

NQPC-14

COMPARISON OF QOL SCALES IN PATIENTS WITH BRAIN TUMORS

Natsuko Tsushita Satomi¹, Ruriko Miyahara¹, Takaki Omura¹, Masamichi Takahashi¹, Makoto Ohno¹, Yasuji Miyakita¹, Yoshitaka Narita¹; ¹Department of Neurosurgery and Neuro-Oncology, National Cancer Center Hospital, Tokyo, Japan

PURPOSE: Measurement of quality of life (QOL) of patients with brain tumors is a challenge, because parameters of the established QOL scales for cancer patients are easily affected by the focal neurological deficits. Thus, simpler QOL scales which are feasible for evaluation of QOL with severe neurological deficits are required. We compared the results of four QOL scales in patients with brain tumors. **METHODS:** From 2015 to 2018, we prospectively performed EORTC QLQ-C30/BN20 (C30/BN20), KPS, EQ-5D and "Distress and Impact Thermometer (DIT)" every three months. **RESULTS:** 2150 QOL evaluations from 710 patients were analyzed. The median age was 54 years (range 14–97). 319 glioma, 93 meningioma, 165 brain metastases and 133 other brain tumors were included. Global health status of C30/BN20 strongly correlated with QOL scores calculated by EQ-5D and DIT; it also showed correlation with KPS (correlation coefficients: 0.632, -0.675, -0.622, 0.412, respectively ($p < 0.001$)). Most items of C30/BN20 showed relatively strong correlation with QOL scores, whereas KPS strongly correlated to physical activities and DIT strongly correlated to items related to psychological status. Seizures did not correlate with any other QOL scales. In patients with KPS \leq 60, wide dispersion of QOL scores and DIT were observed. In these patients, KPS correlated only with items 1–3 of EQ-5D and DIT with item 5. When time course of QOL scores in malignant glioma was evaluated, it was maintained until first remission, and significantly impaired at recurrence, compared to onset ($p = 0.014$). **CONCLUSION:** QOL scores can be used as an alternative for C30/BN20, and QOL time course of glioma can be adequately evaluated with it. KPS and DIT can also be alternative scales. These two scales should desirably be used in combination in patients with low KPS. Evaluations of feasibility and validity of these QOL scales in patients who cannot answer C30/BN20 are warranted.

NQPC-15

COGNITIVE FUNCTION AND ACTIVITY OF DAILY LIFE AFTER TUMOR REMOVAL FOR PATIENTS WITH BIFRONTAL GLIOBLASTOMA

Akiko Kakuta¹, Masayuki Nitta, Takashi Maruyama, Yoshihiro Muragaki, Tetsuo Ikai; ¹Department of rehabilitation, Tokyo Women's Medical University

INTRODUCTION: Glioblastomas often grow in a butterfly shape in the bifrontal lobes. The aggressive removal of these contrast-enhanced lesions may cause serious cognitive dysfunction. In this study, we have analyzed changes of cognitive function, effects on ADL, as well as rehabilitation methods for patients with bifrontal glioblastoma before and after tumor removal. **SUBJECTS:** In this study, 6 patients including 2 males and 4 females with a mean age of 39.8 were reviewed. All patients exhibited bifrontal glioblastoma that was surgically removed. The primary tumor location was lower-left frontal gyrus for four of the patients, the right preSMA-SMA region for one patient, and the lower-right frontal gyrus for the remaining patient. **METHOD:** Patients' cognitive function and ADL evaluated after the tumor removal and at the end of postoperative chemoradiotherapy, were retrospectively analyzed. We compared and verified the features and EOR. An evaluation was performed using MMSE-J, FAB, TMT, RCPM, RBMT, BADS, and FIM. **RESULT:** After completion of chemoradiotherapy, 3 patients returned home, 2 were transferred to the hospital, and 1 returned to work. MMSE score was worsen in two patients, and their tumor were located in the lower-right frontal gyrus and the lower-left frontal gyrus. Two cases in the right frontal lobe and two cases in the lower left frontal gyrus scored lower average on the TMT. In our final evaluation, ADL was not worsening after surgery. **DISCUSSION:** Many patients with bifrontal glioblastoma exhibited disturbance of consciousness due to strong edema before surgery, but they recovered in about two months after the tumor removal and many of them considered back to work. Involvement of prefrontal cortex may be related to severe cognitive dysfunction. Active rehabilitation should be started as soon as possible after surgery to acquire a compensation functions for the cognitive disorders and simulation for social life and work.

