

Gliosarcoma with prominent smooth muscle component (gliomyosarcoma): A report of 10 cases

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ABSTRACT

Background and Aim: Gliosarcoma (GS) is an uncommon malignant tumor of the brain, consisting of malignant glial, usually a glioblastoma (GB), as well as sarcomatous component; the latter is usually in the form of fibrosarcoma. We report a series of 10 GSs with prominent smooth muscle component, which is a rare occurrence. **Settings and Design:** Out of a series of 225 cases of GB admitted in our hospital, 10 were diagnosed as GS with prominent smooth muscle component, gliomyosarcoma (GMS). **Materials and Methods:** This is an observational study based on the experience with 225 cases of GB, encountered between 1995 and 2008, in our hospital. The tumors showing prominent spindle cell component were stained with reticulin and 20 with strongly positive reticulin stain were diagnosed as GS. They were further studied by immunohistochemical staining for glial fibrillary acidic protein (GFAP), smooth muscle actin (SMA), desmin and factor VIII antigen. **Results:** Out of 225 cases of GB, 20 were diagnosed as GS. Ten of these showed prominent smooth muscle component and were diagnosed as GMS. They revealed varying degrees of SMA and factor VIII Ag positivity. In the sarcomatous component, SMA and factor VIII positive cells were seen close to the vessel walls as well as away from them. **Conclusion:** GMS containing prominent smooth muscle component may not be as rare as has been reported in the literature. Both GS and GMS appear to arise from the vessel wall at least in some cases, suggesting their possible vascular origin.

KEY WORDS: Glioblastoma, gliomyosarcoma, gliosarcoma

INTRODUCTION

Gliosarcoma (GS) is an uncommon malignant brain tumor characterized by a biphasic tissue pattern and consists of glial and mesenchymal components, both being malignant. It is considered as Grade IV tumor (World Health Organization, 2007).^[1] GS constitutes about 2% of all glioblastomas (GBs), 5% of all astrocytomas and 8% of anaplastic astrocytomas.^[1-4] The age distribution is comparable to GBs and it manifests between the age of 40 and 60 years. Males are more frequently affected. GS is usually located in the cerebral hemispheres involving the temporal, frontal, parietal and occipital lobes in decreasing order of frequency. The glial component is usually astrocytic in nature showing the morphological features of GB and the sarcomatous component is commonly a fibrosarcoma exhibiting morphological features of malignancy. The origin of mesenchymal component has been controversial. Feigin *et al.*^[5] first suggested the vascular origin of sarcomatous component which has been largely accepted. However, there has been some controversy regarding the histogenesis of sarcomatous component in recent years. Further, the mesenchymal component in GS has been rarely found to be in the form of smooth and skeletal muscle, bone and cartilage.^[6-11] Sarkar *et al.*^[10] reported the largest series of GSs from India. The series included one case showing features of

Access this article online
Website: www.ijpmonline.org
DOI: 10.4103/0377-4929.77324
Quick Response Code:


rhabdomyosarcoma while three others showed areas of osteogenic sarcoma. None had the features of smooth muscle cell differentiation.

We encountered 10 cases of GS with prominent smooth muscle component and report these due to the rare occurrence. The possibility of origin of the sarcomatous component from the blood vessel wall was also investigated.

MATERIALS AND METHODS

A total of 225 cases, diagnosed as GB during a period of 14 years (January 1995–December 2008), were included in this study. The tumors showing a biphasic pattern of GB and prominent spindle cell component with malignant features on paraffin embedded, hematoxylin–eosin stained sections were stained with reticulin to establish a diagnosis of GS. These cases were further studied by immunohistochemical stains using peroxidase–antiperoxidase method for glial fibrillary acidic protein (GFAP), smooth muscle actin (SMA), desmin and factor VIII Ag.

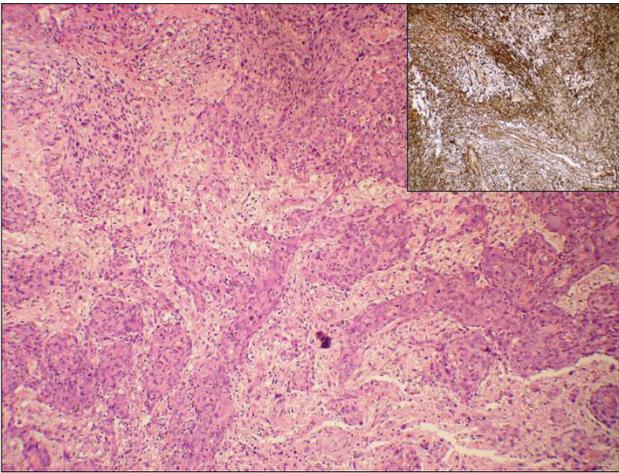


Figure 1: GS: Biphasic nature of tumor with intermixed glial and sarcomatous components (H and E, $\times 10$). Inset shows strong reticulin positivity in sarcomatous areas with relatively small reticulin negative (glial) areas (reticulin stain, $\times 20$)

