

# Clinical Presentation, Approach and Outcome of Gliosarcoma: A Series of 12 Cases

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## ABSTRACT

Gliosarcoma (GSM) is a rare and aggressive type of brain tumour with limited treatment options and a poor prognosis. The present case series aimed to provide further insights into the clinical features, treatment outcomes, and prognosis of GSM. Medical records of 12 histologically confirmed cases of GSM were analysed from 2018 to 2022, revealing a male predominance and a median age of 54 years. The most common symptoms were headache and vomiting due to raised intracranial pressure. All patients underwent maximal safe resection followed by concurrent chemoradiation and adjuvant chemotherapy with Temozolomide (TMZ). Kaplan-Meier analysis showed a median Progression-free Survival (PFS) and overall survival of 8 and 12 months, respectively. The study revealed that the optimal treatment for primary GSM remains a therapeutic dilemma due to the rarity of the disease and the heterogeneity of the patient population and treatment regimens employed. The present study provides valuable insights into the clinical presentation and management of primary GSM in India and highlights the need for further research to improve outcomes for these patients.

**Keywords:** Gliosarcoma, Glioblastoma, Prognosis, Radiotherapy

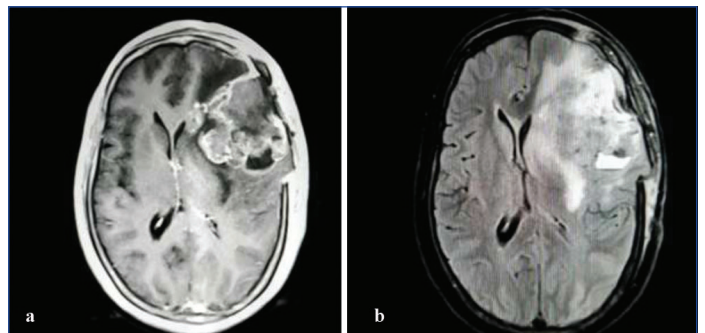
## INTRODUCTION

The Gliosarcoma (GSM) is a rare primary malignant brain tumour and accounts for 1-8% of all adult gliomas [1]. It is a biphasic tumour of the central nervous system and is classified as a grade IV neoplasm by the World Health Organisation (WHO) classification of 2016 [2]. The currently accepted definition of primary GSM is a well-circumscribed lesion with clearly identifiable biphasic glial and metaplastic mesenchymal components [3]. The scarcity of literature regarding GSM in the Indian context hinders the development of an appropriate approach toward these patients. Hence, present retrospective case series aimed to study the clinical presentation, pattern of treatment, and survival outcomes for a series of patients with primary GSM attending a tertiary cancer care facility in India. Medical records were reviewed, and data were collected on all primary GSM patients who visited the Radiotherapy (RT) Outpatient unit from 2018 to 2022. Histologically proven cases of GSM from individuals aged 18-65 years who underwent maximal safe resection and received adjuvant RT were included in the study. Patients with a prior history of RT or chemotherapy and those with any synchronous malignancy were excluded.

## CASE SERIES

A total of 12 patients with primary GSM were retrospectively reviewed. Patient characteristics such as age, gender, Eastern Cooperative Oncology Group (ECOG) score [5], presenting symptoms, duration of symptoms, as well as tumour location were taken into account. Additionally, treatment characteristics including the extent of surgery, the gap between surgery and RT, dose and duration, along with details of concurrent TMZ, were recorded. The duration between the day of surgery and the first sign of clinical or radiological progression of the disease was considered for PFS, while Overall Survival (OS) was calculated from the date of surgery to the day of the patient's death. Kaplan-Meier survival analysis was performed for the calculation of OS and Progression-Free Survival (PFS).

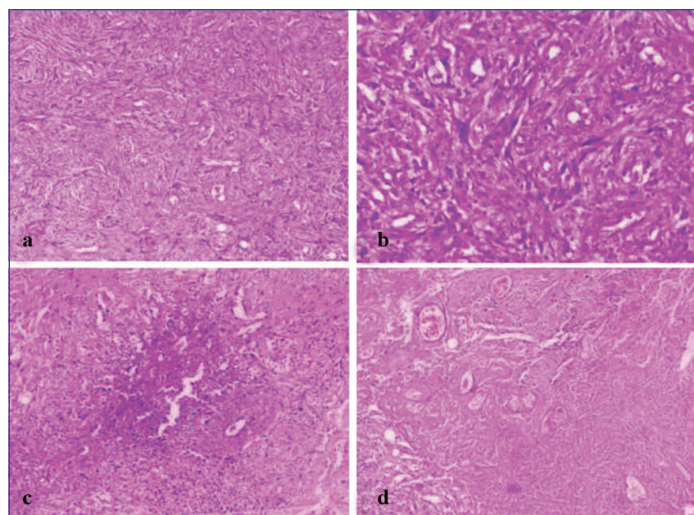
A male preponderance was observed with a male-to-female ratio of 2:1. On radiological images as shown in [Table/Fig-1a,b], tumours were hypo/isointense on T1 images with areas of necrosis. Post-contrast T1 weighted images displayed brilliant enhancement.