PCNSL (ML)

ML-02

MULTIAGENT IMMUNOCHEMOTHERAPY, R-MPV-A, FOR PATIENTS WITH SECONDARY CENTRAL NERVOUS SYSTEM LYMPHOMA

Motoo Nagane¹, Keiichi Kobayashi¹, Kuniaki Saito¹, Daisuke Shimada¹, Yoshie Matsumoto¹, Shohei Iijima¹,

Nobuyoshi Sasaki, Yuki Yamagishi, Nobuyuki Takayama, Yoshiaki Shiokawa¹; ¹Department of Neurosurgery, Kyorin University School of Medicine, Tokyo, Japan

BACKGROUNDS: Standard of care (SOC) for primary central nervous system lymphoma (PCNSL) has been induction therapy with high-dose methotrexate (MTX)-based multiagent immunotherapies followed by consolidation, and we have shown that one such regimen, R-MPV-A have superior efficacy over HD-MTX alone with whole brain radiotherapy (WBRT). While SOC for secondary CNS involvement of systemic diffuse large B-cell lymphoma (DLBCL)(SCNSL) has not been established. Here we report the outcome of R-MPV-A for patients with SCNSL. **PATIENTS AND METHODS:** Fifteen patients with SCNSL treated with R-MPV-A from January 2014 to January 2019 in Kyorin University Hospital were eligible. Prior treatment for systemic DLBCL was mostly R-CHOP. Response and survival outcomes were evaluated. **RESULTS:** Median age was 68.0 y (55–84), male/female 6/9, median KPS 70 (40–90), histopathological confirmation was achieved in 12 patients (80%; biopsy 11). RMPV (rituximab+MTX+procarbazine+vincristine) 3 cycles in 3, 4–7 cycles in 6, 8 cycles in 5. WBRT and cytarabine were delivered in 6 and 9 patients, respectively. R-MPV resulted in 6 CRs/CRus, 5 PRs, 1 SD, and 2 PDs (Response rate 73%). R-MPV-A including consolidation led to 9 CRs/CRus, 2 PRs, 1 SD, and 2 PDs (complete response rate 60%). With median F/U period of 11.2 m (0.1–51.5), 1y-PFS and 2y-PFS of R-MPV-A were 66.0% and 56.6%, 1y-OS and 2y-OS were 72.2% and 72.2%, respectively. Median PFS/OS were not reached. Consolidation cytarabine was associated with better outcome. Three deaths occurred during the treatment (20%; two during R-MPV with aged 70s, KPS 40 and 50; one presented MTX clearance delay). No other serious adverse events were observed. **CONCLUSIONS:** These results suggest the certain efficacy of R-MPV-A for SCNSL. Being heavily pretreated frequently, precautions should be taken to identify high risk cases.

ML-03

RECONSIDERATION OF TREATMENT FOR ELDERLY PATIENTS WITH PRIMARY CENTRAL NERVE SYSTEM LYMPHOMAS

Naoki Shinojima¹, Kenji Fujimoto, Keishi Makino, Takahiro Yamamoto¹, Jun-ichiro Kuroda¹, Kazutaka Ohta¹, Tatsuya Takezaki¹, Kazutaka Oda, Kazumi Nakamura, Hiroshi Jono, Yoshiaki Mikami, Akitake Mukasa¹; ¹Department of Neurosurgery Kumamoto University Hospital

