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IDH-mutant grade 4 astrocytoma: a comparison integrating the clinical, pathological, and survival features between primary and secondary patients

Yanwei Liu ^{1 2}, Dezhi Gao ^{3 2}, Huiyuan Chen ⁴, Jing Zhang ¹, Kun Yao ⁵, Chenxing Wu ⁶,
Shouwei Li ⁶, Wei Yan ⁷, Xiaoguang Qiu ^{1 2}

Affiliations

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Abstract

Objective: IDH-mutant grade 4 astrocytomas (AIDHmut/G4) are divided into primary de novo (pAIDHmut/G4) and secondary with a history of prior lower-grade gliomas (LGGs; sAIDHmut/G4). The mutational spectrum and DNA methylation patterns are homogeneous within de novo pAIDHmut/G4 and evolved sAIDHmut/G4, but the two groups have different diagnoses, management, and outcomes. This study sought to systematically compare the clinical, pathological, and survival characteristics between them.

Methods: Of the 871 grade 4 astrocytomas with data for IDH mutation, 698 (80.1%) were primary and 173 (19.9%) were secondary. Of the 698 primary tumors, 103 (14.8%) were pAIDHmut/G4, and of the 173 secondary tumors, 108 (62.4%) were sAIDHmut/G4. Clinical, pathological, and survival features were compared between pAIDHmut/G4 and sAIDHmut/G4. Multivariate analyses were performed to identify prognostic factors.

Results: Patients with sAIDHmut/G4 had significantly shorter median overall survival (OS; 11.8 vs 34.2 months, hazard ratio [HR] 2.69, 95% confidence interval [CI] 1.367-5.306, $p = 0.004$) and progression-free survival (PFS; 8.5 vs 24.3 months, HR 2.83, 95% CI 1.532-5.235, $p = 0.001$) than patients with pAIDHmut/G4. In patients with sAIDHmut/G4, resection status and chemotherapy were independent prognostic factors for OS and PFS; in patients with pAIDHmut/G4, LGG component, resection status, and O6-methylguanine DNA methyltransferase promoter methylation were independent prognostic factors. The therapeutic strategies of LGGs did not influence survival of patients with sAIDHmut/G4, but patients who had not received radiotherapy or chemotherapy when they were diagnosed with LGGs were found to benefit from radiotherapy or chemotherapy when they progressed to sAIDHmut/G4.

Conclusions: The different clinical characteristics, survival, and risk factors between sAIDHmut/G4 and pAIDHmut/G4 provide a reference to guide treatment decisions in AIDHmut/G4.

Keywords: IDH mutation; LGG component; grade 4 astrocytoma; lower-grade glioma; primary; risk factors; secondary; survival; tumor.