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# Gliosarcomas: Are They Still Dreadful?

Authors
**Balu. S[1], Sridhar. P[2], Rahul Loni[3], Vedamanasa I.[4]**
[1]Associate Professor, Department of Pathology, Kidwai Cancer Institute, Bangalore-29
[2]Assistant Professor, Department of Radiation Oncology, Kidwai Cancer Institute, Bangalore-29
[3,4]Post Graduate Student, Department of Radiation Oncology, Kidwai Cancer Institute, Bangalore-29
Corresponding Author
**Sridhar. P**
Assistant Professor, Department of Radiation Oncology, Kidwai Cancer Institute, Bangalore-29
Email: *sridharkmiort@gmail.com*

**ABSTRACT**
**Introduction:** *Gliosarcomas are highly malignant tumours of the central nervous system, having the worst prognosis. Gliosarcomas have the same epidemiology and natural history like Glioblastoma whereas the incidence is more among Males compared to females. Gliomas can lead to sarcomatous transformation in the supporting mesenchymal element, affecting the temporal lobe commonly. Gliosarcoma is diagnosed based on gliomatous and malignant mesenchymal differentiation seenon biphasic tissue pattern.*
**Materials and Methods:** *16 patients aged between 32 – 70 years were analyzed. 10 cases were Primary gliosarcoma and 6 cases were secondary gliosarcoma. All patients underwent tumor excision and received adjuvant concurrent chemo radiation therapy followed by adjuvant chemotherapy alone.*
**Results:** *In our case series, median survival was 15.6months. Subset analysis showed better median survival in primary gliosarcoma patients.*
**Conclusion:** *Maximal safe resection followed by concurrent chemoradiation and adjuvant chemotherapy should be the standard management in primary/secondary gliosarcoma patients.*
**Keywords***: GBM: Glioblastoma, PGS: Primary Gliosarcoma, SGS: Secondary Gliosarcoma, IMRT: Intensity Modulated Radiotherapy.*

## Introduction

Gliosarcomas are highly malignant central nervous system tumors, which is also considered to be a variant of glioblastoma with very poor prognosiswhen compared to glioblastoma. It accounts for 2-8% of all Glioblastoma (GBM) and 0.48% of all intracranial tumors[(1,2)]. Pathologically gliosarcoma consists of biphasic glial and metaplastic mesenchymal components[(3)]. According to the 2010 statistical analysis by the Central Brain Tumor Registry of the United States, from 2004 to 2006, GBM accounted for 53.8% of all Gliomas, Gliosarcomas accounted for 2% of all GBM. The epidemiology and natural history of Gliosarcomas are similar to Glioblastoma [(4,5,6)]. Males are more frequently affected than females (M: F ratio 1.8:1). It is recognized that gliomas can induce sarcomatous transformation in the supporting mesenchymal elements. It affects the temporal lobe more often. It is difficult to differentiate High grade glioma,

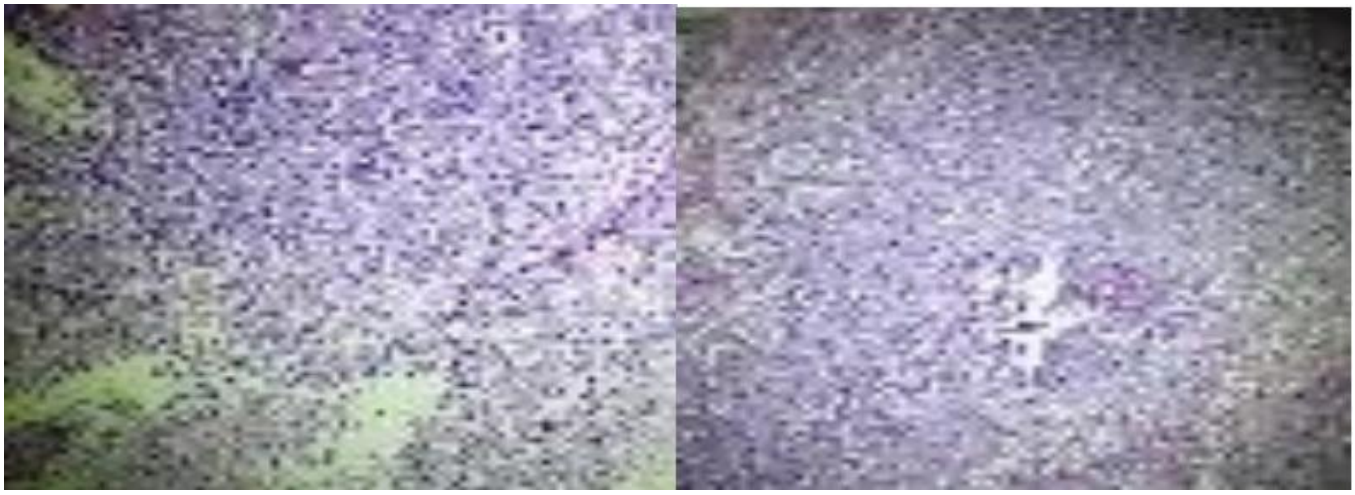
CNS Lymphoma and metastatic carcinoma radiologically and clinically.

