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Biological characteristics and outcomes of gliosarcoma

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Abstract

Gliosarcoma is a highly aggressive primary brain tumour. It is a relatively rare tumour and comprises of two histological components, glial and sarcomatous. Gliosarcomas carry a poorer prognosis than that of Glioblastoma Multiforme (GBM). The current review highlights important histological and radiological features of gliosarcoma in the light of recent literature, and also touches upon the treatment options and outcomes of various types of gliosarcoma.

Keywords: Glioma, Sarcoma, Brain tumour.

Review of Evidence

Gliosarcoma is a rare primary brain tumour with prevalence varying from 1.5-8% in different studies, and accounts for 0.48% of all intra-cranial tumours.[1] It can be further sub-classified into primary gliosarcoma (PGS) and secondary gliosarcoma (SGS), and whereas PGS occurs de novo, SGS is believed to occur as a recurrence or progression of Glioblastoma Multiforme (GBM), or as a consequence of radiation therapy.[2]

The current accepted definition of gliosarcoma is 'a well-circumscribed lesion with clearly identifiable biphasic glial and metaplastic mesenchymal components'.[3,4] The glial component resembles GBM and is richly positive for glial fibrillary acidic protein (GFAP),while the sarcomatous component resembles fibrosarcoma, but may also resemble osteosarcoma, chondrosarcoma, angiosarcoma,or rhabdomyosarcoma,[5,6] and is rich in reticulin and poor in GFAP expression. Reis et al., observed that P53 mutation is seen in 23% of gliosarcomas as compared to 11% of primary GBM, and epidermal growth factor receptor (EGFR) amplification, is found in only 4% of gliosarcomas compared to 35% of GBM. Small differences are also noted in Phosphatase and Tensin homolog (PTEN) mutation and cyclin-dependent kinase (CDK) amplification.[7] Cases of radiation induced gliosarcoma include ependymoma, oligodendroglioma, anaplastic astrocytoma, meningioma, pituitary adenoma, acute lymphoblastic leukaemia and choriocarcinoma. Extracranial metastasis can be seen in patients with SGS.[2,8,9]

Radiologically, Zhang et al., reported gliosarcomas as irregular masses on both CT and MRI, with a smooth external wall, well demarcated from the surrounding brain parenchyma, and significant surrounding oedema. Furthermore, they described that gliosarcomas occur more commonly in the temporal lobe, and can appear similar to meningiomas on gross morphology.[10] Han et al.,[3] described it as generally large lesions that are hypo-intense on T1-weighted images and hyper-intense on T2-weighted images, with areas of necrosis and central calcification (characterized by heterogenous contrast enhancement), and intense peripheral or irregular enhancement and shift of midline structures. Diffusion and mass diffusion coefficient are usually heterogeneous and MR spectroscopy may show choline (Cho) peak, with normal creatinine (Cr) and low N-acetyl-aspartate (NAA), although these findings are non-specific.[11] Despite small differences, gliosarcoma is largely indistinguishable from GBM in most cases as they share identical radiological and clinical characteristics, and their definitive differentiation is based only on histopathology.[4,12]

The treatment is on the same lines as GBM, with maximal safe resection as the cornerstone, followed by Concomitant Chemotherapy and Radiation Therapy (CCRT).[13] Castelli et al., reported their management of gliosarcoma patients with12-months median follow up (2-71 months), and reported Gross total resection (GTR) in 59% patients. Temozolamide based CCRT was administered in 64% patients while 15% patients received adjuvant chemotherapy regimens based on platinum, fotemustine and vincristine. Treatment at recurrence included chemotherapy in 80% of patients, repeat surgery in 17% and chemo-radiotherapy in 2% of the patients.[14] They report a median Overall Survival (OS) of 13 months, and a median Progression Free Survival (PFS) of 7 months. Although it is difficult to conclude as such but CCRT and adjuvant chemotherapy did not improve OS compared to radiotherapy alone. High dose of Radiation Therapy (RT) and salvage treatment appeared to increase OS.[14]

