

Metastatic spinal glioblastoma in a pediatric patient: A case report

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Abstract

Glioblastoma is the most aggressive primary brain tumor, with a generally poor prognosis. While it predominantly affects adults, its occurrence in pediatric patients, especially with spinal drop metastasis, is exceedingly rare and their molecular mechanisms remains poorly understood. This is a case report of an 11-year-old girl diagnosed with a thalamic glioblastoma (IDH1-unmutated, K27M-mutated) who presented with neurological deterioration suggestive of metastatic progression. MRI confirmed the presence of spinal drop metastases, highlighting a rare but significant complication. This case underscores the challenges of managing metastatic spinal glioblastoma in pediatric patients and the need for vigilance in detecting delayed metastases. Given the limited therapeutic options, further research is essential to elucidate the pathogenesis of glioblastoma dissemination and develop targeted treatment strategies for these challenging cases.

Keywords: Pediatric Glioblastoma; Thalamic Glioblastoma; K27M Mutation; Spinal Metastasis

1. Introduction

1.1. Case description

An 11-year-old girl was referred to the neurosurgery department from a local hospital with complaints of progressive headaches, nausea, and episodes of left-sided weakness over several weeks.

The neurological examination revealed deficits and impairments suggestive of right thalamic involvement and the medical history taking showed no significant personal or family medical history.

Initial radiological investigations included cerebral magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA). Imaging identified an extra-axial mass centered on the left cerebellar tentorium, measuring 46 mm × 52 mm × 65 mm. The lesion exhibited heterogeneous T2 hyperintensity and T1 hypo intensity, with intense and heterogeneous contrast enhancement. Central cystic areas were observed, extending both supra- and infratentorial, along with moderate active tri-ventricular hydrocephalus. These findings were consistent with a glial tumor accompanied by subarachnoid dissemination (Figure 1).

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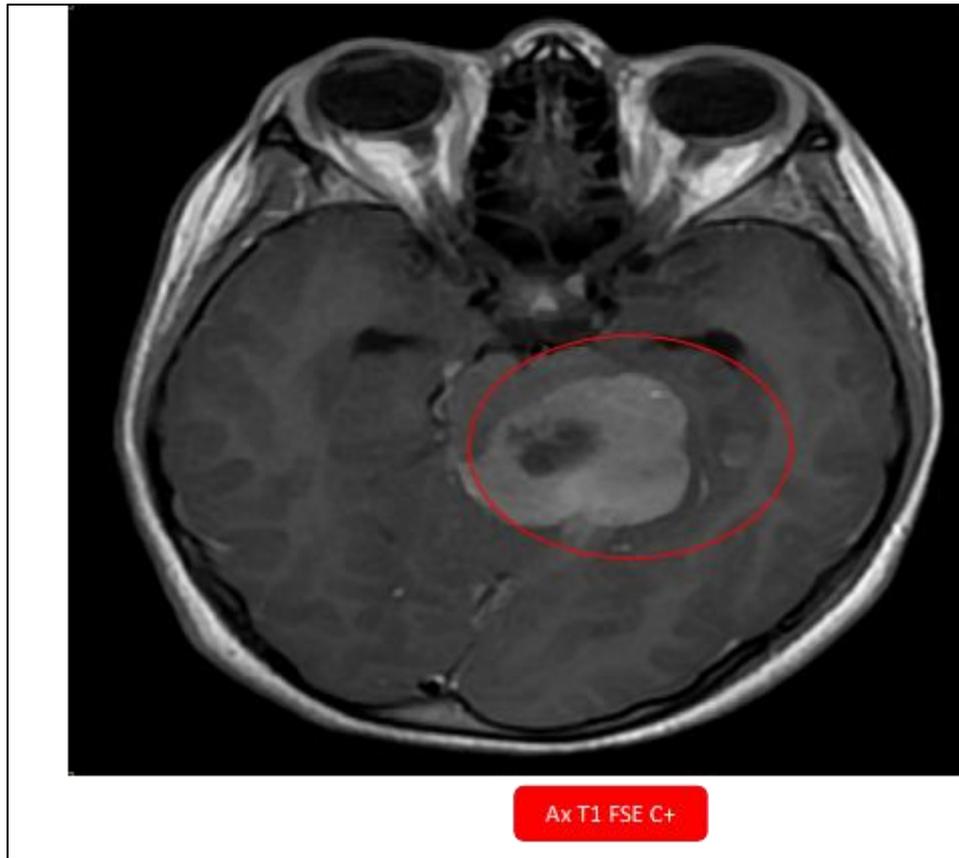


