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Clinical, surgical, and molecular characteristics and outcomes of adult patients with diffuse midline glioma, H3 K27-altered, treated with surgical resection

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Abstract

Purpose: To investigate the clinical, surgical, and molecular features and outcomes of adult patients with diffuse midline glioma (DMG), H3 K27-altered, treated with surgical resection.

Methods: We retrospectively analyzed 52 adult patients with cerebral H3 K27-altered DMG who underwent surgical resection. Next-generation sequencing (NGS) was performed on a subset (n = 20) to characterize the genomic landscape. Survival outcomes were evaluated using Kaplan-Meier analysis and Cox proportional hazards models.

Results: The median overall survival (OS) was 17.8 months. Genomic profiling revealed a distinct molecular landscape dominated by H3F3A mutations, with high-frequency co-occurring TP53 mutation. Crucially, we observed a significant enrichment of mutations within the RTK/RAS/PI3K signaling pathway, primarily driven by NF1, FGFR1, and PIK3CA. In the multivariable Cox regression model, postoperative adjuvant radiotherapy (RT + TMZ) emerged as the sole independent protective factor for overall survival (HR = 0.12, P < 0.001). Conversely, the extent of resection (RANO EOR Class) and molecular targeted therapy did not reach independent statistical significance, despite demonstrating favorable survival trends in univariable analyses.

Conclusion: Adult H3 K27-altered DMG represents a biologically unique entity with distinct genomic alterations. While postoperative radiotherapy (RT + TMZ) remains the irreplaceable prognostic cornerstone, maximal safe resection provides an essential cytoreductive foundation. Future paradigms should integrate safe resection and targeted agents into adult-tailored, multi-modal treatment frameworks.

Keywords: Adult; Diffuse midline glioma; H3K27-altered; Molecular landscape; Prognosis; Surgery.