

Medulloblastoma (MB) is a highly aggressive soft tissue neoplasm, classified as a primitive neuroectodermal tumor. It is the most common posterior fossa tumor in children, but occurs rarely in adults. MB accounts for approximately 20% of all primary central nervous system (CNS) tumors of childhood, while its incidence is around 1% of adult brain tumors. Most often it occurs in the cerebellum. We report a case of multicentric MB involving the bilateral cerebellopontine angle (CPA) and right cerebellar hemisphere. The tumor showed isointensity on T1/T2-weighted images, and slight hyperintensity on T2-weighted fluid-attenuated inversion-recovery (FLAIR) images. The MB had restricted diffusion on diffusion-weighted images (DWI). It was not easy to make an accurate diagnosis before biopsy. The lesion in our patient presented with atypical MR image features of medulloblastoma. To our knowledge, this is the first case of bilateral CPA MB.

Key words: medulloblastoma; bilateral; cerebellopontine angle.

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Atypical bilateral cerebellopontine angle medulloblastoma: differential diagnosis, immunohistochemical features and radiological presentation

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Introduction

Medulloblastoma (MB) is a highly malignant and aggressive embryonal neuroectodermal tumor of the cerebellum [1–12]. This is the most common posterior fossa tumor in children [13], but occurs rarely in adults [14]. MB accounts for approximately 20% of all primary CNS tumors of childhood [8, 15–17] while its incidence is around 1% of adult brain tumors [18].

The World Health Organization (WHO) classification of tumors of the central nervous system (CNS) distinguishes four main histological variants of MB: classic, desmoplastic, extensive nodular, and large cell/anaplastic. According to the most recent molecular consensus, MB has been sub-classified into SHH, WNT, group 3, and group 4 [8, 6, 19–22]. Sonic Hedgehog subgroup (SHH) MB comprises two-thirds of cases in adults [22]. The pathogenesis and etiology of MB have not been elucidated clearly. Anatomically, MBs can be found in the midline, in the cerebellar hemisphere, or extending exophytically into the cerebellopontine angle (CPA) [23]. In adults, MBs are typically observed in the cerebellar hemispheres. CPA medulloblastoma is an extremely rare variant. In fact, there have only been 40 reported cases, with less than 24% in children [23, 24]. Classic and desmoplastic MBs are the most common histological types of CPA MBs [20, 22, 25–26].

We describe a very rare case of bilateral CPA MB in an adult who presented with radiological findings consistent with a CPA lymphoma. To our knowledge, MB with bilateral cerebellopontine angle has never been reported. Herein we present the first case report of bilateral CPA MB in a young woman.

Case report

A 25-year-old immunocompetent female suffered from progressive headache, vertigo and diplopia for 1 month. On neurologic examination, the patient was alert and well oriented. In otherwise good health, the patient suffered from down beat nystagmus, cerebellar dysmetria on the right without truncal ataxia, and right cranial nerve VI palsy, suggesting a posterior fossa lesion. The other cranial nerves were intact, and there was no sensory or motor deficit. There was minimal right sensorineural hearing loss. The patient did not experience dysarthria, dysphagia or choking while drinking. There was no family history of neurological diseases. Gadolinium-enhanced magnetic resonance imaging (MRI) study revealed a 19 × 17 × 13 mm, lobulated, mildly enhanced homogeneous intra-axial mass in the right cerebellar hemisphere, and bilateral CPA lesions, with partial extension into the right

internal auditory canal (IAC). The lesion on the right CPA side measured $17 \times 14 \times 18$ mm; the lesion on the left CPA side was smaller, measuring approximately $13 \times 13 \times 9$ mm. The tumor showed isointensity on T1/T2-weighted images, and slight hyperintensity on T2-weighted fluid-attenuated inversion-recovery (FLAIR) images. The MB had restricted diffusion on diffusion-weighted imaging (DWI). Lumbar puncture was performed, but analysis of the cerebrospinal fluid was normal, and cytological examination revealed no malignant cells. Three more lumbar punctures were performed due to neurological impairment but showed similar results to the first one. Furthermore, as a diagnosis of lymphoma was included in the differential diagnosis, a whole body PET/scan was performed without abnormal results. On the basis of imaging, also a differential diagnosis of lymphoma and bilateral CPA schwannoma was considered preoperatively. A steroid pulse was administered as a therapeutic and diagnostic trial, but significant improvement was not observed.

A right retrosigmoid craniotomy was performed. The patient underwent biopsy under microscope of the right cerebellar and right CPA lesions. Tumors were moderately reddish colored with loss in the cleavage plane with the normal cerebellar tissue, suggestive of tumor infiltration.

The surgical specimen consisted of a mass of soft red-to-grey tissue fragments. The paraffin sections, stained with hematoxylin and eosin, revealed a tumor that displayed the features of the classic variant of medulloblastoma with small polymorphic hyperchromatic cells with carrot-shaped nuclei, surrounded by scanty cytoplasm and neuroblastic rosettes. There was no necrosis or vascular proliferation. The Ki-67 proliferation index was less than 40%.

