects in future clinical trials with NTRK inhibitor.

## **Lymphocytic Hypophysitis with hypertrophic intracranial pachymeningitis: a case report**

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We report a case of lymphocytic hypophysitis with hypertrophic intracranial pachymeningitis. Case: A 44-years-old man presented with headache and was referred to our department. His laboratory investigations revealed panhypopituitarism due to a pituitary mass lesion. Magnetic resonance imaging(MRI) showed a sellar mass and thickening of the pituitary stalk and dura with contrast media dumbbell shaped suprasellar. He was given 15mg daily of hydrocortisone for hypoadrenalism. The lesions were not responded during glucocorticoid treatment for 6 months. Biopsy was done via transsphenoidal approach. Histopathological examination showed massive infiltrating lymphocyte and fibrosing pituitary glands. Immunohistochemical staining revealed B lymphocytes were dominantly infiltrated. Thickend dura mater were also same pathological findings. Lymphocytic hypophysitis were known as T cell predominance and responded to steroid therapy. This case is unique that B cell were conspicuous and hypertrophic pachymeningitis.

## **A case of WHO grade I meningioma metastasized to the lung 26 years after initial surgery**

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**【Back ground】** Meningiomas comprise 13-26% of all intracranial tumors, and are usually slow growing and benign. Distant metastasis of a meningioma is rare and associated with WHO grade II or III meningiomas; metastasis from grade I is especially rare.

**【Case】** A 65 year old male underwent surgery for posterior fossa meningioma WHO grade I 26 years ago at another hospital. Eleven years ago, the tumor recurred and  $\gamma$ -knife radiosurgery was performed. Seven years ago, the tumor recurred again, and he attended our hospital for the second surgery. The tumor was totally excised (Simpson grade II) and histology indicated meningioma WHO grade I. Before admission to our hospital he had suffered headaches and vomiting for four months. The tumor had recurred in the same area and extended from the margin of the previous excisional site to the right middle cranial fossa. Tumor resection was performed after feeder occlusion. Histology again indicated meningioma WHO grade I. Preoperative examination revealed a nodule in the lower lobe of the right lung. Because this nodule gradually grew larger, partial resection of the right lower lobe was performed four months after the third operation. Although the tumor showed a central necrosis, its histology was consistent with meningioma WHO grade I.

**【Conclusion】** Metastasis of meningioma WHO grade I is rare. Grade I histology of the metastatic site is also rare. We discuss our case and review relevant literature.

## **The case of lymphoplasmacyte-rich meningioma invaded to sigmoid sinus**

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Lymphoplasmacyte-rich meningioma (LPRM), the most rare variant of meningiomas, features extensive lymphoplasmacytic infiltrates. We present an extremely rare case of LPRM extended to sigmoid sinus. 72-year-old woman had complaint right visual activity loss. Neurological examination disclosed right visual activity and visual field loss. The magnetic resonance imaging revealed the homogeneous enhancement mass lesion extended in the right middle base to cerebellar tent measuring 25mm in diameter with invaded sigmoid sinus, suggesting meningioma. The operation was performed. The tumor was elastic hard compare to normal meningioma and adhesive to arachnoid strongly. After the operation, the patient's visual activity loss was also improved. Histologically, the tumor showed dense infiltration of lymphocytes and plasma cells with occasional formation of lymphoid follicles. We also found focal collection of epithelioid cells that showed whorl formation and immunoreactivity for epithelial membrane antigen (EMA). These collective findings led us diagnose this tumor as LPRM. The Ki-67 LI was higher than benign meningioma about 10%. The local recurrence of the tumor was not detected at follow-up. LPRM is the most rare variant of meningiomas, classed WHO grade 1 as benign tumor. The neuro-imaging shows thickened enhancement of the dura matter, likes hypertrophic pachymeningitis. The pathological findings features extensive lymphoplasmacytic infiltrates and poor tumor progression. The present case shows typical neuro-imaging and pathological findings, but invaded to sigmoid sinus and higher Ki-67 LI. Since the natural history of this tumor is unclear and reported the recurrent case, careful follow-up is needed.

## **Diagnosis changed from Angiomatous meningioma to solitary fibrous tumor / hemangiopericytoma by molecular analysis**

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Since both SFT and HPC fuse the NAB2 and STAT6 genes and leads to STAT6 nuclear expression, the 2016 WHO classification has created the combined term. We report a case of multiple brain tumors which was changed its diagnosis by IHC from angiomatous meningioma (AM) to solitary fibrous tumor / hemangiopericytoma(SFT/HPC). A 59-year-old male was admitted to hospital for cognitive dysfunction. Magnetic resonance imaging revealed tumors measuring 70X68mm in the right frontal parasagittal and 16X15mm in the left frontal convexity. We performed the surgical removal of the right tumor and diagnosed as angiomatous meningioma(AM), grade I. Four years later after the surgery, the left side of tumor was growing with hemorrhage. The tumor was totally resected. Histological examination revealed the tumor composed of proliferation of spindly cells. Mitotic activity is over 4-5 per 10 high power fields. Immunohistochemical(IHC) studies revealed positivity with CD34, and negative results for S-100 and EMA. STAT6 was positive in nuclear of tumoral cells. The tumor of left side was diagnosed with SFT/HPC, grade III. We investigated the previous tumor of the right side. According to IHC, the tumoral cells revealed the nuclear positivity with STAT6. The diagnose was changed to SFT/HPC from AM. The molecular biological studies were important for the differential diagnosis between SFT/HPC and AM.

## **Intracranial fibrosarcoma with somatic mutations in *NF2* and *ATRX***

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**【Background】** Clinical sequencing has greatly gained prevalence and can facilitate clinical decision-making and understanding of pathogenesis in challenging cases. Herein, we report a case with an intracranial fibrosarcoma, wherein the clinical panel sequencing ("Today OncoPanel" [TOP]) and DNA methylation analysis yielded additional information.

**【Clinical Summary】** A 69-year-old female presented with an intraparenchymal hemorrhage in the right frontal lobe. Additional examinations led to the diagnosis of tumor bleeding suspect of meningioma. While she underwent a near-total tumor resection, we observed discontinuity between the tumor and falx cerebri. Although the postoperative course was initially favorable, the residual tumor displayed a rapid regrowth just two and a half months later. Accordingly, she underwent a second surgery, followed by chemoradiotherapy. To date, the tumor remains under control for eight months.

**【Pathological Findings】** Primary and recurrent tumors shared similar histological findings: tumors comprised of dense, spindle-shaped cells with pale, eosinophilic cytoplasm arranged in interlacing fascicles. Additionally, mitoses were frequently observed (1-4/high-power field). Immunohistochemistry for EMA, PgR, STAT6, GFAP, HMB-45, S-100 stained all negative. Consequently, the diagnosis of an intracranial fibrosarcoma was made. Besides, the TOP analysis detected somatic mutations in *NF2* and *ATRX*. Copy number analysis revealed *MDM2* gain and loss of heterozygosity on chromosome 22q. Furthermore, clustering analysis on DNA methylation status combined with public data revealed the similarity with highly aggressive sarcoma.

**【Conclusions】** We describe a case with an intracranial fibrosarcoma. Along with clinical panel sequencing and DNA methylation analysis, this study will shed light on this rare entity.

## **A rare case of craniopharyngioma with malignant transformation**

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Craniopharyngioma is a benign tumor belonging histologically to WHO grade I. Malignant transformation of this tumor is extremely rare. Here, we report a case considered as craniopharyngioma with malignant transformation. The patient is a 30-year-old female who was initially diagnosed at age 14 as a sellar/suprasellar typical adamantinomatous craniopharyngioma in 2001. She had repeatedly received surgery 8 times, radiation therapy (2001), and gamma knife radiation therapy twice (2005, 2008) for multiple recurrences. From the primary tumor to sixth recurrence (2013), histological findings showed a typical adamantinomatous craniopharyngioma. However, from the 7th recurrence (2015), high cellularity and increased number of mitotic figure and MIB-1 index were observed gradually. At the 9th recurrence, the number of mitotic figure increased to 11/10 HPF. There are only a few reports of malignant craniopharyngioma and no clear criteria for malignant transformation have been established. However, at least the 9th recurrent tumor was considered to be malignant. She received postoperative radiotherapy. At present (May 2018), there is no tumor growth although tumor remains. Several reports suggested that the effects of radiation therapy are one of the possibilities for malignant transformation, but the mechanism remains to be clarified. As the prognosis of malignant craniopharyngioma is considered to be extremely poor, accurate prediction of prognosis and discussion of additional treatment are necessary, and it is desirable to construct appropriate criteria of malignancy in craniopharyngioma.



