J Neurooncol. 2025 Mar 6. doi: 10.1007/s11060-025-04977-3. Online ahead of print.

Extra-central nervous system metastasis from high-grade glioma: a single-institution experience

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PMID: 40055259 DOI: 10.1007/s11060-025-04977-3

Abstract

Purpose: Extra-central nervous system metastasis (ECM) from glioblastoma and other high-grade gliomas (HGGs) is exceedingly rare, likely due to central nervous system barriers and the short overall survival (OS) in HGG patients, limiting the timeframe for metastasis. Improved treatments have extended survival, potentially increasing ECM incidence, though mechanisms remain unclear.

Methods: This retrospective study examines HGG patients (n = 16) with ECM treated at The University of Texas M. D. Anderson Cancer Center from 1993 to 2023.

Results: Median age at HGG and ECM diagnoses were 33.6 and 35.1 years, respectively, with a slight female predominance. Diagnoses included glioblastoma, IDH-wildtype WHO Grade 4 (n = 11), epithelioid glioblastoma WHO Grade 4 (n = 2), astrocytoma IDH-mutant WHO Grade 4 (n = 2), and H3K27-altered diffuse midline glioma (n = 1). Median interval from HGG to ECM diagnosis was 10 months. The temporal lobe was the most common HGG site, with ECM primarily in cervical lymph nodes, bone, parotid gland, and cranial soft tissues. Genomic profiling identified TP53, EGFR, RB1, NF1, TERT promoter, and BRAF V600E mutations. Median OS from HGG diagnosis was 23.4 months, and median OS following ECM diagnosis was 5.9 months. Chemotherapy and radiotherapy to ECM sites extended survival. Leptomeningeal disease was present in 50% of cases and correlated with worse prognosis. ECM typically developed in advanced disease stages.

Conclusion: This study highlights genomic alterations, management, and outcomes associated with ECM in HGG. Tumor spread may stem from neurosurgical manipulation and occur via hematogenous and/or lymphatic routes. Multimodal treatment extends survival. Targeted therapies based on molecular profiles should be explored.

Keywords: Diffuse midline glioma; Extra-central nervous system metastasis; Glioblastoma; High-grade glioma.