

period, of which 16 cases underwent a total of 18 brain biopsies. The final diagnosis was 7 ML (6 PCNSL, 1 brain metastasis), 3 toxoplasma encephalopathy, 1 PML, 1 brain tuberculosis, 1 immune reconstitution syndrome, 1 *Penicillium marneffei* infection, 1 hematoma and one case that could not be diagnosed. In patients with ML, preoperative sIL-2 receptor was higher and EBV positive cases in cerebrospinal fluid tended to be more common ( $p=0.051$ ,  $p=0.086$ , respectively). Five of the six patients with PCNSL were treated at our hospital, four of which were treated with highly active anti-retroviral treatment (HAART) and whole-brain irradiation and one with HAARA alone, resulting four with CR and one with SD. Four patients, except one who had sudden death of unknown cause, were still alive without recurrence (median observation period 44.5 months). CONCLUSION: At the moment, it is difficult to diagnose ML without brain biopsy. HIV-positive status has been regarded as a poor prognosis factor in PCNSL patients, but the prognosis seems to have improved with HAART.

#### ML-10

##### PRIMARY DIFFUSE LARGE B-CELL LYMPHOMA OF THE CRANIAL VAULT: A CASE REPORT

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**BACKGROUND:** Tumors other than meningiomas, cavernous malformations and metastatic tumors rarely originate in the cranial vault. We report a case of primary diffuse large B-cell lymphoma of the cranial vault. **CASE DESCRIPTION:** A 58-year-old woman was referred to our hospital because of a right frontal subcutaneous mass that had rapidly increased in size. The patient had been well until approximately 2 months before this referral, when she had slight difficulty in opening the right eye. Thereafter she had headaches and a swelling of the forehead. She was seen in a neurosurgery clinic and referred to our hospital. She had no past history of serious illnesses, operations or hospitalizations. On examination, there was a fixed firm mass, 13 cm in size, in the right side of the forehead. The skin on the center of the mass was stretched and took on a reddish hue. Neurological examination was negative. Blood chemistry tests showed lactate dehydrogenase four times above normal and a slight increase in alkaline phosphatase, amylase and lipase. Beta-2-microglobulin was normal. Bone windows of computed tomography (CT) of the head showed hyperostosis and permeative lytic changes of the frontal bone. Postcontrast MRI showed a large enhanced subgaleal lesion extending through the bony calvarium with a large subdural component. Histological examination after a biopsy was characteristic for a diffuse large B-cell lymphoma. Postcontrast CT of the abdomen and FDG-PET showed metastatic lesions in the pancreas, kidneys and cervical lymph nodes. The patient has been treated by CHOP chemotherapy and has been well. **CONCLUSIONS:** We present a case of primary diffuse large B-cell lymphoma of the cranial vault. We recommend including this tumor variant in the differential diagnosis of rapid growing cranial vault tumors.

#### ML-11

##### DETECTION OF MYD88 MUTATIONS FROM CELL FREE DNA AIDS IN THE DIAGNOSIS OF CENTRAL NERVOUS SYSTEM LYMPHOMAS

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**BACKGROUND:** Diagnosis of primary central nervous system lymphomas (PCNSL) can be challenging. We have shown that the detection of MYD88 mutation in cell free DNA (cfDNA) taken from cerebrospinal fluid (CSF) is reliable (JCO Precision Oncology, 2019; Leukemia and Lymphoma, 2019). We report four cases in which detection of MYD88 mutation aided in the diagnosis. **CASE 1:** A 67-year-old man with a history of systemic B-cell lymphoma, experienced right hemiparesis. MRI showed a slightly enhancing lesion located in the midbrain. MYD88 L265P mutation was found by digital droplet PCR analysis of cfDNA extracted from CSF. The patient underwent a needle biopsy, and was diagnosed as diffuse large B-cell lymphoma. **CASE 2:** A 32-year-old man was diagnosed as having a demyelinating lesion after experiencing severe headaches. A small enhancing lesion was found in the right frontal lobe, and the patient was treated with steroids. The lesions repeatedly disappeared and reappeared and finally, stopped responding to steroids. MYD88 mutation was detected. A biopsy was performed, and the diagnosis was PCNSL. **CASE 3:** A 49-year-old man underwent a biopsy for a right frontal lesion after experiencing memory loss; the pathology showed broad T-cell infiltration but only some perivascular B-cells with slight atypia. The patient was tapered off steroids, and the lesion spread rapidly. An open biopsy was performed, but the pathology was not typical for B-cell lymphoma. The patient's symptoms rapidly worsened, and

whole brain irradiation was performed. At recurrence, MYD88 mutation was detected. **CASE 4:** An 82-year-old man presented with blurred vision. Vitreous humor biopsy was inconclusive for ocular lymphoma. A head MRI showed an intracranial lesion which spontaneously regressed. MYD88 was detected, and the patient is being closely observed. **CONCLUSION:** Detection of MYD88 mutation from cfDNA extracted from CSF can aid in the diagnosis of CNS lymphoma, especially in atypical cases.

