re-consideration of treatments for tumors diagnosed as so-called PNET. In this study, we propose the optimization of treatments for tumors diagnosed by the new classification to clarify which treatments were effective for the tumors those were diagnosed as PNET. MATERIALS AND METHODS: The tumor samples diagnosed as so-called PNETs were analyzed. The molecular information was extracted from tumor specimens. We used high throughput analysis with microarray, FISH, and immunohistochemistry. They all had treated in our institution in last 6 years and their clinical courses were followed by medical records. Informed parental consent was obtained from their guardians and this study was approved by the institutional review board of Juntendo university. RESULTS: Nine tumor samples were able to be analyzed and they are re-classified into high-grade glioma, neuroblastoma, sarcoma, embryonal tumors with multilayered rosettes, C19MC altered (ETMR). They resembled each other closely in morphology, and therefore, it was not able to be classified by histopathological findings. There was a case of pineoblastoma, whose molecular background suggested that the tumor was re-classified into neuroblastoma. In terms of treatments, we have succeeded in neuroblastoma cases so far, ETMRs were required multiple surgeries and radiations to maintain remissions. CONCLUSIONS: Re-classification of diagnosis based on the molecular background is necessary to clarify the optimization of treatments for pediatric brain tumors, and the comprehensive methods is required. We present our methods for molecular diagnosis in clinical field and future plans.

MPC-11

IDH1/2 MUTATIONS ARE ASSOCIATED WITH SEIZURE ONSET AND VETRY IMAGING IN PATIENTS WITH DIFFUSE GLIOMA VISUALIZING 2-HYDROXYGLUTARATE BY MASS SPECTRUM

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BACKGROUND: Mutations in isocitrate dehydrogenase 1 or 2 genes (IDH1/2) frequently occur in lower-grade gliomas. Mutant IDH1/2 proteins gain a new ability to produce 2-hydroxyglutarate (2HG). IDH1/2 mutations have shown to be related with seizure through the structural similarity of 2HG to glutamate. We, therefore, sought to investigate the relationship between seizure and IDH1/2 mutations and to visualize tissue 2HG distribution in patients with diffuse gliomas. METHODS: We assessed 149 patients with diffuse glioma, and measured tissue 2HG concentrations in 104 patients by using liquid chromatography-tandem mass spectrometry. The matrix-assisted laser desorption/ionization high resolution mass spectrometry imaging (MALDI-HR-MSI) was used to visualize tissue 2HG distribution for 12 tissue samples. RESULTS: Seizure onset was observed in 34 among 56 (60.7%) patients with IDH1/2 mutant tumor, whereas in 18 among 93 (19.4%) patients with IDH1/2 wild-type tumor ($p<0.0001$). The tissue 2HG concentration was significantly higher in IDH1/2 mutant tumor than in IDH1/2 wild-type tumor (median: 4862 ng/mg vs 75 ng/mg) ($p<0.0001$). Multivariate analysis, including tissue 2HG concentration, IDH1/2 status, histology, grade, and location, showed that IDH1/2 mutations was significantly correlated with seizure onset. The MALDI-HR-MSI showed that 2HG spread in various concentration independent of cellularity and also in extracellular space in IDH1/2 mutant tumor tissue. CONCLUSIONS: We demonstrated the association between IDH1/2 mutations and seizure, and the heterogeneous 2HG distribution not only in cellular area but also in extracellular space. These findings suggest the potential role of 2HG as an intercellular mediator to tumor environment, resulting in epileptogenesis formation.

MPC-12

ACCURACY OF INTRAOPERATIVE SIMPLE FLOW CYTOMETER FOR HIGH GRADE GLIOMA OPERATION COMPARED WITH INTRAOPERATIVE FROZEN DIAGNOSIS.

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INTRODUCTION: Intraoperative simple flow cytometer (iFC) was developed in recently, we examined the correlation intraoperative frozen diagnosis (IOFD) and intraoperative frozen section of resection margin (IOFM) to iFC. METHOD AND MATERIAL: Total 33 cases of high grade glioma patients were underwent operation in April 2017 ~ May 2019, and IOFD and IOFM were compared to iFC. Sample of iFC were retrieved just same parts of IOFM and IOFD. We compared to microscopical findings, MIB-1, malignant index (MI), and MI Level (G0-4). RESULTS: Accuracy rate of iFC and IOFD in high grade glioma was 84%, and the concordance rate of grading was17.2%. Correlation coefficients between MIB-1 and iFC of IOFD was r=0.5019 P=0.0065. Accuracy rate of IOFM was 46.8%, and concordance rate of grading was 35.5%. Correlation coefficients between MIB-1 and iFC of IOFM was r=0.5899 P=0.0001. CONCLUSIONS: Although iFC accuracy rates iFC of IOFD and IOFM were high, iFC concordance rates and grade were low. Correlation between MIB-1 and iFC of IOFM was better than that of IOFD. Probably, iFC of IOFD was a little difficult because of sample heterozygosity.

