Cervical Intramedullary Spinal Cord Glioblastoma in a 10 Year-Old Child. Case Report

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ABSTRACT
Among all pediatric tumors in CNS, the intramedullary spinal cord tumors are less than one-third of 1% and only about 1-3% of them are high-grade gliomas. Intramedullary glioblastoma (GBM) is considered highly threatening because of its aggressiveness and, even with intense management, lesion progress and patients develop severe deficits. Authors report a very rare case of a 10-year-old patient with extensive cervical GBM with an unusual outcome.

Keywords: Spine cord tumor; Glioblastoma; Intramedullary tumor; Children

INTRODUCTION
Tumors arising from tissue elements within the spinal cord are a small subgroup of central nervous system (CNS) tumors in children. Among all pediatric tumors in CNS, the incidence of intramedullary spinal cord tumors is less than one-third of 1%.

Low-grade gliomas such as ependymomas and astrocytomas account for the majority, with only about 1-3% being high-grade gliomas¹. The latter are considered highly threatening because of their aggressive behavior and their localization in between the fiber tracts that are responsible for motor control, movement coordination, and different modalities of sensation².
Due to the remarkable aggressiveness of this type of tumor, it is important to establish diagnosis for early definition of therapeutic intervention. However, even with aggressive management — including surgery, radiotherapy and chemotherapy — the lesions eventually progress and patients develop primary disabilities and complications associated with prolonged hospitalization.

The authors report a very rare case of a 10-year-old patient with extensive intramedullary glioblastoma of the cervical segment of the spinal cord. Brief information about the epidemiology, presentation, treatment and outcome are further discussed.

CASE PRESENTATION

Caucasian 10-year-old, male patient, previously healthy, present with a two-months history of lower extremity dysesthesias, which progressed to lower limbs (LL) weakness, gait difficulties, upper limbs (UL) weakness and cervical pain several days before evaluation. Neurological examination demonstrated tetraparesis (grade III in LL and grade II in UL), spasticity and Babinski sign in LL, and hypotonia in UL. All these symptoms are more evident in the right side. In addition, paresthesia with sensitive level at C3 segment was detected. There was no vesical or sphincter dysfunction and no cranial nerve deficit. Finally, no respiratory dysfunction was detected. He was classified with grade IV of McCormick scale due to the upper limbs’ impairment.

Due to the suspicion of a possible spinal cord syndrome, the patient was submitted to brain and spine magnetic resonance imaging (MRI) with contrast injection, and spine, which revealed an extensive infiltrative intramedullary lesion at C3-T2 level (Figure 1).

Microsurgical subtotal excision was performed with intraoperative neurophysiologic monitoring. After opening the dura, a brownish-red, highly vascularized solid mass was identified and the resection of entire visualized tumor area was performed (Figure 2). Further immunohistological analysis confirmed the diagnosis of a grade IV (World Health Organization [WHO] classification) glioblastoma (Figure 3).

The early post-operative period was marked by worsening of the weakness in LL (grade I) and by the developing of urinary retention. No changes in UL deficits were noted.

The patient is currently receiving fractionated radiation therapy to cervical and thoracic spine and oral temozolomide therapy. In the 1-year postoperative follow-up, he did not present severe adverse effects related to adjuvant treatment and he is clinically stabilized with no new deficits and with subtle improvement in the urinary retention and LL weakness. He maintained the McCormick grade IV at clinical examination.
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Due to the remarkable aggressiveness of this type of tumor, microsurgical subtotal excision was performed with intraoperative neurophysiologic monitoring. After opening the dura, a brownish-red, highly vascularized solid mass revealed an extensive infiltrative intramedullary lesion at C3-C7. Intraoperative gross pathology of a cervical spinal intramedullary glioblastoma showed expansiveness and compressive effect on the adjacent structures (Figure 2).

Histopathologic features of the cervical spinal GBM showed positive expression for glial fibrillary acidic protein (GFAP) and ATRX protein, indicating glioblastoma multiforme (GBM) (Figure 3).

In adults, ependymomas are the most common glial neoplasm of the spinal cord, followed by astrocytomas. In children, however, astrocytomas occur more frequently. Most intramedullary astrocytomas are low grade, but 10% to 15% of intramedullary astrocytomas are high-grade (WHO grades III and IV). Most of these are anaplastic astrocytomas (WHO grade III), but 0.2% to 1.5% are glioblastoma multiforme (WHO grade IV) 1,4,6.

