

ROMANIAN NEUROSURGERY

Vol. XXXX | No. 3

September 2026

Left frontal WHO grade 4 gliosarcoma
with glial and sarcomatous component
in a young adult female: a case report
with literature review

Namit Singhal,
Vinay Agarwal,
Mayank Agarwal,
Ankur Agarwal



Left frontal WHO grade 4 gliosarcoma with glial and sarcomatous component in a young adult female: a case report with literature review

Namit Singhal¹, Vinay Agarwal², Mayank Agarwal³, Ankur Agarwal⁴

¹ Department of Neurosurgery, S. S. Hospital of Neurosciences, Spine and Trauma Centre, Agra, Uttar Pradesh, INDIA

² Department of Neurology, Vinay Agarwal Neurology Clinic, Agra, Uttar Pradesh, INDIA

³ Department of Neurosurgery, Sarojini Naidu Medical College, Agra, Uttar Pradesh, INDIA

⁴ Advanced Imaging and Pathology Private Limited, Agra, Uttar Pradesh, INDIA

ABSTRACT

Gliosarcoma (GS) is a rare and aggressive variant of glioblastoma (GBM), accounting for 2–8% of all GBM cases. It is characterized by biphasic histology comprising glial and sarcomatous components and carries a dismal prognosis. A 32-year-old female presented with progressive headache, vomiting, seizures, and right-sided weakness for two months. Magnetic resonance imaging revealed heterogeneously enhancing left frontal lesion with mass effect, for which patient underwent near-total surgical excision. Histopathological examination demonstrated biphasic morphology with glial and sarcomatous components, mitotic activity, giant tumor cells, and extensive necrosis. Immunohistochemistry revealed GFAP positivity in the glial component and vimentin, SMA, and weak GFAP positivity in the sarcomatous component. ATRX was retained, IDH-1 was negative, and Ki-67 index was 50%, confirming WHO grade 4 GS with smooth muscle differentiation. Despite aggressive multimodal therapy including surgery, radiotherapy, and temozolomide-based chemotherapy, the patient succumbed after three cycles, reflecting the poor prognosis associated with GS.

INTRODUCTION

Gliosarcoma (GS) is a rare and aggressive variant of isocitrate dehydrogenase (IDH)-wildtype glioblastoma (GBM), constituting approximately 2% to 8% of all GBMs and 1.8% to 2.6% of all glioblastoma multiforme cases [1,2]. While GS typically affects patients in their fifth to seventh decades of life with a male predominance, it remains exceptionally rare in younger adults [3]. Radiologically, GS often mimics GBM or metastatic lesions, presenting as a well-demarcated, peripherally located supratentorial mass with heterogeneous enhancement and significant perilesional edema [1].

Keywords
case report,
glioblastoma,
gliosarcoma,
immunohistochemistry,
radiotherapy,
temozolomide



Corresponding author:
Namit Singhal

S. S. Hospital of Neurosciences,
Spine and Trauma Centre, Agra, India

singhalnamit77@gmail.com

Copyright and usage. This is an Open Access article, distributed under the terms of the Creative Commons Attribution Non-Commercial No Derivatives License (<https://creativecommons.org/licenses/by-nc-nd/4.0/>) which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is unaltered and is properly cited.

The written permission of the Romanian Society of Neurosurgery must be obtained for commercial re-use or in order to create a derivative work.

ISSN 2344-4959 (online)
ISSN 1220-8841 (print)

© Romanian Society of
Neurosurgery



First published
September 2026 by
London Academic Publishing
www.london-ap.uk

Diagnosis relies on histopathological examination (HPE) and immunohistochemistry (IHC), demonstrating glial fibrillary acidic protein (GFAP)-positive glial areas and reticulin-rich sarcomatous regions [2]. Despite maximal safe resection and adjuvant chemoradiotherapy with temozolomide, the prognosis remains poor, with a median overall survival of around 13.3 months and a high propensity for recurrence [4,5]. We report a rare case of left frontal WHO grade 4 gliosarcoma in a 32-year-old female, highlighting its diagnostic challenge and aggressive clinical course.

