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Gliosarcoma: A Reported Case

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Abstract | **Case Report**

Gliosarcoma is a rare aggressive variant of glioblastoma, classified as WHO grade IV a rare and aggressive variant of glioblastoma, affecting men between the ages of 50 and 60. It is characterized by a biphasic histological pattern combining glial and mesenchymal components. The pathogenesis remains debated. Prognosis remains poor, with median survival ranging from 8 to 17 months. Gliosarcoma remains a diagnostic and therapeutic challenge. Despite histological similarities with GBM, its distinct clinical behavior and metastatic potential warrant further investigation to improve management strategies and patient outcomes. This case study aimed to demonstrate the anatomopathology of gliosarcoma, and its aggressiveness.

Keywords: Gliosarcoma, Gliobastoma, pathogenesis, histology, prognosis.

INTRODUCTION

Gliosarcoma (GSM) is a rare but highly malignant glioblastoma (GBM) that accounts for 2–8% of high-grade gliomas [1]. It was first described by Stroebe *et al.,* in 1895, and increasingly recognized by Feigen *et al.,* in 1955 [2]. In recent years, with the progression of genetic research, the occurrence of similar genetic alterations in both glial and mesenchymal components suggests a monoclonal origin [2] Gliosarcoma presents unique histopathological manifestations characterized by a biphasic growth model of glial and sarcomatous elements [3]. Gliosarcoma has similar radiological and clinical representations to glioblastoma but a comparatively poorer prognosis. Several researches have reported the median overall survival (OS) of gliosarcoma ranging from 6.6 to 18.5 months. At present, special therapies for gliosarcomas are virgin, and treatments still cannot exceed the limits of glioblastoma guidelines, including maximum surgical resection, radiotherapy (RT), and témozolomide [3]. We report the case of a 50-year-old man, affected by grade IV gliosarcome, at the Oncology-Radiotherapy department of the Mohammed VI University Hospital in Marrakech

MATERIEL AND METHODS

- **Clinical examination:** A 50-year-old patient, consulted a private neurosurgeon in June 2024 for headaches unrelieved by analgesic treatment, associated with general deterioration. These symptoms had been ongoing for two years and had worsened with the onset of left hemiplegia.
- **A brain MRI:** Compressed right fronto-temporal tumor process suggestive of high-grade glial tumor, measuring 58 x 45 x 56 mm, with associated peri-lesional edema.
- The patient underwent surgery on August 2, 2024: an excision of a solid fronto-temporo-insular tumor mass.
- Histopathological analysis revealed largely necrotic spindle-cell tumor proliferation, and immunostaining showed:
  - Anti-GFAP antibody: Heterogeneous positivity of tumour cells, Negative on sarcomatous contingent.
  - Anti-IDH1 antibody: Negative.
  - Anti-ATRX antibody: Tumor cell positivity.
  - Anti-Vimentin antibody: Positive on sarcomatous contingent.
  - Anti-EMA Ab-3 antibody: Focal positivity of tumor cells.
  - Anti-P53 antibody: Low tumor cell positivity.

Which is compatible with WHO 2021 grade IV gliosarcoma

The patient was transferred to the Oncology-Radiotherapy Department of the Mohammed VI

University Hospital in Marrakech for adjuvant treatment. Upon admission, the patient was conscious with a Glasgow Coma Scale (GCS) score of 15/15, and the neurological examination revealed a decrease in muscle strength on the left side, rated at 3/5. Multidisciplinary decision was made to perform a post-operative brain MRI, along with a CT scan of the thoraco-abdominal-pelvic region, to decide whether to proceed with further surgery or opt for adjuvant radiotherapy.

The TAP CT scan did not reveal any abnormalities. **Post-operative MRI**: An increase in size of the right fronto-temporal compressive tumor process (measuring 75 x 85 x 77 mm vs 58 x 45 x 56 mm) with active hydrocephalus and subfalcine herniation.

Meanwhile, the patient's condition deteriorated. He was placed under palliative care, fell into a coma (GCS score of 4/15), presented with bilateral mydriasis, and was subsequently admitted to the intensive care unit, where he passed away in October 2024.

