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A 17-year-old boy presented with a 2-week history of lower back pain, progressive gait difficulty and sensory deficit of bilateral lower limbs. Magnetic resonance imaging of neuroaxis showed intramedullary tumor with spinal cord expansion from Th12 to L2 and irregular areas of enhancement. Emergent laminoplasty and biopsy was performed. Histopathological examination showed small atypical cells, but most cells had too much degeneration and necrosis to confirm the diagnosis definitively. Leptomeningeal dissemination caused conscious disturbance, nuchal rigidity and epilepsy. 2 weeks after decompression, we performed cordotomy again for advanced diagnosis, to be found diffuse midline glioma, H3K27M mutant by immunohistopathological examination and DAN sequence. He was treated with combination of whole brain and spine radiation therapy and chemotherapy with temozolomide and bevacizumab. He is still alive over 6 months. The clinical significance of H3K27M mutant in spinal gliomas is unclear. Further examinations are needed.

MPC-17

USEFULNESS OF INTRAOPERATIVE MOLECULAR DIAGNOSIS OF GLIOMA USING REAL-TIME PCR

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BACKGROUNDS: Based on the comprehensive gene association studies in recent years, the revision was issued in 2016 WHO classification, integrating genetic information in glioma diagnosis. Many studies have been reported the correlation between each molecular subtype and prognosis in the new classification. Gliomas surgery is required to maximum tumor resection with functional preservation. Currently, our institute decides a surgical strategy based on the morphological diagnosis and genetic information from the obtained tissue during the operation. We evaluated the IDH 1/2 gene mutations and 1p/19q codeletion by using real-time PCR intraoperatively. We report the usefulness of this method in this presentation. OBJECTIVE: 58 specimens obtained during surgery from March to November 2017, IDH 1/2 gene mutations and 1p/19q codeletion were evaluated intraoperatively by real-time PCR. IDH 1/2 gene mutations were detected using HRM, and SNP genotyping was used for TERT promoter mutations expected as a surrogate marker for 1p/19q codeletion. RESULT: Each gene mutation was detected in approximately 90 minutes from DNA extraction of obtained surgical tissue to analysis. The accuracy of HRM of IDH 1/2 mutations was 97.3% (72/74 cases) evaluated by the result of IDH1-R132H IHC or Sanger sequencing, and SNP genotyping of TERT promoter mutations was 94.3% (50/53 cases). There was almost no difference from final genetic information. CONCLUSION: Real-time PCR is feasible as an intraoperative molecular diagnosis. The accuracy of diagnosis is very high and it can be evaluated in a short time, so it's useful for decision making during operation.

MPC-18

CATEGORIZATION OF LOWER GRADE GLIOMA USING ONCOPANEL.

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PURPOSE: We are developing a 48-gene OncoPanel (Kagoshima Brain Tumor 48 OncoPanel) specializing in glioma diagnosis. Clinical application of genetic diagnosis derived from genetic alterations detected by OncoPanel, including IDH mutation, 1p/19q-codeletion, and other gene mutations in lower-grade glioma was verified. METHODS: The 48 genes consist of 24 genes related to glioma and 24 genes on chromosomes 1 and 19. DNA was extracted from tumor FFPE samples and blood samples, and then single nucleotide variants and copy number variants were detected using next-generation sequencer. RESULTS: Among the 99 diffuse glioma cases that had undergone OncoPanel analysis by July 2019, 40 cases diagnosed histologically as WHO grade 2 or 3 diffuse glioma were included. The integrated diagnosis by conventional gene analysis were Diffuse astrocytoma 10 cases, anaplastic astrocytoma 11 cases, oligodendroglioma 10 cases, anaplastic oligodendroglioma 9 cases. IDH1 mutation was detected in 30 cases, of which in 19 cases 1p/19q-codeletion was detected, all with TERT mutation. Among 11 cases with 1p/19q-non-codeletion, ATRX mutation was detected in 10 cases and was almost mutually exclusive with TERT mutation. In 10 cases without IDH mutation, EGFR amplification or mutation was detected in 6 cases, of which 4 cases were accompanied by TERT mutation. DISCUSSION: KBT48 can detect TERT and ATRX mutations in a mutually exclusive manner and can improve the classification accuracy of oligodendroglioma and astrocytoma. Groups with gene profiles similar to glioblastoma with EGFR amplification/mutation and TERT mutation can also be classified. CONCLUSIONS: In the diagnostic classification of lower-grade glioma, KBT48 can well classify into oligodendroglioma group, astrocytoma group and glioblastoma-like group, and is considered to be applicable in clinical practice.