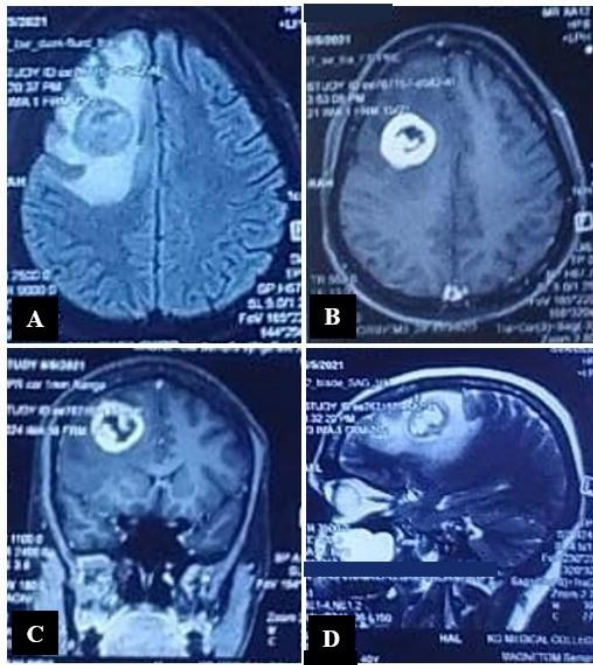


Figure 1. Magnetic resonance imaging of brain [axial (A and B), coronal (C), and sagittal (D)] illustrating heterogeneously peripherally enhancing oval shaped mass lesion is seen in left frontal lobe with central necrosis and adjacent perifocal edema changes causing mass effect with midline shift of around 4.0 mm toward left side.

CASE REPORT

A 32-year-old female presented with progressive headache, vomiting, seizures, and right-sided weakness for two months. There was no significant medical history. Magnetic resonance imaging (MRI) of the brain revealed heterogeneously peripherally enhancing oval shaped mass lesion is seen in left frontal lobe with central necrosis and adjacent perifocal edema changes causing mass effect with midline shift of around 4.0 mm toward left side

suggesting high-grade glioma (Figure 1). Based on these findings, the patient underwent near-total surgical excision of the tumor.

The tissue specimens were sent for HPE. Postoperatively, the patient was clinically and neurologically stable, with no observed complications; thus, he was discharged on the fifth postoperative day. Postoperative MRI brain revealed a tumor cavity.

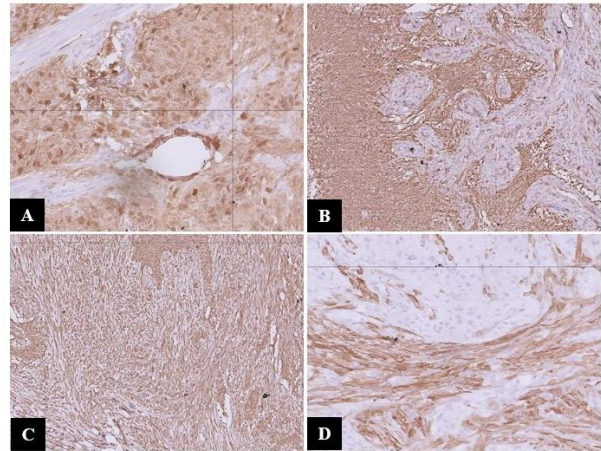


Figure 2. Histopathological examination demonstrating biphasic morphology with glial component showing pleomorphic cells with ovoid nuclei, coarse chromatin, and inconspicuous nucleoli, and the sarcomatous component showing spindle cells arranged in interlacing fascicles.

Microscopically, the tumor demonstrated biphasic morphology involving glial and sarcomatous tissues intimately admixed together. The glial component included pleomorphic cells with ovoid nuclei, coarse chromatin, and inconspicuous nucleoli, while the sarcomatous component included spindle cells arranged in interlacing fascicles (Figure 2). Moreover, there was presence of mitotic activity, giant tumor cells, and extensive areas of necrosis.

