to investigate molecular prognostic markers in 23 medulloblastoma patients who were registered in the Japanese Pediatric Molecular Neuro-Oncology Group and treated with lower-dose CSI relative to standard treatment. A WCA was defined as the presence of at least two of three chromosomal changes as follows: chromosome 7 gain, chr 8 loss, and chr 11 gain. Results: All patients presented with no residue or a residual tumor smaller than 1.3 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 subgroups, there were 5 WNT, 2 SHH, 1 Group 3, and 15 Group 4 medulloblastomas. Seventeen patients with Group 3/4 medulloblastomas showed WCA s 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 113 months after diagnosis, respectively, and one of these patients presented with a WCA. Conclusion: WCA may be a molecular prognostic biomarker not only in patients with medulloblastoma compared with standard-dose CSI but also in those treated with lower-dose irradiation.

Key words: medulloblastoma / molecular classification / whole chromosomal alteration

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 eIMPACT-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 (ZFNYVE21) AUTOANTIBODY AS A NOVEL BIOMARKER FOR OLGIDODERGIOGLIOMA 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 (ZFNYVE21) was a regulator of tumor invasion and migration. In this study, we examined the levels of serum anti-ZFNYVE21 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-ZFNYVE21 protein was co-expressed, and its antibody levels were measured by amplified luminescent proximity homogeneous assay-linked immunosorbent assay (AlphaLISA). Results: The anti-ZFNYVE21 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 1p19q 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 1p19q co-deleted oligodendroglioma with IDH-mutated astrocytoma, the sensitivity and specificity were still 50% and 100%, respectively. Conclusion: Serum anti-ZFNYVE21 antibodies might be a novel diagnostic marker distinguishing 1p19q co-deleted oligodendroglioma from IDH-mutant astrocytoma.

Key words: 1p19q 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 ± 15.4 years old at diagnosis, 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 worse prognosis (p<0.0021). 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 (LGGs) such as codelence of 1p19q 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 LGGs, molecular characteristics were implemented as diagnostic standard for LGGs 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 LGG cases in single institution based on WHO2007 morphological criteria and compared them to the original institutional diagnoses from each era. The study samples were all histologically grade II-III diffuse glioma-diagnosed cases evaluated from 1990 to 2016. Results: The diagnosis was analyzed by Sanger sequence and 1p/19 codelence 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 astrocytomas 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 diagnoses (WHO2016) found that astrocytoma diagnoses in WHO2016 are significantly lower than WHO2007 and meanwhile 45% of oligodendrogliomas diagnoses were shifted into astrocytomas. There is a probability that there are high frequency of morphologically diag-
Abstracts

Nose oligodendroglioma tumors which are having molecular characteristics of astrocytoma. There is a trend that diagnosed grade II LGGs are actually grade III being reassessed diagnosis.

Key words: Neuropathology | WHO2016 criteria | Molecular diagnosis

MPC-17

2021 WHO CLASSIFICATION OF TUMORS OF THE CNS, 5TH ED. Takashi Komori1; Department of Laboratory Medicine and Pathology, Tokyo Metropolitan Neurological Hospital

The grading of gliomas based on histological features has been a subject of debate for several decades. While the traditional grading system has failed to stratify the risk of IDH-mutant astrocytoma, canonical histological and proliferative markers may be applicable to the risk stratification of IDH-wildtype astrocytoma. Numerous studies have examined molecular markers to obtain more clinically relevant information that will improve the risk stratification of gliomas. The C6K23R-driven homozygous deletion for IDH-mutant astrocytoma and the following three criteria for IDH-wildtype astrocytoma: the concurrent gain of whole chromosome 7 and loss of whole chromosome 10, TERT promoter mutations, and EGFR amplification, were identified as independent molecular markers of the worst clinical outcomes. Therefore, the 2021 World Health Organization (WHO) Classification of Tumors of the Central Nervous System adopted these molecular markers into the revised grading criteria of IDH-mutant and -wildtype astrocytoma regarding tumor grading system within glioma types. For diffuse gliomas in children, molecular alteration-based classification was adopted, dividing low-grade and high-grade subcategories. New tumor types and subtypes were introduced, some based on DNA methylation profiling. To achieve this novel classification in a resource-limited setting, an integrated diagnosis combining clinical, histological, and molecular information became more important.

Key words: WHO classification | genetics | pathology

NEUROIMAGING (NI)

NI-2

USE OF NEURITE ORIENTATION DISPERSION AND DENSITY IMAGING (NODDI) FOR EARLY DISTINCTION BETWEEN INFILTRATING TUMOR AND VASOGENSE EDEMA IN NON-ENHANCING LESIONS WITH GLOBLASTOMA PATIENTS

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Background: Globlastoma is a highly infiltrative tumor. In the non-enhancing T2-weighted hyperintense area, differentiating between non-enhancing tumors (NETs) and vasogenic edema is challenging. Neurite orientation dispersion and density imaging (NODDI) is a new diffusion MRI technique that reveals the inhomogeneity of the brain microstructure.

