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Unraveling the Molecular Basis of Extracranial Glioblastoma Metastasis: A Case Report and Literature Review

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Abstract

Glioblastoma (GB), IDH-wildtype (IDH-wt), is the most prevalent primary malignant brain neoplasm in adults. Despite adjuvant therapy, the prognosis for these tumors remains dismal, with a median survival of around 15-18 months. Although rare, extracranial metastases from GB are reported with increasing frequency, likely due to advancements in follow-up, treatments, and improved patient survival. The molecular mechanisms driving the dissemination of GB beyond the central nervous system (CNS) remain elusive, and controversy persists regarding whether these metastasizing tumors possess distinct molecular profiles and whether patients exhibit specific clinical characteristics. We present here a detailed analysis of the molecular evolution of a GB, IDH-wt in a woman in her early forties who subsequently developed extracranial metastases to the liver and spine. This case study provides insights into the mechanisms underlying the dissemination of GB beyond the CNS. By comprehensively reviewing the molecular findings of the literature, we identified frequent TP53 mutations in the tumors at initial diagnosis, as well as evidence of the presence of different clones denoting molecular heterogeneity in those metastasizing tumors. Furthermore, a subset of younger female patients whose tumors at diagnosis present PTEN alterations acquires additional TP53 clonal alterations at recurrence and metastasis. Our findings may contribute to improved prognosis, follow-up, and treatment strategies in GB, IDH-wt patients.

Keywords: PTEN; TP53; extracranial metastasis; glioblastoma; molecular genetic alterations.