ASTROCYTIC TUMORS WITH GAIN ON 7Q AND THOSE WITH GAIN OF WHOLE CHROMOSOME 7 BELONG TO DISTINCT SUBGROUPS CHARACTERIZED BY VARIOUS GENETIC FACTORS INCLUDING IDH1 AND TP53

Yuichi Hirose, MD, DMSc and Hikaru Sasaki; Fujita Health University

BACKGROUND: Many genetic studies on gliomas have reported the utility of DNA copy number aberrations (CNAs) in tumor classification, and we have previously shown that grade II–III adult supratentorial gliomas could be classified into clinically relevant subgroups based on the CNAs. The major CNAs in astrocytic tumors of these grades were gain of whole chromosome 7 (+7) and that on chromosomal arm 7q (+7q), and tumors with +7 had a worse outcome than tumors with 7q. However, it was not confirmed that the former could develop from the latter; that is, it is not clear that a stepwise DNA copy number gain on chromosome 7, beginning as partial gain of 7q, develops along with glioma progression. We then aimed to establish glioma development pathway model by combining information on CNAs and other genetic information.

METHODS: We analyzed the chromosomal DNA copy number aberrations of 160 adult supratentorial gliomas using comparative genomic hybridization as well as mutational status of IDH1 and TP53 by PCR-based direct sequencing. We also performed immunohistochemistry for c-Met whose gene is located in 7q34, that is included in the region with copy number gain in both +7 and +7q tumors. RESULTS: The most frequent aberration in IDH1 mutant tumors was -1p/19q followed by +7q, and, in contrast, IDH1 wild-type tumors showed +7 and, less frequently in grade II-III tumors, -10q. Kaplan-Meier estimates for progression free survival showed that the tumors with mutant IDH1, -1p/19q, or +7q (in the absence of +7p) survived longer than tumors with wildtype IDH1, +7, or -10q. Furthermore, +7q tumors showed TP53 mutation and c-Met overexpression whereas +7 tumors did not show these features. Paired analysis of astrocytic tumors for primary and recurrent disease showed that the majority of +7q tumors progressed without additional gain of 7p. In contrast to tumors with gain on chromosome 7, there is a lack of evidence to indicate that tumors with 1p/19q loss are composed of multiple lineages. CONCLUSIONS: We found +7q tumors were distinct tumor lineage from tumors with whole 7 gain, and, although associated with CNA in common region of the chromosome, tumors with a gain on chromosome 7 (mostly astrocytic) comprise multiple lineages, and such differences in their biological nature should be taken into consideration during their clinical management.

SECONDARY CATEGORY: n/a.