

Primary Gliosarcoma of the Brain: A Case Report and Review of Literature

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Abstract

Case Report

This report describes a case of gliosarcoma (GS), a rare primary malignant brain tumor with a biphasic histological pattern. The patient was a 70-year-old male who presented with gradual memory impairment without signs of increased intracranial pressure. Magnetic resonance imaging (MRI) revealed a heterogeneous right frontal lesion with significant edema, suggestive of a glial tumor. The patient underwent a biopsy, which identified a pseudo-encapsulated, highly vascularized tumor. Histopathological examination showed a malignant, dense tumor proliferation composed of a glial component positive for GFAP and a sarcomatous component positive for vimentin, confirming the diagnosis of GS. The characteristic imaging features of GS, including hypointensity on T2-weighted MRI and ring-like enhancement, were also observed in this case. The patient was treated with maximal safe surgical resection followed by concurrent radiation therapy (60 Gy in 30 fractions) and temozolomide chemotherapy, as per the standard Stupp protocol for glioblastoma. Despite this multimodal approach, the prognosis for GS remains poor, with a median survival time comparable to glioblastoma. This case report illustrates the clinicopathological features of this rare and aggressive primary brain tumor, highlighting the importance of accurate diagnosis and multidisciplinary management. Ongoing research is needed to elucidate the pathogenesis and identify novel therapeutic targets to improve outcomes for patients with gliosarcoma.

Keywords: Gliosarcoma (GS), brain tumor, Magnetic resonance imaging (MRI), glial tumor.

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INTRODUCTION

Gliosarcoma (GS), a subtype of glioblastoma (GBM), is a rare primary malignant tumor of the central nervous system. GS has a bimorphic histological architecture that includes both gliomatous (WHO grade 4) and sarcomatous components [1-4]. Strobe initially reported this tumor in 1895. But Feigen and Gross (1955) were the first to characterize these tumors in detail [1, 2]. They have genetic, clinical, and prognostic similarities to GBM. As therefore, it is not unusual that they are treated in an approach similar to the GBM [4, 5]. However, certain characteristics of GS point to a distinct clinicopathological behavior, including peripheral location on cerebral lobes, a tendency for dural attachment, resemblance to meningiomas, a proclivity to produce intra or extracranial metastasis, and a purportedly poor survival rate when compared to GBM [6]. Because of the disease's rarity and the dearth of large prospective studies, the literature on GS is composed of smaller series with often conflicting findings, particularly related to the role of chemotherapy and survival outcome. In this paper, we present a clinical case of gliosarcoma and discuss the anatomoclinical

characteristics, as well as the diagnostic and therapeutic aspects of this rare entity. In macroscopic examination, the material consisted of multiple fragments of whitish and grayish appearance.

PATIENT AND OBSERVATION

This is a 70-year-old patient with no notable medical history who has developed gradual memory impairment without signs of increased intracranial pressure (ICP) or other neurological symptoms. A brain MRI revealed a heterogeneous right frontal lesion with significant edema, which suggested a glial tumor (Figure 1). The patient received a course of corticosteroid therapy followed by a fragmented excisional biopsy. A pseudo-encapsulated tumor was found. The material was sent to the pathologist. The histopathological examination of the specimens showed a malignant, dense, and highly vascularized tumor proliferation composed of interlacing bundles of fusiform cells with moderately enlarged, slightly hyperchromatic nuclei, often in mitosis. The stroma is remodeled by tumor necrosis. The tumor proliferation is surrounded by a thin rim of glial tissue. In Immunohistochemical study, the

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glial component showed positive staining for GFAP. The sarcomatous component showed positive staining for vimentin and negative staining for GFAP. These findings are consistent with the diagnosis of primary gliosarcoma. The patient received concurrent chemoradiation therapy

according to the Stupp Protocol: Radiation therapy: 60 Gy in 30 fractions over 6 weeks and Temozolomide: 75 mg/m²/day for 42 consecutive days with Adjuvant chemotherapy: Six cycles of 150-200 mg/m²/day on days 1-5, starting every 28 days.

