(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

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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

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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

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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

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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

to investigate molecular prognostic markers in 23 medulloblastoma patients who were registered in the Japan Pediatric Molecular Neuro-Oncology Group and treated with lower-dose CSI relative to standard treatment. A WCAS was defined as the presence of at least two of three chromosomal changes as follows: chromosome (chr) 7 gain, chr 8 loss, and chr 11 gain.Results: All patients presented with no residue or a residual tumor smaller than 1.5 cm2 after surgery without metastasis. The median age at onset was 6.9 years, and the median follow-up period was 80.6 months. CSI was delivered at a median dose of 18.0 Gy. Regarding molecular subgrouping, there were 5 WNT, 2 SHH, 1 Group 3, and 15 Group 4 medulloblastomas. Seven patients with Group 3/4 medulloblastomas showed WCASs and had significantly better prognosis than those without the alteration (5-year progression-free survival 100% vs. 63%, p = 0.046). Two late relapses occurred at 89 and 115 months after diagnosis, respectively, and one of these patients presented with a WCAS.Conclusion: WCAS may be a molecular prognostic marker not only in patients with medulloblastoma treated with standard-dose CSI but also in those treated with lower-dose irradiation.

Key words: medulloblastoma | molecular classification | whole chromosomal aberration

MPC-7

CLINICAL FEATURES OF DIFFUSE HEMISPHERIC GLIOMA, H3 G34-MUTANT IN CHILDREN AND YOUNG ADULTS

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INTRODUCTION: H3F3A G34R/V mutated gliomas are seen predominantly in children and young adults, and have been proposed as “Diffuse hemispheric glioma, H3 G34-mutant” in cIMPACT-NOW Update 6. However, the clinical features of the tumor have not been fully elucidated. METHODS: We retrospectively reviewed 4 cases with H3G34R mutation among 40 cases diagnosed as glioblastoma under 30 years old or primitive neuroectodermal tumor (PNET) in our hospital. RESULTS: There were one male and three female patients with a median age of 21.5 years (range: 17–27 years). All lesions were localized in the cerebral hemispheres, and the initial symptoms were headache in two cases and seizures in two cases. On imaging, there was one case with poor contrast, and unlike the infiltrative growth pattern of the other three contrasted cases, it showed a well-defined mass lesion. DWI showed high signal in all four cases, reflecting the high cell density in histopathology. All cases were IDH-wildtype. CONCLUSION: Although the patient background and genetic characteristics of the glioma with H3 G34R/V mutation at our institution were generally consistent with previous reports, there were some cases with atypical imaging findings. Further investigation is required for a deeper understanding of the clinical features of this tumor.

Key words: H3 G34R/V mutation | glioma | children and young adults

MPC-8

SERUM ANTI-ZINC FINGER FYVE DOMAIN-CONTAINING PROTEIN 21 (ZFYVE21) AUTOANTIBODY AS A NOVEL BIOMARKER FOR OLIGODENDROGLIOMA IDH-MUTANT AND 1P/19Q CO-DELETION

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Background: Glioma is one of the most challenging diseases to cure, and it would be beneficial to discover new serum biomarkers for early diagnosis. Moreover, zinc finger FYVE domain-containing protein 21 (ZFYVE21) was a regulator of tumor invasion and migration. In this study, we examined the levels of serum anti-ZFYVE21 antibodies in patients with glioma. Methods: This is a multicenter observational prospective study to discover a novel serum autologous antibody marker. We analyzed 286 pre-surgically collected sera of CNS tumors and compared them to healthy donors(HD). Bacterially expressed glutathione-S-transferase-fused ZFYVE21 protein was purified, and its antibody levels were measured by amplified luminescent proximity homogeneous assay-linked immunosorbent assay (AlphaLISA). Results: The anti-ZFYVE21 antibody levels were significantly elevated in patients with gliomas (P<0.001) than those in HD, instead of patients with other CNS tumors. Among gliomas, the highest sensitivity was observed for oligodendroglioma containing IDH mutation and 1p/19q co-deletion to HD (sensitivity: 72.00%, specificity: 67.71%, AUC: 0.7565, P<0.0001), while there is no significance in astrocytoma containing only IDH mutation. In comparing 1p/19q co-deleted oligodendroglioma with IDH-mutated astrocytoma, the sensitivity and specificity were 50% and 100%, respectively. Conclusion: Serum anti-ZFYVE21 antibodies might be a novel diagnostic marker distinguishing 1p/19q co-deleted oligodendroglioma from IDH-mutant astrocytoma.

