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Survival analysis of adult midline-located gliomas and diffuse midline gliomas: beyond the H3K27 mutation paradigm

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Abstract

Purpose: Although pediatric midline-located gliomas (MGs) with H3K27 alteration have been widely known to have a poor prognosis, few researchers have assessed adult MGs with H3K27 alteration. We aimed to determine the effect of H3K27 alteration on the prognosis of adult MGs. And we tried to identify the factors affecting the prognosis of diffuse midline glioma (DMG). This is the first study to investigate the prognosis of adult DMGs according to histological grade and is the largest study to investigate the survival of adult patients with DMGs.

Methods: We reviewed the charts of adult patients diagnosed with MG after undergoing resection or biopsy at our institution between 2010 and 2020. The Gehan-Breslow-Wilcoxon test was used for univariate survival analysis, and the Cox regression proportional hazard model was used for multivariate survival analysis.

Results: Among the 124 adult MGs identified, 44 (35.5%) showed H3K27 alterations. Surprisingly, the H3K27 alteration group showed significantly better median survival than the wildtype group in patients of all ages (23.1 vs. 15.9 months, p = 0.040). Crucially, in the rigorous multivariable Cox regression analysis adjusting for age, performance status, and therapeutic modalities across all adult patients, the H3K27 alteration did not demonstrate a statistically significant independent negative effect on overall survival (HR 1.014, p = 0.956). In the survival analysis of 44 patients with DMG, low and intermittent histological grade, KPS ≥ 80, total resection, and concurrent chemoradiation therapy were associated with significantly better survival.

Conclusion: Unlike their pediatric counterparts, adult MGs with H3K27 alterations do not inherently confer a poor prognosis when adequately adjusted for clinical confounders. In adults, the survival trajectory of WHO grade 4 DMGs is profoundly dictated by their underlying morphological aggressiveness, functioning alongside KPS, extent of tumor resection, and adjuvant treatment strategies.

Keywords: Adjuvant chemoradiotherapy; Diffuse intrinsic pontine glioma; Diffuse midline glioma; H3K27 alteration.