

toxicities was high (92%), but mostly manageable without major complications. Fourteen patients received 3 g/m², 4 patients received 2 g/m², 7 patients received 1 g/m² of cytarabine, and the rate of grade 4 leukopenia/thrombocytopenia was 64%/57%, 25%/50%, and 29%/29%, respectively. **DISCUSSION:** HD-cytarabine consolidation therapy with dose modification according to age groups for PCNSL was feasible and well-tolerated in patients 80 years of age or younger. The efficacy of HD-cytarabine was undetermined and further investigation is warranted.

ML-09

THE REAL-WORLD OF ELDERLY PCNSL THERAPY IN TOHOKU AND NIIGATA AREA ACCORDING TO RETROSPECTIVE ANALYSIS: A COLLABORATIVE INVESTIGATION OF THE TOHOKU BRAIN TUMOR STUDY GROUP

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INTRODUCTION: Recently, the number of cases of primary central nervous system lymphoma in elderly patients (EL-PCNSL) has been increasing. However, the treatment may be insufficient because of poor performance status and pre- and posttreatment complications. Therefore, we analyzed the risk factors for EL-PCNSL in the Tohoku and Niigata areas of Japan and clarified the REAL-WORLD of EL-PCNSL therapy. **MATERIALS & METHODS:** We investigated surgical and nonsurgical cases of patients aged 71 years or older from eight facilities during the last 8 years. We analyzed patient information, radiotherapy/chemotherapy or not, PFS, OS, RRs, second-line therapy, pre- and posttreatment complications, outcomes, and risk factors for poor prognosis. The log-rank test was used for univariate analysis, and Cox regression analysis was used for a multivariate analysis of risk factors. **RESULTS:** Of the 142 cases registered, five differed from PCNSL pathologically, three receiving BSC were excluded, 31 were treated without biopsy, three were treated based on CSF-findings, and 100 were treated with biopsy. Total 134 cases were followed. The median age was 76 years, pretreatment KPS was 50%, and 118 cases (88%) had 217 pretreatment complications. The treatment contents consisted of various combinations depending on the attending physician. The retrospective overall PFS was 16 months and OS was 24 months. In the early treatment phase, out of 16 cases with dropout, four tumor and four complication deaths occurred. There were 77 deaths (58%), 39 internal tumor deaths (51%), and 33 complication deaths (43%). Poor prognostic risk factors were <60% posttreatment KPS, complications involving pretreatment cardiovascular and central nervous system disease, posttreatment pneumonia or severe infection, and absence of radiation or chemotherapy. **CONCLUSIONS:** Pretreatment KPS did not affect poor outcomes, but posttreatment KPS <60% and pre- and posttreatment complications did. Radiotherapy and chemotherapy are reportedly effective, but additional research to clarify the details of these modalities is needed.

ML-13

THE PRIMARY TREATMENT OUTCOMES AND FUTURE PROBLEMS OF PCNSL ELDERLY PATIENTS IN OUR INSTITUTE

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BACKGROUND AND PURPOSE: Since the introduction of HD-MTX, cognitive symptoms after irradiation have become a problem mainly in elderly patients. In this study, we evaluated the treatment outcomes of over 70 years old PCNSL patients after HD-MTX introduction. **Subjects and METHODS:** From April 2009 to December 2019, there were 46 cases of PCNSL patients who had been treated in our institute. The HD-MTX treatment group had 42 cases and the R-MPV-A treatment group had 4 cases. In the HD-MTX treatment group, 30–40 Gy of whole brain irradiation was performed (n=32), but cases of SRS or no irradiation (n=10) were included due to poor PS. The R-MPV-A treatment group was performed with whole brain 23.4 Gy + local 21.6 Gy or no irradiation. The remission rate and outcome (mOS) were examined. **RESULTS:** The background of all 46 patients was 28 males and 18 females, with an average age of 75.8 years (70–87 years). The pathological diagnosis was DLBCL in all cases. The remission rate after chemotherapy in the HD-MTX treatment group was 52.4% (22/42). The post-irradiation remission rate was 78.6% in cases of whole-brain irradiation (n=14) among non-remission cases (n=20). The mOS of the whole-brain irradiation cases was 58.5 months (n=18) in the remission cases (n=22), but was 38.7 months (n=14) in the non-remission cases (n=20). The mOS of patients with SRS or

no irradiation (n=10) was 12.4 months. The R-MPV-A treatment group (n=4) had a remission rate of 100% after chemotherapy. Of the 26 cases whose cause of death could be identified in the HD-MTX treatment group, 58% (15/26) had tumor-related death and 30% (8/26) had pneumonia or suffocation. **CONCLUSION:** R-MPV-A has a high remission rate even in elderly patients, and if the irradiation dose can be reduced or avoided with R-MPV-A, ADL maintenance will be expected in elderly patients.