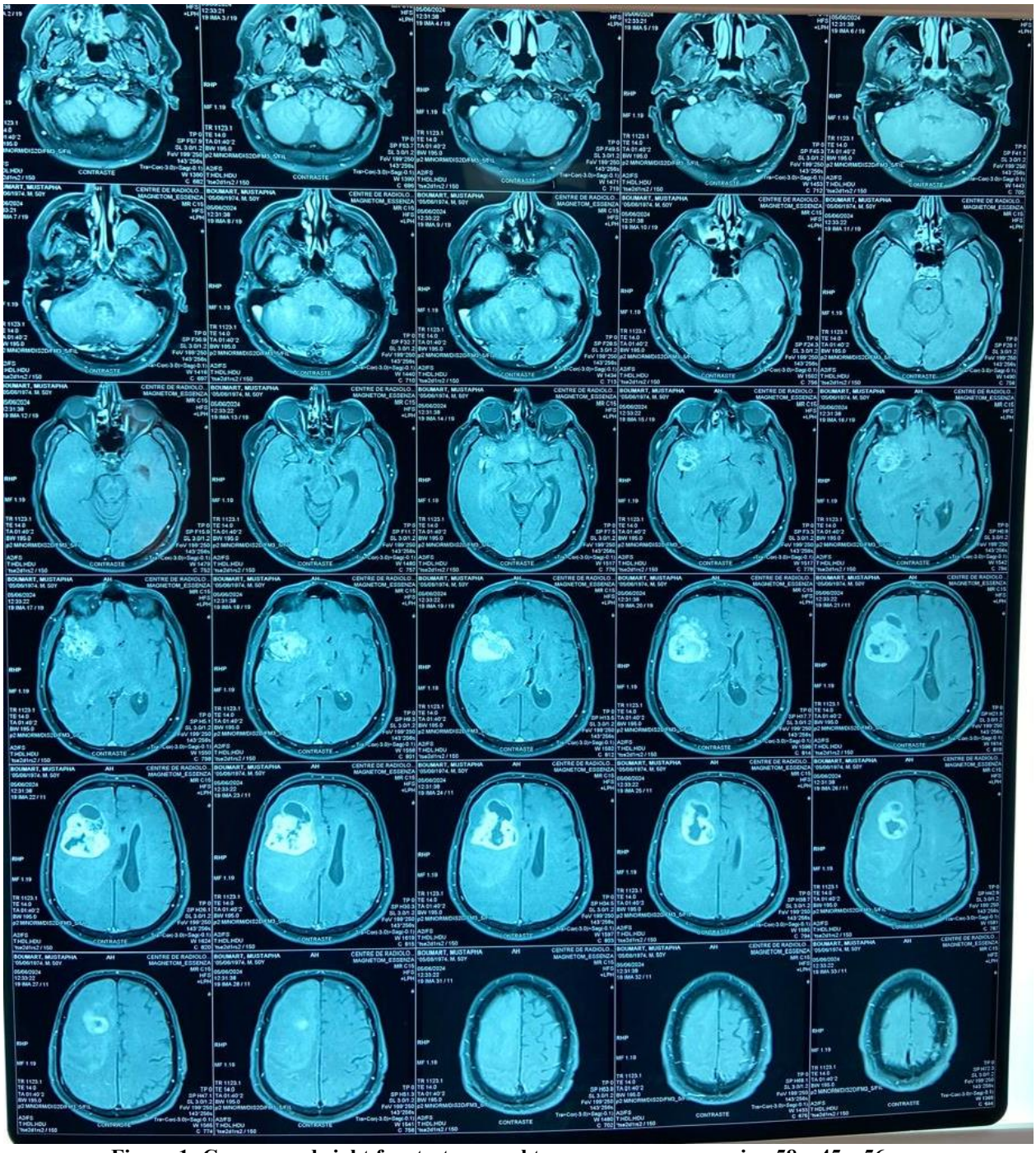

Figure 1: Compressed right fronto-temporal tumor process measuring 58 x 45 x 56 mm

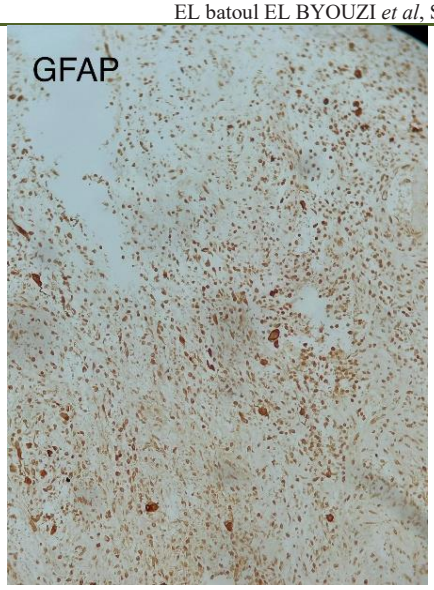

Figure 2: Heterogeneous GFAP expression in tumour cells; absent in sarcomatous area