## **A case of methotrexate associated lymphoproliferative disorders**

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**【Introduction】** Methotrexate (MTX) plays an important role in the treatment of rheumatoid arthritis (RA) but reports on lymphoproliferative diseases (LPD) associated with the use of MTX have been increasing in recent years. We report cases of central nervous system lymphoproliferative diseases due to methotrexate related lymphoproliferative disease (MTX - LPD). **【Case】** A 75-year-old female. She visited us with complaints of cerebral movement disorder and gait disturbance on the right hand two weeks ago. MRI revealed 3 cm neoplastic lesions in left parietal lobe. **【Surgical findings】** The lesion was exposed to the brain surface and was elastic hard. The boundary with normal tissue was relatively clear, mainly composed of granulomatous necrotic tissue. Lesions were completely excised. **【Pathological diagnosis】** The invasion of inflammatory cells and the proliferation of heteromorphic cells of the lymphoid lineage were observed. Heterotypic cells are GFAP negative, olig 2 negative, IDH 1 negative, CD 3 partial positive, CD 20 partial positive, EBER - ISH partially positive. MIB 1 index is about 40% by hot spot. ALK - 1 negative. It was thought to be diffuse large B cell lymphoma than morphology and trait. In the last 7 years ago MTX was continuously administered to RA and oligoclonality was confirmed by IgH rearrangement, it was diagnosed as central nervous system lymphoma by MTX-LPD. **【Conclusion】** Although the report of MTX - LPD has been increasing in recent years, there are not many cases reported in the central nervous system. We reported to share experiences of rare cases.

## **A case of primary central nervous system T-cell lymphoma seems to be caused by long-term administration of adalimumab**

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Many of primary central nervous system lymphoma (PCNSL) are diffuse large B-cell lymphoma and T cell lymphoma is rare. we report a case of primary central nervous system T-cell lymphoma seems to be caused by long-term administration of adalimumab. A 41-year-old male was suffering from Headache, nausea and dizziness 2 weeks before admission. He was administered adalimumab for Crohn 's disease from 6 years ago. CT showed a tumor in the right cerebellum. At the time of admission, Japan Coma Scale I -1 and no neurological abnormal findings were observed. MRI revealed a 44 x 40 mm tumor in the right cerebellum that was ring-enhanced with gadolinium. The day6, his consciousness got worse because of rapid deterioration of hydrocephalus, then tumor resection by craniotomy was performed. Histopathological findings showed proliferation of atypical lymphocytes which are CD3 (+), CD4 (+), CD5 (+), CD20 (-), therefore we diagnosed peripheral T cell lymphoma. Postoperatively, consciousness disturbance was improved. Adalimumab is known to increase the risk of developing malignant tumors such as lymphoma during long-term administration to children and young adults. Considering that susceptible age for PCNSL is 50-70s and T cell lymphoma is rare, this case seems to be caused by long-term administration of adalimumab. Using TNF antagonists such as adalimumab may occasionally causes complications of PCNSL, therefore we need careful follow-up.

## **A case of central nervous system methotrexate-associated lymphoproliferative disorders (MTX-LPD)**

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**【Introduction】** Methotrexate (MTX) is one of the central drugs in the treatment of RA and other autoimmune diseases, but its report of MTX-related lymphoproliferative disease (MTX-LPD) has increased. Here we report one case of central nervous system lymphoproliferative disorder by MTX-LPD. **【Case】** A 65-year-old woman. We visited our hospital with complaints of dysphagia, diplopia and gait disturbance two weeks ago. MRI revealed a 2 cm tumor massive from the left medulla to the left cerebellar limb with contrasting margin. Tumors were also found in soft tissues around the left femur and subcutaneous tissues such as inguinal lymph nodes. Since 7 years ago MTX was orally administered to palmoplantar cystic disease, MTX-related lymphoproliferative disease was suspected and left hip tumor mass was biopsied. **【Pathological diagnosis】** Large heteromorphic cells with enlarged nucleus proliferated diffusely, and nuclear fission images were scattered. Heterotypic cells showed CD20 positive, CD3 negative, EBER - ISH negative, and the Ki - 67 labeling rate was 80%, which was diagnosed as Diffuse large B - cell lymphoma. **【Progression】** After diagnosis, oral administration of MTX was stopped and treated with steroids. Cerebellar lesions and subcutaneous masses also shrunk and symptoms improved. **【Conclusion】** A tumor of the whole body including the central nervous system disappeared due to discontinuation of MTX administration, and a case of MTX-LPD was reported. There are not many cases reported in the central nervous system. We reported to share experiences of rare cases.

## **Lymphomatoid granulomatosis of the brain: A case report**

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A 75-year-old male was followed every year for old cerebral infarction and unruptured cerebral aneurysm. Magnetic resonance imaging (MRI) of the brain unexpectedly revealed a mass with a large cerebral edema in the right frontal lobe, which was not found the year before. Neurological examination did not showed any symptoms. A computerized tomography (CT) scan did not demonstrated any other mass lesions. The patient was hospitalized and underwent a right frontal lobectomy using the Brainlab navigation system. Pathology reported polymorphous, CD20-positive, Epstein-Barr virus (EBV)-positive, lymphohistiocytic, inflammatory infiltrate within the walls of the vessels with associated necrosis and diagnosed a lymphomatoid granulomatosis. The patient received no adjuvant treatments because of complete resection of tumor. Four months after his diagnosis, brain MRI showed no recurrence. Lymphomatoid granulomatosis is a rare disorder of the central nervous system (CNS) with few cases being reported in literature. We discuss the process of evaluation and management.

## **Reappraisal of multiple cerebral lesions characterized by dense T cell infiltration in patient with DLBCL in past history and PTCL-NOS developing two years later**

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**【Case】** 56 year-old male **【Past history】** DLBCL of tonsil in complete remission three years ago **【Present history】** He had general fatigue, intense daytime sleepiness and taste disorder. Multiple lesions located by MRI suggested primary lymphoma, lymphomatoid granuloma (LYG). Thorough investigation of blood, CSF, skin random biopsy etc. did not reveal definite diagnosis. The cerebral lesion removed by craniotomy disclosed dense small T cell infiltration in parenchyma, showing CD3 +, CD5 +, CD10-, CD20+ (very few), CD4<CD8, EBV-ISH -. Relapse of DLBCL and LYG were unlikely diagnosis. Polyclonal pattern of TCR $\gamma$  and B cell (CDRIII) clonality tests from the lesion suggested reactive infiltration. Steroid therapy was administered based on the possible diagnosis of Clippers syndrome. Some of the CNS lesions disappeared. Two years later, he developed PTCL-NOS in bone marrow characterized by dense T cell infiltration and complex karyotype abnormalities. In retrospective evaluations, brain lesions were examined by the clue of specific karyotype abnormalities whether they can be regarded as an early lesion of PTCL-NOS.

## **A case of cauda equina primary extramedullary plasmacytoma**

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**【Case presentation】** 78 years old male patient had suffered from buttock and leg pain from 2016 and the symptoms had been progressed. He visited neurosurgeon and magnetic resonance imaging (MRI) as axial imaging showed swollen nerve of cauda equina, at levels of L4-S1 and this lesion was diffusely enhanced with Gd. Lymphoma was mostly suspected by MRI features, but laboratory data such as value of LDH and sIL-2 receptor were within normal range. Other differential diagnoses were myxopapillary ependymoma, neurofibroma, metastatic spinal tumor, and infectious inflammatory disease including military tuberculosis. **【Histopathological findings and disucssion】** Tumor biopsy were performed in April 2018, and cauda equina were swollen and there were no involvement of spine. Histologically, neoplastic plasma cells which had axle-like nuclear and a lot of Russel body were massively proliferated within the peripheral nerves of cauda equina, and the neoplastic cells were demonstrated immunohistochemical positivity for CD138 with Ig-G kappa light chain restriction. CD20 and CD3 positive cells were small and had no atypia excluding malignat lymphoma, or negativity for AE1/AE3 suggested no metastatic carcinoma, and diagnosed as plasmacytoma. Extramedullary plasmacytomas account for about 4% of all plasma cell tumors. This tumor occurs mainly in upper gastrointestinal and respiratory tract, and also in lung, thyroid gland, orbita, and lymph node. Cauda equina is very rare region affected by primary extramedullary plasmacytoma, reported as 5 cases as literature previously in worldwide.