Key words: 1p/19q co-deletion | glioma | serum marker

MPC-10

PROGNOSTIC ANALYSIS IN IDH MUTANT ASTROCYTOMA PATIENT WITH CDKN2A/B HOMOZYGOUS DELETION.

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Background: IDH mutant astrocytoma has good prognosis compared with IDH wildtype one. In IDH mutant astrocytoma, However, patients with CDKN2A/B homozygous deletion (HD) are worse prognosis than non CDKN2A/B HD. Here we analyzed the prognosis of glioma patients identified with CDKN2A/B HD in our hospital. Method: There were 62 cases, and female was 26. Mean age of all cases was 41.2 and median age was 38. In IDH gene status, R132H was 59 cases (95.2%), R172K 2 (3.2%) and R132S 1 (1.6%). All 62 cases were TERT wildtype. CDKN2A/B HD were 12 cases (19.4%). In log-rank test, the group of CDKN2A/B HD was poor prognosis than non HD. In astrocytoma grade 3, CDKN2A/B HD had significantly poor prognosis (p=0.002). In Cox proportional hazard model analysis, CDKN2A/B HD was effective predictive prognostic factor as well as age and grading (p=0.03). Discussion/Conclusion: We showed that CDKN2A/B HD was good predictive prognostic factor in IDH mutant astrocytoma.

Key words: astrocytoma | IDH mutation | CDKN2A/B homozygous deletion

MPC-13

THE EVALUATION OF THE SHIFT OF TREND IN LOWER GRADE GLIOMA DIAGNOSES BASED ON EACH ERA`S CRITERIA

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It is found that molecular characteristics in lower grade gliomas (LrGGs) such as codeletion of 1p/19q and IDH mutation was found to be more accurate to predict the patient`s clinical outcome compared to morphological diagnoses alone. Since the revision WHO2016 classification of LrGGs, molecular characteristics were implemented as diagnostic standard for LrGGs diagnoses. In the other hand, morphological diagnostic standard before WHO2016 classification era was determined by different considerations and therapeutic strategies. The malignancy grades were also majorly determined by morphological diagnoses only. This study re-evaluated 20 years of LrGG cases in single institution based on WHO2007 morphological criteria and compared them to the original institutional diagnoses from each era. The study samples were originally grade II-III diffuse glioma-diagnosed cases resected from 1990 to 2016. Biopsy cases were excluded. IDH mutation was analyzed by Sanger sequence and 1p/19 codeletion status was analyzed by Comparative Genome Hybridization (CGH). As the result 93 cases were collected and based on original diagnoses, more than 50% cases are astrocytomas. Compared to re-assessment by morphological diagnoses (WHO 2007), case numbers of astrocytoma diagnoses are decreased whereas oligodendroglioma and oligoastrocytoma case numbers are increased. But, based on WHO2016 criteria, the case number of astrocytomas is again found to be increased. From comparison between original institutional diagnoses and re-assessment results, it is found that there is a shift of trend from astrocytoma to oligodendroglioma and from grade II to grade III. Comparison between morphological diagnoses (WHO2007) and molecular (WHO2016) found that astrocytoma diagnoses remain unchanged meanwhile 45% of oligodendroglioma diagnoses were shifted into astrocytomas. There is a probability that there are high frequency of morphologically diag-