**[Table/Fig-1]:** MRI of brain showing heterogenous tumour involving the left frontoparietal lobe with midline shift. (a) Tumour shows brilliant contrast enhancement on post-contrast T1 W axial section. (b) T2 FLAIR images with enhancement, perilesional oedema, mass effect and midline shift.  
MRI: Magnetic resonance imaging; FLAIR: Fluid attenuated inversion recovery

Hyperintense lesions were seen on T2 weighted MR images with enhancement, perilesional oedema, and mass effect. These patients had supratentorial lesions in terms of location, with the temporal lobe being the most common site of the tumour, observed in 6 (50%) patients. While half of the patients underwent gross total resection, only biopsy was safely feasible in 4 (33.3%) patients, and subtotal resection was performed in another 2 (16.7%) patients. Histopathological study of the surgical specimen showed a biphasic tumour comprising predominantly sarcomatous components and focal glial components [Table/Fig-2a-d]. The sarcomatous component comprised randomly arranged spindle-shaped tumour cells with moderate to markedly pleomorphic nuclei, coarse chromatin, and a moderate amount of cytoplasm. Glial components in the form of astrocytes with moderately pleomorphic nuclei were also observed. Areas of necrosis and vascular proliferation were noted. Immunohistochemistry was employed to arrive at a definite conclusion, which showed spindle cells positive for vimentin and Glial Fibrillary Acidic Protein (GFAP) positivity in tumour cells. These findings were consistent with the diagnosis of GSM.

The median duration of the gap between surgery and RT in present patients was 40 days (range: 25 to 75 days). All GSM patients received concurrent chemoradiation and adjuvant chemotherapy. Steroids, antiemetics, and other supportive treatments were used according to individual patients' symptoms. RT was delivered to all



**[Table/Fig-2]:** a) Shows sarcomatous component comprising of randomly distributed malignant spindle cells. (H&E stain, 40X); (b) Shows spindle shaped tumour cells having markedly pleomorphic nuclei. (H&E stain, 100X); (c) Shows high grade glial component. (H&E stain, 40X); (d) Shows large areas of necrosis.

patients using intensity-modulated RT technique on a 6 MV linear accelerator. A total dose of 60 Gy was delivered at 2 Gy/fraction to the clinical target volume. Concurrent and adjuvant Temozolomide was administered following Stupp’s protocol [4]. The patients were then clinically followed up, and contrast-Enhanced MRI (CE-MRI) of the brain was performed at three months and thereafter if clinically indicated. All the patients completed their adjuvant chemoradiation. The median age was 54 years (range 38-61 years), and the majority (58.3%) of patients had an ECOG performance status of 2. The patient characteristics are enumerated in [Table/Fig-3]. The median RT duration was 51.5 days (range: 43-58 days), and all patients received an RT dose of 60 Gy/30#. The treatment characteristics along with survival outcomes are shown in [Table/Fig-4]. The median PFS and OS in the present study were 8 and 12 months, respectively, as depicted in [Table/Fig-5a,b].

Patient characteristics	Values
<b>Median age (years)</b>	54 years (Range 38-61)
<b>Sex</b>	
Male	8 (66.6%)
Female	4 (33.3%)
<b>Performance status</b>	
ECOG 1	5 (41.6%)
ECOG 2	7 (58.3%)
Median duration of symptoms (months)	2 months ( Range 1 to 8 )
<b>Presenting symptoms</b>	
Headache±Vomiting	11 (91.6%)
Motor weakness	5 (41.6%)
Seizures	2 (16.6%)
Memory loss	1 (8.3%)
<b>Tumour Site</b>	
Temporal	6 (50%)
Parietal	3 (25%)
Frontal	2 (16.6%)
Multicentric	1 (8.3%)
<b>Baseline imaging modality</b>	
CE-MRI	8 (66.6%)
CECT	4 (33.3%)