**Pathogenesis**

Gliosarcoma has sarcomatous components which originated from neoplastic transformation of hyperplastic blood vessels as seenin High grade gliomas. Histological reaction to factor VIII, Von Willebrand factor and CD34 is noted in sarcomatous component (7). The mutations in p-53, PTEN, CDK amplification, p-16 deletion was also seen. EGFR, MDM2, P53 (binding and inactivation protein) amplification and over expression are seen in primary gliosarcoma [8].

The genetic alterations seen in secondary Gliosarcomas are PTEN mutation, P16 deletion and TP53 mutation and lack of EGFRamplification. The genetic changes in Gliosarcomas are intermediatebetween primary and secondary Glioblastoma [9]

**Histopathology**



**Gliosarcoma:** Pleomorphic tumor cellshaving areas of necrosis and spindle cells with pleomorphic nucleus (sarcomatouscomponent).

**IHC:** Presence of glial fibrillary acid protein, Vimentin, Desmin, Ki 67 index-60%. Gliosarcoma are diagnosed based on biphasic tissue pattern composed of gliomatous and the malignant mesenchymal differentiation. Rare variants which is seen are herring bone pattern of fibrosacroma, malignant osteiod cells, cartilaginous differentiation of an osteosarcoma or chondrosarcomal differentiation [10].

**Materials and Methods**

16 histologically confirmed post safe maximal resection cases of gliosarcoma aged between 32-70 years with KPS more than 70 wereanalysed.

**Treatment**

**Surgery:** Patients underwent maximal safe resection

**Radiation therapy:** Target volumes were prescribed according to the RTOG 98-03 and 08-25 which recommended volumes: CTV1 = surgical bed and/or residual tumor +20–25mm, CTV2 = surgical bed and/or residual tumor +5mm. The planning target volume (PTV) is an additional margin of 3–5mm. For patients who developed recurrences, reirradation was done. Dose given was 50 Gr/25 fr. Planning target volume consisted of CTV + 5mm margin.

Primary gliosarcoma patients received doseof 60 Gy/ 30 fr [14]; GBM patients who developed recurrence with gliosarcoma histology received a dose of 50 Gy/25 fr via IMRT technique.

**Chemotherapy:** Adjuvant radiotherapy with Tab. Temozolomide 75 mg/ m2 daily, followed by adjuvant chemotherapy (Temozolomide 150 mg/ m2 OD x 5days -6 cycles) [12].

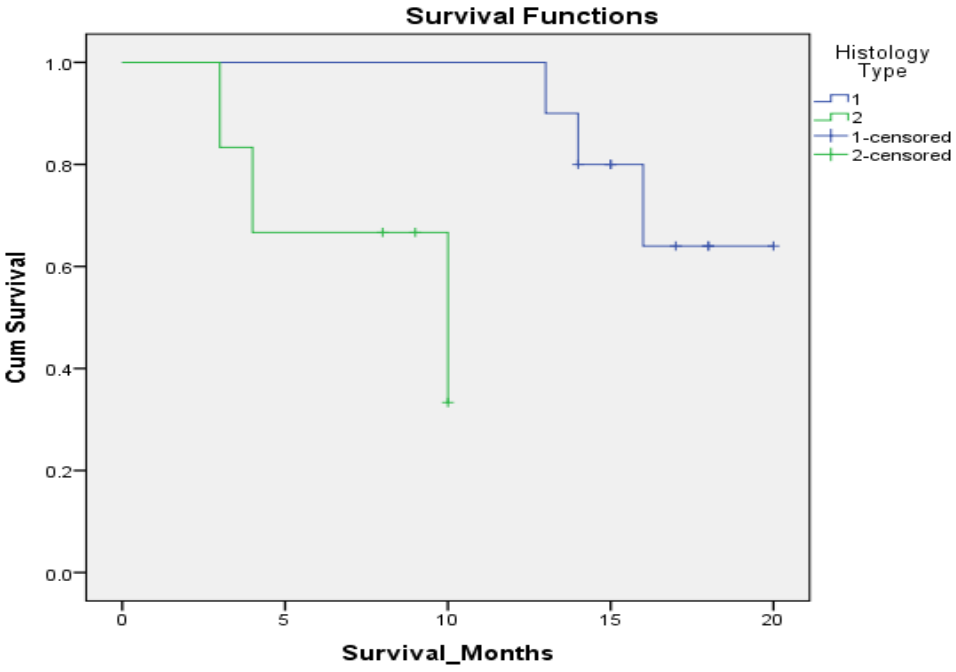
**Follow up:** Patients were followed up every 3 monthly and evaluated by CT/MRI scans, Brain SPECT scans was alsodone to know the viability of tumor.

