ML-18

CLINICAL DIAGNOSIS FOR SUSPECTED PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA PATIENTS WITHOUT HISTOPATHOLOGICAL CONFIRMATION

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BACKGROUND: The gold standard of the diagnosis of primary central nervous system lymphoma (PCNSL) is the histopathological diagnosis by biopsy surgery. However, we experience some cases with a high risk of biopsy surgery or difficulty in general anesthesia. We perform radiation and chemotherapy without histopathological confirmation for such patients based on imaging findings, ophthalmological evaluation, and cerebrospinal fluid examinations. In this study, we investigated clinical diagnosis and outcomes for patients suspected PCNSL.

METHOD: From April 2016 to December 2019, all adult brain tumor patients that were diagnosed with PCNSL without histopathological confirmation and underwent radiation and/or chemotherapy were included. The following criteria were retrospectively analyzed. 1) Intraorbital lymphoma, 2) SUV_{max}>12 in ^{18}F FDG-PET, 3) ADC_{mean}<0.98×10^{-3} mm^2/s in MRI diffusion-weighted images, 4) tumor to normal ratio >1 in late phase of ^{123}I IMP SPECT, 5) CSF β2 microglobulin >2.1 mg/l, 6) CSF sIL2R >77 U/ml, 7) Improvement of imaging findings or clinical symptoms by steroid.

RESULT: 9 suspected PCNSL patients were included. 8 patients were positive for 3 or more above criteria. All these patients achieved CR by initial treatment with radiation or chemotherapy which indicated appropriate diagnosis for PCNSL. The remaining 1 patient was SD by radiotherapy, which was an atypical clinical course of PCNSL. The above criteria were positive in 2 and negative in 3. There were no examinations that could be performed in all cases before the treatment.

CONCLUSION: Some useful markers for the diagnosis of PCNSL have been reported. However, all have limited sensitivity and specificity. Each examinations are also restricted by patient, institution and time. The combination of the useful examinations will improve the diagnostic accuracy of PCNSL.

ML-20

OUTCOME OF HIGH-DOSE METHOTREXATE-BASED CHEMOTHERAPY WITH OR WITHOUT RITUXIMAB FOR PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA

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High-dose methotrexate based chemotherapy(HD-MTX) improved outcome of primary central nervous system lymphoma(PCNSL), but the prognosis is still poor. Recent studies showing that Rituximab is very effective for systemic lymphoma, the role of Rituximab for PCNSL is unclear. 34 patients diagnosed PCNSL received HD-MTX chemotherapy adding rituximab. Response rates were 74%(20/27) for newly diagnosed PCNSL patients, 85.7%(6/7) for recurrent PCNSL patients. Major side effects were infusion reaction and respiratory infections disease. We have to compare the outcome of HD-MTX chemotherapy retrospectively.

ML-21

TIRABRUTINIB MONOTHERAPY FOR RELAPSED/REFRACTORY PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA

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BACKGROUNDS & PURPOSE: Prognosis of patients with primary central nervous system lymphoma (PCNSL) remains poor despite multiagent immunochemotherapy, and standard of care for relapsed or refractory (r/r) PCNSL has not been established. Recent progresses on molecular genetics and biology of PCNSL have led to development of novel molecular targeted therapies, especially targeting Bruton's tyrosine kinase (BTK), located in the B-cell receptor and Toll-like receptor signaling pathways. Tirabrutinb, a second generation BTK inhibitor, was approved for r/rPCNSL in March 2020 in Japan. METHODS: Patients with r/rPCNSL treated with tirabrutinib since December 2017 were eligible for this retrospective study. Tirabrutinib was given orally at doses 320–480 mg/day daily until progression or unacceptable toxicity. RESULTS: A total of 7 patients were enrolled (6 relapses, 1 refractory), 4 males, median age was 73 (range, 54–80 years), and median KPS was 70 (70–90). Three patients had received prior whole brain radiotherapy. Median number of prior therapies was 1 (1–2). Best overall response rate was 57.1%; 42.9% with a complete response (CR/CRu), 14.3% with a partial response (PR), while there were 3 PDs (42.9%). Four patients experienced PD and estimated median progression-free survival (mPFS) was 29.6 months. All patients were alive at the data cutoff with median follow up of 21.4 months (2–30.4). Common adverse events (AEs) include grade 4 neutropenia (n=1), grade 3 lymphopenia (n=3), and hepatic dysfunction (n=1). Toxic rash was observed in four patients (grade 3 in one, grade 2 in three) leading to discontinuation of tirabrutinib in two patients, while others continued on TIR with dose reduction and steroid use. The median time to rash presentation was 28 days (12–28). CONCLUSIONS: Tirabrutinib was well tolerated with frequent minor to moderate skin rash emerging within one month and active for r/rPCNSL. Long-term efficacy and safety profile need to be determined with a larger cohort.

