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Gliosarcoma: A Diagnostic and Therapeutic Challenge – A Case Report and Review of Recent Literature

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Abstract **Case Report**

Gliosarcoma (GS) is a rare malignant tumor of the central nervous system, representing an aggressive variant of glioblastoma (GBM) grade IV according to the 2021 WHO classification. Characterized by an architecture combining glial and sarcomatous components, this tumor preferentially occurs between 40 and 70 years of age with a male predominance. We report the case of a 53-year-old patient treated in our institution. The review of recent literature highlights the heterogeneity of clinical presentations, the importance of molecular tools for accurate diagnosis, and the limitations of current therapeutic strategies. Despite advances in molecular biology, the prognosis remains bleak with a median survival of 6 to 18 months, underscoring the need for novel targeted therapeutic approaches.

Keywords: Gliosarcoma, Brain Tumor, Case Report, Surgery, Radiotherapy, Temozolomide.

INTRODUCTION

Gliosarcoma is a rare primary tumor of the central nervous system, initially described by Stroebe in 1895, but it was not until 1955 that Feigin and Gross formally defined it as a variant of glioblastoma multiforme [1, 2]. According to the 2021 World Health Organization (WHO) classification, it is classified as an IDH-wildtype grade IV glioblastoma, characterized by a dual histological component: glial and sarcomatous [3].

This tumor accounts for approximately 1.8 to 8% of all glioblastomas, with incidence varying across series [4]. The median age at onset is around 52 years, with a slight male predominance (sex ratio of 1.4 to 1.8) [4, 5]. The location is primarily supratentorial, preferentially affecting the temporal region [6]. Rarer locations in the posterior fossa or spinal cord have also been described.

The clinical history is generally short, with a duration of evolution ranging from one week to three months [7]. The symptomatology is polymorphic, dominated by intracranial hypertension syndrome, motor deficits, and seizures. The extracranial metastatic potential of gliosarcoma is higher than that of classic glioblastoma, with approximately 11% of cases developing metastases, mainly pulmonary, hepatic, and nodal [8].

We report here the case of a 53-year-old patient diagnosed with gliosarcoma after surgical resection, discussing the diagnostic, therapeutic, and prognostic particularities in light of the most recent data in the literature.

CLINICAL OBSERVATION

A 53-year-old patient, with no significant medical history, presented to the neurosurgery department of our hospital with rapidly progressive worsening headaches, episodes of vomiting, without seizures or initial motor deficit. This occurred in a context of weight loss.

Brain magnetic resonance imaging (MRI) revealed a right temporo-parietal mass with a dual cystic and solid component measuring 82 × 66 × 54 mm. The solid part showed very intense contrast enhancement, with intralesional hemorrhagic changes. This lesion was responsible for a moderate mass effect on adjacent structures (Figure 1). These radiological characteristics, although suggestive of a high-grade glial tumor, did not allow for certain distinction between glioblastoma and

gliosarcoma. On MRI, gliosarcomas typically appear as hypointense on T1 and as mixed or hyperintense signal on T2, with significant enhancement after gadolinium injection.

A right temporo-parietal craniotomy with right temporal lobectomy was performed. Upon opening, the tumor measured approximately 4.5 × 4.5 × 4.0 cm, reddish in appearance, solid, firm in consistency, and highly vascularized. It had a clear demarcation from the adjacent brain tissue but adhered closely to neighboring veins. Pathological and immunohistochemical examination of the surgical specimen established the diagnosis of gliosarcoma. The tumor exhibited a characteristic biphasic architecture: a glial component, positive for the GFAP marker (glial fibrillary acidic protein), and a sarcomatous component positive for vimentin. Postoperative MRI showed persistence of a tumor remnant with a right temporal porencephalic cavity (Figure 2).

The patient was referred to our radiotherapy department for postoperative irradiation. Conformal radiotherapy using volumetric modulated arc therapy (VMAT) was delivered at a total dose of 60 Gy in 30 fractions of 2 Gy, in accordance with recommendations. The clinical target volume (CTV) was defined as the resection cavity and areas of residual enhancement on T1 sequences, with the addition of a 20 mm margin including T2/FLAIR signal abnormalities, respecting anatomical barriers. The planning target volume (PTV) was obtained by adding a 5 mm geometric margin (Figure 3). Concomitant temozolomide at a dose of 75 mg/m² per day was administered during radiotherapy, followed by adjuvant temozolomide chemotherapy.