NEUROIMAGING (NI)

NI-01

CONTRAST-ENHANCED MRI AND POSITRON EMISSION TOMOGRAPHY FOR DISTINGUISHING THE GRADE OF GLIOMA

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OBJECTIVE: Grading of glioma according to the WHO classification plays an important role in the treatment of patients with glioma. It is widely recognized that malignant gliomas exhibit contrast enhancement on MRI, whereas low-grade gliomas do not exhibit contrast enhancement. However, we sometimes encounter malignant gliomas without contrast enhancement on MRI. In this study, we evaluated the diagnostic accuracy of contrast-enhanced MRI and PET for distinguishing the WHO grade of glioma. METHODS: A total of 105 patients with newly diagnosed cerebral glioma were included in the study. All patients underwent 11C-Methionine (MET), 11C-Choline (CHO), 18F-Fluorodeoxyglucose (FDG) PET and MRI. The specificity and sensitivity of MRI contrast enhancement and mean T/N ratios of these three tracers for each WHO grade were analyzed. RESULTS: Contrast enhancement was observed in 35 patients (33%) of the total. Contrast enhancement was observed in 1/30 (3%) in grade 2, 8/43 (19%) in grade 3, and 26/30 (87%) in grade 4. The sensitivity and specificity of MRI for differentiating grade 2 from grade 3 was 11.1% and 54.7%, respectively. In contrast, the cutoff value, sensitivity, and specificity of each tracer for differentiating grade 2 from grade 3 were: 1.70, 66.7%, and 58.1% for MET; 2.15, 76.7%, and 51.2% for CHO; and 0.64, 80.0%, and 32.6% for FDG, respectively. DISCUSSION: A correlation between contrast enhancement of MRI and WHO grade was observed to some extent; however, only 19% grade 3 gliomas showed contrast enhancement. The sensitivity and specificity of PET for differentiating between grade 2 and 3 was relatively higher than that of MRI; however, it was not suitable for clinical use. CONCLUSION: Contrast-enhanced MRI may not be reliable for determining the WHO grade for glioma, in particular differentiating between grade 2 and 3. Comprehensive evaluation with MRI and PET can provide more accurate diagnosis.

NI-02

THE ASSOCIATION BETWEEN ^{11}C-METHIONINE UPTAKE, IDH GENE MUTATION, AND MGMT PROMOTER METHYLATION IN PATIENTS WITH GRADE II AND III GLIOMAS

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AIM: We evaluated the association between ^{11}C-methionine positron emission tomography (^{11}C-methionine PET) findings, isocitrate dehydrogenase (IDH) gene mutation, and O^6-methylguanine-DNA methyltransferase (MGMT) promoter methylation in patients with grade II and III gliomas. MATERIALS AND METHODS: Data were collected from 40 patients with grade II and III gliomas who underwent both magnetic resonance imaging (MRI) and ^{11}C-methionine positron emission tomography (PET) as part of their pre-surgical examination. We examined IDH mutation through DNA sequencing, and MGMT promoter methylation through quantitative methylation-specific polymerase chain reaction (PCR).

RESULTS: A threshold of MGMT promoter methylation of 1.0% was significantly associated with tumor/normal tissue (T/N) ratio. The T/N ratio in samples with MGMT promoter methylation ≥1.0% was higher than that in samples with MGMT promoter methylation <1.0%, and the difference was statistically significant ($p = 0.011$). Reliable prediction of MGMT promoter methylation (<1.0% vs ≥1.0%) was possible using the T/N ratio under the receiver operator characteristic (ROC) curve with a sensitivity and

specificity of 75% each (cut-off value = 1.6) (p = 0.0226, AUC = 0.76172). Conversely, the T/N ratio had no association with IDH mutation (p = 0.6). The ROC curve revealed no reliable prediction of IDH mutation using the T/N ratio (p = 0.606, AUC = 0.60577). CONCLUSION: ^{11}C-methionine PET parameters can predict MGMT promoter methylation but not IDH mutation status. ^{11}C-methionine uptake may have limited potential to reflect DNA methylation processes in grade II and III gliomas.