**[Table/Fig-3]:** Baseline characteristics of patients.

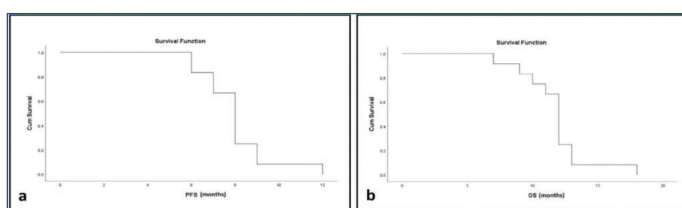
## DISCUSSION

Gliosarcoma has been managed similarly to glioblastoma with a poorer prognosis [1]. Literature evaluating the prognostic variables,

Treatment/Outcome variables	Values
<b>Extent of surgery</b>	
GTR	6 (50%)
STR	2 (16.6%)
Biopsy	4 (33.3%)
Gap between surgery and RT	40 days (Range 25-75 days)
RT dose	60 Gy in 30#
Median RT duration (days)	51.5 days (Range 43-58 days)
Median concurrent TMZ Dose (mg)	100 mg (Range 80 mg to 120 mg)
<b>Number of adjuvant TMZ cycles</b>	
6 cycles	7 (58.3%)
3-5 cycles	2 (16.6%)
0-2 cycles	3 (25%)
Median PFS	8 months (Range 6-12 months)
Median OS (months)	12 months (Range 7-18 months)

**[Table/Fig-4]:** Treatment characteristics and patient outcomes.

GTR: Gross total resection; STR: Subtotal resection



**[Table/Fig-5]:** Kaplan-Meier plot for: (a) Progression-free survival; and (b) Overall survival.

treatment approach, and outcomes is limited due to the rarity of the disease, the heterogeneity of the patient population, and the treatment regimens employed. Hence, the optimum treatment for these patients remains a therapeutic dilemma.

The GSM predominantly affects adults from the sixth to seventh decade of their life with a greater propensity in the male population [6]. In the present study, the median age at the time of presentation was 54 years, and a male predilection was observed in terms of incidence. This was in concordance with similar studies conducted on patients from the same geographical area, as shown in the case series by Biswas A et al., where the median age of presentation was found to be 50 years with a male predominance [7]. The median duration of symptoms at the time of presentation in this study was two months, with features of raised Intracranial Tension (ICT), i.e., headache and/or vomiting, being the most common presentation (91.6%). Rath GK et al., reported similar findings with a median symptom period of 1.5 months and raised ICT being the most common symptom observed in 81% of the patients [8]. GSM usually arises in the cerebrum with a relatively higher propensity towards the temporal lobe [8], and the same was observed in the present study, where 50% of the patients had the lesion located in their temporal lobe.

In present study, all the patients were treated with maximal safe resection followed by adjuvant chemoradiation and chemotherapy. The benefit of radiation therapy on the patients’ survival was described by Kozak KR et al., in their study, which showed that RT-treated patients had a median survival of 10 months as opposed to four months in patients not receiving RT [1]. The addition of chemotherapy in the form of TMZ has only shown a modest improvement in the survival of GSM patients [9,10].

All the patients eventually experienced a relapse of the disease during subsequent follow-ups. The site of relapse was local in all 12 cases, and it occurred within the Planning Target Volume (PTV) of RT. This finding was in line with the results reported by Lutterbach J et al., where they observed local relapse in all their cases of GSM following RT [11].

The median PFS in present study was eight months. Dejonckheere CS et al., reported a similar PFS of 7 months in their 26 cases of GSM treated with RT and chemotherapy following surgery [12]. The median OS of the patients in the present study was 12 months. Similar survival outcomes have been reported in the case series by Lutterbach J et al., and Zhang G et al., where the median OS was 13 months and 11.5 months, respectively [11,13]. Additionally, all the patients in the present study had died due to neurological causes following their relapse of the disease.

## CONCLUSION(S)

In conclusion, GSM is a rare and aggressive brain tumour that has a poor prognosis despite aggressive treatment. Treatment strategies included maximal safe surgical resection, followed by concurrent chemo-RT and adjuvant TMZ therapy. The present case series provides valuable insights into the clinical characteristics and treatment outcomes of patients with GSM. The findings suggest that GSM is a distinct clinical entity with a poorer prognosis compared to glioblastoma. The study highlights the importance of further research to improve understanding of present entity. Additionally, clinicians need to be aware of the unique features of GSM to improve patient management and optimise treatment outcomes.

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