ML-14

RE-CHALLENGE AND MAINTENANCE THERAPY OF METHOTREXATE FOR ELDERLY PCNSL PATIENTS WITH LOW SCORED KPS

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PURPOSE: The delayed neuronal toxicity after high dose methotrexate (HD-MTX) followed by radiotherapy (RT) is a serious problem for elderly primary CNS lymphoma patients. We started maintenance therapy (MT) with MTX after achieving complete remission (CR) to defer RT for elderly and poor Karnofsky Performance Scale (KPS) patients.

METHODS: We performed HD-MTX (3.5g/m²) therapy until achieving CR for the patients over 70 years whose KPS were equal to or less than 60%. After having CR, 3 courses of MT of MTX (3g/patient) for 3 weeks were introduced every 3–4 months for 2 years. At the time of recurrence, HD-MTX was repeated. But when CR was not achieved by HD-MTX alone, RT was introduced. Moreover, additional use of rituximab was considered if patients' condition became better.

RESULTS: Number of patients was 9. Median age, median KPS, and median follow up periods were 73y.o. (71–78), 40% (30–60), and 14.0 months (1–55), respectively. CR rate was 78% and two patients were not achieved CR due to the adverse events (AEs) which were acute tubular necrosis and pneumocystis pneumonia. But meanwhile, there was no AE by MT. Median OS, median PFS, median time of radiation free period and delayed neuronal toxicity were 19.5 months (95%CI 3-NA), 5.0 months (95%CI 2–22), 2.5 months, and 8.2 months, respectively.

DISCUSSION: The results of this study might be inferior to other reports of elderly patients due to poor median KPS. And low introduction rate of MT was undesirable. However, once MT was introduced, MT itself was safe and easy to manage and the long-term prognosis was excellent.

CONCLUSION: Rechallenge of HD-MTX and maintenance therapy of MTX might be promising but the problems of some serious AEs and low CR rate with HD-MTX alone should be resolved.

ML-15

THE FUTURE DIRECTION OF TREATMENT DEVELOPMENT FOR PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA (PCNSL)

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PURPOSE: We found that the combination of high-dose Methotrexate (HD-MTX)-based therapy and histone deacetylase inhibitor (HDACI) had a therapeutic effect on PCNSL. In addition, this year, tirabrutinib, a Bruton's tyrosine kinase inhibitor, was approved for marketing as a single agent for relapsed/refractory PCNSL, and new therapeutic development is expected. We will examine the treatment results of PCNSL in our department retrospectively and discuss the future direction of treatment development. **METHODS:** From 2001 to 2014, 82 newly diagnosed PCNSL patients treated with HD-MTX/Procarbazine (MP) as initial remission induction chemotherapy were retrospectively analyzed. **RESULTS:** Complete response (CR) was obtained in 38 patients (46.3%) after initial chemotherapy, and the median overall survival (OS) in the CR and non-CR groups was 2636 days and 728 days, respectively, and significantly shorter in the non-CR group (p<0.01). In the CR group, 27 cases (71.1%) recurred and 12 cases received HD-MTX re-challenge (M-re), 14 cases received treatment other than M-re (1 case did not receive treatment), the median OS after relapse was 590 days. The median post-relapse progression-free survival (PFS) of the 10 patients undergoing M-re at the first relapse was 116 days, the median OS after relapse was 590 days. The median post-relapse PFS of 16 patients receiving other treatments was 428 days, the median OS after relapse was 532 days. There was no difference in PFS and OS after recurrence in treatment at the first recurrence (p=0.15, p=0.55). **CONCLUSION:** The OS of non-CR patients in the initial chemotherapy and the OS after recurrence after CR were short. The possible directions of PCNSL treatment development include 1) increasing the CR rate with initial chemotherapy and maintaining CR for a long time for newly diagnosed PCNSL, and 2) finding an effective treatment for recurrence. New drugs such as tirabrutinib and HDACIs may be breakthroughs.