MPC-14

BRAF V600E MUTANT OLIGODENDROGLIOMA-LIKE TUMORS WITH CHROMOSOMAL INSTABILITY IN ADOLESCENTS AND YOUNG ADULTS

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We performed genome-wide methylation analysis on 136 pediatric low grade gliomas, identifying a unique cluster consisting of oligodendroglioma-like BRAF V600E mutant tumors with Recurrent gain of Chromosome 7 and loss of Chromosome 10 (OLIVER). Hierarchical clustering and t-stochastic neighbor embedding analyses cluster them with previously described pediatric-type low grade gliomas, separate from adult gliomas. OLIVERS exhibit distinct clinical behavior as temporal lobe lesions in adolescents and young adults, prolonged history of seizures and all are alive with no recurrence (follow-up 3.2 to 13.2 years). Morphogically, all showed oligodendroglioma-like features, including round nuclei with perinuclear halos, a chicken-wire pattern of branching capillaries and microcalcification. None showed astrocytic features or characteristics suggestive of high-grade tumors including necrosis or mitotic figures. All tumors harbored multiple chromosomal copy number abnormalities (more than 10 chromosomes per OLIVER), but none showed 1p/19q co-deletion or IDH1 mutation. Interestingly, one tumor showed a TERT promoter mutation. Although the series is small, OLIVER may represent a new category of IDH wild-type low grade gliomas which may be confused with molecular GBM. Further, they highlight the heterogeneity of IDH wild-type gliomas and the relatively indolent behavior of pediatric-type gliomas.

MPC-15

FEASIBILITY OF GLIOMA SPECIFIC ONCOPANEL IN THE DIAGNOSIS OF GLIOMA

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AIM: Molecular classification of glioma is a mandatory in the diagnosis of glioma according to the WHO 2016 classification of tumors of the central nervous system. However, WHO does not indicate the molecular methodology to be integrated, and the versatility and cost-effectiveness of molecular diagnosis is a concern. In this study, we evaluate the feasibility of a glioma specific tailored NGS panel where driver gene mutation and 1p/19q codeletion can be analyzed in a single platform. MATERIALS AND METHODS: We developed a glioma specific tailored NGS panel consisting of 48 key driver genes including IDH1/2, TP53, PTEN, EGFR, PDGFR, NF1, RB1, CDKN2A, and the TERT promoter. DNA was extracted from FFPE tumor tissues histologically identified by a pathologist, and from patient derived blood to serve as a control. In this system, gene mutations and copy number alterations can be precisely characterized, thus 1p/19q co-deletion can also be evaluated. We have analyzed 106 glioma patients (Grade II: 19 cases, Grade III: 23 cases, Grade IV: 64 cases) using this system.

RESULTS: From these 106 cases, IDH1 and TERT promoter mutations were detected in 33 cases (28%) and 55 cases (52%), respectively. 1p/19q co-deletion was detected in 19 cases (18%), with IDH1 mutations in all cases. In 57 Grade IV cases, TP53, PTEN, RB1, NF1, PDGFRA mutations were detected in 25 cases (43%), 24 cases (41%), 10 cases (17%), 8 cases (14%) and 6 cases (10%). Although EGFR mutation frequency was low (3%), amplification was detected in 14 cases (24%). As for deletion, PTEN and CDKN2A loci were deleted in 36 cases (62%) and 30 cases (52%), respectively. To note, MET alterations were detected in 2 cases. The cases in which histopathological diagnosis is difficult to make have a tendency to show atypical genetic alterations.

CONCLUSION: Diagnosis of glioma patients with this glioma-specific tailored NGS panel is feasible.

MPC-16

RAPID PROGRESSIVE SPINAL DIFFUSE MIDLINE GLIOMA, A CASE REPORT

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