**Results**

Results were statistically analyzed using 'R' software

**Patient characteristics**

| | Age (Yrs) | Sex (M/F) | Histology | Radiological response to treatment | Survival (Months) |
|---|---|---|---|---|---|
| 1 | 52 | M | Primary Gliosarcoma | Progressive disease | 13 |
| 2 | 45 | M | Primary Gliosarcoma | Progressive disease (death) | 14 |
| 3 | 40 | M | Primary Gliosarcoma | NED | 14 |
| 4 | 32 | F | Primary Gliosarcoma | Progressive disease (Death) | 15 |
| 5 | 46 | M | Primary Gliosarcoma | Stable disease | 15 |
| 6 | 52 | F | Primary Gliosarcoma | Stable disease | 16 |
| 7 | 40 | M | Primary Gliosarcoma | Progressive disease (Death) | 17 |
| 8 | 60 | M | Primary Gliosarcoma | Stable Disease | 18 |
| 9 | 63 | F | Primary Gliosarcoma | Stable disease | 18 |
| 10 | 70 | M | Primary Gliosarcoma | NED | 20 |
| 11 | 48 | F | Secondary Gliosarcoma | Progressive disease (death) | 3 |
| 12 | 60 | M | Secondary Gliosarcoma | Small residual disease present | 4 |
| 13 | 34 | M | Secondary Gliosarcoma | Progressive disease (death) | 8 |
| 14 | 54 | M | Secondary Gliosarcoma | Progressive Disease | 9 |
| 15 | 57 | F | Secondary Gliosarcoma | Stable disease | 10 |
| 16 | 65 | M | Secondary Gliosarcoma | Progressive disease | 10 |




The median survival was 15.6 months.The median survival was better in Primary Gliosarcoma patients (18 months v/s 7 months) (p=0.006).

**Discussion**

Gliosarcomas are rare variant of Glioblastoma[11]. Diagnosing the gliosarcoma is a challenging task as it can be mistaken for metastatic carcinoma or CNS lymphoma. Hence micro dissection genotyping is used to better characterize these tumors [12]. Age, Extent of resection, use of adjuvant radiotherapy and chemotherapy are the important variables in improving survival in this devastating disease[13]. Further the EGFR

expression, MGMT methylation, IDH1 mutation must also be analyzed to explore the scope of various other chemotherapeutic agents.Contrary to the belief that Gliosarcoma fares worse than Glioblastoma, if patients are treated optimally with Radiotherapy and Chemotherapy (Temozolomide 75 mg/m2 OD) and Adjuvant Chemotherapy (Temozolomide 150 mg/m2 OD x 5 days for 6 months), the prognosis remains almost the same as Glioblastoma patients.

No statistically significant difference in survival was found between Gliosarcoma and glioblastoma [14,15,16,17] although these studies predate the current treatment protocol for glioblastoma. Salvatiet al.[18] studied 11 cases, four of which received RT and temozolomide with a median survival of 17.4 months and five received RT alone with a median survival of 15.7 months. They concluded that chemotherapy seems to have an added benefit; our study also correlates with the same finding. Hence trimodality treatment should be the standard of care for gliosarcoma patients.

## Conclusion

Patients who undergo tumor excision followed by adjuvant concurrent chemoradiotherapy and followed by adjuvant chemotherapy have better survival outcomes. The Incidence of developing Gliosarcomas in recurrence cases is showing a raising trend. Diagnosing this rare variant of high grade gliomas at the earliest and treating optimally will help in achieving better overall survival.

## Conflict of Interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

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