Glioblastoma Multiforme in the Cerebellopontine Angle in a Pediatric Patient

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Abstract

Posterior fossa tumors are frequently diagnosed in children compared to their adult counterparts, representing 54 to 70% of the cases. Tumors located in the cerebellopontine angle are rare and represent 10% of the posterior fossa lesions in children. In addition, glioblastoma multiforme is a malignant primary tumor of the central nervous system and represents 3% of the tumors in children. We present the fourth reported case of a glioblastoma multiforme, confirmed by histopathology and located in the cerebellopontine angle in a 6-year old child, which was treated with surgery and subsequently with radiotherapy and chemotherapy. Thus, the presence of a glioblastoma multiforme in the cerebellopontine angle is extremely rare and needs a high-index of suspicion in children.

Keywords
- cerebellopontine angle
- glioblastoma multiforme
- near-total resection

Introduction

Posterior fossa tumors in children are relatively frequent. The majority of posterior fossa tumors in childhood are located in the fourth ventricle, cerebellar vermis and brainstem, and include medulloblastomas, ependymomas and gliomas. Cerebellopontine angle (CPA) tumors in this population are rare and represent less than 10% of all the posterior fossa tumors.[1,2]The most common tumors in the CPA are schwannomas and meningiomas in adults, but in children, they are rare and are only found in cases of type 2 neurofibromatosis. Other intra-axial tumors such as ependymomas, gliomas, and atypical teratoid rhabdoid tumor/primitive neuroectodermal tumor (ATRT/PNET) are found according to the series.[1,2]

Glioblastoma multiforme is a rare and malignant primary tumor of the central nervous system, with an incidence of less than 3% in children, which is less frequently located in the posterior fossa, specifically in the CPA. When this tumor is diagnosed, multimodal treatment with surgery, radiotherapy, and chemotherapy is recommended.

Only three cases of CPA glioblastomas originating from the brain stem have been reported in the literature in children.[3-5] Herein, we present the case of a 6-year-old child with a CPA mass which was initially catalogued as a malignant schwannoma versus an ependymoma, but the histopathological examination revealed a glioblastoma multiforme.

Case Report

A 6-year-old child without relevant past medical history was admitted with a 2-month period of headache, nausea, vomiting, and gate ataxia. Right facial paresis, rotatory nystagmus, and anisocoria were also present. A contrast-enhanced brain CT scan revealed a severe obstructive hydrocephalus and a posterior fossa mass in the right CPA and brain stem with absence of contrast enhancement (►**Fig. 1A**, **B**). At that moment, neuroendoscopy was not available at the institution, so the decision was made to place a ventricular peritoneal shunt (VPS) with resolution of the hydrocephalus and without complications (►**Fig. 1C**). A contrast-enhanced

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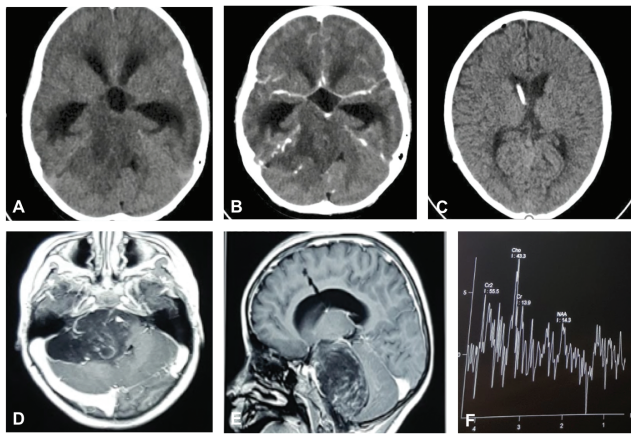

Fig. 1 (**A**) Brain CT scan revealed a severe hydrocephalus. (**B**) Contrast-enhanced CT scan revealed a hypodense mass in the CPA without contrast enhancement. (**C**) Postoperative CT scan revealed the adequate position of the ventricular catheter and resolution of the hydrocephalus. (**D, E**) T1, contrast-enhanced MRI showed a large mass in the right CPA involving the brain stem. There is a differentiation plane between the tumor and cerebellum, but not between the tumor and the brain stem, suggesting its origin from this structure. **(F)** Spectroscopy showed an increased peak of choline and a decreased peak of NAA. Abbreviation: CPA, cerebellopontine angle.