BACKGROUND: The therapeutic response to high-dose methotrexate therapy (HD-MTX) for primary central nervous system lymphoma (PCNSL) varies. Polyglutamylation (PG) is a reversible protein modification, tumor cells show frequent occurrence of PG. Intracellularly polyglutamylated MTX is not subject to competitive inhibition by leucovorin (LV). Tumor cells with high PG levels are selectively killed, whereas normal cells with lower PG are rescued by LV. We previously reported that PG is a predictor of therapeutic response to HD-MTX in PCNSL. However, PG did not affect overall survival (OS) in the elderly unlike the young patients, suggesting that there are other significant predictors in the elderly. The aim of this study is to identify the prognostic factors in aged PCNSL. **METHODS:** The prognostic factors were investigated in 48 patients (M/F=23/25) aged 65 and older undergoing HD-MTX in our institute with data of area under the concentration-time curve of MTX, AUC_{MTX} ($\mu\text{mol/L/h}$). **RESULTS:** The median OS of elderly PCNSL was 937 days. In the AUC_{MTX} high group (median 1706.3 or more, n=24) and the low group (median below, n=24), OS was significantly shortened in the high group compared with the low group (median 728 vs 1290 days, $p = 0.032$). Even in multivariate analysis, AUC was the only independent poor prognostic factor of OS ($p = 0.031$). On the other hand, AUC was not a prognostic factor for OS in PCNSL younger than 65 years. AUC_{MTX} of aged PCNSL was significantly higher compared with younger patients ($p < 0.01$). These results suggested that PG may be a good prognostic factor of OS when AUC_{MTX} is low. **CONCLUSION:** In the aged PCNSL, OS was shortened when AUC_{MTX} was high. With the results of the previous research, it is suggested that if PG levels is high in elderly PCNSL, the OS prolongation can be expected if the MTX dose is reduced.

ML-04

PROGNOSTIC SIGNIFICANCE OF IMMUNOHISTOCHEMICAL SUBTYPES BASED ON THE STAGE OF B-CELL DIFFERENTIATION IN PRIMARY CNS LYMPHOMA

Akihiro Inoue¹, Shohei Kohno, Shirabe Matsumoto¹, Satoshi Suehiro¹, Masahiro Nishikawa¹, Saya Ozaki¹, Hideaki Watanabe¹, Takanori Ohnishi, Takeharu Kunieda¹; ¹Department of Neurosurgery, Ehime University School of Medicine, Ehime, Japan

PURPOSE: Primary central nervous system lymphoma (PCNSL) has been immunohistochemically classified into two subtypes, germinal center (GC) B-cell and non-GC B-cell, but prognostic impact of these subtypes

remains debated. We investigated clinical features and prognostic significance of newly defined immunohistochemical subtypes that were identified by expression patterns of three B-cell differentiation markers in PCNSL. In addition, we analyzed a factor related to responsiveness to high-dose methotrexate (HD-MTX) chemotherapy. **METHODS:** Tumors from 32 PCNSL patients were immunohistochemically evaluated regarding expression of CD10, BCL-6, and MUM-1 and classified into subtypes according to the expression patterns of these markers. Clinical features and prognostic outcome of these subtypes were investigated. **RESULTS:** Twenty-three patients were treated with HD-MTX-based chemotherapy followed by whole-brain radiation therapy (WBRT), and nine were treated with WBRT alone. Three immunohistochemical subtypes were identified, including A-type expressing CD10, BCL-6, and MUM-1 (12 patients), B-type expressing BCL-6 and MUM-1 (12 patients) and C-type expressing MUM-1 only (8 patients). Response rate in the HD-MTX therapy group was 57.1% (4/7) in A-type, 87.5% (7/8) in B-type, and 75% (6/8) in C-type. C-type with the lowest metabolic activity showed significantly longer overall survival than A-type with the higher uptake of methionine (71.6 versus 39.6 months). **CONCLUSIONS:** Immunohistochemical identification of PCNSL based on the B-cell differentiation stage revealed three types of tumors, showing different metabolic activity and survival time. Refined immunohistochemical classification of PCNSL subtypes may become a useful tool for predicting more accurate prognosis and accessing the sensitivity to HD-MTX therapy.