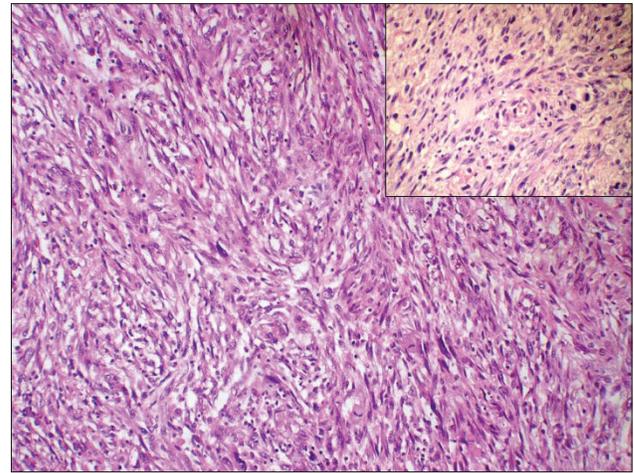


Figure 2: Photomicrograph showing sarcomatous component with nuclear pleomorphism (H and E, $\times 20$) and increased mitotic activity (inset)

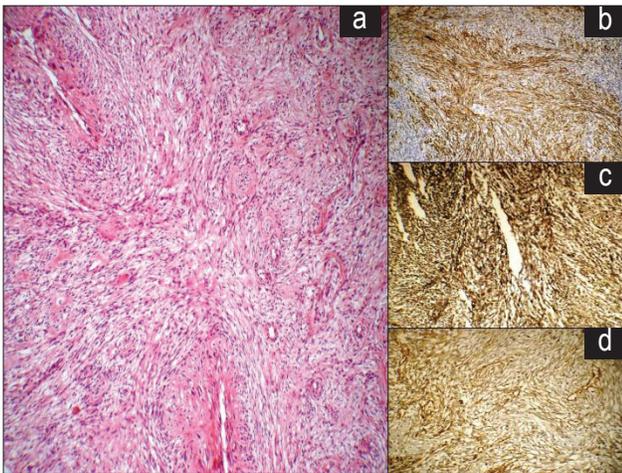


Figure 3: (a) Photomicrograph showing many spindle cells with eosinophilic cytoplasm. Note the tumor cells are in continuity with the vessel wall (H and E, $\times 20$); (b) SMA positive tumor cells in continuity with the vessel wall and also in large areas away from the vessels (SMA stain, $\times 20$); (c) reticulin positive fibers are also in continuity with vessel wall and involving large areas of the tumor (reticulin stain, $\times 20$); (d) factor VIII positive tumor cells, close to vessel wall and also away from it (factor VIII Ag, $\times 40$)

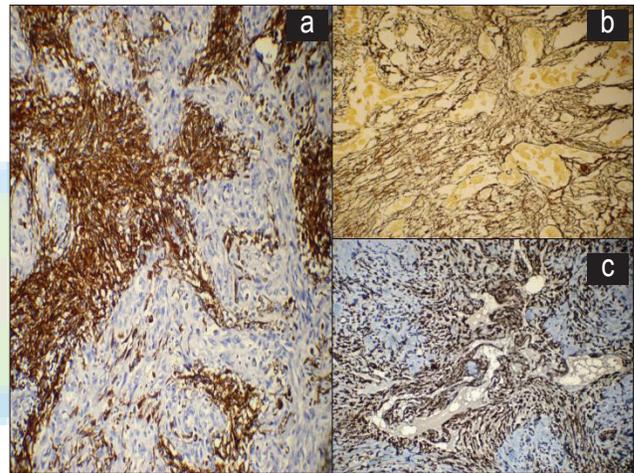


Figure 4: (a) Photomicrograph showing large groups of GFAP positive glial areas intermingled with predominantly GFAP negative sarcomatous areas (GFAP stain, $\times 10$); (b) reticulin stained spindle cells around groups of reticulin negative glial cells (reticulin stain, $\times 40$); (c) photomicrograph showing SMA positive reaction of the sarcomatous cells in the same area confirming the diagnosis of GMS (SMA stain, $\times 40$)

RESULTS

Out of the 225 cases of GB, 20 (8.8%) showed a biphasic pattern [Figure 1] with features characteristic of GB along with large areas of prominent spindle cell component. These were diagnosed as GS on the basis of strong reticulin positive reaction in large areas showing sarcomatous features [Figure 1, inset] and GFAP positivity in the glial component. The sarcomatous areas showed features of malignancy, including nuclear atypia and increased mitotic activity [Figure 2 and inset]. In some of these cases, the spindle cells had eosinophilic cytoplasm, suggesting the possibility of their myogenic nature [Figure 3a] which was subsequently confirmed by immunohistochemical staining with

SMA [Figure 3b]. In many cases, the sarcomatous components with strongly positive reticulin stain were found to be in continuity with the wall of markedly hyperplastic blood vessel walls and extending further into the tumor [Figure 3c]. Varying degrees of positive staining of the tumor cells for factor VIII Ag were seen in 10 cases of GS [Figure 3d].

