



Primary bulbo-medullary glioblastoma in a child: case report

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Abstract

Glioblastoma (GBM) of the spinal cord represents a rare entity in children and account for less than 1% of all central nervous system (CNS) cancers. Their biology, localization, and controversial treatment options have been discussed in a few pediatric cases. Here, we report a case of primary spinal cord glioblastoma in a 5-year-old girl having the particularity to be extended to the brainstem. This tumor has been revealed by torticollis and bilateral brachial paresis. The patient underwent subtotal resection; unfortunately, she died in reanimation 1 week later by severe pneumopathy. To the best of our knowledge, this is the first case in the literature reporting this particular localization in a child. Beyond their dismal prognosis, we discuss the rarity of the disease and describe the peculiar characteristics, management, and prognosis of this rare tumor in pediatric oncology. This case appears to be unusual for both the histological type and the extension to brain stem.

Keywords Children · Spinal glioblastoma · Spinal cord · Brain stem · Multidisciplinary treatment

Abbreviations

GBM Glioblastoma
CNS Central nervous system

Introduction

Spinal cord glioblastoma (GBM) accounts for approximately 7.5% of all intramedullary gliomas and 1.5% of all spinal cord tumors [7]. These tumors are only rarely seen in children and represents 1–5% of all GBMs [20, 28]. They have a predilection for development in the cervical or cervicothoracic region and are associated with severe disability and poor prognosis.

Here, we report a case of primary spinal cord glioblastoma having the particularity to be extended to the brainstem. To the best of our knowledge, this is the first case in the literature reporting this particular localization in a child. This case appears to be unusual for both the histological type and the extension to brain stem.

Little is known about the peculiar clinical characteristics of primary spinal glioblastomas and his optimal treatment.

However, this report describes one case of cervical glioblastoma in a 5-year-old child and reviews other cases reported in the literature (Table 1) and discuss the clinical features, current multidisciplinary therapeutic approaches, and prognostic factors of this rare pathology with a review of pertinent literature.

Case Description

Clinical Presentation

A 5-year-old girl presented at our department complaining of severe cervical back pain, torticollis, and progressive weakness of her two upper limbs. Clinical examination found a conscious child, having severe torticollis (Fig. 1) and symmetric bilateral brachial paresis. No neurological deficit was found in the lower limbs.

Plain X-rays were normal, although CT scan showed an enlargement of the cervical spinal canal. However, MRI revealed a large and a heterogeneous cervical intramedullary mass with irregular enhancement after gadolinium injection that filled the spinal canal until T2. The mass was extended from the bulbo-medullary junction to the cervicothoracic spinal cord (T2) and appear hyposignal T1 and hypersignal T2. Craniospinal MRI did not show any signs of hydrocephalus or leptomeningeal metastases (Fig. 2).

The patient underwent surgery, and the tumor was approached through a suboccipital craniotomy, C1

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Table 1 Review of the literature on primary cervical/CT GBM in pediatric patients

Case no.	Author and year	Age (years)/sex	Level of tumor	Surgery	RT/CT	Survival (months)
1	Narayana et al. 2010 [21]	14/M	C2-C7	STR	–/–	2
2	Perkins et al. 2011 [23]	15/F	C6-C7	STR	+/+	6
3	O Halloran et al. 2013 [22]	10/F	Cervical	GTR	+/+	14
4		12/F	Cervical	GTR	+/+	14
5		4/F	Cervical	STR	+/+	10
6		10/F	CT	STR	+/+	12
7	Lober et al. 2010 [17]	8/M	Cervical	STR	+/-	4
8		16/M	CT	STR	+/+	6
9		11/M	CT	STR	+/+	17
10	Prasad et al. 2012 [25]	10/M	Cervical	Biopsy	–/–	3
11	Ansari et al. 2012 [3]	12/F	Cervical	STR	+/-	6
12	Russel et al. 1959 [27]	14/M	C2-C7	STR	+/+	9
13		18/F	C7-T7	GTR	+ /NR	21
14		18/F	CT	GTR	+/-	21
15		18/F	CT	GTR	+/-	21
16		18/F	CT	GTR	+/-	21
17	Johnson et al. 1987 [9]	8/F	Cervical	STR	+/+	1
18	Kim et al., 2011 [12]	12	C1-C7	STR	–/–	2
19	Adams et al. 2016 [2]	13/F	Cervical	GTR	+/+	15
20		15/M	Cervical	STR	-/+	8
21	Caroli et al. 2005 [5]	10/F	C2-C7	STR	+/-	3
22	Minehan et al. 2009 [19]	18/F	Cervical	STR	+/-	4
23		1/M		STR	–/–	10 days
24	Raco et al. 2005 [26]	11/F	Cervical	NR	–/–	6
25	Wisoff et al. 1998 [31]	1/F	CT	NR	+/-	64
26	McGirt et al. 2008 [18]	2/F	C7-T7	GTR	+/-	14
27		1/M	C7-T2	STR	+/+	13
28		1/M	C3-T7	Biopsy	+/+	24
29	Lam et al. 2012 [15]	14/F	C6-T5	GTR	+/+	10
30		8/F	C3-T4	STR	+/+	14
31	Our case Lakhdar et al. 2019 [14]	5/F	CT	STR	–/–	1 week