ML-05

A CASE OF NEUROLYMPHOMATOSIS ARISING SECONDARILY FROM PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA

Keishi Horiguchi¹, Hirofumi Asano¹, Tadashi Osawa¹, Masahiko Tosaka¹, Yuhei Yoshimoto¹; ¹Department of Neurosurgery, Gunma University, Maebashi, Japan

A woman in her 40s. A biopsy of multiple intracranial lesions was performed, and the patient was diagnosed with DLBCL. As an initial treatment, 6 courses of high dose MTX therapy were performed and CR was achieved. Radiation therapy was not desired by the patient. On the 19th month after initial treatment, tumor recurrence was confirmed by MRI and added 2 courses of HD-MTX. On the 23rd month, second recurrence around the left basal ganglia were observed. One additional course of HD-MTX was performed, but due to the appearance of renal damage that was thought to be acute tubular necrosis, additional HD-MTX was not performed and whole brain irradiation was performed. She began complaining of pain in the trunk and extremities during radiation. When MRI and FDG-PET were performed in the 25th month, multiple lesions were found in the ganglia, plexus, and peripheral nerves from the cervical spinal cord to the sacral spinal cord. Cerebrospinal fluid cytology revealed atypical lymphocytes and lymphoma dissemination in the spinal cord. When intrathecal administration of the anticancer agent was performed nine times weekly, the CSF cytology was negative. Imaging findings showed that the lesions relapsed, although the lesions were temporarily reduced. After confirming that the renal function had recovered, two additional courses of HD-MTX were performed. Accumulation of FDG-PET in the lesion disappeared in the 29th month. However, peripheral neuropathic pain and paraplegia remained. **Discussion:** Neurolymphomatosis is considered to be a clinically rare disease that presents invasion of lymphoma into peripheral nerves including the cranial nerves, nerve roots or plexus. Diagnosis of NL has been required to be proved by nerve biopsy or autopsy, but noninvasive FDG-PET has been reported to be effective. In this case, CR was not obtained with anticancer drug intrathecal injection, and HD-MTX therapy was successful.

ML-07

R-MPV-A THERAPY FOR PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA IN THE ELDERLY: OUTCOME AND PROBLEM

Hirota Fudaba¹, Yasutomo Momii¹, Kouhei Onishi¹, Daigo Asou¹, Minoru Fujiki¹; ¹Department of Neurosurgery, Faculty of Medicine, Oita University, Oita, Japan

PURPOSE: R-MPV-A therapy has recently been reported to improve the outcomes of primary central nervous system lymphoma (PCNSL). Our patients have received R-MPV-A therapy since 2017 and elderly patients have only been treated with whole brain radiotherapy when they do not show a complete response after induction chemotherapy. We report the therapeutic outcomes and problems of elderly PCNSL patients treated with R-MPV-A. **MATERIALS & METHODS:** Eight newly diagnosed PCNSL patients received R-MPV therapy from September 2017 to June 2019. We retrospectively reviewed the cycles of R-MPV therapy, radiotherapy, consolidation high-dose Ara-C (HD-Ara-C) therapy, and the G8 score (a geriatric assessment). **RESULTS:** Patients were divided into three groups: Group A (71–75 years; n=2), Group B (76–80 years; n=4), and Group C (>81 years; n=2). All Group A patients finished 5 cycles of R-MPV therapy, showed a complete

response, and underwent consolidation HD-Ara-C therapy. Two Group B patients showed a complete response on R-MPV therapy. One of the other patients showed a partial response after 3 cycles of R-MPV therapy, and a >3 kg reduction in body weight. The patient's G8 score was 12 points. Whole brain radiotherapy (23.4 Gy) was administered followed by local radiotherapy (21.6 Gy). One patient showed a partial response after 7 cycles of R-MPV therapy and started radiotherapy. One Group C patient received radiotherapy after 3 cycles of R-MPV because of a new lesion. The other Group C patient showed acute renal damage after 3 cycles of R-MPV. **CONCLUSION:** R-MPV-A therapy was relatively safe for our elderly PCNSL patients. Notably, patients >76 years of age sometimes had severe adverse effect with increased R-MPV cycles. A promising therapeutic strategy based on age and geriatric assessment is needed.

