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Clinical, molecular and radiological predictors of prognosis in newly diagnosed astrocytoma, IDH-mutant, WHO grade 4

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Abstract

Background: Astrocytoma, isocitrate dehydrogenase-mutant, WHO grade 4 (Astro4), is a new tumor type in the 2021 WHO classification of central nervous system tumors that has been poorly characterized in the literature. This study evaluates predictors of prognosis in a large cohort of newly diagnosed Astro4.

Methods: We retrospectively identified 128 consecutive adult patients who presented with an initial diagnosis of Astro4 at Dana-Farber Cancer Institute and Massachusetts General Hospital between 2010 and 2021. Clinical, molecular, and radiological characteristics were recorded, and their associations with overall survival (OS) and progression-free survival (PFS) were measured by log-rank test and Cox proportional hazards model.

Results: The median age at diagnosis was 37.1 years, and 61.7% were men. The median OS was 5.9 years (95% confidence interval, 4.4 - 7.3), while the median PFS was 2.7 years (1.8 - 3.6). Age ≥ 50 and homozygous CDKN2A/B deletion were independent negative prognosticators of OS on univariate and multivariate analyses [hazard ratio (HR), 2.21 (1.16 - 4.21), $p=0.019$; HR, 2.61 (1.27 - 5.38), $p=0.013$]. Maximal resection of enhancing disease was associated with longer PFS on univariate and multivariate analyses [HR, 0.48 (0.26 - 0.87), $p=0.019$]. There were no significant differences in OS or PFS based on MGMT promoter methylation status, T2/FLAIR extent of resection, T2/FLAIR mismatch, radiological pseudoprogression, or enhancement on the pre-operative scan.

Conclusions: Our study comprehensively characterizes a large cohort of newly diagnosed patients with Astro4, emphasizing the prognostic value of CDKN2A/B deletion, age, and the extent of resection of enhancing disease in these patients.

Keywords: CDKN2A/B deletion; IDH-mutant; WHO Grade 4; astrocytoma; prognosis.