(1.34.0) and Rtsne (0.15) packages. [Result] Twenty-three out of 54 IDHwt LGGs matched known methylation classes using the DKFZ methylation classifier. In t-Distributed Stochastic Neighbor Embedding clustering analysis, 20 cases formed a cluster within the methylation class family glioblastoma, IDH-wildtype, mainly subclass RTK I ("GBM" cluster). Another 29 IDHwt LGGs formed an independent cluster ("LGG" cluster) separate from any of the existing reference groups near but not overlapping with several subtypes of pediatric-type lower grade gliomas. The "LGG" cluster cases had significantly longer overall survival than the "GBM" cluster cases. Discussion: Methylation profiling showed that IDHwt LGGs without molecular features of GBM were heterogeneous group of tumors. Our data suggested the presence of "true" IDHwt LGGs with intermediate prognosis.

Key words: glioma | IDH-wildtype | DNA methylome

MPC-2

CLINICAL COURSE AND PROGNOSIS OF LOWER-GRADE GLIOMA, IDH WILDTYPE AND PTERT MUTANT

Yoshinobu Takahashi[1], Hayato Takeuchi[1], Seisuke Tanigawa[1], Takanari Okamoto[1], Naoya Hashimoto[1]; [1]Department of Neurosurgery, Kyoto Prefectural University Graduate School of Medical Science, Kyoto, Japan

Background and Purpose: In the cIMPACT-Now update 3, it was proposed that grade 2 astrocytic gliomas without IDH-mutations and grade 3 astrocytic gliomas with TERT promoter mutations should be designated as diffuse IDH wildtype astrocytic glioma with molecular features of WHO grade IV glioblastoma. Therefore, we investigated whether this group of tumors actually corresponds to grade IV prognostically in cases that we encountered ourselves. Cases and Methods: Among the 65 patients having primary astrocytic glioma who were operated in our hospital from January 2016 to March 2021, the prognostic values of seven patients with lower-grade glioma, IDH wildtype, and pTERT mutant were investigated. Results: Among the seven patients, the median age was 59 years (50–66 years). Four of them had anaplastic astrocytoma, two had diffuse astrocytoma, and no tumor lesion could be identified upon histological examination for one patient. The male-to-female ratio was 1:6. MGMT methylation was observed in two patients (29%). The median survival was 20 months, with a significantly worse prognosis when compared with lower-grade glioma without the TERT promoter mutation (13 patients: median survival 40 months), but a better prognosis when compared with glioblastoma (45 patients: median survival 13 months) (Log-rank p = 0.0051). Conclusion: Although EGFR amplification, combined whole chromosome 7 gain, and whole chromosome 10 loss were not examined, the prognostic value of lower-grade glioma, IDH wildtype, and pTERT mutant was not as poor as that of glioblastoma. Further investigation is required to confirm whether these groups of tumors should be treated in the same way as grade IV glioblastoma.

Key words: lower grade glioma | TERT | prognosis

MPC-4

MALIGNANT TRANSFORMATION OF DIFFUSE LOW-GRADE GLIOMAS: SYSTEMATIC REVIEW AND META-ANALYSIS

Satoshi Nakasu[1], Yoko Nakasu[2]; [1]Division of Neurosurgery, Kusatsu General Hospital, Kusatsu, Japan [2]Shiga University of Medical Science

While malignant transformation of diffuse low-grade glioma (LGG) is a critical event affecting the patient survival, the incidence and related factors have been inconsistent in the literature. According to the PRISMA guideline, we systematically reviewed articles from 2009, meta-analyzed the incidence of malignant transformation and clarified factors related to the transformation. Forty-one articles were included in this study (n = 7122). We identified two definitions of malignant transformation: histologically proven (Htrans) and clinically defined (Ctrans). The malignant transformation rate curves in Htrans and Ctrans were almost in parallel when calculated from the results of meta-regression by the mean follow-up time. The true transformation rate was supposed to lie between the two curves, namely about 40% at the 10-year mean follow-up. Risk of malignant transformation was evaluated by the hazard ratio (HR). Pooled HRs were significantly higher in tumors with a larger pre- and postoperative tumor volume, lower degree of resection and notable preoperative contrast enhancement on magnetic resonance imaging than in others. Oligodendroglial histology and IDH mutation (IDHm) with 1p/19q codeletion (Codel) also significantly reduced the HRs. Using Kaplan-Meier curves from 8 studies with molecular data, we extracted data and calculated the 10-year malignant progression free survival (10yMPFS). The 10yMPFS in patients with IDHm without Codel was 30.4% (95% confidence interval (95%CI) [22.2–39.0]) in Htrans and 38.3% (95%CI [32.3–44.3]) in Ctrans, and that with IDHm with Codel was 71.7% (95%CI [61.7–79.5]) in Htrans and 62.5% (95%CI [55.9–68.5]) in Ctrans. The effect of adjuvant radiotherapy or chemotherapy could not be determined.