Figure 1 Brain MRI revealing a tumorous process centered on the pons, predominantly left-sided, demonstrating intense and heterogeneous contrast enhancement with well-defined central cystic areas

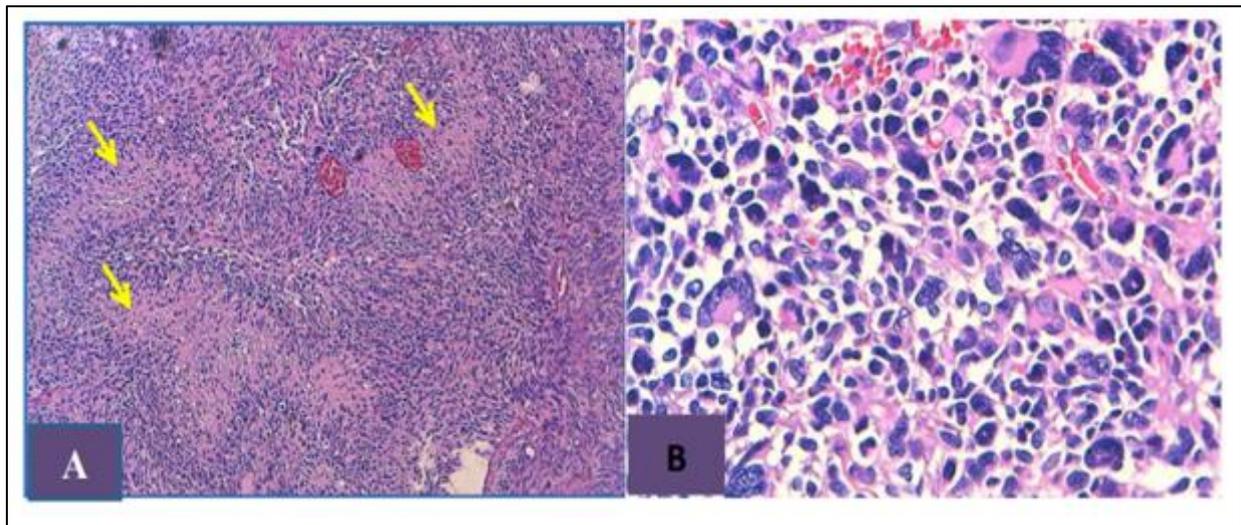


Figure 2 Histopathological Characteristics of the Patient's Glioblastoma A: High cellular density with palisading tumor necrosis (arrows) (H&E, $\times 100$). B: High cellular density with cytonuclear atypia and mitotic activity (H&E, $\times 400$)

The patient underwent ventriculoperitoneal shunting to address hydrocephalus, followed by a stereotactic biopsy to confirm the tumor's histopathology, given its surgical inaccessibility. Pathological and immunohistochemical analyses confirmed a diagnosis of diffuse thalamic glioma, WHO grade 4, classified as glioblastoma, K27M-mutated, with IDH1 non-mutated status. No additional genetic testing, such as NMDAR gene analysis, was performed (Figure 2).

Following a multidisciplinary team (MDT) decision, the patient was referred to the radiotherapy department to initiate adjuvant chemoradiotherapy as per the Stupp protocol [1]. On clinical evaluation, she exhibited right hemiparesis, right central facial paralysis, and an increased base of support. Pupils were equal and reactive, with no other cranial nerve deficits except for facial nerve (VII) involvement. The remainder of the somatic examination was unremarkable.

The treatment plan included radiotherapy delivering 60 Gy in 30 fractions combined with concurrent daily Temozolomide at 75 mg/m². This was followed by six cycles of adjuvant Temozolomide chemotherapy at 150–200 mg/m² [1]. However, one month after completing chemoradiotherapy, the patient's symptoms worsened. A follow-up MRI revealed tumor progression. The MDT and the patient's family opted to proceed with palliative chemotherapy.

Despite continuing Temozolomide up to the fifth cycle, her neurological condition further deteriorated. Decubitus complications, including stage III sacral pressure sores, necessitated a spinal MRI, which identified secondary intradural extramedullary lesions causing spinal cord and cauda equina compression consistent with metastatic spinal dissemination (MSD) (Figure 3).