NR not reported, CT cervicothoracic

laminectomy, and C2–C7 laminotomy. Microsurgical subtotal excision was performed with intraoperative neurophysiologic monitoring. After opening the dura, a greyish, highly vascularized solid mass appeared, infiltrating the cervical spinal cord and the brain stem. At the end of the procedure, the excision appeared to be partial because the infiltration of brain stem (Fig. 3).

Histopathology

Microscopy demonstrates a neoplastic proliferation of polymorphous glial cells characterized by anisocaryosis and atypical mitosis, focal necrosis, calcifications, and areas with

multinucleated cells are present. Moreover, immunohistochemistry shows positivity for glial fibrillary acidic protein (GFAP) and S100 and negativity for synaptophysin, neurofilaments, and the epithelial membrane antigen (EMA). The final histological study was compatible with spinal cord glioblastoma (GBM).

Outcome

In the immediate postoperative stage, the patient developed quadriplegia with breathing difficulties. She was hospitalized in the intensive care unit where unfortunately, she died 1 week later because of severe nosocomial pneumonia.



Fig. 1 The little girl presenting a torticollis

Discussion

Intramedullary gliomas are uncommon clinical entities especially in children accounting for less than 10% of all central

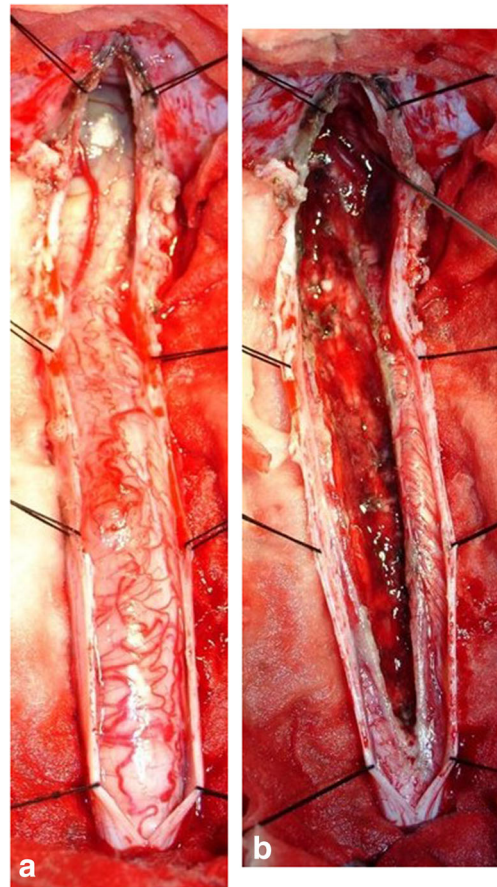
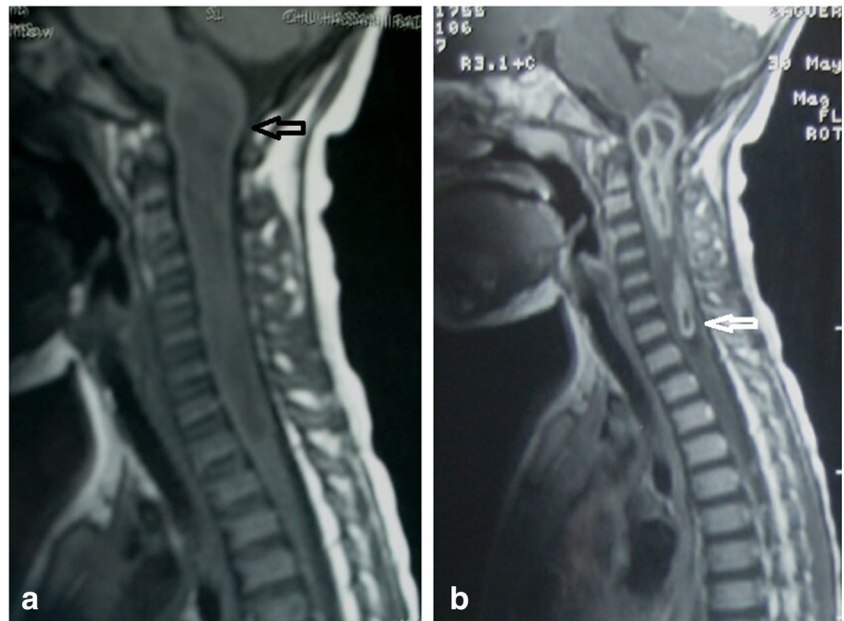


