ABSTRACT

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Clinical, histopathological, and molecular features of IDH-wildtype indolent diffuse glioma: comparison with typical glioblastoma.

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PURPOSE: IDH-wildtype (IDHwt) diffuse gliomas are treated as glioblastoma, however, some of these may show less aggressive clinical courses. The authors investigated the clinical, histopathological, and molecular characteristics of such IDHwt indolent diffuse gliomas (iDGwt), which have not been well documented in the literature.

METHODS: Adult patients with IDHwt gliomas admitted between 2011 and 2020 were surveyed. In this particular study, the clinical indolence was defined mainly as having a small enhancing lesion and a stable period for more than 1 month before surgery. The current WHO diagnostic criteria were adapted for the diagnoses. Gene mutations and copy number changes in 43 representative glioma-associated genes, MGMT promoter methylation status, and survival data were compared with those of The Cancer Genome Atlas reference cohort.

RESULTS: Nine out of 180 surveyed cases (5.0%) fulfilled the present criteria of the iDGwt. Considering the representative regulatory pathways, 8 (88.9%), 4 (44.4%), and 1 (11.1%) case had genetic alterations in the PI3K/MAPK, TP53, and RB pathways, respectively. The frequency of the RB pathway alteration was significantly lower than that in the reference cohort (281 of 362 cases: 77.6%). Two cases (22.2%) showing EGFR amplification met the diagnostic criteria for glioblastoma, and the frequency was significantly lower than that in the reference cohort (412 of 426 cases: 96.7%). The overall survival (median: 37.5 months) in the present series was significantly longer than that in the reference cohort (n = 426, median: 13.9 months).

CONCLUSIONS: iDGwt lacked the molecular features of glioblastoma except for the PI3K/MAPK pathway alteration.

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