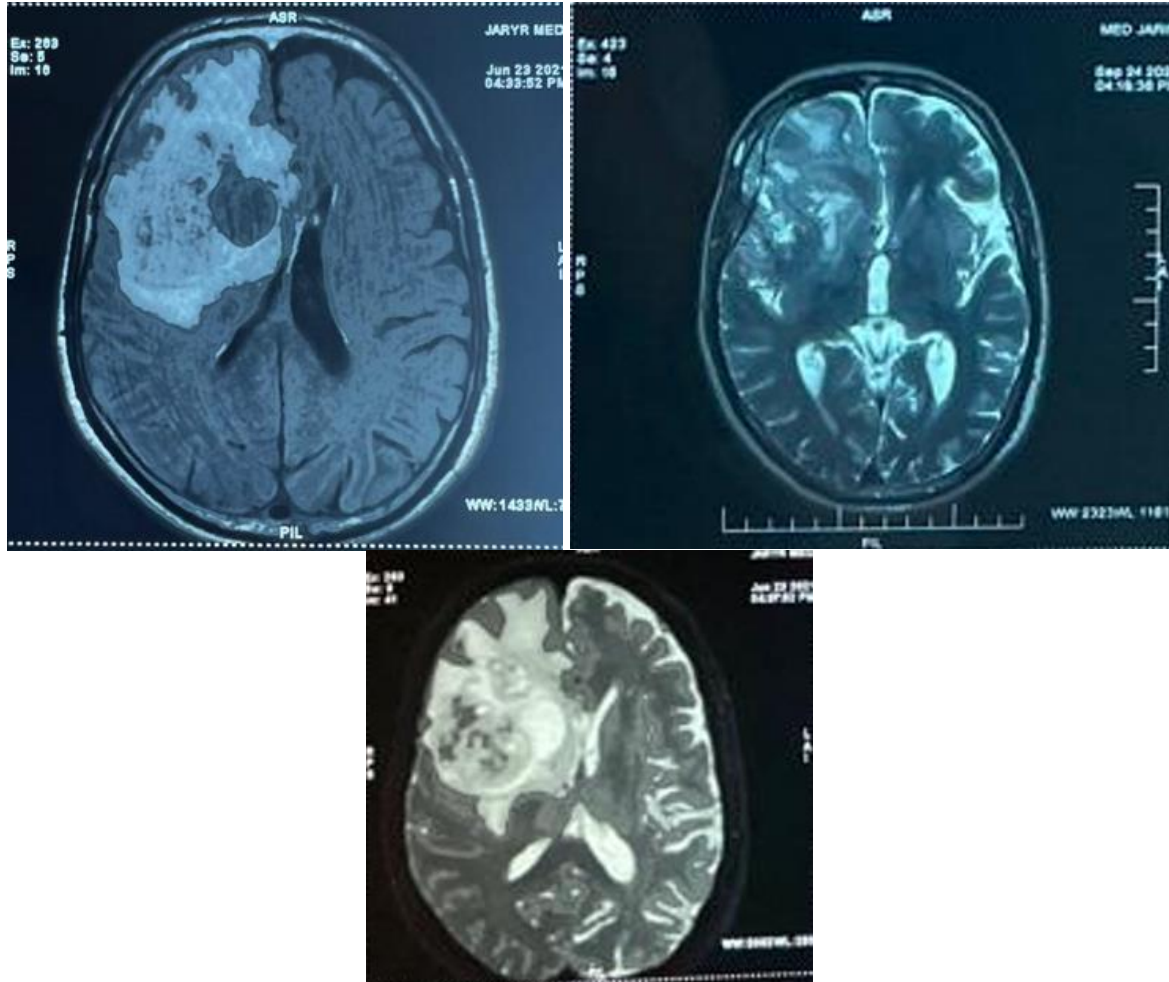


Figure 1: 70-year-old men with Primary Gliosarcoma of the Brain

DISCUSSION

Gliosarcoma (GS) is a rare primary malignant tumor of the central nervous system, accounting for 2% of all glioblastomas and 0.59-0.76% of all brain tumors [2]. GS is a glial tumor formed by a dual proliferation associating two distinct components, one high-grade glial and the other mesenchymal. The glial component is often of the glioblastoma type or exceptionally of the oligodendroglioma type [3]. The mesenchymal component can present with varied morphological aspects, it is a malignant type component [4, 5]. The age of onset of gliosarcoma is similar to that of glioblastoma, with a preferential occurrence between 40 and 60 years of age and an average age of 52.1 years. Rare cases have been reported in children. Men are more frequently affected [6] with a sex ratio of 1.4 to 1.8/1 [7-9]. Gliosarcomas are most commonly located in the temporal or parietal lobes, accounting for over 65% of cases. These lobes are situated on the sides and top of the

brain, respectively. Frontal, parietal, and occipital lobe locations are less frequent [10-12]. These lobes are found at the front, top-back, and back of the brain, respectively. In rare instances, gliosarcomas may affect the infratentorial region, which includes the brainstem and cerebellum, or the spinal cord [7, 13]. The clinical Presentation of gliosarcoma is typically rapid, with symptoms developing over a period of one week to three months. The symptomatology varies depending on the affected brain region. Common manifestations include: Signs of increased intracranial pressure, such as headaches, nausea, and vomiting, Hemiparesis, Homonymous hemianopsia, and aphasia [14]. Due to the presence of the sarcomatous component, gliosarcomas have a higher propensity to metastasize compared to glioblastomas. In some cases, gliosarcomas are first detected at the metastatic stage [15]. The computed tomography (CT) appearance of gliosarcomas may resemble glioblastomas on CT scans. Gliosarcomas typically present as Well-defined, hyperdense mass with