## **Case report: Low-grade primary central nervous system lymphoma suspected by biopsy**

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Low-grade PCNSL is a rare tumor (account for 3 to 4% of the total PCNSL) and the treatment is still not established. Here we report a 46 years old gentleman presented with sudden hemiparesis of right upper and lower limbs. Brain MRI revealed a lesion located on left parietal lobe, with high intensity on T2WI with perifocal swelling and enhancement. Biopsy was performed. Pathological sample from the biopsy revealed proliferation of small atypical cells with CD3, CD20 positive and MIB-1 20% positive. Bodian and LFB stain showed a small proportion of demyelination. From the pathological finding low grade PCNSL was suspected, so we have done a steroid pulse therapy and maintenance therapy. Repeated MRI after the therapy showed a reduction of tumor and improvement of the swelling. Right hemiparesis also improved. Today, the patient is continuing rehabilitation at outpatient. It is reported that PCNSL occasionally progresses resisting to steroid (Suzuki, 2009). Therefore, MR imaging follow up is considered as important.

## **Intracranial methotrexate-associated lymphoproliferative disorder in a rheumatoid arthritis patient treated with methotrexate: a case report**

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**【Background】** Methotrexate (MTX) is one of the most common drug for rheumatoid arthritis (RA). However, some studies have shown that methotrexate induced lymphoproliferative disorders in the patients treated with methotrexate for a long term, namely methotrexate-associated lymphoproliferative disorders (MTX-LPD). We describe a rare case of MTX-LPD with intracranial lesion under MTX therapy for RA. **【Case presentation】** A patient is 68-year-old female. A diagnosis of RA had been made 15 years before and she has received MTX therapy for 5 years. She experienced progressing palsy of right limbs and magnetic resonance imaging of brain showed a ring enhancing lesion in the left parietal lobe. Operation Open biopsy was performed for making a definite diagnosis and planning treatment. HE stain showed perivascular cuffing of a lymphoma with tumor cell infiltration. Immunohistochemistry showed a positive reaction to CD20 and lesion was demonstrated strong nuclear signal by in situ hybridization for Epstein Barr early region. Finally we made a diagnosis of MTX-LPD. We discontinued MTX and treated with steroid. The intracranial lesion has been decreased in size and right palsy was resolved two years after the discontinuation of MTX. **【Conclusions】** An intracranial MTX-LPD is extremely rare. The authors describe their particular case and review the literature pertaining to MTX-LPD.



## **A case of primary central nervous system lymphomatoid granulomatosis ameliorated completely after treatment of corticosteroids**

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**【Background】** Lymphomatoid granulomatosis (LYG) is an angiocentric and angiodestructive lymphoreticular proliferation which usually involves the lungs, but may also involve the central nervous system (CNS). But, unique primary LYG of the CNS has been reported rarely. We report our experience of primary CNS-LYG with good prognosis with corticosteroid treatment. **【Patients and Methods】** A 37-year-old female presented with headache and left leg weakness. There was no evidence of systemic disease. Her MRI of brain showed multiple small enhancing nodules in her right hemisphere with diffuse high intensity lesion on T2/FLIR image. **【Results】** Brain biopsy showed atypical lymphohistiocytic cells with CD3+ and CD20+ infiltrate around the vessels. EBER-ISH was negative. Thus primary CNS-LYG was diagnosed. Systemic high dose corticosteroid therapy following oral corticosteroid was performed and complete remission was achieved **Conclusions** Primary CNS-LYG is a rare disease that seems not to be associated with EBV and appears to have a better prognosis than systemic LYG with CNS localization which is frequently EBV positive.

## **Autopsy case report of intravascular large B-cell lymphoma with nephrotic syndrome**

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A 74-year-old man with nephrotic syndrome was admitted to previous hospital due to systemic edema after 3 years of complete remission (CR). He had been treated with cyclosporine A (CyA) and prednisolone. In this hospitalization, Steroid intensive therapy was started. After a month, he developed psychological symptoms such as delusions of persecution and anorexia following tremor of face and bilateral upper limbs. Since he was suspected as steroid-induced psychiatric disorder, he transferred to our hospital. His symptoms were rapidly deteriorated. His laboratory findings revealed elevated transaminase of liver, dysfunction of kidney and dehydration. MRI revealed fresh multiple infarction in bilateral cerebrum and cerebellum. Soon, he suffered from shock and died despite rehydration and administration of antibiotics. In autopsy, multiple infarction was found in bilateral cerebrum and cerebellum especially cingulate gyrus with plugging of vessels by atypical cells. The atypical cells were also found in other organs (lung, pericardium, prostate, kidney). Immunohistochemistry showed that these atypical cells were lymphoid origin and B-cell in type, staining positively with CD20, CD79 $\alpha$ , BCL6, and MUM1. A diagnosis of intravascular large B-cell lymphoma (IVLBCL) was made. Since this patient had history of treatment of immunosuppressive agents (CyA and steroid), 'other iatrogenic immunodeficiency-associated lymphoproliferative disorders (oii-LPD)' might be in consideration.

## **A case of probably CNS infiltration developing in a patient with IgM MGUS**

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Immunoglobulin (Ig) M monoclonal gammopathy of undetermined significance (MGUS) is characterized as a serum IgM monoclonal protein < 3 g/dL, bone marrow lymphoplasmacytic infiltration < 10%, and no evidence of constitutional symptoms, symptomatic anemia, or hyperviscosity, but sometimes develops plasma cell myeloma, Waldenstrom's macroglobulinemia (WM), or non-Hodgkin lymphoma. We present a patient with suspected central nerve system (CNS) infiltration of IgM MGUS. A 63 year-old male with IgM $\kappa$  monoclonal gammopathy of undetermined significance (MGUS) diagnosed 5 years ago, had an onset of brain tumors causing consciousness disorder and right-sided hemiparesis in the basal ganglia, midbrain, temporal lobe, and frontal lobe. Needle biopsy disclosed diffuse large B-cell lymphoma. These tumors were uncontrollable after standard chemotherapy of high-dose MTX and whole brain radiation, and the patient was dead 2 months after diagnosis of CNS lymphoma. Immunohistochemistry revealed positive CD20, bcl-2, IgM, and c-myc, and negative CD 3 and CD138, suggesting of highly malignant lymphoma. Few reports of IgM MGUS developing DLBCL with CNS infiltration have been described before. Previous reports showed lymphoplasmacytic lymphoma/WL of associated disease of IgM MGUS sometimes occurs CNS infiltration and the case of DLBCL developed from WM/LPL cells by histological transformation as a result of clonal evolution. This patient probably CNS infiltration developing in a patient with IgM MGUS.

## **A case of subdural mass lesion with chronic myeloid leukemia**

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This case was a wide-spreading subdural mass lesion that we could not diagnose. Patient was a 64-year-old woman with chronic myeloid leukemia, which was treated by Dasatinib and was in complete remission since two years ago. She complained swelling of cervical, axillary and inguinal lymph node since 10 days before hospitalization. We performed lymph node biopsy suspecting Malignant lymphoma, but we could not observe any specific findings except for proliferation of various cells. We stopped Dasatinib and replaced it with prednisolone(10mg/day) 4 days before hospitalization because of increasing pleural effusion. She was hospitalized for rapidly progressing occipital headache, and CT scan showed subdural mass lesion widely spreading on left hemisphere. MRI showed homogeneously contrasted subdural mass lesion without mass effect and with low intensity on DWI. Dural metastases of malignant lymphoma, chronic myeloid leukemia, subdural abscess or subdural hematoma were suspected, and we performed open biopsy. Intraoperative findings were dark-red colored elastic tissue involving dura matter without infiltration of arachnoid. Pathological findings showed diffuse infiltration of lymphocytic or plasmacytic mononuclear cells in the fibrous tissue. Histiocytic cells with rich cytoplasm were also observed. At least, no tumor cell was observed. Some kind of inflammatory disease was suspected, but we could not determine diagnosis. We would like to ask for the clinical pathology review meeting.

## **A case of progressive multifocal leukoencephalopathy with severe inflammation which differential diagnosis with brain tumor is difficult**

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**【Introduction】** progressive multifocal leukoencephalopathy (PML) is rare disease which present in the white matter of immunocompromised patients. We report a case of PML which differential diagnosis with brain tumor is difficult. **【Case description】** 72-year-old woman with long-term steroid for dermatomyositis presented dysarthria and memory disturbance. Brain MRI demonstrated slightly high signal of DWI, high signal of FLAIR, and punctate pattern of enhanced image in the white matter of bilateral frontal. The diagnosis from radiological image was difficult. We resected one gyrus of right frontal lobe for pathological diagnosis. **【Pathologic finding】** Many inflammatory cells such as lymphocytes, plasma cells, and macrophage were detected mainly on perivascular of the white matter. According to the lymphocytes, there were more CD3 positive cells than CD20 positive cells, and the large lymphocytes were also detected. In the background, many cells which had oval swelling nucleus were distributed. Although the initial tentative diagnosis was T cell malignant lymphoma, many cell with swelling nucleus were positive to JC virus capsid protein VP1 and minor capsid protein VP2/3 indicating they were JC virus infected cells. The final diagnosis was PML with severe inflammation. **【Clinical course】** Initially she was treated by high dose methotrexate therapy because of initial diagnosis T cell lymphoma. Neurological image and clinical symptom were improved after initial treatment. After diagnosis of PML, She was treated by anti-JC virus medicine, and neuroradiological image and clinical symptom was improved further. **【Conclusion】** PML with severe inflammation has difficulty with diagnosis of malignant lymphoma in radiological and pathological.