Clinical Presentation
Neurological deficits are related to the region of the spinal cord...
that is involved. Because these tumors asymmetrically involve white matter tracts within the spinal cord, the presentation is characteristically asymmetrical. The major difference in presentation between low-grade and high-grade astrocytomas is the onset of symptoms before diagnosis. For low-grade tumors, symptoms are present on average for 3.5 years before diagnosis. In contrast, malignant astrocytomas have a shorter history and are typically diagnosed about 6 months after the onset of symptoms because of neurological deterioration.

Neurologic dysfunction manifests as sensory dysesthesias, muscular weakness, progressive difficulty of ambulation and urinary dysfunction. The most common symptoms include pain (42%), motor regression (36%), gait abnormalities (27%), torticollis (27%), and progressive kyphoscoliosis (24%) \(^5^\). Exacerbation and worsening of the neurological status are progressive and often related to the progression and the growth rate of the tumor or intratumoral bleeding\(^1^,^4\).

In this case, the patient presented with LL dysesthesias, which progressed to asymmetrical weakness and gait difficulties in a period of 2 months. This presentation can be considered rapidly progressive compared to the literature data and suggest the highly aggressive behavior of the lesion.

**Evaluation**
The gold standard exam to evaluate spinal cord tumors is the contrasted MRI, although computed tomography (CT) may also be used for evaluation of bone complications \(^1^,^2\). The analysis of some aspects is important to the characterization of the lesion, like spinal cord expansion, contrast enhancement, and presence of cysts. Malignant astrocytomas often are characterized by images hypo- to isointense on T1W, hyperintense on T2W and FLAIR, heterogeneous contrast enhancement, areas of hemorrhage, necrosis and edema, which are not usually seen in lower grade lesions \(^4^,^7^,^9\).

Nevertheless, the histopathological and immunological evaluations are necessary, once there are no pathognomonic findings in MRI for exact differentiation of the intramedullary tumors. In addition, the choice of subsequent therapy with chemotherapy and radiation therapy is guided by the histological type of the lesion \(^1^,^5\).

This case presented a hypointense image in T1W and hyperintense in T2W, with heterogeneous contrast enhancement. In addition, although it was a high-grade lesion, there were no cystic components or signs of hemorrhage.

**Management**
The surgical management of these rare tumors remains controversial due to the lack of prospective randomized studies with regard to treatment, and the majority of patients with malignant astrocytoma of the spinal cord undergo some sort of cancer-directed surgical treatment, ranging from biopsy alone to partial or gross total resection\(^1^,^4\).

After surgery, rates of local and distant recurrence are high, and many authors recommend adjuvant treatment \(^6\). The majority (80%) of patients with malignant astrocytoma of the spinal cord undergo radiation treatment, and several studies have demonstrated a survival benefit from radiotherapy in this group \(^6^,^10\).

Chemotherapy is also an option for treatment of malignant intramedullary astrocytomas. There is limited evidence that temozolomide (TMZ) and bevacizumab may be beneficial in the treatment of malignant astrocytomas of the spinal cord, although their role remains unclear \(^1^,^4\).

RT is considered the standard post-surgical management in infiltrative high-grade astrocytomas \(^10\). In patients with severe paraparesis high doses have been reported in the literature. However, when used in conjunction with chemotherapy or potential radiosensitizer (TMZ), a lower dose of radiotherapy is reasonable \(^1,^10\).

**Outcomes**
High-grade intramedullary spinal cord lesions have a poor prognosis in the pediatric population \(^11,^12\). The most important factor affecting the prognosis of patients with spinal cord...
tumors is the histological grade of the tumor and, among the patients with grade IV lesions, the cervical location is associated with a poorer outcome (survival rate of 6 months) when compared with thoracic or lumbar involvement (12-13 months). This difference probably occurs due to the involvement of the fibers of the phrenic nerve, causing respiratory complications. Furthermore, literature reviews suggest that survival rate is better in patients with an age less than 7 years. Despite the large infiltration in this area, our patient had no respiratory symptoms and is stable after 1 year of follow-up, keeping only the same deficits prior to surgery. This outcome can be considered uncommon analyzing the high-grade of the lesion, localization, and the estimated survival for these patients.

CONCLUSION

The spinal cord is a rare site of pediatric GBM, which has a poor overall survival despite the multimodality therapy. Surgery followed by adjuvant therapy with radiation and chemotherapy are the recommended standard approach of these lesions. However, even with aggressive intervention, the outcomes are unfavorable. Thus, more studies regarding the management of these patients should be stimulated with the aim of obtaining a better understanding of this complex pathological process.

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