IHC revealed that the glial component expressed GFAP, S100, and Vimentin, while it was negative for SMA, Desmin, H-Caldesmon, and CD31. The sarcomatous component expressed Vimentin, SMA, GFAP (weak), and Factor VIIIa (weak), while it was negative for S100, Desmin, H-Caldesmon, and CD31. Moreover, ATRX was retained, P53 was mild type (patchy), Ki67 index was 50%, and isocitrate dehydrogenase (IDH)-1 was negative. Use of reticulin stain highlighted reticulin fibres in sarcomatoid areas. These findings led to the final diagnosis of

WHO grade 4 gliosarcoma with prominent smooth muscle component.

Postoperatively, the patient received adjuvant radiotherapy with temozolomide-based chemotherapy. However, after three cycles, the patient succumbed.

DISCUSSION

Gliosarcoma (GS) was first described by Stroebe in 1895 and later characterized by Feigin *et al.* in 1955 [6]. According to the World Health Organization (WHO) classification, GS is considered a grade IV tumor and a subtype of IDH-wildtype GBM [3]. GS typically affects adults in their fifth to sixth decades of life, with a mean age of approximately 59 years and a slight male predominance (1.8:1) [1,2]. Our patient, a 32-year-old female, represents a younger demographic, though cases in young adults have been documented [7]. While most GSs arise *de novo* with no identifiable risk factors, as in our patient, a subset is secondary, linked to prior therapeutic cranial irradiation or progression from lower-grade gliomas [8,9].

The clinical presentation of GS mirrors that of GBM [6], dictated by tumor location and mass effect. The most common clinical presentation includes headache, focal neurological deficits, seizures, and signs of raised intracranial pressure [8], consistent with presenting feature of our patient, including progressive headache, vomiting, seizures, and right-sided weakness. These are classic sequelae of a rapidly expanding frontal lobe lesion causing significant midline shift.

The pathogenesis of GS remains debated, with two main theories proposed. The collision tumor hypothesis suggests that the sarcomatous component arises from neoplastic transformation of hyperplastic blood vessels within the glioma [6]. However, the monoclonal origin theory, supported by similar genetic alterations in both components, is currently favored [10]. IHC findings, in our patient, strongly support this and demonstrated the classic biphasic morphology with GFAP-positive glial cells and vimentin-positive spindle cells, along with a prominent smooth muscle component (SMA positivity), representing an unusual mesenchymal differentiation pattern [6,8]. The high Ki-67 index of 50% reflects the aggressive proliferative drive [8], and retained ATRX expression with negative IDH-1 status are consistent with primary GS [10].

MRI typically reveals a well-demarcated supratentorial mass with heterogeneous signal intensity and rim-like enhancement [1]. In our patient, heterogeneously enhancing left frontal mass with perilesional edema aligns with these findings. The differential diagnosis for an MRI showing a peripherally enhancing mass with central necrosis primarily includes GBM and cerebral metastasis [2]. Key histological mimics include desmoplastic GBM, malignant solitary fibrous tumor, and high-grade meningioma [9]. The presence of a true biphasic pattern with reticulin-rich sarcomatous zones and GFAP-rich glial zones, as highlighted by the reticulin stain in our patient, is diagnostic for GS [2]. IHC is paramount in resolving this differential, with our panel effectively ruling out solitary fibrous tumor (negative CD31, factor VIIIa weak) and pure glioma.

Standard treatment follows GBM protocols: maximal safe resection followed by radiotherapy and temozolomide-based chemotherapy [5]. Our patient underwent near-total resection followed by adjuvant chemoradiotherapy, yet succumbed after three cycles, reflecting the aggressive nature of this tumor. Despite treatment, mean overall survival is 13 months (6.9 - 19.4 months), with a 2-year survival rate of 32.6% [7]. Primary GS has a slightly worse prognosis than GBM, and the presence of mesenchymal differentiation does not appear to confer a survival advantage [1,2]. Recurrence rates exceed 90%, and GS exhibits a higher propensity for extracranial metastasis (approximately 11%) compared to GBM [2,5].