Fig. 3 Peroperative aspect of cervical spinal cord after open the dura matter (a) and after surgical excision (b)

Fig. 2 Sagittal T1-weighted craniocervical MRI (a), with gadolinium (b) showing spinal cord GBM extending from the bulbo-medullary junction (brainstem) (black arrow) to cervicothoracic (T2) (white arrow)



nervous system tumors [11]. Data on childhood malignancies from the European Union show that only 3% of all children with CNS tumors are affected by this disease [10]. These

tumors are often misdiagnosed or diagnosed late because of their rarity. The commonly reported locations of GBM are the cervicothoracic segments, with the cervical spine being the most affected region, followed by the thoracic spine [24]. To the best of our knowledge, there are no other radiologic reports of primitive glioblastoma in cervical spine extended to brain stem in childhood.

The study of Konar et al. showed that the mean age at presentation for primary spinal GBM was 10 ± 5.1 years [13]. Clinical presentation is related to the region of spinal cord involved. The most common symptoms in children include pain, motor regression, torticollis, and progressive kyphoscoliosis. These lesions are highly aggressive, with rapid neurological deterioration and death following a short clinical history [8] as seen in this report, usually less than a year [6].

However, spinal cord glioblastoma shows a tendency to spread via the subarachnoid space at the spinal and, more rarely, at the brain level. This can be explained by the proximity of the neoplastic cells to the cerebrospinal fluid pathways [5]. In the same way, the extension to the brain stem may be a tumoral progression from spinal cord or on the contrary the starting point of GBM. These patients develop not only local recurrences but frequently widespread leptomeningeal metastases.

MRI is the diagnostic procedure of choice for spinal tumors. In the presented case, MRI was able to accurately define the tumor extending from brain stem to T2. Full neuraxis MRI is always recommended in order to detect possible metastases. The main aim of the differential diagnosis of gliomas in the pediatric population is to exclude demyelinating disease, neurosarcoïdosis, vascular malformations, ischemia, pseudotumor, chronic arachnoiditis, transverse myelitis, gangliogliomas, ependymomas, and epidermoid/dermoid tumors [7].

Historically, pediatric spinal GBM has been treated surgically with adjuvant radiotherapy (RT) followed by chemotherapeutic regimens, although neoadjuvant chemotherapy did not offer any survival benefit compared with RT and adjuvant standard chemotherapy [29].

In addition, controversial management protocol and contradictory reports on the benefit of resection, radiation, and chemotherapy limit neurosurgeons' or oncologists' ability to formulate clear guidelines and consensus on optimal treatment strategies. However, some studies have advocated for aggressive surgical removal, but the lack of a clear plane between the infiltrative tumor and the adjacent normal tissue makes total removal largely unrealizable [8]. Furthermore, treatment always requires an individual decision-making process. Although surgical decompression/resection of spinal cord GBM is the treatment of choice (with varying degree of extent of resection ranging from partial debulking to gross total resection and even cordectomy), it is often accompanied by

significantly increased morbidity without necessarily increase survival; therefore, some authors recommend biopsy [7]. Use of chemotherapy and temozolomide may prove helpful, despite aggressive treatment combining surgery and irradiation [4]. Moreover, laminoplasty should be performed in spinal surgery in children, to avoid the high incidence of spinal deformities following laminectomy [5].

Pediatric GBM usually has a grim prognosis. Many reported cases had survival ranges from 6 and 16 months, with a mean survival period of 12 months after diagnosis [20]. An exceptionally long survival of 144 months has been reported for a patient with spinal GBM [30]. In the analysis of Adams et al., only the histological subtype, age at diagnosis (child and adult), sex, and the extent of resection were associated with survival [1]. On the other hand, Liu et al. report that tumor size and the extend of surgery had no significant impact on survival of adult patients, whereas postoperative radiotherapy is associated with prolonged survival [16] (Table 1).

The analysis of all published cases of spinal GBM (Table 1) demonstrate female predominance with sex ratio $\frac{1}{2}$, and GTR performed only in 29% with median survival of 17 months against 8 and 11 months after STR/Biopsy and all resection degrees, respectively. In addition, half of the cases underwent chemotherapy, 78% radiotherapy, and only 6 cases without any adjuvant treatment (RT/CT) with median survival of 2 months. Also, further studies are required to elucidate the best treatment strategy for pediatrics spinal cord glioblastoma.

Conclusion

Spinal cord glioblastoma is a deadly disease that is so rare, exceptionally extends to brain stem with grim prognosis. Even with aggressive management, these tumors are generally associated with a dismal outcome.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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