## **A case of giant mature teratoma in third ventricle**

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Intracranial teratoma occur frequently in children and young people and is rare about 0.4% in brain tumors. We report a case of the giant mature teratoma in third ventricle. A 5-years old male had presented with a tremor two years before. He pointed out a large tumor of third ventricle and hydrocephalus on Computed Tomography(CT). The tumor size was 56mm×48mm. It was well-demarcated with the surrounding brain and it contained calcification. The tumor indicated a high signal partly on T1WI and T2WI of magnetic resonance imaging(MRI). We thought preoperative diagnosis was a teratoma. First of all, we biopsied the tumor and detained Ommaya reservoir using neuroendoscopy. The biopsy results were fat-like tissue and fibroblasts. Next, we removed totally through interhemispheric transcallosal transchoroidal approach. The tumor included fat tissue, hair tissue, calcification like tooth. It was adhered strongly to the near of the pineal gland. Pathologically, the diagnosis was mature teratoma. After the operation, the tremor was disappeared, and he was discharged from the hospital without neurological deficit. For diagnosis of teratoma, a combination of the images and pathology is very important.

## **Supratentorial purely cortical anaplastic ependymoma -A case report-**

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**【Introduction】** Ependymomas that occur in the brain surface are rare. Purely cortical anaplastic ependymoma has examined past literature but few reports. Since we experienced a case that considered as supratentorial purely cortical anaplastic ependymoma this time, we will report a case and review of the literature. **【Case】** A 16-year-old man. He has no special medical history nor family history. Because he was aware of headaches, left facial paralysis, numbness of the left hand, he consulted his previous doctor. Intracranial hemorrhage was suspected by the head computed tomography. The head MRI of our hospital confirmed a contrast lesion of 5 cm large in contact with the dura of the right frontal lobe. Differential diagnosis considered meningioma, solitary fibrotic tumor, etc., but none of the typical findings were found. Intraoperative findings did not adhere to the dura mater, and the boundary with the brain was completely removed except adhesion of the tumor except for the bottom of the tumor. The pathological diagnosis was anaplastic ependymoma. After surgery, radiation therapy is done, there is no recurrence. **【Discussion】** Typical rosette structure was not apparent, but the present case was approved RELA fusion. From the viewpoint of recognizing a branched capillary network with clear cell as the background, the possibility of supratentorial clear cell ependymoma with branching capillaries was also thought. The age at onset, under 18 years of age, also considered a possibility that the prognosis is relatively good. **【Conclusion】** Differential diagnosis with supratentorial tumor needs to keep this disease in mind.

## **Juvenile xanthogranuloma mimicking brain stem tumor in an infant: A case report and a review of literatures**

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**【Introduction】** Juvenile xanthogranuloma (JXG) is an uncommon disorder of histiocytic cell proliferation. It typically arises from cutaneous tissue usually occurring in childhood. The lesion in the central nervous system (CNS) is rare. An operated case of the solitary CNS-JXG is reported with a thorough review of English literatures. **【Clinical summary】** An eight-month male infant was admitted because of the left hemiplegia. Brain MRI showed a tumor localizing in the brain stem. Low grade glioma, such as pilocytic astrocytoma or pontine glioma, was suspected. Tumor resection was performed. Histopathological examination indicated the diagnosis of JXG as described in detail below. There were no skin lesions. Bone XP, chest CT and abdomen CT showed no lesions in other visceral organs. Therefore, we concluded it as a brain-localized single lesion. **【Pathological findings】** Histopathological examination revealed diffuse proliferation of histiocytes and fibroblastic cells, admixed with lymphocytes, foamy macrophages and a small number of multinucleated giant cells. There was no necrosis. Immunohistochemical studies demonstrated most of the cells being positive for CD68, factor XIIIa and negative for CD1a, GFAP, neurofilament, BRAF(V600E). S-100 immunostaining was equivocal. Histopathological findings and immunostaining pattern of this lesion were consistent with JXG. **【Conclusion】** We reported a case of solitary CNS-JXG with histological and immunohistochemical examinations.



## **Germinoma recurrence outside the previous radiation field 15 years after complete remission**

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Germinoma is curable disease presenting 90% survival at 10-years, due to appropriate radiation and chemotherapy. However, SEER database suggested that germinoma might recur a few decades later. The germinoma patient, who present recurrence 15 years after the initial treatment, is reported.

A 36 year-old woman has a history of neurohypophysial germinoma, which was thought to be completely cured after 30Gy of extended local irradiation with 10Gy local boost and chemotherapy, including cisplatin and etoposide. 15 years later, she presented cerebral tumor outside the radiation field, and it was pathologically diagnosed as germinoma recurrence. Carboplatin and etoposide were administered, and tumor completely disappeared. However, tumor recurred 9 months after the treatment, and stereotactic radiosurgery followed by additional chemotherapy, including ifosfamide, cisplatin and etoposide, could achieve complete remission, again.

Several reports suggested germinoma could recur long time after the initial treatment. In our case, tumor recurred at extra-radiation field, which means that some tumor could not be cured by only chemotherapy without irradiation, even if it showed long-term remission. For better quality of life in the long-time surviving germinoma patients, lowering the dose of radiation with intensive chemotherapy is required, but to assess the survival results, long follow-up, more than 15 years, is essential.

## **A case of medulloepithelioma in the posterior cranial fossa**

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Medulloepithelioma is a rare and highly malignant primitive neuroectodermal tumor that usually occurs in childhood. The diagnosis of this entity required only morphological analysis until the World Health Organization classification of central nervous system (CNS) tumors has been revised, in which genetic analysis is necessary. We report a case of medulloepithelioma in the posterior cranial fossa that was diagnosed by both, morphological and genetic analyses based on this classification. A 10-month-old girl was admitted to our hospital with consciousness disturbance and vomiting. Neuroimaging revealed a partially calcified mass and cyst formation in the posterior cranial fossa. Partial resection of the tumor was performed and histological findings revealed multilayered rosettes with LIN28A staining, but genetic analysis showed no amplification of the C19MC microRNA cluster at 19q14.32. Therefore, we diagnosed the tumor as medulloepithelioma belonging to other CNS embryonal tumours. The patient was immediately treated with systemic high dose chemotherapy. Follow-up neuroimaging 10 months later showed no signs of recurrence. Medulloepitheliomas are difficult to diagnose by routine hematoxylin and eosin staining and require combined morphological, immunohistochemical and genetic analyses to provide an accurate diagnosis.

## **Primary intracranial peripheral PNET case report**

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In 2016 CNS WHO classification, the term CNS PNET that termed in 2007 was removed from the diagnostic lexicon. Time before 2007, these tumor were termed supratentorial PNET. On the other hand, the peripheral PNET(pPNET) is originating from soft tissue and bone like Ewing's Sarcoma. These two types have similar histological appearance but different prognosis. 9-year-old girl had suffered from vomiting without nausea. CT scan revealed a right fronto temporal cystic tumor. MRI shows an irregular contrast enhancement. An urgent craniotomy with complete removal of the lesion was performed. The tumor was located above the pia mater with a dural implantation. The frozen section diagnosis was of small round cell tumor. On the basis of this diagnosis the patient was planned to undergo CSI(craniospinal irradiation) after the chemotherapy following the protocol of the medulloblastoma. After the first chemotherapy, the FISH was performed and EWSR1 gene-related rearrangement was detected. Then we diagnosed the tumor as pPNET and changed the radiation therapy from CSI to local radiation therapy. CNS PNET and pPNET have similar histological appearance but have different originating and immunohistochemical results. We report one case of intracranial pPNET. The occurrence of pPNET at this site is unusual. Immunophenotypical as well as genetic analysis play a key role in the diagnosis and the distinction from CNS PNET.

## **Recurrence of biphenotypic sinonasal sarcoma with cerebral hemorrhaging: A case report with an 11-year follow-up**

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Biphenotypic sinonasal sarcoma (BSNS) is a newly classified tumor that is characterized by neural and myogenic differentiation. We herein report a rare case of the recurrence of BSNS with intracranial hemorrhaging and a review of the literature. A 70-year-old man presented with disturbance of consciousness and vomiting blood. He had undergone resection of a sinonasal tumor 11 years earlier and shown no recurrence at his last follow-up 4 years ago. Computed tomography showed cerebral hemorrhaging around a low-density mass that occupied the left frontal base and left ethmoid sinus. Total resection was performed. A histological examination of tumor specimens obtained from the first and the second resections revealed almost the same characteristic morphological features and the patient was diagnosed with BSNS. The lesion was negative for any fusion genes, such as PAX3-MAML3, PAX3-FOXO1 or PAX-NCOA1 fusion. The long-term progression of BSNS is not clear. This case appears to be the first reported recurrence of BSNS with cerebral hemorrhaging. BSNS should be considered to need long-term follow-up.

