IDH1 mutations in grade II astrocytomas are associated with unfavorable progression-free survival and prolonged postrecurrence survival.


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Abstract

BACKGROUND: The favorable prognostic impact of mutations in the IDH1 gene is well documented for malignant gliomas; its influence on World Health Organization (WHO) grade II astrocytomas, however, is still under debate.

METHODS: A previously published database of 127 predominantly surgically treated patients harboring WHO grade II astrocytomas was revisited. Patients were screened for TP53 mutations (sequencing analysis), IDH1 mutations (pyrosequencing), and MGMT promoter methylation (methylation-specific polymerase chain reaction and bisulfite sequencing). Endpoints were overall survival, progression-free survival (PFS), time to malignant transformation, and postrecurrence survival. Radiotherapy was usually withheld until tumor progression/malignant transformation occurred.

RESULTS: IDH1 mutations, TP53 mutations, and methylated MGMT promoters were seen in 78.1%, 51.2%, and 80.0% of the analyzed tumors, respectively. IDH1 mutations, which were significantly associated with TP53 mutations and/or MGMT promoter methylation ($P < .001$), resulted in shortened PFS (median, 47 vs 84 months; $P = .004$); postrecurrence survival, however, was significantly increased in those patients undergoing malignant transformation (median, 49 vs 13.5 months; $P = .006$). Overall survival was not affected by IDH1. A similar pattern of influence was seen for MGMT promoter methylation. Methylated tumors did significantly worse (better in terms of PFS (postrecurrence survival)); a low number of unmethylated tumors, however, limited the power of this analysis. Conversely, TP53 mutations were stringently associated with a worse prognosis throughout the course of the disease.

CONCLUSIONS: IDH1 mutations are associated with a Janus headlike phenomenon; unfavorable prognostic influence on PFS turns into favorable impact on postrecurrence survival. A similar pattern of influence might exist for MGMT methylation.

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