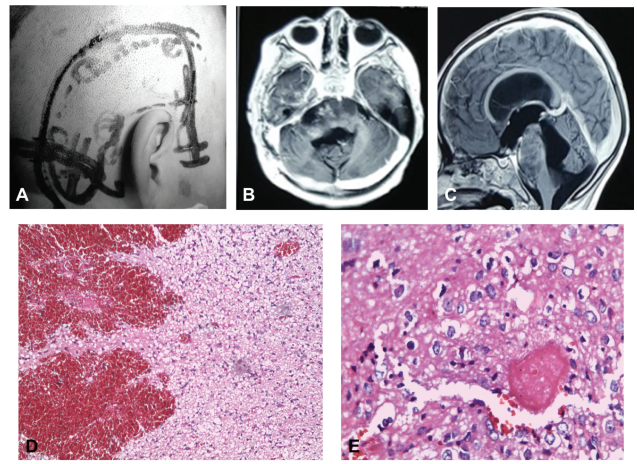

Fig. 2 (**A**) Preoperative planification of the surgical approach. (**B, C**) Postoperative T1, contrast-enhanced MRI showed a subtotal resection of the tumor. (**D, E**) Histological study of the tumor showed a glioblastoma with necrosis, high-mitosis index, atypical round cells, and microneovascularization.

brain MRI revealed a right cystic and solid CPA infiltrative lesion toward the brainstem with intratumoral enhancing and necrosis areas, suggestive of a malignant tumor. In addition, the spectroscopy revealed an increased peak of choline and a decreased peak of N-acetyl-aspartate (►**Fig. 1D–F**) The differential diagnosis at that moment was a malignant schwannoma, astrocytoma, or an atypical teratoid/rhabdoid tumor (ATRT)/primitive neuroectodermal tumor (PNET).

One week after the VPS surgery, the patient developed neurologic impairment. The CT scan revealed absence of hydrocephalus but mass effect of the tumor, and with these findings, emergent surgical resection of the lesion was decided. A combined approach was performed: A U-shaped incision was done and subtemporal and retrosigmoid craniotomies were performed (►**Fig. 2A**). Intraoperative neurophysiological monitoring (IONM) was not employed. During the microscopic resection of the lesion, a large, infiltrative, noncapsulated, reddish tumor without a cleavage border and with a rich vascularized network within the mass was found. Infiltrative tumor involving the brainstem, basilar artery, and cranial nerves were observed and softly dissected, especially the facial and lower cranial nerves. After surgery, the patient was stable and awakened with facial paralysis and lower cranial nerves compromise. Postoperative MRI showed a near total resection of the tumor with a remnant portion in the ventrolateral surface of the brainstem (►**Fig. 2B**, **C**). Histopathologic examination revealed a tumor compatible with a glioblastoma multiforme. Immunohistochemistry examinations revealed the following pattern: PAGF positive, Ki-67: 30%, neurofilament: enhanced axonal entrapment, p53: positive, IDH: negative, AXTR: retained nuclear expression. After surgery, the patient underwent radiotherapy and chemotherapy with temozolamide. Unfortunately, the patient was lost after 1 year of follow-up.

Discussion

CPA tumors in children are rare and it is necessary to differentiate them from intra-axial tumors, which extend to the CPA in an exophytic fashion such as gliomas, and from extra-axial lesions such as meningiomas and schwannomas. Clinical manifestations of intra-axial and extra-axial lesions of the CPA include the compromise of cranial nerves and progressive development of hydrocephalus. Overall, medulloblastomas and ependymomas are the most frequent tumors in the posterior fossa in children, and among these tumors, malignancy is high.