Of the 20 cases of GS, 12 were males and 8 were females. The age range was between 15 and 72 years and 13 of the patients were between 40 and 70 years of age. Majority of the tumors occurred in temporal, frontal and parietal lobes.

Histochemical and Immunohistochemical Stains

The distinction between the two components of GS is facilitated by histochemical and immunohistochemical staining with

reticulin and GFAP. Sections stained for GFAP showed variable degrees of positive reaction in all the 20 cases, confirming their astrocytic origin. GFAP-positive areas were either geographically separated from or intermingled with the reticulin positive sarcomatous areas [Figure 4a and b]. In 10 cases (4.4%), tumor cells with sarcomatous features in areas of variable size showed positive staining for SMA, suggesting their leiomyomatous nature [Figure 4c]. All the cases were negative for desmin. Many tumor cells, positive for both SMA and factor VIII Ag, were found close to the vessel wall as well as further away in the tumor areas and at places they were in continuity from the vessel wall into the tumor [Figure 3a, d]. The sarcomatous component in the other 10 cases of GS was fibrosarcoma in nature with no other differentiation.

DISCUSSION

Stroebe^[12] was the first to recognize the occurrence of GS as an entity in 1895. However, the term did not find acceptance till Feigin and Gross^[3] reported the occurrence of sarcoma in GB in 1955 and subsequently in 1958.^[5] Since then, the GSs have been firmly established as an entity and many cases have been reported in the literature. Most of them show a combination of features of GB and fibrosarcoma. However, rarely, cases with other mesenchymal elements, such as smooth muscle, skeletal muscle, bone and cartilage, constituting the sarcomatous component, have been reported.^[6-11] In the present series, we have 20 cases of GS, and out of these, 10 were with smooth muscle as a component of sarcoma [gliomyosarcoma (GMS)]. Such an occurrence is a rare phenomenon and has been reported earlier by Haddad *et al.*^[6] and Jones *et al.*^[13]

The cell of origin of sarcomatous component has not been fully established. Feigin and Gross (1955)^[5] suggested that the sarcomatous component in GS develops as a result of neoplastic transformation in markedly hyperplastic blood vessels, commonly found in GB. Sarcomatous change has been considered to be from endothelial, pericytic or undifferentiated mesenchymal cells. This view has been generally accepted and progressive transformation of sarcoma from hyperplastic blood vessels has been recorded in human^[2,4,5,13] as well as in an experimental study, reported by Green and Harvey (1968).^[14] Endothelial markers such as factor VIII-related antigen^[14-16] and Ulex europaeus agglutinin (UEA-1)^[14] have been identified in the sarcomatous tumor cells. However, some studies in recent years have suggested that the sarcomatous component is the result of progressive loss of GFAP in some parts of glioma along with the acquisition of sarcomatous phenotype.^[16-19] These studies are indicative of origin of both the components from glial cells, the sarcomatous change representing a phenotypic transformation of GB cells.^[20-24] This change results in negative immunohistochemical staining of such transformed cells for GFAP and they acquire antigenic characteristics of other different cell types. They then react with appropriate antibody such as anti-smooth muscle and anti-desmin antibodies. Therefore, it seems possible that in GS, both the components are of monoclonal origin. However, the origin of GS is still debatable and alternative pathways cannot be ruled out.^[25,26] Kepes *et*

al.^[27] reported chondroid cells in astrocytomas resulting from metaplastic change since they were positive for GFAP. In GB, metaplastic change to epithelial cell has also been reported.^[28]

In the present study, we found GS in 20 cases (8.8%) of GB, a relatively higher incidence than that reported in the literature. This may be due to the fact that reticulin stain is not always used in case of GB with prominent spindle cell component. We observed the continuity of reticulin positive sarcomatous component from vessel wall into the tumor in some of the cases, suggesting its vascular origin [Figure 3c]. Further, we observed the occurrence of smooth muscle as a sarcomatous component, a rare phenomenon, in 10 cases (4.4%). It is to be noted that in many of our cases some of the SMA-positive tumor cells also appeared to be in continuity with the blood vessel wall within the tumor [Figures 3b and 4c] and they were negative for GFAP. Factor VIII Ag-positive cells were also found to be in continuity from vessel wall into the tumor [Figure 3d]. These observations are highly suggestive of origin of sarcomatous as well as smooth muscle component of the tumor from the vessel wall. Thus, the origin of sarcomatous element including leiomyosarcomatous elements from the vessel wall, at least in some cases of GS, as suggested by Feigin, appears to be a strong possibility.

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Source of Support: Nil, **Conflict of Interest:** None declared.