Unfortunately, the outcome was unfavorable. The patient experienced progressive deterioration of his neurological and general condition. He died 5 months after the completion of radiotherapy, before completing adjuvant chemotherapy.

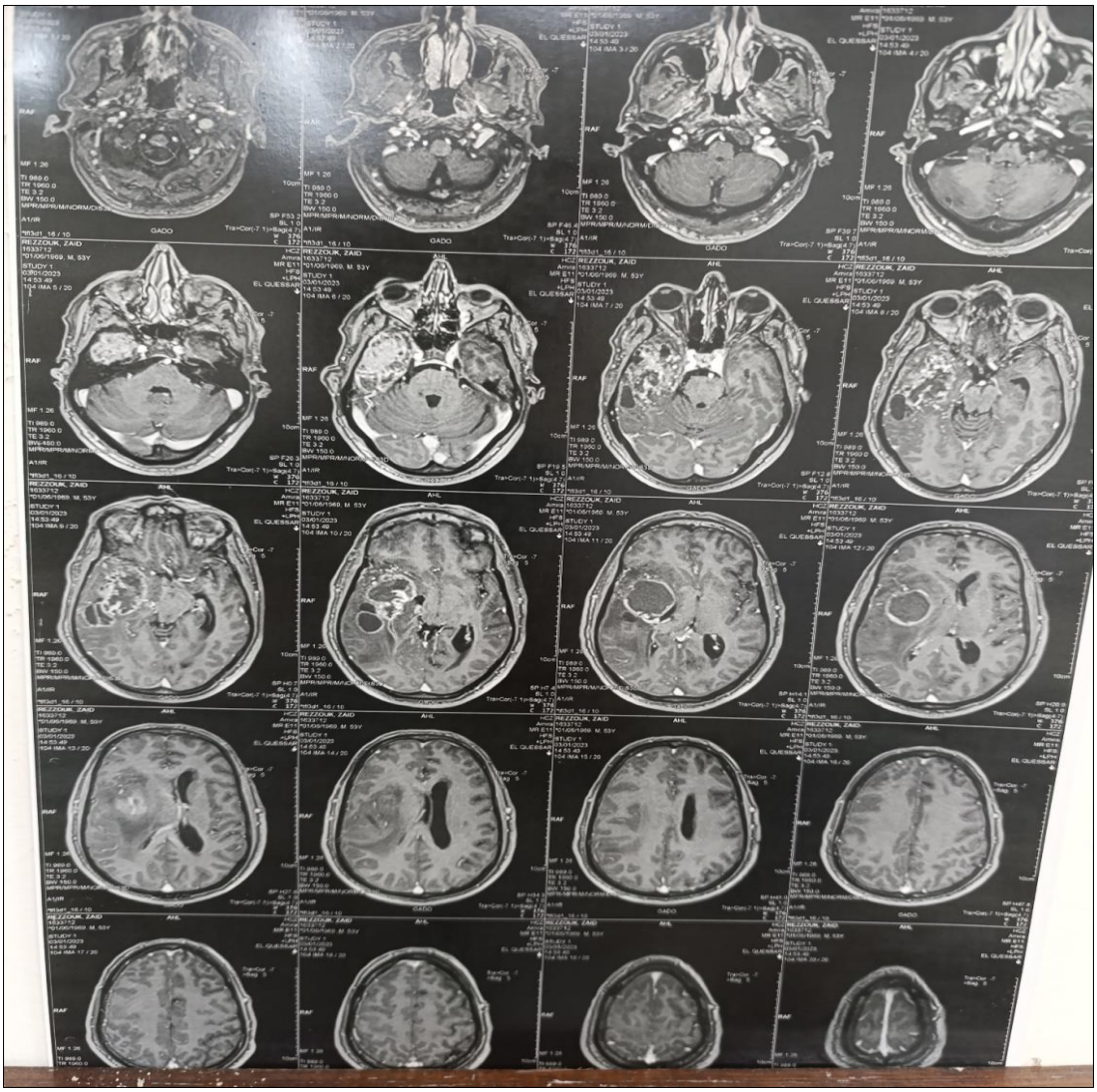

Figure 1: Brain MRI in axial sections. Showing a heterogeneous right temporo-parietal mass with a dual cystic and solid component and intense enhancement