The aim of this study is to differentiate between NETs and edema based on NODDI. Methods: Data were collected from 20 patients with glioblastoma as well as three patients with metastasis and two with meningioma (control), who underwent MRI as part of pre-surgical examination. The MRI data included T2- and T1-weighted contrast-enhanced images and NODDI images. The NODDI was manually placed the volume of interest (VOI) on the NETs and edema based on the previously reported reports. ICV, ODI, ISOVF, FA, and ADC were calculated for each VOI. Results: Fifteen and 13 VOIs were placed on NETs and edema, respectively. Each parameter was measured and the unpaired t-test revealed a significant difference between NETs and edema (p < 0.0001). The ROC curve analysis revealed a large difference in the ADC, FA, and ISOVF between NETs and edema compared to ICV and ODI. Principal component analysis of the five parameters showed that ADC, ISOVF, and FA contributed to the differentiation between NETs and edema. Multiple logistic regression analysis was performed with the three aforementioned parameters. A predictive formula could be created to discriminate between NETs and edema, following the use of which, the ROC curve revealed an AUC value of 0.88. Furthermore, this formula was applied to the edematous regions of the images of the negative control group, and the prediction degree of the tumor was well below 0.5, thus enabling differentiation as edema. Conclusions: NODDI may prove to be a useful tool to discriminate between NETs and edema in the non-contrast T2 hyperintensity region of glioblastoma.

Key words: glioblastoma | non-enhancing tumor | NODDI

NI-3

MAGNETIC RESONANCE RELAXOMETRY FOR TUMOR CELL DENSITY IMAGING FOR GLIOMA: AN EXPLORATORY STUDY VIA 11C-METHIONINE PET AND ITS VALIDATION VIA STEREOTACTIC TISSUE SAMPLING

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Objective: To evaluate the feasibility of MR-based cell density imaging utilizing NODDI for the differential diagnosis between NETs and edema. When compared the cell density imaging with the conventional histological analysis, we were able to demonstrate that the VOI on the NETs and edema based on the previous histopathological analysis. Methods: We retrospectively analyzed 30 adult supratentorial glioma cases with methionine (MET) positron emission tomography (PET). PET images were compared with the values from qMRI and DWI were correlated. Study 2: Seventy-nine stereo-tactically sampled tissues from 22 glioma patients were correlated with Met-PET, qMRI, and DWI measurements regarding tumor cell density. qMRI acquisition: Imaging was performed on either a 1.5 or 3 T MR scanner (Prisma or Aera; Siemens Healthcare, Erlangen, Germany). T1-relaxometry was achieved by first acquiring MP2RAE images, then converting those images into T1-relaxation time maps. At the same time, T2-relaxometry was achieved by first acquiring multi-echo T2-weighted images and then converting those images into T2-relaxation time maps, with both relaxometries performed via Bayesian inference modeling (Olea Nova; Canon Medical Systems, Tochigi, Japan). Results: Study 1 revealed that regions of 1850ms < T1-relaxation time < 3200ms and 115ms < T2-relaxation time < 225ms tended to be Met-PET T/Nr > 1.5. DWI was not useful to separate areas between low and high Met-PET. Study 2 showed that regions of 1850ms < T1-relaxation time < 3200ms showed high cell tumor density than other areas (p<0.04). Conclusions: Our results supported the hypothesis that qMRI is useful for predicting the tumor load within the brain among glioma patients. T1-relaxometry was not useful for this means. On the other hand, ADC measured from DWI was limited for tumor load prediction.

Key words: glioma | MRI | tumor cell density

NI-6

PREOPERATIVE DIFFERENTIAL DIAGNOSIS OF GRADE II AND GRADE III IN CASES WITH ASTROCYTOMA, IDH MUTANT

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Objective: To evaluate the feasibility of MR-based cell density imaging utilizing NODDI for the differential diagnosis between NETs and edema. When compared the cell density imaging with the values from qMRI and DWI were correlated. Study 2: Seventy-nine stereo-tactically sampled tissues from 22 glioma patients were correlated with Met-PET, qMRI, and DWI measurements regarding tumor cell density. qMRI acquisition: Imaging was performed on either a 1.5 or 3 T MR scanner (Prisma or Aera; Siemens Healthcare, Erlangen, Germany). T1-relaxometry was achieved by first acquiring MP2RAE images, then converting those images into T1-relaxation time maps. At the same time, T2-relaxometry was achieved by first acquiring multi-echo T2-weighted images and then converting those images into T2-relaxation time maps, with both relaxometries performed via Bayesian inference modeling (Olea Nova; Canon Medical Systems, Tochigi, Japan). Results: Study 1 revealed that regions of 1850ms < T1-relaxation time < 3200ms and 115ms < T2-relaxation time < 225ms tended to be Met-PET T/Nr > 1.5. DWI was not useful to separate areas between low and high Met-PET. Study 2 showed that regions of 1850ms < T1-relaxation time < 3200ms showed high cell tumor density than other areas (p<0.04). Conclusions: Our results supported the hypothesis that qMRI is useful for predicting the tumor load within the brain among glioma patients. T1-relaxometry was not useful for this means. On the other hand, ADC measured from DWI was limited for tumor load prediction.

Key words: glioma | MRI | tumor cell density

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