**P3-101**

**Preservation of staining property STAT6 immunostaining in solitary fibrous tumor/haemangiopericytoma with preoperative embolization**

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We examined conditions adequate immunoreactivity of STAT6, using a specimen of solitary fibrous tumor/haemangiopericytoma (SFT/HPC) which underwent preoperative embolization. **【Patient】** A 26 y.o. man who had solid, irregularly shaped and well-enhanced extraaxial tumor. Angiography and tumor embolization were performed followed by the resection at the same day. Intraoperative diagnosis was the SFT/HPC. Warm ischemic time from the start of embolization to complete tumor excision and immersion in 10% neutral buffered formalin was about 17hrs. **【Samples】** The tumor specimen were cut into about 5\*10mm size and formalin-fixed as follows: 15hrs, 39hrs (also prepared the specimens for routine path-diagnosis), 63hrs, 87hrs, 7days, 15days, 22days. **【Antibody】** polyclonal anti-STAT6(S-20): sc-621, 1:50, Santa Cruz, Dallas, TX **【Results】** The STAT6's nuclear positivity were more distinct with short-time-fixed samples, but contained the area that were kept relatively good even for specimens of the longest 22-days-fixed. On the other hand, in the specimen of the largest diameter of tumor prepared for routine path-exam, adequate immunopositivity were at the only within 500 mcm of the tumor surface or within 100 mcm around the relatively large blood vessel branch within the tumor. Immunoreactivity remarkably weakened inside the tumor in which formalin permeation was delayed. **【Conclusion】** The time-lag from the ischemia to the formalin penetration, which affected the immunoreactivity of STAT6, was remarkable attenuation even within a relatively short period of time within 40 hours after immersion in the formalin. It might be improved by dividing the tumor before the immersion in formalin for tumors larger than 1 cm in diameter.

## **$\delta$ -catenin modulates bevacizumab-induced glioma invasion**

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**【INTRODUCTION】** While bevacizumab suppresses angiogenesis, it has also been reported to cause invasive proliferation. We evaluated the effects of bevacizumab on the invasiveness of glioma cells and determined target genes involving in the regulation of bevacizumab-induced invasion. **【MATERIAL AND METHODS】** Human glioma U87 $\delta$ EGFR cells were stereotactically injected into the brains of mice. Bevacizumab was administered intraperitoneally three times per week. At 18 days after tumor implantation, the brains were removed for histopathology observations and mRNA was extracted from the orthotopic U87 $\delta$ EGFR glioma cells. Gene expression was assessed by qRT-PCR arrays, which included factors such as adhesion molecules. Expression of genes-of-interest was compared between the bevacizumab and control groups. The cytotoxicity of bevacizumab and its effect on U87 $\delta$ EGFR, U251MG, A172, Gli36 and its invasiveness were investigated. Expression of key factors was targeted by siRNA, and shRNA knockdown, and cell invasiveness was analyzed. **【RESULTS】** In vivo, bevacizumab treatment increased glioma cell invasion. qRT-PCR array analysis revealed upregulation of  $\delta$ -catenin (CTNND2) and several other factors. Down regulation of  $\delta$ -catenin by shRNA decreased bevacizumab-induced glioma invasion. In vitro experiments showed that a low concentration of bevacizumab was not cytotoxic, but tumor cell motility was increased. And  $\delta$ -catenin was upregulated by a low dose of bevacizumab treatment. Silencing of  $\delta$ -catenin decreased the bevacizumab-induced glioma invasion. **【CONCLUSION】** This study showed that some ECM factors were changed, and glioma cell invasion was induced during bevacizumab therapy. The findings suggest that  $\delta$ -catenin regulates bevacizumab-induced glioma cell invasion, and may be a novel target for glioma treatment.

## **A case of radionecrosis, 2 years after radiation therapy**

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**【Introduction】** Here we report a case of radionecrosis developed 2 years after temozolomide concomitant radiation therapy for anaplastic astrocytoma.

**【Case】** A 60 years old men was diagnosed as right frontal brain tumor, and admitted in our hospital in August 20XX. The first surgery was performed. The diagnosed was anaplastic astrocytoma (WHO2007). After the surgery, Stupp's regimen was performed. In March 20XX+1, the tumor recurred and the second surgery was performed. Placement of BCNU wafer was performed, too. The diagnosis was anaplastic astrocytoma, IDH-mutant (WHO2016). Maintenance therapy was continued, however, the tumor recurred in January 20XX+3. The third surgery was performed in February.

**【Histological findings】** Extensive geographical coagulative necrosis was found below resected lumen. In brain tissue around the lesion, astrocytosis and invasion of lymphocytes and histiocytes were observed. No tumor cell was found under the BCNU wafer. Hyaline degeneration was remarkably observed in a part of vessels. Coagulation necrosis of vessels was also observed frequently. We diagnosed this case as radionecrosis, however, IDH mutated cells existed partially.

**【Discussion】** Radionecrosis is reported to occurs within six to fifteen months after the radiotherapy, which mimics recurrence of metastatic brain tumor or malignant glioma. We experienced a case of radionecrosis developed 2years after the radiotherapy, and thought it unlikely to be the radionecrosis. Here we report the pathological findings, clinical course and radiographical findings of this case with consideration from literatures.

## **A case of primary intracranial rhabdomyosarcoma**

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Primary intracranial rhabdomyosarcoma is a very rare tumor that poses great diagnostic challenges to pathologists. We report a case of a 10-year old female who presented with symptoms of increased intra-cranial pressure, dressing apraxia and upper extremity paralysis secondary to recurrent hematoma formation in the left occipital area. A neoplasm was identified after the second hematoma evacuation and the primary pathologic consideration at that time was primitive neuroectodermal tumor. Initially, chemotherapy and radiotherapy were given, however, therapy subsequently shifted to more powerful chemotherapeutic agent with the confirmed diagnosis of rhabdomyosarcoma. Therapy response was noted and lasted for few years until development of recurrence. The patient had survived for 53 months from initiation of therapy. Histologically, the tumor consisted of diffuse proliferation of immature spindle cells with marked cytologic atypia and eosinophilic cytoplasm, arranged in fascicular and storiform pattern. There are frequent mitoses and scattered multi-nucleated giant cells with eosinophilic cytoplasm. Immunohistochemically, the tumor cells show expression of skeletal muscle differentiation (myogenin, desmin, HHF35) and INI1 expression was retained. To the best of our knowledge, there are only 50 cases of primary intracranial rhabdomyosarcoma published. It is important to include rhabdomyosarcoma as a differential diagnosis when dealing a poorly differentiated tumor in the central nervous system. In this case, an accurate diagnosis of primary intra-cranial rhabdomyosarcoma contributed to appropriate treatment and long-term survival of a patient.



## **A case of mucinous carcinoma considered malignant transformation from intracranial germ cell tumor**

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**【Introduction】** To our best knowledge, there is no report of primary intracranial mucinous carcinoma so far. **【Case】** A four-year-old male child underwent a partial removal of a pineal tumor. Pathological diagnosis was mixed germ cell tumor including mature teratoma and choriocarcinoma. After the surgery, he received radiation therapy (whole brain and local), followed by chemotherapy up to 6 years old. Over 20 years has passed without tumor progression. However, the residual tumor growth and a hydrocephalus was recognized at the age of 27. He underwent an endoscopic third ventriculostomy (ETV) and a partial tumor removal. Pathologically, layered keratinized material with monocyte infiltration was found, however, there was no malignancy. The tumor progression was recognized about a half year later. Therefore, we diagnosed growing teratoma syndrome and performed CARE chemotherapy (carboplatin and etoposide) twice and a subtotal tumor removal. Pathological examination revealed glandular epithelium containing goblet cells with a lot of mucus. We diagnosed mucinous carcinoma. **【Conclusion】** If a residual tumor of germ cell tumor grows rapidly, a tumor removal should be necessary to diagnose pathologically.