Key words: low-grade glioma | malignant transformation | 1p19q codeletion

MPC-5

CHARACTERISTICS OF H3 G34-MUTANT GLIOMAS

Yuji Kibe[1], Fumiharu Ohka[1], Kazuya Motomura[1], Kosuke Aoki[1], Sachi Maeda[1], Masaki Hirano[1], Tomohide Nishikawa[1], Junya Yamaguchi[1], Shintaro Yamazaki[1], Atsushi Natsume[1], Ryuta Saito[1]; [1]Department of Neurosurgery, Nagoya University Graduate School of Medicine, Aichi, Japan

Introduction: Diffuse hemispheric gliomas, H3 G34-mutant (DHG H3G34-mutant) are newly recognized infiltrating gliomas of the cerebral hemispheres of pediatric and young adult patients. We experienced 6 DHG H3G34-mutant cases. In this study, we describe the clinical, radiological and pathological characteristics of these cases. Result: Mean age at diagnosis was 16.8 years (range:10–26). Three patients were male. Among six cases, tumors located in cerebral cortex in five cases and multiple sites including basal ganglia and cortex in a case. All tumors showed no or only a faint contrast-enhancement and harbored restriction of diffusion. One patient underwent total resection, four underwent partial resection and one underwent biopsy. Pathological diagnosis were CNS embryonal tumors (n=3/6), glioblastoma, IDH-wildtype (n=2/6) and anaplastic astrocytoma, IDH-wildtype (n=1/5). All cases were negative for Olig2 and positive for GFAP in immunohistochemistry. Mean Ki-67 index was 38% (range: 10–60%). All cases revealed at least one of mitosis, necrosis or microvascular proliferation. Especially, mitosis was the most frequently found (n=5/6). The *H3F3A* mutations were G34R mutations in all cases. One case revealed a characteristic mutation pattern, therefore now we are performing further examination. Adjuvant chemoradiotherapies were performed for all cases. Mean progression free survival was 10.1 months (range: 1.6–33.1). Discussion: As published literatures reported, all cases exhibited restriction of diffusion and negative for Olig2. For a cerebral hemispheric tumor of pediatric or young adult patient which shows restriction of diffusion and no contrast-enhancement, and of which pathological findings is malignant and olig2 is negative, genetic analysis of *H3F3A* gene might be essential.

Key words: Glioma | H3 G34-mutant | Diffuse Hemispheric Glioma

MPC-6

CLINICAL SIGNIFICANCE OF WHOLE CHROMOSOMAL ABERRATION SIGNATURES IN NON-METASTATIC MEDULLOBLASTOMAS TREATED WITH 18GY OF CRANIOSPINAL IRRADIATION

Kohei Fukuoka[1], Jun Kurihara[2], Makiko Mori[1], Yuki Arakawa[1], Ema Yoshioka[3], Tomoko Shofuda[3], Yuko Matsushita[4], Yuko Hibiya[4], Satoko Honda[5], Atsuko Nakazawa[5], Chikako Kiyotani[6], Naoki Kagawa[7], Kai Yamasaki[8], Ryo Ando[9], Dai Keino[10], Yosuke Miyairi[11], Atsushi Sasaki[12], Ryo Nishikawa[13], Isao Date[14], Motoo Nagane[15], Katsuyoshi Koh[1], Koichi Ichimura[4], Yonehiro Kanemura[3]; [1]Department of Hematology/Oncology, Saitama Children's Medical Center, Saitama, Japan [2]Department of Neurosurgery, Saitama Children's Medical Center [3]Department of Biomedical Research and Innovation, Institute for Clinical Research, Osaka National Hospital, National Hospital Organization [4]Division of Brain Tumor Translational Research, National Cancer Center, Research Institute [5]Department of Clinical Research, Saitama Children's Medical Center [6]Children's Cancer Center, National Center for Child Health and Development [7]Department of Neurosurgery, Osaka University Graduate School of Medicine [8]Department of Pediatric Hematology and Oncology, Osaka City General Hospital [9]Department of Neurosurgery, Chiba Children's Hospital [10]Division of Hematology/Oncology, Kanagawa Children's Medical Center [11]Department of Neurosurgery, Nagano Children's Hospital [12]Department of Pathology, Saitama Medical University [13]Department of Neuro-Oncology/Neurosurgery, Saitama Medical University International Medical Center [14]Department of Neurological Surgery, Okayama University Graduate School [15]Department of Neurosurgery, Kyorin University Faculty of Medicine

Background: One of the most significant challenges is a reduction in the dose of craniospinal irradiation (CSI) in patients with medulloblastoma to minimize neurological sequelae. However, a North American clinical trial failed to show the prognostic non-inferiority of lower-dose irradiation compared to that associated with standard-dose radiation therapy for non-metastatic medulloblastomas. A European retrospective study revealed that whole chromosomal aberration signatures (WCASs) are a potential prognostic factor in Group 3/4 medulloblastoma without metastasis, but whether the molecular signature has the same clinical impact in patients treated with lower-dose CSI remains unknown. Methods: We conducted DNA methylation analysis using an Illumina Infinium Human Methylation EPIC BeadChip array