TUMOR RELATED EPILEPSY AND IDH MUTATIONS IN GLOMOMS

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ABSTRACT: Tumor related epilepsy (TRE) is an important complication in the treatment of brain tumors. In recent studies, it is assumed that isocitrate dehydrogenase (IDH) mutations are concerned with TRE in gliomas. Here, we examined the association between IDH mutations and TRE in our cases.

METHODS: 115 patients who had a supratentorial glioma and were treated in our hospital from February 2009 to November 2018 were retrospectively assessed for IDH mutations and TRE. RESULTS: 38 patients were the IDH mutant group (16 females, mean age 43.7±12.9 years, mean follow-up time 44.0 months). 77 patients were the IDH wild group (35 females, mean age 61.6±16.6 years, mean follow-up time 18.1 months).

Compared to the IDH wild group, the IDH mutant group was significantly younger and mean follow-up time was longer. There were no differences in the postoperative radiation and chemotherapy in both groups. The incidence of seizures as presenting symptom was 20 patients (32.6%) in the IDH mutant group and 16 patients (20.8%) in the IDH wild group, and was significantly higher in the IDH mutant group (p=0.03). 27 patients (71.1%) in the IDH mutant group had TRE at least once during follow-up time and 39 patients (50.0%) in the IDH wild group (p=0.06). In addition, the median OS for the group with seizure onset (36 patients) was 69.2 months and the group with the other onset forms (79 patients) was 22.4 months. The seizure onset group had a significantly better prognosis (p<0.05). CONCLUSION: Gliomas with IDH mutations have a higher incidence of TRE. Although IDH mutations are considered to be a risk factor for TRE, which is consistent with previous studies, but it is suggested that differences in survival may have an effect on the incidence of TRE.

PRIMITIVE NEUROECTODERMAL TUMORS WITH MOLECULAR MARKER TO PREDICT PROGNOSIS AND HISTOLOGICAL MALIGNANCY IN iGCTs

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CLINICOPATHOLOGICAL ANALYSIS OF 12P GAIN IN INTRACRANIAL GERM CELL TUMORS

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BACKGROUND: Gain of short arm of chromosome 12 (12p) is commonly observed in testicular germ cell tumors (gGCTs). 12p gain is frequently seen in intracranial germ cell tumors (iGCTs). However, little is known about the clinical significance of 12p gain in iGCTs.

MATERIALS AND METHODS: We have collected 200 fresh frozen tissue samples of iGCTs through the Intracranial Germ Cell Tumor Genome Analysis Consortium in Japan. Firstly, we analyzed DNA methylation status in 83 iGCTs. 3 seminomas and 6 normal control samples using Infinium Human Methylation 450K BeadChip array (Illumina, CA). Idat files were processed using R (Version 3.5.3) and minfi package (1.3.0) to generate copy number variations. Compared with average genome-wide copy number level, 12p gain was determined. Then, we performed clinical-pathological information were analyzed for progression-free survival (PFS) and overall survival (OS). Those tumors that consist of only either germininoma and/or mature teratoma components were classified as Favorable Histology (FH) and all the others that contains malignant histological components were classified as Unfavorable Histology (UH). RESULTS: 12p gain was observed in 100% (3/3) of seminoma, 13.6% (3/22) of germinoma, 16.7% (1/6) of mature teratoma, 25% (1/4) of immature teratoma, 55% (11/20) of mixed germ cell tumor, 100% (4/4) of yolk sac tumor, 100% (1/1) of embryonal carcinoma, and 100% (1/1) of choriocarcinoma. In total, 44.6% (73/165) of all iGCT showed 12p gain. Regarding histological classification, the 12p gain rate in FH (72%, 18/25) was significantly higher than that in UH (12.1%, 4/33, P=0.01). Both PFS and OS were significantly worse in iGCTs with 12p gain compared with those without 12p gain.

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INTRODUCTION: In the present WHO classification of central nervous system tumors, the supratentorial tumors comprise several round blue cells with aggressive clinical features had been defined as primitive neuroectodermal tumor (PNET). Recent molecular analysis revealed that they do not belong to a single entity, but they are re-classified as the tumors of other well-defined subtypes and newly defined tumor species. Morphological changes of the WHO classification of tumors of the central nervous system were related to recent molecular classification.

IN THIS STUDY: We aimed to classify the iGCTs, which are included in the current WHO classification of central nervous system tumors, to the new classification.

RESULTS: We classified 200 fresh frozen tissue samples of iGCTs based on many molecular markers, including DNA methylation status, gene expression, Copy number variations, and the nuclear magnetic resonance imaging analysis. The classification results were compared with the clinical-pathological information and survival analyses. We found that the 12p gain was associated with worse survival of iGCTs.

CONCLUSION: The classification of iGCTs based on many molecular markers is expected to provide more accurate information on their clinical-pathological features and survival analyses.

Mechanisms of Better Prognosis in IDH-Mutated Astrocytoma with 19q-Loss

We previously reported that there was a subgroup of IDH-mutated astrocytomas harboring only 19q-loss showing oligodendroglioma-like morphology and an overall survival (OS) compared with 19q-intact astrocytomas (Otani et al. Cancer Sci 2018). The purpose of the present study was to reveal how 19q-loss contributed to better prognosis and the morphology in the subgroup. We compared expression pattern between five 19q-loss and 19q-intact IDH-mutated astrocytomas by using IDH mutation and 136 up-regulated genes and 203 down-regulated genes were extracted in 19q-loss astrocytomas compared with 19q-intact astrocytomas. Significantly changed genes distributed throughout all chromosomes, but more down-regulated genes were on 19q and 4p, and more up-regulated genes were on 4q. Genes associated with apoptosis, cell adhesion, and antigen presentation were up-regulated, and genes associated with Ras signaling pathway were down-regulated. These changes could result in better prognosis. By contrast, there was no expression change detected gene associated with oligodendroglioma-like morphology although up-regulation of genes associated with axon guidance and down-regulation of genes associated with cell shape might result in the morphology or neuronal differentiation. Expression pattern of 19q-loss astrocytomas indicated no tendency of oligodendroglial differentiation.

Better prognosis of 19q-loss astrocytomas was derived from expression changes associated with tumor proliferation and tumor immunity.