## **A case of front-temporal suprasellar papillary glioneuronal tumor**

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Papillary glioneuronal tumors are rare tumor type, which were only recently recognized and histologically characterized by their pseudopapillary architecture associated with compact areas composed of neuronal elements in different maturation states. The authors present 16-year-old woman with papillary glioneuronal tumor. She was admitted to our institute because of her visual disturbance. Imaging showed a demarcated, mainly solid and cystic calcified frontal base to suprasellar extending tumor. The patient underwent surgery with bifrontal craniotomy. Histologically, it was observed pseudo-papillary growth of GFAP positive cells and synaptophysin-positive interpapillary collections of neurocytes. The cell nuclear fissions were not noticeable and Ki-67 was 4.1% at the maximum site. After surgery, her visual disfunction was improved.

## **A Case of Solitary Fibrous Tumor of NAB2 Exon 6-STAT6 Exon 17**

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The solitary fibrous tumor (SFT) is a relatively rare tumor among primary brain tumors. The NAB2-STAT6 fusion gene is a driver mutation of SFT and has genetic changes similar to those of hemangiopericytoma (HPC). Recently, various NAB2-STAT6 genotypes have been confirmed, and the relationship between genotypes and malignancy has been reported. A 49-year-old woman was referred to our department because of a 2-week history of left occipital headache and nausea. Brain magnetic resonance imaging (MRI) showed a well-demarcated and strongly enhanced mass with multi cystic compartments in the left occipital region. The mass was approximately 40 mm in diameter. A subarachnoid space was found between the tumor and the left occipital lobe, suggesting an extramedullary situated tumor. However, there was no dural tail sign. Surgical resection of the tumor was performed. The tumor was mildly elastic and hard and bled easily. The tumor was grayish, with a clear boundary between the tumor and the brain surface. The tumor was resected sub-totally because it had invaded into the left transverse sinus. Histological examination showed moderate cellularity with round or oval nuclei, collagenous stroma, 1 mitosis per 10 high-power fields, and no necrotic areas. Immunohistochemical examination showed diffuse positivity for STAT 6 and CD 34. Genetic analysis showed NAB2 exon 6-STAT6 exon 17 fusion gene. We finally diagnosed SFT.

## **Usefulness of PCR direct sequence on definitive diagnosis for chondrosarcoma : -two case reports-**

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**【Introduction】** Performing a differential diagnosis between chondrosarcoma (CS) and chordoma (CH) is sometimes difficult. Because CH has a poorer prognosis than CS, it is critical to perform an accurate diagnosis. We report two cases of CS where the PCR-direct sequence proved to be useful in differential diagnoses. **Case1;** A 73-year-old woman with bilateral abducens paralysis onset. Imaging showed the heterogeneously enhanced mass lesion on MRI with destruction of clivus bones. Tumor resection under endoscope was performed by endonasal approach. **【Pathological findings】** Polygonal cells proliferated with reticular, funicular and solitary pattern formation in myxomas-like extracellular matrix. Immunohistochemical staining (IHC) showed positive for S100, but negative for AE1/AE3, CAM5.2, and EMA. The MIB1-LI was 1%. IDH1-R132G mutation was detected by PCR-direct sequence, while IDH2-R172 was wild type. **Case2;** A 33-year-old man with right trigeminal neuralgia onset. Imaging showed the ring-like enhanced tumor bulk located in right cavernous sinus to cerebellopontine angle. Tumor resection was performed by right suboccipital craniotomy. **【Pathological findings】** While chondroid tissue was mainly seen, the tumor cells with palisading arrangement in myxoid stroma were partially visible. IHC was negative for AE1/AE3, CAM5.2, and EMA. The MIB1-LI was 2%. IDH1-R132G mutation was detected in PCR-direct sequence, while IDH2-R172 was wild type. **【Discussion and conclusions】** The IDH1 mutation was found to be common in CS and rarely so in CH, although the imaging and the pathological findings of both tumors were very similar. We conclude that PCR-direct sequence is useful in differential diagnosis between CS and CH.

## **A Case of intraventricular giant cell glioblastoma**

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Giant cell glioblastoma (GCG) is a rare histological variant of glioblastoma (GBM). We report a case of a 60-year-old man who presented short-term memory impairment. Magnetic resonance imaging (MRI) showed a well-circumscribed mass approximately 6 cm in size, which was located within the inferior horn of the right lateral ventricle. He presented progressive left-sided hemiparesis and impaired consciousness after admission. The patient underwent surgical removal through transcortical route 15 days after admission. Grossly, the tumor was seen as hypervascular mass with very hard consistency. Histological examination revealed pleomorphic nuclei and necrosis. Most striking feature was numerous bizarre multinucleated cells. Staining for IDH-1 R132H, GFAP, EMA, vimentin, and S-100 were negative in the tumor cells. Staining for p53 was positive. MGMT promoter hypermethylation and 1p/19q co-deletion were not detected. The final pathological diagnosis was GCG. The patient underwent radiotherapy and temozolomide chemotherapy. However, MRI showed cerebellar new lesion during adjuvant therapy, which we highly suspected to be a dissemination. We performed whole brain radiotherapy and added bevacizumab. After adjuvant radiochemotherapy, a follow up MRI demonstrated decrease of enhanced lesions. Because intraventricular GCG is extremely rare, we also reviewed pertinent literature regarding this case.

## **A case of pontine glioma occurring 14 years after chemoradiotherapy of NGGCT**

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We report a rare case of pontine glioma that occurred 14 years after chemoradiotherapy of nongerminomatous germ cell tumors (NGGCT). An 8-year-old girl presented with rapid reduction of visual acuity with high level of serum AFP and b-HCG. As she had suprasellar lesion and was diagnosed as NGGCT, she underwent radiotherapy (local 26 Gy, whole ventricle 24 Gy) and chemotherapy (CPA, CDDP, VP-16). Although the tumor was contracted without recurrence in 14 years, T2 / FLAIR high-intense lesion on the pons appeared at the age of 22 and gradually grew with gadolinium-enhanced portion. As methionine PET showed high accumulation in that lesion, she underwent stereotactic biopsy. Histopathological examination showed that it was composed of small round cells with round nucleus and partial high cell density similar to oligodendroglioma-like cells. Neither microvascular proliferation nor necrosis was found. Immunohistochemical study showed positive staining for ATRX, GFAP, and Olig2, whereas negative for IDH1 R132H, MGMT, and p53 staining. The Ki-67 labeling index was 10%. Only 1p loss was identified using FISH analysis. Therefore, it was diagnosed as low-grade glioma, WHO grade 2. Then she received temozolomide and her enhanced-lesion was reduced. Pontine glioma (diffuse midline glioma in WHO 2016) occurs frequently in childhood, and morphologically consisted of astrocytic component. Radiation induced glioma is rare with a high incidence in young people, but it has been reported to be no difference in genetical alterations between radiation-induced gliomas and spontaneously occurring gliomas. We discuss the molecular analysis of this case.

## **A case of gliofibroma in adults who underwent oncogene panel test**

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**【Introduction】** gliofibroma is a tumor with glia component and mesenchymal component, and it is a very rare tumor that has only been reported to date by about 40 cases. It occurs mainly in children and is often a benign tumor. We report a case of adult patient with gliofibroma who had recurrence early postoperatively and underwent oncogene panel examination (Todai Onco Panel, TOP). **【Case】** A 40-year-old man who had no medical past history presented with repeated eye sticky seizures. In the head MRI, a contrast lesion with a diameter of 3 cm was recognized in the left temporooccipital region. The tumor was total removed by surgery. About 2 months after surgery, because nodules appeared in the removed cavity, we considered recurrence and the patient underwent radiotherapy. **【Pathologic findings】** Histologically, tumor cells with distinct chromatin-deforming distortion and notches with a circular to spindle-shaped nucleus were densely proliferated and accompanied by a desmoplastic response. Neurons and glia cells, which are thought to be non-neoplastic, are intervened between islands. The nuclear fission image was not clear. Results of immunostaining were as follows. EMA (-), LCA (-), EG (-), PFR (-), SIGMA (-), SIAP BRAF (-), CD21 (-), CD34 (-). The MIB1 positive rate is about 7% in the high part. **【Oncogene panel test result】** Mutation of ARID1B was confirmed. **【Discussion】** Because gliofibroma is a rare disease, the characteristics of the disease are still unclear. The accumulation of cases and pathological and genetic analysis are necessary in the future.