#### ML-12

##### MECHANISMS OF CELL DEATH INHIBITION THROUGH CHANGE IN SUBCELLULAR LOCALIZATION OF PIM-1 BY PIM1 GENE MUTATION RECURRENTLY FOUND IN PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA.

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**BACKGROUNDS:** In a study of Next Generation Sequencing in primary central nervous system lymphoma (PCNSL), we have previously reported several mutations of high frequency, in comparison with systemic diffuse large B cell lymphoma (DLBCL)s. Consequences of these specific mutations in PCNSL are unknown. In this study, we have analyzed the functional consequence of mutations in the PIM1 gene, observed in 100% of PCNSL patients, which encodes a serine/threonine kinase and is known to drive tumorigenesis in several malignancies. **METHODS:** Four most frequent mutations of PIM1 in PCNSL, S77N, K115N, P216S, L275F, were chosen from our previous study, and each mutant was generated by site directed mutagenesis in PIM1 cDNA cloned in an expression vector. Resulting vectors were transiently transfected into human cancer cell lines. Functional studies were carried out using various biochemical methods. **RESULTS:** Among the four mutants, increased phosphorylation of BCL-2 associated death promoter (BAD) at Ser112, which is a phosphorylation target of Pim-1, was observed by expression of K115N mutant compared with wild type PIM1 in HeLa and Nagai cells expressing endogenous BAD. Decreased cell death under camptothecin treatment was also observed in K115N mutant expressing Nagai cells compared with wild type PIM1-expressed cells. We also observed a significant shift in subcellular localization of Pim-1 carrying K115N mutant; from the nucleus, main sublocalization for wild type Pim-1, into the cytosol determined by immunocytochemistry and immunoblotting of nuclear and cytosolic fraction of the cells. Augmented cytosolic localization of Pim-1 carrying K115N mutant was suppressed by inhibition of glycosylation. **DISCUSSION:** It is suggested that PIM1 K115N mutant may drive chemoresistance through increased BAD phosphorylation that suppresses cell death compared with wild-type PIM1 through modification of its subcellular localization, which might be regulated by its glycosylation status.

#### ML-13

##### AN ATTEMPT OF RECHALLENGE OF HD-MTX AND MAINTENANCE THERAPY OF MTX FOR PATIENTS WITH PCNSL

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**PURPOSE:** High dose methotrexate (HD-MTX) followed by radiotherapy (RT) is a standard therapy for primary CNS malignant lymphoma. However, the delayed neuronal toxicity due to RT is a serious problem especially for elderly patients. To avoid RT toxicity, we performed re-challenge of HD-MTX until complete remission (CR). Furthermore, we started maintenance therapy (MT) with MTX for elderly and poor Karnofsky Performance Scale (KPS) patients and reported the interim results. **METHODS:** We performed HD-MTX (3.5g/m<sup>2</sup>) therapy until achieving CR for patients whose ages were older than 70 years old and KPS were less than or equal to 60%. After having CR, 3 courses of MT of MTX (3g/patient) for 3 weeks were introduced every 3–4 months for 2 years. In cases of recurrence, HD-MTX was repeated. But when CR was not achieved by HD-MTX, RT was introduced. **RESULTS:** Number of patients was 8. Median age, median KPS, and median follow up periods were 73.5y.o. (71–78), 40% (30–60), and 4.5mo. (1–42), respectively. CR rate was 75% but two patients did not achieve CR. One patient had a complication of acute tubular necrosis just after first use of HD-MTX and another died due to pneumocystis pneumonia after 4<sup>th</sup> HD-MTX. Two patients without RT maintained CR and good KPS over 2 years. Four patients with RT maintained CR but their KPS gradually deteriorated. **DISCUSSION:** Rechallenge of HD-MTX exhibits better results and comparable safety with standard treatment, but RT was unavoidable. In order to avoid RT, we started MTX maintenance therapy for elderly and poor KPS patients before recurrence. Our maintenance therapy is easy and good disease control for patients who had not received RT, however there were two serious adverse events. **CONCLUSION:** Rechallenge of HD-MTX and maintenance therapy of MTX might be promising but dangerous for elderly patients. Further careful assessment is needed.