NI-03

USEFULNESS OF IMP-SPECT IN PREOPERATIVE GRADE EVALUATION OF INTRAORBITAL TUMOR.

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INTRODUCTION: The frequency of intraorbital tumors is small as 0.9% of all brain tumors, but its pathological type is diverse. Among them, the diagnosis of whether particularly malignant tumor scan clinically, is extremely important. Nuclear medical testing is essential for non-invasive differential diagnosis in brain tumors. SPECT, good malignancy differentiation, evaluation of malignancy, usefulness such as differentiation of non-tumorous lesions have been reported many. However, there are few reports that SPECT was useful in preoperative differential diagnosis of orbital tumors. Since 123IMP-SPECT was useful in preoperative differential diagnosis of intraorbital tumors, we report some literature considerations. METHOD: Among the 27 cases of intraorbital tumors that were operated on in our clinic between August 2005 and August 2016, 14 cases of SPECT prior to surgery were examined for the usefulness of preoperative differential diagnosis. Breakdown of cases, as the malignant tumor, two cases of malignant lymphoma, MALT lymphoma 2 cases, adenoid cystic carcinoma 1 case, in one case plasma cytoma, as a benign tumor, false tumors 4 cases, three hemangioma cases, neurocytoma 1 case it was. RESULTS: In IMP early image, accumulation of clear IMP was observed in all six cases of malignant tumors. In benign tumors, there is no accumulation in hemangioma and neurosheath, there is a strong accumulation in one of the four cases in false tumors, it was observed mild accumulation in the remaining two cases. Tumor to normal ratio of IMP early image was an average of 2.39 in six malignant tumors and 1.52 in 8 benign tumors. CONCLUSION: This time, we examined the usefulness of 123IMP-SPECT in preoperative differential diagnosis of intraorbital tumors. The T/N ratio of intraorbital malignant tumors is higher than benign tumors, and it was thought to help to evaluate preoperative malignancy of intraorbital tumors.

NI-04

WHICH RADIOLOGICAL IMAGING IS BEST TO DISCRIMINATE RADIATION NECROSIS FROM TUMOR PROGRESSION? - SUBANALYSIS OF SYSTEMATIC REVIEW FOR RADIOLOGICAL DIAGNOSIS OF RADIATION NECROSIS -

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BACKGROUND: It is challenging to discriminate radiation necrosis from tumor progression, especially in malignant glioma. Therefore many radiological imaging studies have been reported. In this study, we performed a systematic review of radiological diagnosis for radiation necrosis and analyzed the best radiological imaging for malignant glioma. METHODS: We divided diagnostic approaches into two categories as follows-CT and MRI (conventional radiological imaging studies), and SPECT and PET (nuclear medicine studies). Our librarians conducted a comprehensive systematic search on Pub Med, Cochrane Library, and the Japan Medical Abstract Society up to March 2015. The searching keywords included radiation necrosis, recurrence, imaging modalities such as MRI, diagnosis, and differential. In a meta-analysis, diagnostic odds ratio (DOR) was calculated. A subanalysis was performed, dividing into tumor types, gliomas and metastatic brain tumors. RESULTS: Of 188 and 239 records extracted from the database, 20 and 26 studies were included in the meta-analysis after exclusion of case reports and studies with incompatible content and insufficient information. Gd-enhanced MRI exhibited the lowest sensitivity (63%) and DOR (2.2). On the other hand, combined multiple imaging studies including MRS and perfusion image displayed the highest sensitivity (96%) and DOR (5.9). In the subanalysis for glioma, Gd-enhanced MRI and 18F-FDG-PET revealed low DORs (1.7 and 2.3). Conversely, 18F-FET-PET and combined multiple imaging studies showed high DORs (6.8 and 5.9). CONCLUSIONS: Gd-enhanced MRI had low diagnostic ability for differentiation of radiation necrosis. In glioma patients, 18F-FDG-PET was not useful to discriminate radiation necrosis from tumor progression. Combined multiparametric imaging including lesional metabolism and blood flow could enhance diagnostic accuracy and be useful to differentiate radiation necrosis from tumor progression even in glioma patients.