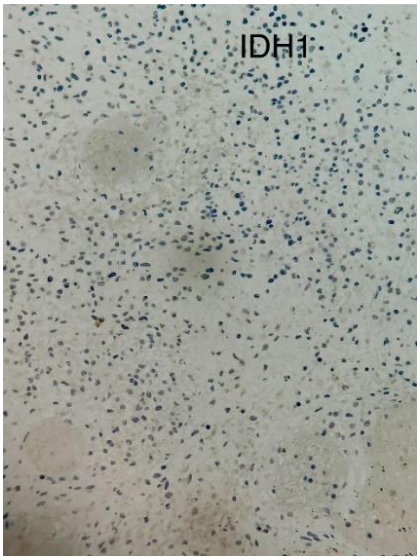

Figure 3: Anti-IDH1 immunostaining negative in tumour cells

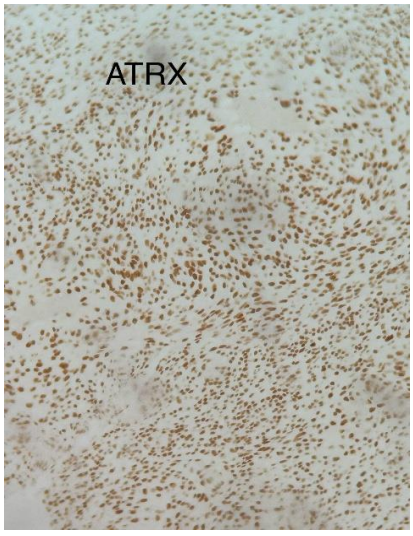

Figure 4: Anti-ATRX immunostaining: Positive in tumour cells

DISCUSSION

Gliosarcoma grade IV is a rare variant of Isocitrate Dehydrogenase wild type glioblastoma, with both glial and mesenchymal differentiation and accounts for approximately 2% of glioblastomas [4]. With slight predominance in males, age ranging from the sixth to seventh decade, and a predilection for the temporal lobes, although it can also affect the frontal, parietal and occipital lobes [5]. Rarely gliosarcome can be seen in the posterior fossa or spinal cord [2]. It is often located superficially, and presents surgically as a firm lesion adherent to the meninges where it has occasionally been mistaken for meningioma at surgery [6].

On CT scan, gliosarcoma can either resemble glioblastoma with lesions, areas of necrosis and heterogeneous enhancement-or it can resemble meningiomas with hyperdense lesions having well-defined borders and homogeneous enhancement. On MRI, the tumors showed heterogeneous contrast enhancement, well-demarcated or irregular borders and peritumoral edema [2].

There is some controversy regarding the pathogenesis of gliosarcoma. Some authors suggested the sarcomatous components originated from neoplastic transformation of hyperplastic blood vessels commonly found in high grade gliomas [5]. This ‘‘collision tumor’’ concept was supported by early descriptions by Feigin of hyperplastic vessels and perivascular arrangement of sarcomatous elements in gliosarcoma [7]. An alternative theory that has recently gained favor, points to a monoclonal origin of both components of gliosarcoma, with sarcomatous component originating through aberrant mesenchymal differentiation of the malignant glioma [5].

The diagnosis of gliosarcoma is based on some minimal histological criteria, which were introduced by Meis *et al.,* in 1991 and requires the tumour to be bimorphic; composed of two distinct malignant cell populations: one component to be astrocytic with areas of necrosis, the criteria for glioblastoma, the sarcomatous component to resemble a spindle cell sarcoma, and a minimum of one confluent sarcomatous area. In addition, immunohistochemistry for GFAP in conjunction with Reticulin stain is required to distinguish the glial from the sarcomatous components of the tumour. Staining for Vimentin is not helpful in the differential diagnosis, since both gliomas and sarcomas show positive staining [7].

Reticulin and GFAP helped to distinguish the glial and mesenchymal elements. The sarcomatous areas are Reticulin-rich and GFAP-negative, whereas the glial component is Reticulin-poor and GFAP positive [5]. In our case, GFAP was negative in the sarcomatous contingent, and positive in the glial component, and Vimentin was positive on the sarcomatous component, in line with what was already been described.

In the largest known histologic study of 36 patients, gliosarcoma was found to be universally IDH wild type, suggesting that it is a derivative, or genetic variant of primary glioblastoma [9]. Similarly, IDH1 and IDH2 were shown to be correlated with prognosis in IDH1-mutated glioblastoma as compared to wild-type. However, no prognostic significance has been found in gliosarcoma patients.