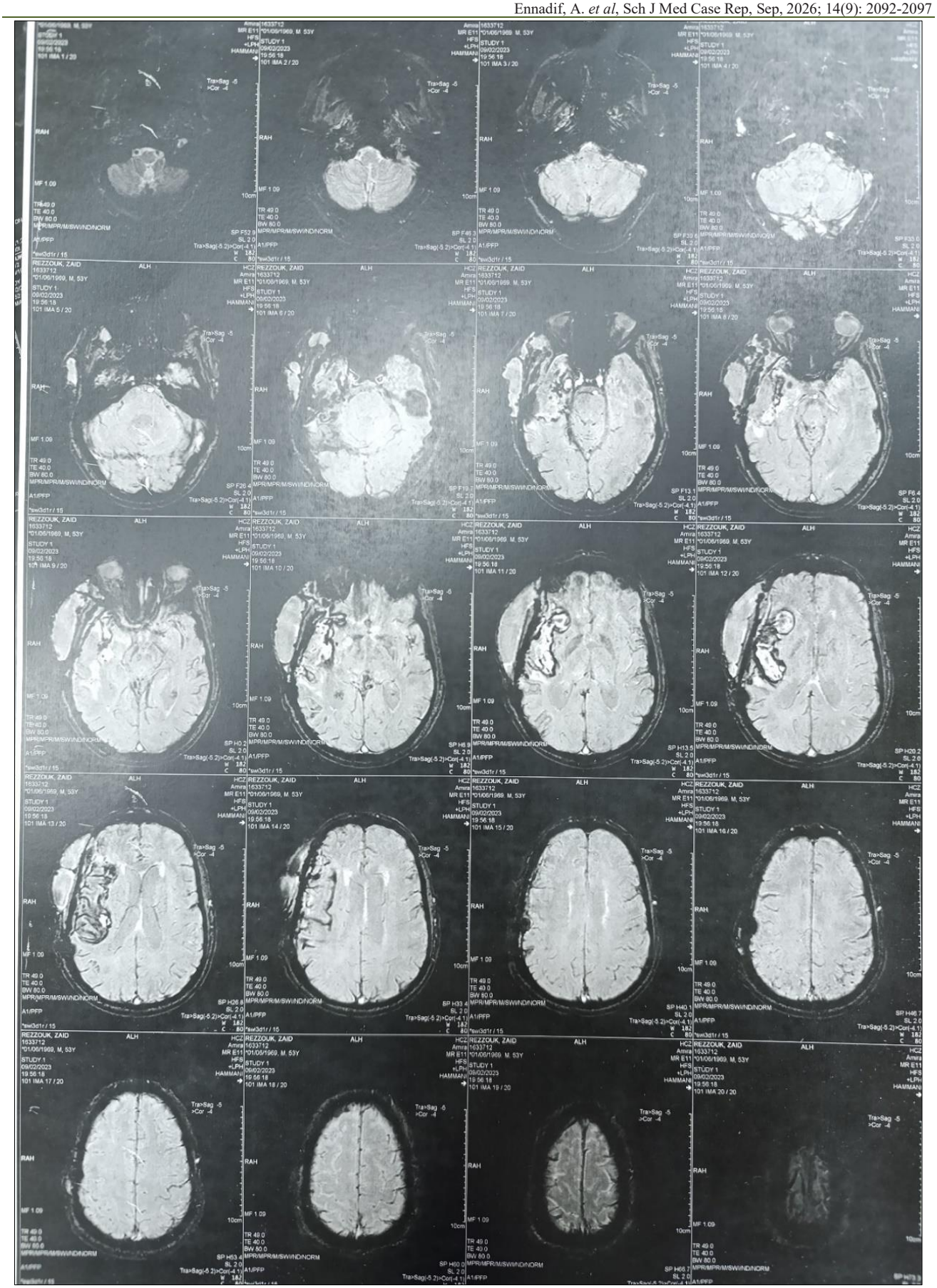

Figure 2: Early postoperative MRI in axial sections. Showing a tumor remnant with a right temporal porencephalic cavity

