CASE REPORT

Irradiation of Two Cases of Gliosarcoma: Place and Modalities of Radiotherapy

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Abstract

Introduction: Gliosarcoma is a rare histopathologic variant of glioblastoma traditionally associated with a poor prognosis. We present two cases of Gliosarcoma treated in our department.

Discussion: Gliosarcoma (GSM) is a variant of glioblastoma (GBM), the most common primary malignant brain tumor that occurs in adults. GSM is characterized by its biphasic components: the gliomatous and sarcomatous components and categorized into primary and secondary GSM. Intrinsic to the brain parenchyma, GSM is usually managed by gross total resection, and radiotherapy with/without chemotherapy.

Conclusion: Despite the notable advances and improvement in overall survival (OS), a consensus on the optimal treatment for GSM patients is unclear.

Keywords: Gliosarcoma, two cases report, radiotherapy, TMZ, surgery

1 | INTRODUCTION

Gliosarcomas are a variant of glioblastoma (along with epithelioid glioblastoma and giant cell glioblastoma) recognized in the current WHO classification of CNS tumors (1). They are highly malignant (WHO grade IV) primary intraaxial neoplasms with both glial and mesenchymal elements. Peak presentation is around the 6th decade and there is a male predilection (1, 2). Histologically, GSM tumors are characterized by a biphasic growth pattern consisting of both glial components and areas of sarcomatous, mesenchymal differentiation often resembling fibrosarcoma (3). GSM patients are typically managed as conventional GBM in accordance with the Stupp’s regimen of trimodality therapy including maximal safe resection; radiotherapy (RT) with concurrent and adjuvant temozolomide (TMZ) based chemotherapy (4).

We present here two cases of gliosarcoma who were treated at our institute.

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2 | CLINICAL CASES

2.1 | Case 1

A 47-year-old male consulted for signs and symptoms associated with raised intracranial pressure, seizure and aphasia. Brain MRI showed an approximately 45*30mm sized heterogeneous lesion in left frontal region surrounded by significant vasogenic edema with a mass effect shifting the midline. A left-side frontotemporal craniotomy and complete macroscopic resection were performed. Histological examination showed a malignant tumor proliferation made of large pleomorphic cells with atypical hyperchromatic nucleus and numerous mitoses, associated with component of fusiform atypical cells with a nucleus ovoid and hyperchromatic. Immuno histochemistry was performed and showed tumor cells that express GFAP (glial fibrillary acidic protein), P53 and CD34. The patient was then referred to our department and underwent a post-operative radiotherapy treatment using an isocentric field technique, with 18MV photons, receiving a total dose of 60Gy in 30 fractions (2Gy per fraction ). The patient’s condition continued to deteriorate and he died few days later.

2.2 | Case 2

A 51-year-old female admitted in emergency for loss of consciousness. She also complained of headache and vomiting for 3 days before her hospitalisation. Brain MRI revealed hyperintense lesion in the right temporal region measuring 6cm with perifocal edema, mass effect was seen causing compression over right lateral ventricle with midline shift and subfalcine herniation to left with descending transtentorial herniation. The patient underwent right frontal free bone flap craniotomy and gross total excision of tumor.

Histological examination revealed poorly differentiated, largely necrotic malignant tumor process suggesting either glioblastoma or metastasis of a carcinomatous process. Immunohistochemistry was positive for Ac anti GFAP; and negative for Ac anti CKAE1/AE3. The patient was referred to our department, where an adjuvant three- dimensional conformational radio the treatment was performed, with 6 and 18MV photons, delivering a total dose of 60Gy in 30 fractions (2Gy per fraction). Adjuvant Temozolamide therapy was administered. The patient was followed until 5 months later, when there was a decline in his general condition, leading to death soon afterwards.

3 | DISCUSSION

Gliosarcoma (GSM), a variant of GBM, the reported incidence is 1-8% of all malignant gliomas and thus represents an exceptionally rare malignancy (2).

It is a malignant tumor that arises from glial cells and is characterized by its biphasic components: gliomatous and sarcomatous (2, 5). Gliosarcoma is further categorized into primary and secondary( SGS), after prior GBM diagnosis (6). Exact pathogenesis is unknown, but earlier it has been postulated that the
FIGURE 2: axial CT showing GTV (gross tumor volume: red line; CTV(clinical target volume)=GTV +2cm: magenta line).

sarcomatous components originated from malignant transformation of hyperplastic blood vessels commonly found in high grade gliomas (7, 8).