## **Epithelioid hemangioendothelioma that metastasizes to the temporal lobe and cerebellum**

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**【Background】** Epithelioid hemangioendothelioma is a non-epithelial tumor derived from vascular endothelium discovered by Sharon Weiss et al. in 1975. Pathologically it shows the findings between angiosarcoma and hemangioma, but from genetically it shows different properties from both. Metastasis often occurs with a relatively slow course, and no effective treatment has been established. We report on a case of epithelioid hemangioendothelioma with intracranial metastasis. **【Case】** 20 year old male. An abnormal shadow was pointed out in the lung at the screening examination, and multiple examination showed multiple granular shadows in the lung. Since it was asymptomatic, three years passed and again an examination pointed out an abnormal shadow in the lung. Therefore, it was a close examination, in addition to multiple granular shadows in both lungs, multiple hepatic metastasis and cortical metastasis were observed. TBLB was performed, and diagnosis of Epithelioid hemangioendothelioma was obtained. It was introduced to our hospital for the purpose of treatment, and the head MRI revealed an expansion of the edematous change of the lesion. **【Conclusion】** Epithelioid hemangioendothelioma develops in the whole body, in particular occurs in lung, liver, bone, soft tissue, rarely occurs in the skull. This time, we discovered Epithelioid hemangioendothelioma on the left temporal lobe, and relapsed after 5 and 20 months. Sensitivity to radiation and chemotherapy is low from previous reports and surgical treatment should be selected for resectable cases.



**P3-113**

**A case of hemangioblastoma with disseminating recurrence**

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**【Case presentation】** A 41-year-old man presented with headache, nausea and dizziness. MRI showed a solid tumor suspecting hemangioblastoma in his left cerebellum. He underwent tumor resection and histopathological diagnosis could be hemangioblastoma but showing the similar findings of ependymoma. Three years and 11 months after the removal, MRI showed newly two lesions in his right cerebellum and a lesion in his Th2 level of thoracic spinal cord. The cerebellar lesions were removed and they were recurrent hemangioblastoma. One year later, MRI showed multiple disseminating lesions in his cerebellum and thoracic spinal cord. He received stereotactic radiotherapy in these recurrent lesions. **【Discussion】** Histologically, hemangioblastoma is characterized by capillary network development and stromal cell proliferation. The stromal cells have abundant cytoplasm packed with lipid vacuoles and can exhibit a clear cell-like appearance in specimens. It has been known to be difficult to distinguish hemangioblastoma from clear cell ependymoma. The leptomeningeal dissemination of hemangioblastoma was rare. We discuss this rare case with literature consideration.

## **An elderly patient with massive dissemination diagnosed with pineal parenchymal tumor of intermediate differentiation (PPTID): An autopsy case**

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A 71-year-old male presented with disorientation and gait disturbance. MRI demonstrated a 13mm-sized pineal tumor, with multiple disseminations to the lateral ventricle and the whole spinal cord. Whole-body CT scan were negative of primary tumor. There were no definitive findings, the result of cerebrospinal fluid cytology suspected of carcinoma, thus diagnosis of brain metastases with unknown origin was made. He died of a progressive respiratory failure 3 months after the onset. The autopsy findings revealed no primary lesions in the body, and there was a 20mm-sized tumor at the pineal body with diffuse infiltration into the surrounding brain tissue and dissemination to the ventricle wall. The tumor cells harbor high N/C ratio, a so-called salt and pepper chromatin, and mitosis. There was also necrotic region. Immunostaining demonstrated negative AE1/AE3, and positive Synaptophysin and NCAM, thus diagnosis of PPTID was made. Pineal tumor is extremely rare accounts for below 1% of all intracranial tumors, and 21-54% of the pineal tumor is PPTID. Furthermore, elderly PPTID patients is rare. In the present case, considering the result of cytology and old age, we diagnosed with brain metastasis with unknown origin. Due to his poor general condition, it is doubtful that we successfully provide radiation therapy, but we should have done the biopsy of pineal tumor for the early and right diagnosis. We experienced a pineal tumor with massive dissemination, which was diagnosed by an autopsy. We should keep in mind that PPTID may be the diagnosis among brain metastases of unknown origin.

## **Papillary tumor of the pineal region: Two cases report and review of the literature**

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**【PURPOSE】** A variety of neoplasms such as pineal parenchymal cell tumors, germ cell tumors, papillary tumor of the pineal region (PTPR), and others arise in and around the pineal gland. Among them, PTPR is rare and has not been well recognized. Thus, this report describes two cases of PTPR and reviews the literature.

**【METHODS】** The first case was a 57 years-old man who visited to examine neurological condition. No deficits were revealed. MRI showed a relatively high-intensed mass on T1-WI with homogeneous enhancement. The second case was a 68 years-old man who was suffered from gait and memory disturbances for five months. Neurologically, cognitive decline was revealed. MRI showed a relatively low-intensed mass with mildly heterogeneous enhancement. Both of them were totally removed through the right occipital transtentorial approach, and have not recurred for 113 and 36 months respectively.

**【RESULTS】** The histology both revealed the proliferation of epithelia-like cells around the blood vessels showing papillary and solid areas. Anaplastic features such as mitosis or necrosis were only seen in the second case. The tumor cells were immunoreactive for CK, Vim., and S-100, but not for GFAP, Olig2, EMA, NFP, SYN, and chromogranin. MIB-1 SI was around 1.5 and 3.5% and MGMT-immunoreactivity was moderately and highly recognized respectively. The ultrastructure of the deparaffinized specimen demonstrated intermediate filaments and reminiscent junctions.

**【CONCLUSION】** Rare cases of PTPR were reported and review of the literature will be discussed.

**P3-116**

**A case of 16 years old, right cerebellar tumor consisting of monotonous proliferating undifferentiated small cells**

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Case of A 16-year-old man. Right cerebellar tumor with multilocular cyst was pointed out with CT following head injury. There were no neurological deficits. Angiography didn't show tumor staining. Although PETCT had accumulation of methionine and choline, no accumulation of FDG. Undergoing craniotomy, the whole tumor was excised macroscopically. Microscopically, fragments with a maximum of 15 x 9 x 7 mm, tumor cells which had small round nucleus and eosinophilic cytoplasm with a high nuclear cytoplasm ratio, were diffuse and dense monotonous proliferating. Tumor cells lobulating by blood vessels, reactive glial cells was observed, the desmoplasia was not recognized. In the region where the spindle-shaped cells proliferated, six mitosis appeared in one high power fields. The boundary with the brain parenchyma was clear, tumor clusters infiltrated alveolar pattern. Necrosis was not clear. Immunohistochemically, tumors showed EMA, keratin (AE1 / AE3) and desmin staining. Neurofilament Protein and NeuN stained in a small number of cells, synaptophysin weakly positive. p53 and INI1 was positive. Negative stains included GFAP, Olig 2, chromogranin A, beta-tubulin, myogenin, IDH1. The maximal MIB 1 labeling index was 40-50%. Glioma, medulloblastoma, AT / RT were denied. In the mesenchymal tumor, the desmoplasia was not recognized, We diagnosed of desmoplastic small round cell tumor (DSRCT). Reconfiguration of EWSR1 and WT1 was also confirmed. Up to now, there are 6 cases of intracranial DSRCT reports. Tumor cells without desmoplasia made pathological diagnosis difficult. Despite its rarity, DSRCT expands the differential diagnosis of small round cell tumors of the CNS.

## **A case of acromegaly in which a growth hormone producing pituitary adenoma recurred rapidly after administering pegvisomant**

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Pegvisomant is a growth hormone receptor inhibitor, which suppresses serum IGF-1 level and improves clinical symptoms of acromegaly. Here, we report a patient with acromegaly who was introduced pegvisomant in place of somatostatin receptor ligands (SRL) followed by rapid regrowth of the pituitary adenoma. The patient was a 63-year-old woman with treatment-resistant diabetes mellitus, in whom acromegaly and an invasive pituitary tumor were pointed out. We performed the first trans-sphenoidal surgery (TSS), and removed the tumor subtotally, except the tumor in the bilateral cavernous sinuses. Pathological findings showed relatively high Ki-67 labeling index (10%). Although we had administered SRLs (octreotide and lanreotide), we had to stop them due to their side effect, flatulence. So, instead of SRLs, we introduced pegvisomant to control the disease. Two months after administering pegvisomant, a cystic tumor recurred rapidly, so the second TSS was performed. At this time, the pathological exploration showed almost same findings as that of first specimens. We restarted pegvisomant, resulting in regrowth of the tumor in seven months, and the third TSS was performed. Pathological finding showed that Ki-67 labeling index increased from 10 % to 18 %, and p53 converted to positive. Immunostaining for somatostatin receptor showed positivity for both subtype 2 and subtype 5. As pegvisomant seemed to be related to rapid regrowth of the tumor, we stopped pegvisomant and started to use pasireotide.