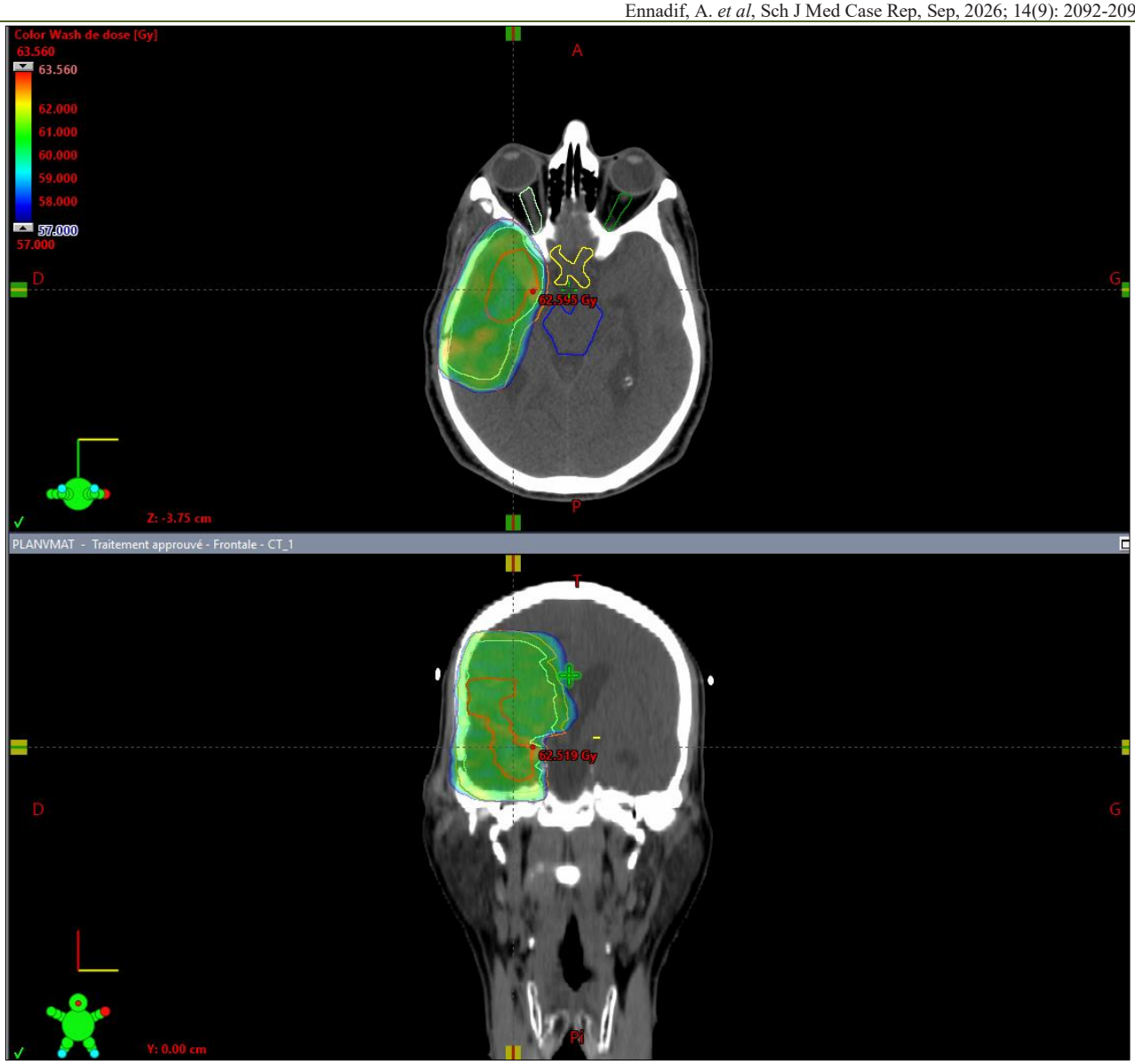

Figure 3: VMAT dosimetry image. Conformal dose distribution covering the planning target volume (PTV) while sparing organs at risk

