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Histopathological and molecular characteristics of IDH-wildtype glioblastoma without contrast enhancement: implications for clinical outcomes

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Abstract

Background: Glioblastoma (GB) heterogeneity poses substantial challenges for diagnosis and treatment. IDH-wildtype GB may lack contrast enhancement on MRI and exhibit a "low-grade radiologic appearance" (non-CE GB), a phenomenon with unclear clinical implications. This study investigates the histopathological and molecular differences and survival outcomes between contrast-enhancing (CE) and non-CE GB.

Methods: This retrospective study at Heidelberg University Hospital analyzed 457 IDH-wildtype GB cases (09/2009-01/2021). Contrast enhancement on preoperative MRI was volumetrically assessed, classifying tumors as non-CE/CE GB using a 1 cm^3 cut-off. Molecular and histopathological features, including microvascular proliferation, necrosis, and overall survival (OS), were compared between the groups.

Results: Of the initial cohort, 352 (77%) patients met the inclusion criteria, with 44 (12.5%) non-CE and 308 (87.5%) CE GB. The histopathological assessment revealed that non-CE GB was less likely to present traditional hallmarks of glioblastoma, such as microvascular proliferation (39% vs. 94%) and necrosis (25% vs. 92%) ($p<0.001$). In the non-CE group, 24 patients (55%) were diagnosed as molecular-GB, compared to only 8 patients (3%) in the CE group ($p < 0.001$). A significant difference was observed in Ki-67 levels, with non-CE GBs having a lower mean Ki-67 index of 18 ± 12% compared to 26 ± 13% in CE tumors ($p<0.001$). The median OS was 27.2 months (95%CI 19.8-NA) for non-CE and 14.7 months (95% CI, 13.2-17.1) for CE GB ($p=0.0049$).

Conclusions: IDH-wildtype GBs without contrast enhancement are often diagnosed based on molecular criteria due to less frequent histopathological hallmarks and are associated with prolonged OS.

Keywords: IDH-wildtype glioblastoma; MRI; contrast-enhancement; histopathology; low-grade radiologic appearance.