ML-23

THE OUTCOME OF MALIGNANT LYMPHOMA OF THE CENTRAL NERVOUS SYSTEM IN A SINGLE INSTITUTION

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BACKGROUND: Although high dose-methotrexate therapy has been performed for primary central nervous system malignant lymphoma (PCNSL), R-MPV (rituximab, methotrexate (MTX), procarbazine and vincristine) therapy is currently the first line therapy for (PCNSL) in our hospital. This study examines the results of R-MPV therapy comparing with past treatment. METHOD/SUBJECTS: Thirty-seven patients treated at our hospital from 2009 to 2020 were included. Overall survival time, progression free survival time, and toxicities were evaluated. RESULTS: The average age of patients was 65.7 years. Patients included 21 males and 16 females. Thirty-six patients were diagnosed DLBCL by resected brain tumor tissues, and one was diagnosed DLBCL by vitreous biopsy. As initial treatment, rituximab±HD-MTX therapy (R±MTX group) was performed in 20 cases, HD-MTX therapy plus radiation (R±MTX+RT group) was performed in 12 cases, and RMPV therapy was performed in 5 cases (R-MPV group). Median OS of all cases was 69 months and median PFS was 38 months. Median OS was 69 months in R±MTX group and could not be calculated in R±MTX+RT, and R-MPV groups. Median PFS was 16 months and 56 months in R±MTX group and R±MTX+RT, respectively, and could not be calculated in the R-MPV group. Although the R-MPV group had a short follow-up period, the results were considered to be comparable to those of the R±MTX+RT group. On the other hand, grade 3/4 adverse events occurred in 50%, 25%, and 100%, respectively. CONCLUSION: R-MPV therapy may delay the timing of radiation and reduce the amount of radiation. On the other hand, the frequency of adverse events is high, and more strict management of treatment is required.

CNS METASTASIS (MET)

MET-01

LINAC-BASED FRACTIONATED STEREOTACTIC RADIOTHERAPY WITH MICRO-MULTILEAF COLLIMETER FOR LARGE BRAIN METASTASIS UNSUITABLE FOR SURGICAL RESECTION

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To assess clinical outcomes using linac-based, fractionated, stereotactic radiotherapy (fSRT) with a micro-multileaf collimator for large brain metastasis (LBM) unsuitable for surgical resection. Between January 2009 and October 2018, we treated 21 patients with LBM using linac-based fSRT. LBM was defined as a tumor >30mm maximal diameter in gadolinium-enhanced magnetic resonance images. LBMs originated from the lung (n=17, 81%), ovary (n=2, 9.5%), rectum (n =1, 4.8%), and esophagus (n=1, 4.8%). The median pretreatment Karnofsky Performance Status was 50 (range: 50~80). Recursive partition analysis (RPA) was as follows: Classes 2 and 3 were 7 and 14 patients, respectively. The median follow-up was 5 months (range: 1~86 months). The range of tumor volume was 8.7~26.5 cm3 (median: 17.1 cm3). All patients were basically treated with fSRT ranged from 35 Gy with 7 Gy daily fractions, except in three cases. The progression-free survival was 3.0 months. The median survival time was 7.0 months. There was no permanent radiation injury in any of the patients. Radiation-caused central nervous system necrosis, according to the Common Terminology Criteria for Adverse Events version 4.0, occurred in one patient (grade 3). One patients received bevacizumab for radiation necrosis. Two patients underwent additional surgical resection due to local progression and cyst formation. For patients with LBM unsuitable for surgical resection, linac-based fSRT is a promising therapeutic alternative.