PCNSL (ML)

ML-3

A CASE OF PRIMARY CENTRAL NERVOUS SYSTEM ANAPLASTIC LYMPHOMA KINASE POSITIVE ANAPLASTIC LARGE CELL LYMPHOMA AT NEUROHYPOPHYSIS AND PINEAL GLAND.

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The majority of primary central nerve system (CNS) lymphomas (PCNSL) are diffuse large B-cell lymphomas. Anaplastic large cell lymphoma (ALCL) that is a type of T-cell tumor is very rare in the PCNSL. ALCLs are divided into two entities: anaplastic lymphoma kinase (ALK)-positive and ALK-negative. We report a case of a 26-year-old woman who presented with a one month historyof headache and nausea. Magnetic resonance imaging (MRI) of the brain revealed pituitary and pineal gland mass diagnosed as ALK-positive ALCL by endoscopic brain biopsy. She underwent chemotherapy following methotrexate (MTX) and cyclophosphamide + doxorubicin + vincristine + prednisolone (CHOP). The follow-up contrast-enhanced brain MRI showed no recurrent lesion after chemotherapy. In previous reports, most of the lesions were in cerebral hemisphere, dura mater and spinal cord. Many of these patients were given primary diagnoses of meningitis. To our knowledge, there is no case report of initial diagnosis of germinoma due to lesions in Neurohypophysis and pineal gland as in this case.

Key words: primary central nerve system lymphomas | naplastic large cell lymphoma | anaplastic lymphoma kinase | Neurohypophysis and pineal gland

ML-4

A CASE OF PRIMARY CNS LYMPHOMA DIAGNOSED 5 YEARS AFTER STEREOTACTIC RADIOSURGERY.

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Central nervous system primary malignant lymphoma (PCNSL) is rarely diagnosed as multiple metastatic brain tumors. Almost tumors recure early after receiving stereotactic radiosurgery (SRS). Regardless of the fact, the following case report displays PCNSL, diagnosed five years after the initial treatment with SRS as brain metastases of unknown primary origin. This extraordinal case suggests long-term follow-up regarding PCNCL. The case was a 55-year-old woman with a history of a total hysterectomy for cervical cancer. She developed left paralysis. Brain MRI confirmed a 27 mm contrast-enhanced lesion in the right frontal lobe and three other lesions. SRS was performed as a diagnosis of multiple brain metastases for urgent symptom relief. No extra-cranial cancerous lesions were found. Unknown primary cancer was a probable diagnosis at that time. Two years after SRS, local regrowth of tumor of the right frontal primary motor area was discovered. Re-irradiation was performed. Cerebral edema, contrast enhancement, and left paralysis progressed following five months, taking an oral corticosteroid. Craniotomy and debulk. The pathological diagnosis was brain radiation necrosis due to no viable tumor cells. New lesions in the left temporal lobe and basal ganglia appeared three years after surgery. Awake craniotomy was performed for the left temporal lobe lesion. Histopathology showed diffuse growth of tumor cells with a high nucleocytoplasmic ratio and irregular nuclear shape. Immunohistochemistry revealed positive CD10, CD20, CD45 (LCA), MUM1, and negative CD3, CD5. The Ki- 67 labeling rate was as high as almost 100% to diagnose diffuse large B-cell lymphoma, PCNSL. Multidrug chemotherapy consisting of rituximab, high-dose methotrexate, procarbazine, and vincristine were performed. Complete remission was obtained without any serious adverse events. Considering the residual radiation necrosis, whole-brain irradiation was avoided. Moreover, consolidation therapy was performed only with high-dose cytarabine therapy.