ML-08

THE ROLE OF MAINTENANCE HIGH-DOSE METHOTREXATE CHEMOTHERAPY IN ELDERLY PRIMARY CNS LYMPHOMA PATIENTS

Kazuhiro Mishima¹, Mitsuki Shirahata¹, Jun-Ichi Adachi¹, Tomonari Suzuki¹, Takamitsu Fujimaki¹, Ryo Nishikawa¹; ¹Department of Neuro-Oncology/Neurosurgery, Saitama Medical University, Saitama, Japan

BACKGROUND: The addition of high-dose methotrexate (HD-MTX)-based chemotherapy to whole brain irradiation (WBRT) has improved the prognosis of primary central nervous system lymphoma (PCNSL). However, the high neurotoxicity rates observed, especially in the elderly, raised interest in chemotherapy-only treatments. Withholding radiotherapy substantially decreases the risk of neurotoxicity, however, disease control may be compromised. In the elderly who cannot tolerate WBRT as a consolidation, maintenance treatment may serve as a feasible approach after an initial response. We treated ePCNSL with induction immunochemotherapy, maintenance chemotherapy with HD-MTX and deferred WBRT. Here, we retrospectively investigated the prognosis for ePCNSL that became CR after the induction chemotherapy. **MATERIAL AND METHODS:** Newly diagnosed ePCNSL (median age: 74 years) received biweekly rituximab/HD-MTX for 6 cycles (induction) followed by monthly rituximab/HD-MTX for 2 cycles (consolidation) and then were treated differently according to the radiological response. With CR patients, HD-MTX was continued with every 3 months (maintenance) for 2 years. Patients who did not obtain consent for maintenance therapy were followed up. For PD patients, immunochemotherapy was interrupted and WBRT initiated immediately. Patients with PR and SD were treated with alternative chemotherapy with temozolomide and/or stereotactic radiotherapy or WBRT. **RESULTS:** The median PFS was 24.6 months and median OS was 27 months for the entire cohort. Of the 42 ePCNSL, 26 had CR after induction and consolidation, of which 18 cases were carried out maintenance (M+) and 8 cases were followed up (M-). Median PFS was 73 months in the M+ group and 24.5 months in the M- group. Median OS is 102.2 months versus 27.6 months, respectively. Both mPFS (P=0.0125) and mOS (P=0.0015) were significantly prolonged by maintenance therapy. **CONCLUSION:** It was suggested that maintenance treatment with HD-MTX may improve the prognosis for ePCNSL that reached complete response after induction therapy.

ML-09

DIAGNOSIS AND TREATMENT OF PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA IN HIV POSITIVE PATIENTS

Koji Takano¹, Keisuke Nishimoto¹, Hiroki Yamazaki¹, Koki Murakami¹, Tetsuro Tachi¹, Tomoki Kidani¹, Yonehiro Kanemura¹, Shin Nakajima¹, Tomohito Masuda, Tomomi Kurusu, Kazuyuki Hirota, Takashi Uechi, Dai Watanabe, Yasuharu Nishida, Tomoko Uehira, Toshiyuki Fujinaka¹; ¹Department of Neurosurgery, National Hospital Organization Osaka National Hospital, Osaka, Japan

INTRODUCTION: HIV infection is known to cause a variety of central nervous system complications, such as malignant lymphoma (ML), toxoplasma encephalopathy, cryptococcal encephalopathy, progressive multifocal leukoencephalopathy (PML), brain tuberculosis and HIV encephalopathy. In our hospital, we performed brain biopsy for HIV-positive patients with central nervous system lesions suspected malignant lymphoma, or cases difficult to diagnose with blood, cerebrospinal fluid, and imaging alone. In this study, we retrospectively examined HIV-positive patients who underwent brain biopsy at our hospital, and analyzed diagnosis and treatment of patients with ML. Methods HIV-positive patients who underwent brain biopsy in our hospital from January 2010 to April 2019 were examined in this study. We analyzed background factors, preoperative examination results, pathological diagnosis, treatment and prognosis. **RESULTS:** There were 1,894 HIV-positive patients who were treated at our hospital during the