NI-05

CLINICOPATHOLOGICAL ANALYSIS AND METHIONINE PET ANALYSIS IN PATIENTS WITH GLIOMATOSIS CEREBRI

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OBJECTIVE: Gliomatosis cerebri (GC) was defined as the tumor infiltrating into more than three lobes in WHO2007, but was deleted in WHO2016 because they include genetically heterogeneous tissues. However, we often encounter the cases with strongly invasive glioma. Then, we clinically analyzed the cases of GC. PATIENTS AND METHODS: Seven cases (five men, median age: 57 years (23-89y)) diagnosed as GC in our hospital were included. Data of methionine-positron emission tomography (Met-PET), IDH and p53 mutation, MIB1-labeling index (LI) by immunohistochemistry were searched. We compared the accumulation areas of the Met-PET with the hyperintensity area (T2/FLAIR-high) and gadolinium-enhanced area on the MRI. We also examined a biopsy method, sites and a treatment regimen and analyzed overall survival (OS) and progression-free survival (PFS). RESULTS: The primary symptoms were disorientation in five, epileptic seizure and abnormal vision were two, respectively. The largest lesion area with the image was T2/FLAIR-high, followed by Met-PET and Gd in all. The surgical methods were stereotactic biopsy (2), navigation-guided biopsy (2), endoscopic biopsy (1), and craniotomy (2), The average of tumor/normal ratio in Met-PET was 2.92 (1.97–5.0). The pathological grade was diagnosed as Grade III in 4 and Grade II in 3. IDH1R132H was negative in all, p53 was positive in 5, and an average of MIB-1LI was 12% (2–35). The radiotherapy was performed in 6 cases, and, temozolomide was given to all, and bevacizumab was in 3. Six patients died of a tumor. Median PFS and OS were 8mos and 16.5mos, respectively. CONCLUSION: Because the GC cannot expect improvement by surgery, it is necessary to obtain the pathological diagnosis by a quick and correct biopsy, and the neurologic deterioration by the biopsy technique should be avoided. The Met-PET suggesting the highest grade site was useful for the plan of the biopsy site.

NI-06

MOLECULAR DIAGNOSIS, 11C-METHIONINE UPTAKE AND PROGNOSIS IN GRADE 2 AND 3 GLIOMAS

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OBJECT: The revised 2016 WHO Classification of Tumours of the Central Nervous System incorporates genetic alterations into the classification system, with the goal of creating more homogenous disease categories with greater prognostic value. In this study, we reclassified 103 consecutive lower grade gliomas using the revised 2016 WHO classification and examined for 11C-methionine uptake and prognosis. METHODS: 103 consecutive lower grade glioma patients (Grade 2 in 41 patients, Grade 3 in 62 patients) treated at Tokyo Medical and Dental University Hospital from 2000 to 2018 were included in this study. The IDH1/2, ATRX and 1p19q status were analyzed using tumor samples. The tumor-to-normal ratio (T/N) of 11 C-methionine uptake was calculated by dividing the maximum standardized uptake value (SUV) for the tumor by the mean SUV of the normal brain. RESULT: In the integrated diagnosis, 11 astrocytomas and 17 anaplastic astrocytomas were diagnosed as “IDH-mutant”, while 14 astrocytomas and 29 anaplastic astrocytomas were diagnosed as “IDH-wild”. In the 32 oligodendroglial tumors, 12 oligodendrogliomas and 9 anaplastic oligodendrogliomas were diagnosed as “IDH-mutant and 1p/19q-codeleted”. The concordance rate with 1p19q co-deletion and ATRX retention was 94.7%. The median T/N ratios in oligodendroglial tumors with “IDH-mutant and 1p/19q-codeleted” were 1.83 in Grade 2 and 2.83 in grade 3, which were significantly higher than those in astrocytic tumors with “IDH-mutant” (G2: 1.38, G3:1.62). Kaplan-Meier survival analysis revealed that oligodendroglial tumors with “IDH-mutant and 1p/19q-codeleted” had significantly better outcomes regardless of WHO grade. Overall survival was 90.9% at 5 years and 77.9% at 10 years in oligodendroglial tumors with “IDH-mutant and 1p/19q-codeleted”. CONCLUSIONS. The results indicated that lower grade glioma categories reclassified with molecular classification correlate with the T/N ratio of methionine and the prognosis.