

Observational Study

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High-grade glioma, IDH- and H3-wildtype in young adults: a rare condition with a distinct epigenetic landscape

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Abstract

Purpose: High-grade glioma, IDH- and H3-wildtype in young adults is a rare and poorly known entity. We compared newly diagnosed cases in young adults (18-39 years) to those in adult patients (> 39 years).

Methods: We performed an observational, retrospective, single-centre cohort study at a tertiary neurosurgical oncology centre between January 2006 and December 2023.

Results: We included 1.139 adult patients with a newly diagnosed high-grade glioma, IDH- and H3-wildtype. Young adults: (1) represent a small proportion of patients with high-grade glioma (n = 33, 2.9%); (2) have a high rate of unclassified cases based on epigenetics (n = 5, 15.2%); (3) have a longer progression-free survival (p = 0.003) and overall survival (p = 0.001) and; (4) do not have higher surgically-related adverse event rates (p = 0.198). Concerning young adults, surgical resection was associated with improved progression-free and overall survival (p < 0.001 and p < 0.001, respectively). The DNA-methylation class significantly impacts the overall survival (p = 0.028), however, the MGMT methylation status is not significantly associated with either progression-free or overall survival (p = 0.320 and p = 0.639, respectively).

Conclusion: High-grade glioma, IDH- and H3-wildtype is a rare histo-molecular subtype in young adults with a better prognosis than older adults. In young adults, DNA-methylation subtypes are different from their adult counterpart and had a significant impact on survival unlike MGMT status. Given the rarity in young adults, a dedicated management in specialized neurosurgical oncology centres is preferred. Further molecular and epigenetic analyses are required to understand the differences in prognosis compared to adult patients.

Keywords: Epigenetic; High-grade glioma; Neuro-oncology; Neurosurgery; Young adult.

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