Peak incidence is seen in the sixth and seventh decades of life (1, 2). GSM are clinically indistinguishable from GBM (9).

They are generally located in supratentorial region with the commonest site being temporal region followed by the frontal, parietal and occipital lobes (10).

CT of GSM can show a well-defined hyperdense lesion with a marked perilesional edema, necrotic areas and a mass effect. MRI showed a hyperintense lesion in T1. An isointense lesion is visible in the T2 sequence (11, 12).

Histologically two GSM subtypes have been identified and described, each having its own prognosis and treatment plan (13). Sarcomatous predominant GSM is characterized by its similarity to meningioma, production of reticulin and lack of GFAP positivity; gliomatous predominant GSM is characterized by necrosis seen on pathological examination, lack of reticulin and expression of GFAP (1–13).

In clinical practice, GSM and GBM are managed and treated similarly, although several studies have shown different outcomes when these tumors are identically treated (14, 15). The precise treatment recommendations are still not available due to small number of patients in the available case series and case reports. Thus, tumor resection, postoperative radiation therapy, and chemotherapy with nitrosoureas, misonidazole, dacarbazine, mithramycin, ametopherin, thalidomide, temozolomide, irinotecan, vincristine, cisplatin, or doxorubicin are the treatment modalities for gliosarcoma (16). Treatment with concurrent chemoradiation with temozolomide is suggested to improve overall survival (17).

Several studies investigate the efficacy of radiotherapy in the treatment of GSM patients. A significant increase in overall survival was seen in patients treated with adjuvant radiotherapy compared to patients undergoing surgery only (46 vs. 13 weeks; p=0.025) (18). Similarly, in a study conducted by Castell et al., it was concluded that surgery followed by radiotherapy offered a superior outcome than surgery alone (15). In multivariate analysis, a high total dose of radiotherapy (minimum dose of 54 Gy) correlated with improved overall survival (HR=0.97, p=0.007).

While addition of chemotherapy failed to improve survival, it has been speculated that dose escalation of chemotherapeutic agents could still improve overall survival beyond that reached with RT and surgery (15). The role of radiotherapy in the treatment of GSM was further emphasized in the large study conducted by Kozak et al (2). Han et al attributed the worse outcomes in SGS patients who had received radiotherapy and TMZ for GBM to the possible role of some characteristic mutations absent in primary GSM, such as MGMT(methyleneguanine-DNA-methyltransferase) or EGFR (epidermal growth factor receptor) positivity (16). This reasoning could not be confirmed since molecular profiles of GBMs and SGS were absent. This raised the need for detailed molecular analyses to identify the unique alterations and characteristics of those GBMs that recur as GSM.

Few studies addressing immunotherapy for recurrent glioblastoma included patients with gliosarcoma. Af-
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After its favorable response in increasing long term survival in high-grade gliomas including gliosarcoma (Phase I), a phase II trial of DNX-2401, an oncolytic adenovirus, along with Pembrolizumab, a PD-1 receptor blocker, is currently underway (CAPTIVE/KEYNOTE-192: NCT02197169). Sharing similar targets, another phase I/II trial addresses the efficacy of atezolizumab, a PD-L1 inhibitor in conjunction with temozolomide and radiotherapy (NCT03174197) (18).

Apart from single modality treatments, current guidelines set by the national comprehensive cancer network (NCCN) state that maximal safe surgical resection followed by RT along with concurrent and adjuvant TMZ is recommended for GSM treatment (19, 20).

Although the prognosis of GSM is known to be generally poor, multimodality treatment seems to extend survival (13).

4. CONCLUSION

Gliosarcoma is a rare central nervous system malignancy, it is treated similarly to GBM but optimum treatment recommendations are yet to be defined. Gliosarcoma carries poor prognosis. The studies focusing on cellular and molecular biology of gliosarcoma are required which would aid in identifying new modalities of treatment and bring hope to improve outcomes in patients diagnosed with gliosarcoma.

REFERENCES


4. ; 2011.