Glioblastoma multiforme is the most frequent primary tumor in adults, whereas it only represents 3% in the pediatric population[6] The optimal management of these type of tumors is the complete resection followed by radiotherapy and chemotherapy. Despite this, the reported mean survival time is 12 months. In addition, if temozolamide is initiated, the mean survival time is improved in 2 months.[7]

Pontine and cerebellar glioblastomas can spread to anatomic corridors and infiltrate important neurovascular structures. There are reports of exophytic cerebellar glioblastomas involving the CPA which were treated surgically.[8,9]

There are some differences in the clinical presentation of an intra-axial tumor with exophytic comprise into the CPA in comparison with an extra-axial tumor. The short duration of symptoms, cranial nerve comprise, and rapid progression of hydrocephalus and brain stem dysfunction are suggestive of an intra-axial lesion.[8]

Phi reported a cohort of 267 patients with posterior fossa tumors and only two cases of glioblastoma multiforme were found[1] Nevertheless, no case was located at the CPA. The CPA-located tumors represented 9.7% of the cases. In their analysis, they found a higher incidence of malignancy (70%) compared to previous studies. This finding is explained due to the younger age of diagnosis of the patients (mean 5.8 years) compared to the previous reports (mean 9.4 and 12.9 years).[1]

Table 1 Reported cases of cerebellopontine angle glioblastomas arising from brain stem in children

Case	Author	Sex/ age	Clinical history	CT/MRI findings	Treatment	Outcome
1	Rasalingam[3]	M/9	Right ear discharge, fever, double vision, ataxia, headache, bilateral papilledema, right 6th nerve palsy, nystagmus	CT: lesion in the right CPA with mild enhancement, hydrocephalus.	Retrosigmoid suboccipital craniectomy + subtotal resection	Dead
2	Jhawar[4]	M/12	Intracranial hypertension, ataxia, right facial paresis and hypoacusia.	MR: irregular solid and cystic mass with irregular ring enhancement and perilesional edema	Retrosigmoid suboccipital craniectomy+ near total resection	Mild paresis of facial nerve
3	Kaushik[5]	F/14	Intracranial hypertension, left-sided hemiparesis, right-sided cranial nerve palsy	CT: hypodense mass, hydrocephalus MRI: T1: isointense, T1-weighted: irregular peripheral enhancement T2: hyperintense	1st: VP shunt 2nd: Right retromastoid suboccipital craniectomy	Dead

Abbreviations: CPA, cerebellopontine angle; F, female; M, male; VP, ventriculoperitoneal.

Tomita analyzed the data of 44 infants and only 1 glioblastoma was found at the CPA, but did not report if the tumor arose from the brain stem or the cerebellum.[2] Also, 50% of the tumors were benign in histology, and a high-rate of cranial nerve injuries were reported but recovered within 2 years.

Three authors reported isolated cases of CPA glioblastomas which arose from the brain stem and mimicked other etiologies (►**Table 1**): Rasalingam reported one case of a pontine glioblastoma that mimicked a cerebellopontine angle otogenic abscess.[3] Intraoperatively, a near total resection was performed, and the tumor's appearance resembled a schwannoma. Jhawar reported an exophytic pontine glioblastoma that was supposed to be a tuberculoma or ependymoma due to the radiological characteristics.[4] A near total resection was performed and received subsequent radiotherapy. On the other hand, Kaushik reported the case of a CPA glioblastoma with intracranial hypertension and atypical findings on MRI, which underwent VPS placement and subsequent resection of the tumor.[5]

In our case, the radiological features of the tumor (brain stem infiltration, necrosis areas) and the clinical symptoms oriented to a rapid progressive malignant etiology, which was confirmed with the histopathological examination. The sequence of the procedures performed were similar to previous reports. Nevertheless, endoscopic third ventriculostomy (EVT) has some advantages over VPS in terms of lower mortality rates, postoperative infections, and hematomas.[10,11] Moreover, for severe intracranial hypertension cases, the EVT is less reliable for its control.[11,12] The combined approach was selected in order to obtain an adequate corridor to the CPA space, prepontine space, and the lateral aspect of the clivus.[13,14]

This is one of the only four CPA glioblastoma cases in children reported in the literature with histological confirmation which arose from the brain stem. Other authors reported exophytic cerebellar tumors which involved the CPA. Similar to the previous reports, the real etiology was not suspected from the beginning due to the rarity of the tumor and the atypical imaging characteristics. A careful histopathological examination is required for an ascertain diagnosis. Molecular biology tests showed that overexpression of the p53 protein and the presence of naïve IDH are associated with a poor prognosis.[15,16]

Conclusion

CPA glioblastoma multiforme in childhood is a rare lesion. Differential diagnosis should be considered among other tumors in this location. Histologic confirmation and immunohistochemistry play important roles in deciding the appropriate management and defining the prognosis.

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Conflict of Interest
None declared.

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