disproportionate peritumoral edema relative to the tumor size. The magnetic resonance imaging (MRI) appearance is characteristic, showing a well-defined, intra-axial tumor in contact with the dura mater. The Intermediate signal intensity on T2-weighted images, similar to gray matter but hypointense compared to other glial tumors. Following gadolinium injection, the tumor shows significant ring enhancement on T1-weighted images. Sometimes a ring-like appearance is observed. Therefore, the diagnosis of gliosarcoma should be considered for any intra-axial, primary tumor that is hypointense on T2-weighted images and in contact with the dura mater [15]. For Macroscopic Appearance of Gliosarcoma, it exhibit distinct macroscopic features that aid in their initial identification: The tumor tissue is typically firm and solid to the touch, unlike softer and more gelatinous glioblastomas, the tumor often presents with a lobulated appearance, characterized by rounded or irregular projections on its surface and Unlike infiltrative glioblastomas, gliosarcomas tend to have well-defined margins, meaning they are more clearly demarcated from the surrounding brain tissue. But the extent of the mesenchymal component can influence the macroscopic characteristics of gliosarcoma: When the mesenchymal component is more prominent, the tumor becomes even harder and more well-defined. This can lead to misdiagnosis as a metastasis or, if attached to the dura mater, a meningioma [14]. Microscopically, gliosarcoma exhibits a biphasic pattern with a mixture of two components. The first component consists of a glial component typical of glioblastoma with varying degrees of anaplasia. The second component is sarcomatous, often resembling a fibrosarcoma, with highly atypical characterized by spindle-shaped cells (fibroblasts) arranged in bundles. The sarcomatous component can also resemble a malignant histiocytoma or exhibit other types of differentiation such as cartilage formation, bone tissue, smooth or striated muscle tissue, and even adipocytic differentiation [6]. The distinction between the glial and mesenchymal components in gliosarcoma is crucial for accurate diagnosis and understanding the tumor's behavior. Histochemical and immunohistochemical techniques have proven invaluable in aiding this differentiation: The mesenchymal component expresses vimentin, an intermediate filament protein characteristic of mesenchymal cells. In contrast, the glial component expresses GFAP, a marker protein specifically found in glial cells. Additionally, Masson's trichrome staining shows the presence of collagen in the mesenchymal component [15]. The histogenesis of gliosarcoma is controversial due to the lack of standardized diagnostic criteria, conflicting findings from immunohistochemical analyses, and the intricate interplay of potential formation mechanisms contribute to this enduring mystery. According to Meyer's classification, three primary mechanisms could explain the formation of biphasic tumors like gliosarcoma: a collision mechanism, where Two distinct tumors, arising from different cell lineages, fortuitously encounter and merge

to form a single biphasic tumor; an induction mechanism, where A pre-existing tumor, typically a glioma, induces the transformation of surrounding cells into a different tumor type, the sarcomatous component in the case of gliosarcoma ; and a transformation mechanism, where A portion of a primary gliomatous tumor undergoes a poorly understood transformation, giving rise to the sarcomatous component within the initial tumor itself [16].

Genetically, gliosarcomas exhibit a distinct genetic profile that sets them apart from their glioblastoma counterparts. While glioblastomas are classified into primary and secondary variants, gliosarcomas share more genetic similarities with secondary glioblastomas, suggesting a potential shared developmental pathway. Reis *et al.*, (2000) reported mutations in TP53 in 23%, mutations in PTEN in 38%, deletions of p16INK4 in 37%, but rarely show amplification of EGFR (<8%) [17]. The treatment of gliosarcomas relies on surgical resection, radiation therapy, and chemotherapy. Each modality plays a crucial role in maximizing patient outcomes [18]. Surgical resection can be partial or total depending on the extent of the tumor and is followed by radiotherapy delivering a total dose of 60 Gray (Gy), typically divided into 30 daily fractions of 2 Gy each. Studies have demonstrated the clear benefits of adjuvant radiation therapy following surgical resection for gliosarcoma. Research by Chang *et al.*, (2005) compared the outcomes of patients treated with surgery alone to those who received surgery followed by radiation therapy. The results showed a significant improvement in median survival for patients in the adjuvant radiation therapy group (10.6 months) compared to those who received surgery only (6.2 months) [19]. Despite their chemoresistant nature, temozolomide at a dose of 75 mg/m² remains the most commonly used molecule in conjunction with radiotherapy, followed by an adjuvant dose of 150 mg/m² over 5 cycles. This protocol has led to improved survival [20]. However, recent studies have shown that primary and secondary gliosarcomas, as well as glioblastomas, have nearly equivalent prognoses. The respective median survival times for glioblastomas, primary gliosarcomas, and secondary gliosarcomas (after the initial diagnosis of glioblastoma) are 12 to 18 months, 13.9 months, and 12.6 months [6, 21].

CONCLUSION

Gliosarcoma is a rare and aggressive brain tumor characterized by its dual glial and sarcomatous components. Clinical presentation varies depending on tumor location and infiltration, with common symptoms including focal neurological deficits, seizures, and increased intracranial pressure. Imaging modalities like CT and MRI aid in diagnosis, while definitive confirmation relies on histological examination.

Surgical resection remains the mainstay of treatment, with the extent of resection significantly impacting prognosis. Adjuvant radiation and chemotherapy may be employed post-surgery to eliminate residual tumor cells and reduce recurrence risk. Prognostic factors include age, overall health, tumor location and size, and molecular profile.

Ongoing research focuses on developing more effective treatment strategies and identifying novel therapeutic targets to improve survival rates and quality of life for gliosarcoma patients.

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