Key words: primary CNS lymphoma | stereotactic radiosurgery | delayed diagnosis

ML-7

LIQUID BIOPSY FOR MYD88 MUTATION IN CEREBROSPINAL FLUID IN PATIENTS WITH SUSPECTED PRIMARY CNS LYMPHOMA

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Background: Treatment intervention for central nervous system lymphoma (CNSL) requires pathological diagnosis by surgical biopsy. However, there are some cases in which the risk of surgery is high due to age, comorbidities, localization of lesions, etc. We are developing a CNSL diagnostic method based on the detection of MYD88 L265P mutation by digital PCR (dPCR) using CSF-DNA, and a high accuracy with a sensitivity of 92.9% and a specificity of 100% has been reported. Here, we report two cases with suspected brain stem CNSL, whose treatment strategy was determined by integrated clinico-laboratory information including neurological presentations, imaging, and the result of liquid biopsy. Result: Case 1. A 63-year-old woman visited our hospital with a complaint of right hemiplegia, which deteriorated in two months. MR images revealed a contrast-enhancing lesion in the left midbrain-ventral pons, suggesting CNSL. Biopsy was not considered because of its location, while dPCR using CSF-DNA showed a cluster of MYD88 mutation signals. Based on these work-ups, she was treated with high-dose methotrexate-based chemotherapy, resulting in a complete response with marked improvement of symptoms. Case 2. An 83-year-old man was referred for a history of diplopia and ataxic gait lasting for a month. MR images revealed an invasive lesion on his right midbrain-dorsal pons. Biopsy was declined due to the location, and liquid biopsy using CSF-DNA was performed to assist the diagnosis. In the first test, the CSF-DNA yield was too insufficient to determine the mutation signal by dPCR. The second dPCR using sufficient amount of CSF-DNA resulted in the Target/Total value of 0.049% which was lower than the threshold, suggesting the absence of MYD88 mutation. The patient underwent radiation therapy accordingly.Conclusions: CSF MYD88 mutation analysis by dPCR may have clinical utility and requires sufficient amount of CSF-DNA for exclusion of noise signals.

Key words: liquid biopsy | MYD88 | digital PCR

ML-10

TIRABRUTINIB, A SECOND-GENERATION BTK INHIBITOR IN RELAPSED AND REFRACTORY PRIMARY CNS LYMPHOMA: A SINGLE INSTITUTE STUDY

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BACKGROUND: The prognosis of relapsed and refractory (r/r) primary CNS lymphoma (PCNSL) is poor, and the development of new therapeutic agents is desirable. Comprehensive genetic analysis of PCNSL has shown that MYD88 and CD79B are frequently mutated and are oncogenic drivers, suggesting that Bruton's tyrosine kinase (BTK), which is located downstream of MYD88 and CD79B, may be a reasonable therapeutic target. Tirabrutinib is a second-generation oral BTK inhibitor recently approved in Japan for the treatment of r/r PCNSL. In this study, we evaluated the efficacy and safety of tiraburtinib treatment of r/r PCNSL at Saitama Medical University. MATERIAL AND METHODS: Eighteen patients with r/r PCNSL to HD-MTX-based regimens were treated with 480 mg tiraburtinib daily under fasting conditions until disease progression. RESULTS: The median age was 63.5 years, and the median KPS was 70. Nine patients (50%) achieved a CR, 2 (11%) had a partial response, 3 (17%) had stable disease, and 4 (22%) had progressive disease. After a median follow-up of 17.3 months, the median progression-free survival was 7.9 months, and the median overall survival was 23.6 months. There were four cases of long-term treatment lasting more than one year. Grade 3 or higher adverse events were observed in 1 case of maculopapular rash, 1 case of cardiac failure, 1 case of neutropenia, and 1 case of lymphopenia. CONCLUSION: Tiraburtinib can be administered relatively safely to patients with relapsed or refractory PCNSL, and a certain degree of efficacy can be expected. Which patients can be treated with tiraburtinib over the long term, when can stop tirabrutinib treatment for patients with long-term CR, and the mechanism of tiraburtinib resistance needs to be determined.

Key words: primary CNS lymphoma | Bruton's tyrosine kinase inhibitor | Tirabrutinib

ML-11

TIRABRUTINIB TREATMENT FOR RECURRENT OR REFRACTORY PCNSL

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Since 2020, tirabrutinib which is a Bruton's tyrosine kinase (BTK) inhibitor has been available for recurrent or refractory PCNSL cases. The number of studies reporting efficiency and adverse effect of tirabrutinib