Malignant Transformation in the Biphasic Gliosarcoma

2022 Lifespan Research Day Abstract

Research Category: Clinical & Translational

Primary Research Location: Department of Neuropathology, Rhode Island Hospital, Lifespan, The Warren Alpert Medical School of Brown University, Providence, RI 02903, USA

Funded By: –

Authors(s):

Karin S Ludwig, MD, Post–Doctoral, Rhode Island Hospital. Dept of Pathology & Laboratory Medicine

John E Donahue, MD, Associate Professor, Rhode Island Hospital, Brown University. Dept of Neurology, Pathology & Laboratory Medicine

Suzanne De La Monte, MD, MPH, Professor, Rhode Island Hospital, Brown University. Dept of Neurosurgery, Pathology & Laboratory Medicine

Abstract

Background & Aim: Primary gliosarcoma (PGS) is a rare, malignant brain tumor consisting of glial and mesenchymal elements and categorized as a variant of glioblastoma (GBM) per the WHO classification. The purpose of this study is looking first at how the mesenchymal foci are diagnosed based on current practices examining typical histomorphology, stains, and molecular studies. The second is examining the pathogenesis of the sarcomatous foci, given its CNS location and monoclonal glial origin and fibroblastic changes that enable this tumor to shift glio–mesenchymal boundaries.

Methods: This is a PubMed literature review using 'pathology of gliosarcoma' keywords. Review articles were selected if pertaining to PGS pathogenesis, in particular the sarcomatous foci, and its diagnosis using stains, molecular, and genetic studies of this rare tumor.

Results: The current protocol for diagnosing PGS includes GBM histopathologic features (nuclear atypia, mitoses, necrosis, and endothelial proliferation) and sarcomatous foci showing densely–packed, spindle–shaped cells with herringbone architecture; however, it may present as fibroblastic, osteogenic, chondrogenic, adipogenic, and smooth/skeletal muscle lineages. The glioma is positive for GFAP/Olig2 and lacks IDH mutation. The sarcoma is positive for reticulin and vimentin. The pathogenesis of gliosarcoma remains elusive. It was conceived as hyperplastic vessels with perivascular sarcomatous elements; however, further studies showed identical genetic abnormalities in both glial and mesenchymal components, suggesting a common cell origin. The current view has shifted towards glial cells with aberrant mesenchymal gene expression and subsequent differentiation.

Conclusion: The current WHO classification of CNS tumors recognizes PGS as one of three GBM histologic subvariants. PGS differs from GBM by incorporating sarcomatous elements with malignant glioma. The mesenchymal foci arise in high–grade gliomas that enable aberrant mesenchymal gene expression with subsequent glial–mesenchymal transformation. PGS then behaves in typical sarcomatous fashion with propensity to metastasize outside the CNS.

Clinical Implications: It remains unclear why 2% of GBMs are able to express mesenchymal genes allowing glial–mesenchymal cell transformation (GMT). Given the similarity between GMT and epithelial–mesenchymal transition (EMT), a physiologic and pathologic process, GMT may also be physiologic or a response to other brain pathologies like trauma or stroke.