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Outcomes of HSV-1 encephalitis infection in glioblastoma: An integrated systematic analysis

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Abstract

Introduction: Herpes Simplex Virus-1 (HSV-1) is a neurotropic DNA virus with neural latency and stereotypic viral encephalitis. It has been reported to conceal underlying glioblastoma (GBM) due to similar radiographic imaging and clinical presentation. Limited data exist on the co-occurrence of GBM and HSV-1. To better describe the pathophysiology of HSV-1 superinfections in GBM, we performed a comprehensive review of GBM cases with superimposed HSV-1.

Methods: A comprehensive literature search of six electronic databases with apriori search criteria was performed to identify eligible cases of GBM with HSV-1. Relevant clinic-radiographic data were collected, Kaplan-Meier estimates, Fisher's exact test, and logistic regression analyses were used.

Results: We identified 20 cases of HSE in GBM with an overall survival (OS) of 8.0 months. The median age of presentation was 63 years (range: 24-78 years) and the median interval between GBM or HSE diagnosis was 2 months (range: 0.05-25 months). HSE diagnosis before GBM diagnosis was a predictor for improved survival (HR: 0.06; 95% CI: [0.01-0.54]; $p < 0.01$). There is a significant reduction in OS in patients with concomitant HSE and GBM compared to the cancer genome atlas (TCGA) cohort (median OS: 8 months vs. 14.2 months; $p < 0.05$). Finally, HSV does not directly infect GBM cells but indirectly activates a local immune response in the tumor microenvironment.

Conclusions: Superimposed HSE in GBM may contribute to a significant reduction in OS compared to uninfected controls, potentially activating proto-oncogenes during active infection and latency. Preoperative HSE may induce an antiviral immune response, which may serve as a positive prognostic factor. Prompt antiviral treatment upon co-occurrence is necessary.

Keywords: Encephalitis; GBM; Glioblastoma; HSV; Herpes encephalitis; Herpes simplex.