Epithelial membrane antigen (EMA) is a cell surface-associated glycoprotein widely expressed in nearly all epithelial cells, but also in meningothelial cells. In glial tumors, EMA staining can be helpful in supporting ependymal differentiation [8]. The Ki-67 labeling index (LI) in diffuse gliomas generally increases with malignancy grade (roughly <5% in low grade diffuse gliomas, 5–10% in anaplastic gliomas, and >10% in glioblastomas) [9]. In our case, KI 76 represents 10-30%, which indicates the aggressiveness of the tumor.

Gliosarcoma has a higher propensity to metastasize extra cranially than glioblastoma, via hematogenous dissemination. The sarcomatous component seems to have a higher propensity for such dissemination, often the only component in the metastases. Han *et al.,* reviewed 34 reports of 219 cases of gliosarcoma in the literature and found that most extracranial metastases of gliosarcoma are located in the lung and liver, although there are some reports of metastases on spleen, adrenal glands, kidneys, oral mucus, skin, bone marrows, skull, ribs and cervical lymph nodes. However, dissemination within the neuraxis is less common but still has been reported [2].

Several factors influencing the overall survival have been studied via bivariate and multivariate analyses. Kozac *et al.,* concluded that age, extent of resection, and adjuvant radiotherapy were the most significant predictors of overall survival. On the other hand, gender seemed to have only a slight effect, with male patients’ survival slightly better than that of females. In another study conducted by Walker *et al.,* a multivariate Cox regression analysis showed that overall survival decreased with advanced age at diagnosis and lack of radiotherapy. Similarly, other factors were reported to influence prognosis, such as lack of surgical resection, race, gender and marital status [10].

Traditionally, gliosarcoma patients have been treated with glioblastoma appropriate therapy, and adjuvant radiotherapy is recommended for all gliosarcoma patients after surgery. However, the debate over the value of Temozolomide chemotherapy has still not been resolved due to the lack of a large-scale clinical trial [12].

Wang *et al.,* meta-analysis investigated the efficacy of various treatments among patients with

gliosarcoma. The study found that both Temozolomide-dominated chemotherapy and high-dose radiotherapy were highly associated with a reduction in all-cause mortality among Gliosarcoma patients. Despite substantial heterogeneity, gross total resection might play a clinically favorable prognostic role in patients with gliosarcoma [1].

In the study of Morantz *et al.,* [12] radiation therapy was given to a total dose of 50–60 Gy in 13 of 18 cases (dose per fraction not specified). Perry *et al.,* [15] administered 50 Gy in 25 fractions. In the study of Sarkar *et al.,* [16] the total doses given were between 40 and 60 Gy. Planned total doses ranged from 45 to 81 Gy in the study of Meis *et al.,* (various fractionation schemes), and from 60 to 65 Gy in the study of Galanis *et al.,* but the authors provide no information on how many patients completed therapy. Except for Perry *et al.,* [15], who treated patients with whole brain radiation therapy, none of the other authors described target volume concepts or treatment techniques used. Morantz *et al.,* comment on the effect of chemotherapy on outcome: they found a modest increase in survival in gliosarcoma patients with additional chemotherapy (36 weeks) compared with radiation therapy alone (33 weeks, no P value given) [11]. According to Winkler *et al.,* none of the treatment regimen (radiation or chemotherapy or radiation and chemotherapy) improved the survival of gliosarcoma over glioblastoma [7].

Prognosis of both gliosarcoma and glioblastoma was shown to be poor with median survival of almost 9 months. Median overall survival reached 17.5 months for gliosarcoma patients [10]. Among primary gliosarcoma patients, estimated median survival was 11.0 months. During the past 15 years, nearly all retrospective studies examining adult primary gliosarcomas have reported similar estimates ranging from 8.3 to 16.7 months [13]. In a series of 16,388 high-grade gliomas patients (of which gliosarcoma represented 353 patients), gliosarcoma was associated with a worse prognosis compared to that of glioblastoma [14]. Winkler *et al.,* reported that the longest patient survival known following initial diagnosis has been 22 years [2]. Meis *et al.,* reported a median survival of 8.3 months and found no significant difference compared with the prognosis of patients with glioblastoma [15].

Conclusion

This work reports a case of gliosarcoma, a rare malignant tumor with a multitude of risk factors, in a 55-year-old patient who died before the beginning of treatment, due to the aggressiveness of the disease. Gliosarcoma represents a clinically challenging group of tumors, due to its rarity, poor prognosis, and the limited experience in published literature [16]. The treatment of gliosarcoma follows the recommendations for glioblastoma. The prognosis for gliosarcoma patients appears slightly worse than that observed for GBM patients [17].

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