Poor prognostic factors include advanced age, low Karnofsky performance status, incomplete resection, and TP53 mutation [4,11]. In our patient, young age might have favored a better outcome, but the high Ki-67 index (50%) and extensive necrosis suggested aggressive behavior.

CONCLUSION

This case of a young female with WHO Grade 4 gliosarcoma demonstrates a rapidly fatal outcome despite aggressive multimodal treatment, consistent with its characteristically poor prognosis compared to conventional GBM. The case highlights the critical role of a thorough IHC panel in distinguishing its biphasic glial and sarcomatous differentiation from other conditions with similar presentation.

Acknowledgements

Authors would like to thank Dr. Vikas S. Sharma (MD), CEO, Maverick Medicorum® (), for manuscript writing, editing, submission, and post-submission services.

Author contributions

NS: data collection and research project execution. VA: contribution to the concept and design, drafting the manuscript. MA: conception of the work, manuscript revision. AA: conception of the work, approved the version to be published.

REFERENCES

1. Sampaio L, Linhares P, Fonseca J. Detailed magnetic resonance imaging features of a case series of primary gliosarcoma. *Neuroradiol J.* 2017;30(6):546-553. doi: 10.1177/1971400917715879.
2. Fan H, Yu Y, Du J, Liu L, Luo Y, Yu H, *et al.* Computed Tomography, Magnetic Resonance Imaging, and Pathological Features of Gliosarcoma. *Neuropsychiatr Dis Treat.* 2022;18:2577-2589. doi: 10.2147/NDT.S386616.
3. Din NU, Ishtiaq H, Rahim S, Abdul-Ghafar J, Ahmad Z. Gliosarcoma in patients under 20 years of age. A clinicopathologic study of 11 cases and detailed review of the literature. *BMC Pediatr.* 2021;21(1):101. doi: 10.1186/s12887-021-02556-9.
4. Zhang Y, Ma JP, Weng JC, Wang L, Wu Z, Li D, *et al.* The clinical, radiological, and immunohistochemical characteristics and outcomes of primary intracranial gliosarcoma: a retrospective single-centre study. *Neurosurg Rev.* 2021;44(2):1003-1015. doi: 10.1007/s10143-020-01285-4.
5. Wang X, Jiang J, Liu M, You C. Treatments of gliosarcoma of the brain: a systematic review and meta-analysis. *Acta Neurol Belg.* 2021;121(6):1789-1797. doi: 10.1007/s13760-020-01533-w.
6. Awadalla AS, Al Essa AM, Al Ahmadi HH, Al Ojan A, Muazen Y, Alsayyah A, *et al.* Gliosarcoma case report and review of the literature. *Pan Afr Med J.* 2020;35:26. doi: 10.11604/pamj.2020.35.26.17577.
7. Kakkar N, Kaur J, Singh GK, Singh P, Siraj F, Gupta A. Gliosarcoma in Young Adults: A Rare Variant of Glioblastoma. *World J Oncol.* 2017;8(2):53-57. doi: 10.14740/wjon998w.
8. de Macedo Filho LJM, Barreto EG, Martins PLB, Filho ENS, Gerson G, de Albuquerque LAF. IDH1-mutant primary intraventricular gliosarcoma: Case report and systematic review of a rare location and molecular profile. *Surg Neurol Int.* 2020;11:372. doi: 10.25259/SNI_586_2020.
9. Athinodorou IP, Kolios K, Koumoundourou D, Constantoyannis C. A Challenging Diagnosis of Gliosarcoma: A Case Report. *Cureus.* 2025;17(6):e85292. doi: 10.7759/cureus.85292.
10. Otsu Y, Matsumoto Y, Higaki K, Furuta T, Moritsubo M, Yoshitake H, *et al.* Gliosarcoma with unusual glial components: Two case reports. *Neuropathology.* 2022;42(4):282-288. doi: 10.1111/neup.12803.
11. Tan AC, Ashley DM, López GY, Malinzak M, Friedman HS, Khasraw M. Management of glioblastoma: State of the art and future directions. *CA Cancer J Clin.* 2020;70(4):299-312. doi: 10.3322/caac.21613.