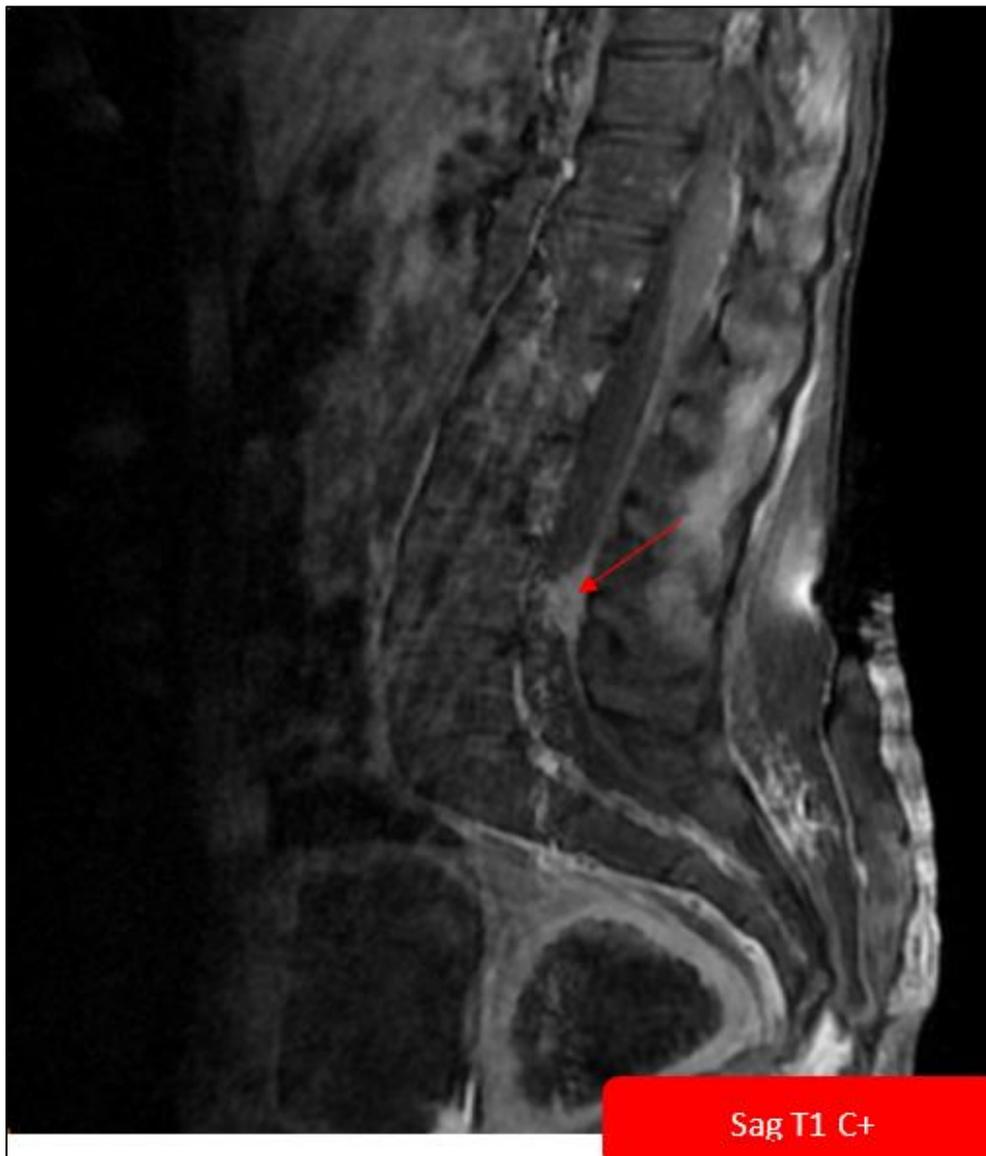


Figure 3 Sagittal MRI of the spine revealing an intradural extramedullary lesion at the L4 level, demonstrating intense contrast enhancement. The lesion extends to involve the cauda equina nerve roots

The patient's treatment shifted to best supportive care. Unfortunately, she discontinued follow-up after the fifth chemotherapy cycle. Her family later informed the medical team of her passing.

2. Discussion

Glioblastoma (GBM) is the most common and least prognostic malignant glioma of primary origin in the central nervous system (CNS). It has a median survival time of 14.6 months after standard treatment with the Stupp regimen, and the vast majority of patients die due to progression of tumor recurrence [2]

Pediatric glioblastoma multiforme (GBM) involving the spine is an aggressive tumor with a poor quality of life for patients. Despite this, there is only a limited number of reports describing the outcomes of pediatric spinal GBMs, both as primary spinal GBMs and metastases from an intracranial tumor. [3]

It was previously believed that extracranial GBM is uncommon because of the presence of physical barriers, such as the thickened basement membrane, the dura mater, and the blood brain barrier. [2] The specific mode of spread remains unclear, although a number of hypotheses have been proposed. The primary mechanism is believed to be tumor extravasation directly through the cerebrospinal fluid (CSF), with surgical debulking increasing the likelihood of tumor seeding. [4]

There is typically an average lag time of 8.5 months after GBM diagnosis prior to detection of spinal drop metastasis. [5] In our case, however, spinal metastasis was detected shortly after the end of radio chemotherapy. In previous reports, this diagnosis occurred after surgical resection of GBM and reported cases of GBM metastasis in the absence of surgical intervention remain rare, and existing accounts have been retrospective post mortem reports. To date, there has been only few reported cases of diagnosis of pediatric GBM spinal drop metastasis prior to surgery.