DISCUSSION

Gliosarcoma, due to its rarity and dismal prognosis, poses real diagnostic and therapeutic challenges. Its recognition relies on histological and immunohistochemical examination, which reveals the dual glial and sarcomatous component [3]. Recent genetic studies have shown that gliosarcoma has a distinct molecular profile from that of classic glioblastoma. A retrospective cohort study including 87 patients with gliosarcoma revealed that alterations in NF1, PTEN, and TP53 were more frequent than in glioblastoma, while EGFR amplification was less frequent [9]. Alterations in CDKN2A/CDKN2B were associated with inferior survival (HR = 5.4, p = 0.023) [9].

A particularly instructive case was reported by Bhangale *et al*., in 2025, describing a 30-year-old female patient with a heterogeneous lesion in the right parietal region crossing the midline [10]. This case highlights the difficulty of radiological diagnosis, as gliosarcoma can mimic classic glioblastoma or a metastasis, and the necessity of histological confirmation.

The infiltrative nature of gliosarcoma makes complete surgical resection rarely achievable, although macroscopic total resection (GTR) is associated with better clinical and prognostic outcomes. In a 2024 study on prognostic factors for primary gliosarcoma, age ≤ 65 years, complete resection, Ki67 ≤ 25%, postoperative Karnofsky score ≥ 70, and adherence to the Stupp protocol were associated with improved survival [11]. Cases of complete resection have led to rapid resolution of neurological deficits, underscoring the importance of prompt and precise surgical management [12].

Adjuvant management, modeled on the glioblastoma protocol, is recommended, although its efficacy in gliosarcoma remains debated [13, 14]. A recent meta-analysis suggested that temozolomide chemotherapy and high-dose radiotherapy offer a survival benefit, and that total resection is associated with reduced mortality [15]. However, studies have shown that progression-free survival was inferior to that of glioblastoma, despite similar overall survival [9]. The median survival of patients with gliosarcoma ranges from 6 to 18 months [10-16].

The extracranial metastatic potential of gliosarcoma, higher than that of glioblastoma, is a particularity to consider. Pulmonary, bone, nodal, and subcutaneous metastases have been described [8-17]. In the study by Li *et al*., (2024), a patient developed a subcutaneous metastasis during treatment, illustrating the need for extended surveillance in these patients [11].

Recent advances in molecular biology have paved the way for potential targeted therapies. The identification of alterations in CDKN2A/B, LRP1B, RB1, and TSC2 as prognostic factors could guide therapeutic choices [9]. Furthermore, understanding the signaling pathways involved, particularly the PI3K/AKT/mTOR and MAPK/ERK pathways, could lead to the development of new therapeutic strategies [18]. It has been suggested that gliosarcoma may constitute a distinct clinicopathological entity from glioblastoma, justifying the development of specific therapeutic protocols [19].

Abbreviations
GS: Gliosarcoma
GBM: Glioblastoma Multiforme
CNS: Central Nervous System
WHO: World Health Organization
IDH: Isocitrate Dehydrogenase
MRI: Magnetic Resonance Imaging
GFAP: Glial Fibrillary Acidic Protein
GTR: Gross Total Resection
VMAT: Volumetric Modulated Arc Therapy
CTV: Clinical Target Volume
PTV: Planning Target Volume
TMZ: Temozolomide
NGS: Next-Generation Sequencing

Conclusion

Gliosarcoma is a rare and aggressive primary brain tumor, constituting a major diagnostic and therapeutic challenge. Diagnosis confirmation relies on histological and immunohistochemical analysis, revealing its dual glial and sarcomatous component. Management, modeled on that of glioblastoma, combines maximal surgical resection, radiotherapy, and adjuvant temozolomide chemotherapy. Despite these treatments, the prognosis remains bleak, with median survival limited to a few months.

Hope lies in the identification of novel molecular pathways and the development of targeted or immunological therapies capable of improving the prognosis of this formidable tumor.

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