## **Invasive skull base aspergillosis in a patient with lactotroph adenoma**

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Aspergillosis is the most common fungal infection on the skull base, and it remains a difficult disease to diagnose and treat. We recently encountered a case of invasive aspergillosis who have lactotroph adenoma controlled by cabergoline. A 47 year-old man had presented with nasal bleeding and diagnosed lactotroph adenoma invading the sellar floor and sphenoid sinus eleven years ago. The cabergoline treatment has been shown to be effective, and ongoing. He developed headache and visual disturbance on the left side in few weeks. MRI shows new tumor mass located medial to the optic canal. Higher doses of cabergoline was ineffective, and we therefore consider surgical resection for tumor and optic canal decompression on transsphenoidally. Although visual acuity did not recover, surgical samples show branching septate hyphae in the inflammatory granulation tissue. Antifungal agent was started immediately, *Aspergillus fumigatus* was identified from the culture of surgical samples subsequently. There were no significant data with blood chemical values and cerebrospinal fluid examination, therefore histopathological diagnosis is imperative in this case. We report a rare case of invasive aspergillosis presenting with lactotroph adenoma with a review of the literature.

## **A case of cavernous angioma of the optic chiasma**

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A 59-years-old male presented with angioma originating from the optic chiasma manifesting as visual disturbance. Magnetic resonance imaging revealed a heterogeneous signal intensity mass at optic chiasma with a low signal intensity on T2\* imaging. Right front-temporal craniotomy was performed by the pterional approach. A subpial hematoma situated at the optic chiasm lesion.

The hematoma with angiomatous component was adherent to optic chiasma, but finally resected from surrounding structure. Histological examination of the specimens confirmed that optic chiasmal lesion was cavernous angioma. Eighteen cases of cavernous angioma of optic nerve have been described, and some presenting with visual disturbance.

Postoperatively, his left visual acuity was slightly improved.

According to our case and reviews, it is the best management that surgical resection with preservation of optic nerve function.

## **IgG4 related tumor-like or hypertrophic disease mimicking skull base meningiomas**

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**【Subjective】** IgG4 related disease (IgG4-RD) is an entity characterized by elevated serum immunoglobulin 4 and pseudo-tumors which contain lymphoplasmacytic infiltration of IgG4-positive plasma cells. Lymphoplasmacyte rich meningioma and Rosai-Dorfman disease are the differential diagnoses of the intracranial lesions related with IgG4-RD. Here we report 2 cases of intracranial lesion of IgG4-RD mimicking skull base meningioma.

**【Cases】** (1) A 62-year-old woman underwent brain MRI because of transient global amnesia. It showed a well-enhanced lesion enlarging along petrous bone dura and tentorium. Craniotomy was performed. There were many lymphocytes and IgG4-positive plasmacytes histologically. Serum IgG4 was high (219 mg/dL). She was diagnosed with IgG4-RD. (2) A 63-year-old woman who suffered from anosmia and underwent brain MRI. A homogeneously enhanced lesion which covered anterior skull base dura, anterior falx and convexity dura was detected. Pathological diagnosis of the exenterate specimen was IgG4-RD with bases of infiltration of IgG4-positive lymphoplasmacytes and elevated serum IgG4.

**【Discussions/Conclusions】** Though there have been a few cases on intracranial pseudo-tumor related with IgG4-RD, all cases were middle-aged patients. The site of predilection was skull base. The lesion was homogeneously well enhanced with gadolinium on MRI, like an en plaque meningiomas. But no tumor cells positive for vimentin or EMA were detected in contrast to lymphoplasmacyte rich meningiomas. Diagnostic criteria have already established and high dose steroid is effective for this disorder. It is important to suspect IgG4-RD primarily and check the serum IgG4 if there was the finding described above on brain MRI. We have to avoid unwanted surgery.



## **A case report of a mass lesion in the brain stem positive for anti-MOG antibodies**

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**【Background】** The differential diagnosis between glioma and tumefactive demyelinating lesion (TDL) can be difficult to distinguish based on magnetic resonance imaging (MRI) findings. Here, we report a case of MOG-antibody-associated disease, in which the patient first received a diagnosis of TDL by biopsy, and relapsed after the treatment. **【Case Presentation】** A healthy 22-year-old man was aware of weakness in his right side and presented to a local doctor. Brain MRI revealed a lesion in the left ventral side of the medulla oblongata, so he was referred to our hospital for further examination. We considered this case as brain stem glioma according to MRI and performed a biopsy. Kluver-Barrera staining showed extensive demyelination, and we found CD68-positive cells at the same site. Anti-aquaporin 4 antibody in the serum and oligoclonal band in the cerebrospinal fluid (CSF) were negative. Consequently, the pathological diagnosis was TDL. The lesion shrank after administration of steroid and we continued to observe the patient. After half a year, the patient developed generalized convulsion, and MRI revealed a scattered lesion in the right frontal lobe. He was readmitted to our hospital, and we diagnosed this case as MOG-antibody-associated encephalitis because MOG antibody was positive in the serum and CSF. The patient's condition improved by administration of steroid. **【Conclusions】** We report a case of MOG-antibody-associated disease that was initially misdiagnosed after the first biopsy. The definition of MOG-antibody-associated disease is controversial, but as preferable treatment can lead to favorable outcomes, this disease should be considered as a differential diagnosis.

## **A case report of granuloma arising from peri-third ventricle**

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**【Presentation of Case】** We document the case of 51 years old woman presented with a month of memory disturbance and apathy. The MRI imaging of brain revealed a homogenously enhancing lesion occupying peri-third ventricle. On day five she got high fever and hyponatremia. Hypothalamic disturbance and hypopituitarism were suspected. We prescribed hydrocortisone. The tumor was biopsied with neuroendoscope. Dexamethasone was prescribed post-operative days. And memory disturbance and apathy were recovered. And tumor was disappeared from the MRI imaging. **【Pathology】** Section of the brain tissue shows diffuse infiltration of an admixture of inflammatory cells including lymphoid cells and macrophages. A relatively small number of enlarged atypical cells are also infiltrated in the tissue. **【Discussion】** Prior steroid administration may obscure the histopathologic diagnosis.

**P3-123**

**Extremely delayed metastasis to the brain originated once completely cured cervical cancer of uterus**

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**【Background】** We experienced a rare case of a brain metastasis from cervical small cell neuroendocrine cancer (SCNEC) of uterus 13 years after the first diagnosis. **【Case】** 51-year-old female patient of disturbed consciousness was admitted. She had previous history of a surgery and adjuvant chemotherapy for cervical SCNEC 13 years before. Her annual checkup was continued for 8 years without any recurrence thus terminated 5 years before admission. Her brain MRI demonstrated a cystic tumor at the right frontal lobe which sized 6cm in diameter. An immediate surgery was done and her consciousness fully recovered. The p16 and synaptophysin immunostain were positive thus the tumor was diagnosed as a metastasis of SCNEC. CT showed no signs of uterine recurrence but an enlarged lymph node at mediastinum. The lymph node was biopsied and diagnosed as a metastasis as well. She now undergoes chemotherapy. **【Discussion】** SCNEC is a rare subtype of cervical cancer which accounts for 0.5-10%. While ordinary cervical cancer rarely shows metastasis to the brain as 0.4-2.3%, SCNEC was reported as 5 out of 15 patients had brain metastasis. The average period between the first diagnosis and metastasis to the brain was 17.2 months, however, the maximum period was reported as long as 127 months. There has not been any consensus about how long we should follow a patient. **【Conclusion】** We experienced a rare case of SCNEC with extremely delayed metastasis to the brain suggesting that longer period of observation is necessary. A guideline is desired for long term observation.

## **Neuropathological change after radiotherapy for HPV-related multiphenotypic sinonasal carcinoma**

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**【Introduction】** HPV-related multiphenotypic sinonasal carcinoma(HMSC) is HPV-related tumor including myoepithelial, ductal and squamous differentiation. Surgical resection with/without postoperative radiotherapy was common, however the efficacy of each treatments (surgical resection, chemotherapy and radiotherapy) were unknown. All past patients had good clinical outcome, but brain invasion wasn't reported. We treated HMSC with brain invasion by radiotherapy alone. We retrospectively discuss about effectiveness of radiotherapy from pathological findings. **【Patient and method】** A 69-year-old man with right frontal lobe intracranial hemorrhage underwent contrast MRI and it showed tumor at right frontal lobe and sinonasal tract. We performed transnasal biopsy and IMRT (40 Gy, 20 fraction). Neuroimaging study showed tumor reduction. However, he got to be coma, and died for respiratory failure at 41st day after radiotherapy. Autopsy was performed. **【Result】** Biopsy specimens showed immature tumor originating from epithelial and mesenchymal cell. Epithelial component consisted of basaloid cells, ductal cells and squamous differentiation. Mib-1 index was over 30%. There were p16-positive cells and HPV-RNA-ISH was partially positive. In autopsy, intranasal specimens showed necrotic changes. Therefore intracranial specimens showed same pathological findings as biopsy. **【Conclusion】** We performed radiotherapy alone for HMSC with intracranial invasion. This is the 1st HMSC report about the efficacy of radiotherapy comparing biopsy and autopsy pathology. Radiotherapy has some effectiveness in HMSC, especially sinonasal lesion.