The exact mechanisms and contributing factors for metastatic spinal dissemination in GBM patients are not yet well understood. However, the presence of a ventricular opening, subventricular infiltration, or a tumor located near the ventricles may serve as potential indicators of risk [6, 7]. According to Tsung, factors such as undergoing multiple surgical resections, being male, ventricular invasion, rupture of the ventricular epithelium, and a weakened immune system could increase the likelihood of spinal dissemination. Tsung further emphasized that repeated surgeries, ventricular involvement, epithelial disruption, and immune suppression may elevate the risk of MSD [8].

In the majority of cases, patients with spinal drop metastasis remain asymptomatic, with pain radiation apparent in only 25% to 33% of cases [9]. Pediatric spinal GBM is associated with a decreased quality of life [11]; however, reports on the factors associated with patient prognosis in relation to treatment approaches for spinal GBM are limited, and the only factor associated with an improved outcome is younger age [12, 13].

This highlights the importance of considering the possibility of spinal drop metastasis in asymptomatic GBM patients and emphasizing the value of MRI spine even in such patients.

The most common symptoms of a spinal metastasis are radicular or local pain, paresthesia's and other sensory symptoms followed by motor weakness [10].

Since symptoms of metastatic spinal dissemination (MSD) often emerge in the late stages of the disease, motor and sensory deficits caused by intracranial GBM progression can obscure its detection. When recurrent GBM presents with rapidly worsening symptoms that cannot be attributed to intracranial lesions, MSD should be considered as a potential cause.

Currently, contrast-enhanced MRI of the entire spinal cord remains the most effective diagnostic tool for MSD in clinical practice. However, no standardized treatment guidelines exist. Available therapeutic approaches include radiotherapy, chemotherapy, intrathecal administration of chemotherapeutic agents, and targeted drug therapy.

This case underscores the aggressive nature of pediatric glioblastoma and the necessity of early diagnosis and molecular profiling to guide treatment strategies and improve prognostic predictions.

Identifying specific genetic markers can refine therapeutic approaches, while clinical trials remain essential for exploring novel therapies. Additionally, comprehensive supportive care plays a crucial role in symptom management and enhancing quality of life. A key takeaway from this case is the importance of vigilant monitoring for metastases, even in the absence of initial surgical intervention.

Pediatric glioblastomas with spinal dissemination are rare, with most cases reported after surgical resection. In contrast, this patient developed metastasis shortly after chemoradiotherapy, highlighting the heterogeneity of disease progression. Previous studies, including those by Tsung et al., suggest that factors such as ventricular involvement and decreased immunity contribute to metastatic risk, aligning with our findings while emphasizing the need for further research into non-surgical dissemination mechanisms, particularly in pediatric patients [1–8].

Optimal management requires proactive spinal imaging, even in asymptomatic patients, as early detection of metastatic spinal dissemination (MSD) enables timely interventions to prevent neurological decline. Tumor proximity to ventricles and ventricular invasion should be closely monitored as potential predictors of metastatic spread. Multidisciplinary collaboration remains critical for managing complex cases, ensuring individualized treatment plans that balance survival outcomes and quality of life. Ethical considerations are also paramount in such cases, necessitating transparent communication with families regarding prognosis, treatment limitations, and potential outcomes.

Respect for patient and family autonomy is crucial, particularly when weighing palliative versus aggressive treatment options.

Future research should focus on refining therapeutic protocols for pediatric glioblastoma with spinal metastases, leveraging clinical trial data to establish evidence-based guidelines but balancing aggressive treatment approaches with quality-of-life considerations will remain a significant challenge in the management of these patients.

3. Conclusion

Spinal seeding of pediatric glioblastoma is rare and associated with poor prognosis due to limited treatment options. This case emphasizes the importance of early identification through whole-spine MRI in patients presenting with unexplained symptoms. Additional studies on molecular pathways and biomarkers are crucial to enhance treatment strategies and patient outcomes.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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