Cachia et al., in their series reported GTR in 53 % patients and CCRT in 70% of patients. Bevacuzimab based regimens were used in 47% of patients, with half receiving single agent and half another agent in combination.[8] Patients with GTR had a better Overall Survival (OS) (24.7 vs. 10.1 months), although this did not reach statistical significance. Overall, patients treated with bevacizumab had a PFS of 4.2 months and an OS of 8.7 months from initiation of treatment. Patients with PGS had the same outcomes, however, SGS patients treated with

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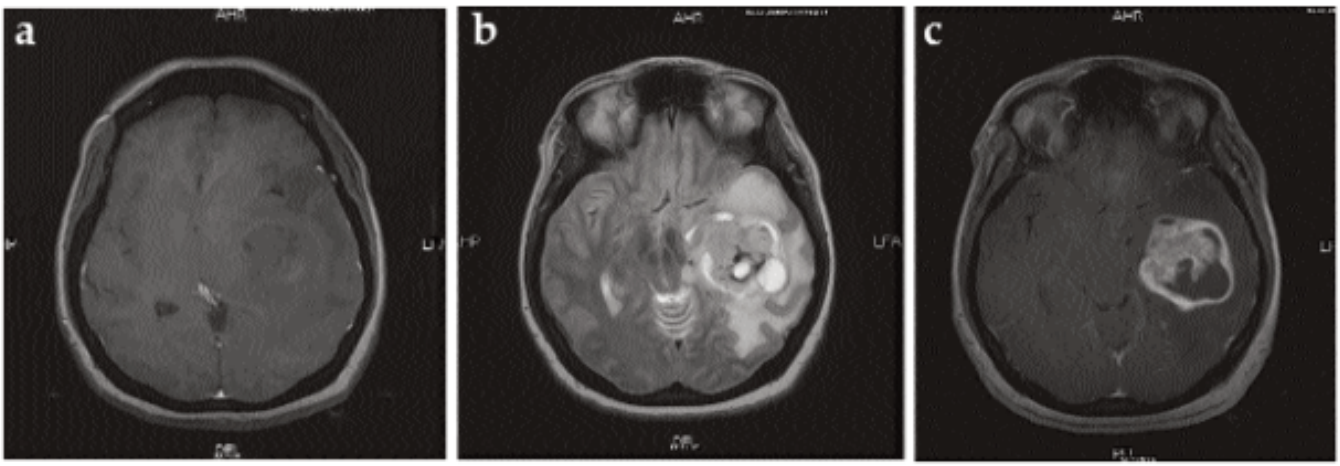

Figure: a) T1WI showing iso-hypo-intense lesion in left parieto-temporal region. b) T2WI showing hyper-intense lesion in left parieto-temporal region. c) T1- contrast enhanced image showing heterogenous enhancement.

bevacizumab, had a OS of 7.3 months and PFS of 3.8 months.[8] Treatment with bevacuzimab along with temozolamide based CCRT did not show any benefit in OS of patients with SGS.[8]

Kozak et al., also reported a median OS of 9 months. Age at presentation, extent of resection, and adjuvant RT were significantly associated with better survival.[15] SGS patients were defined as those with a prior history of GBM, and in this sub-group PFS was 3.1 months from the time of sarcomatous transformation.[8] Twenty-one percent of patients developed tumour metastases and 15% showed leptomeningeal dissemination. Extra-axial spread occurred to the infratemporal region outside the temporal bone, cervical lymph nodes, and temporal bone. The cumulative OS of PGS and SGS was 17.5 months and PFS was 6.5 months.

There appears a wide variation in reported OS for gliosarcoma patients, from 4-11.5 months.[3,5] Interestingly, the OS for SGS is 25 months, and is the same as PGS if measured from the time of first diagnosis of GBM.

Conclusion

Gliosarcoma is a rare tumour that is difficult to differentiate from GBM on clinical or radiological information although can be differentiated on histopathology. GTR followed by temozolamide based CCRT may provide the best outcome.

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