Initially, a wide surgical tumor resection was suggested, but the patient refused this plan because of potential unacceptable neurological worsening. The patient was discharged with slight improvement of her symptoms, and no major postoperative complication was observed. She received external beam radiation therapy to the craniospinal axis at a dose of 36 Gy for 4 weeks, followed by a boost to the posterior fossa at a dose of 54 Gy for 6 weeks. Posteriorly, chemotherapy with temozolomide and irinotecan was administered, followed by cyclophosphamide. The MRI after radiotherapy and chemotherapy revealed no significant tumor growth but rather an apparent decrease in size.

Eight months after biopsy the patient continued to be free of neurological deterioration, and showed improvement of diplopia and ataxia.

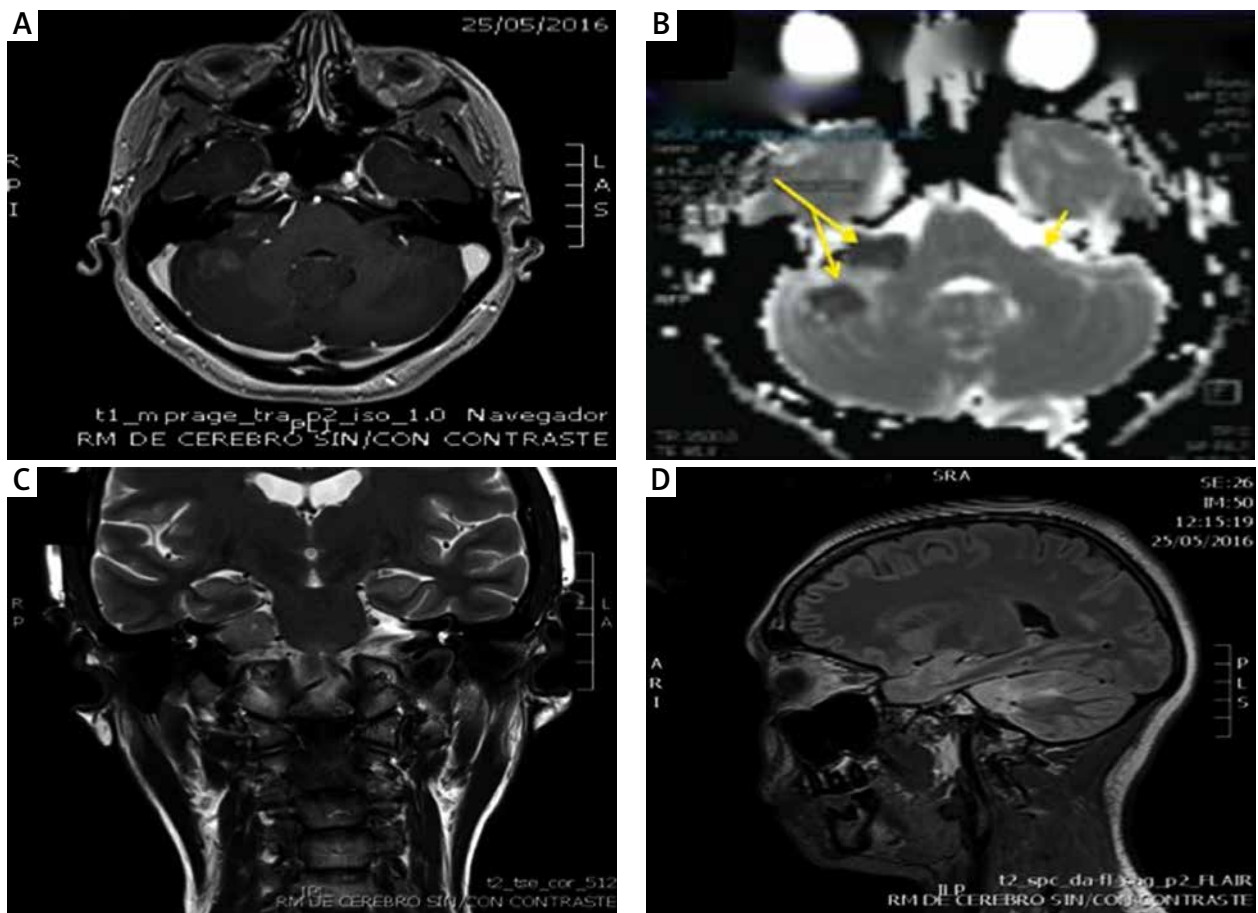


Fig. 1. A) Axial T1-weighted MRI shows intra- and extra-axial tumor in the bilateral CPA and right cerebellar hemisphere. B) Axial ADC demonstrates strong restricted diffusion on the tumor (arrows). C, D) Coronal T2-weighted and sagittal MRI shows mass effect of the tumor in the right CPA

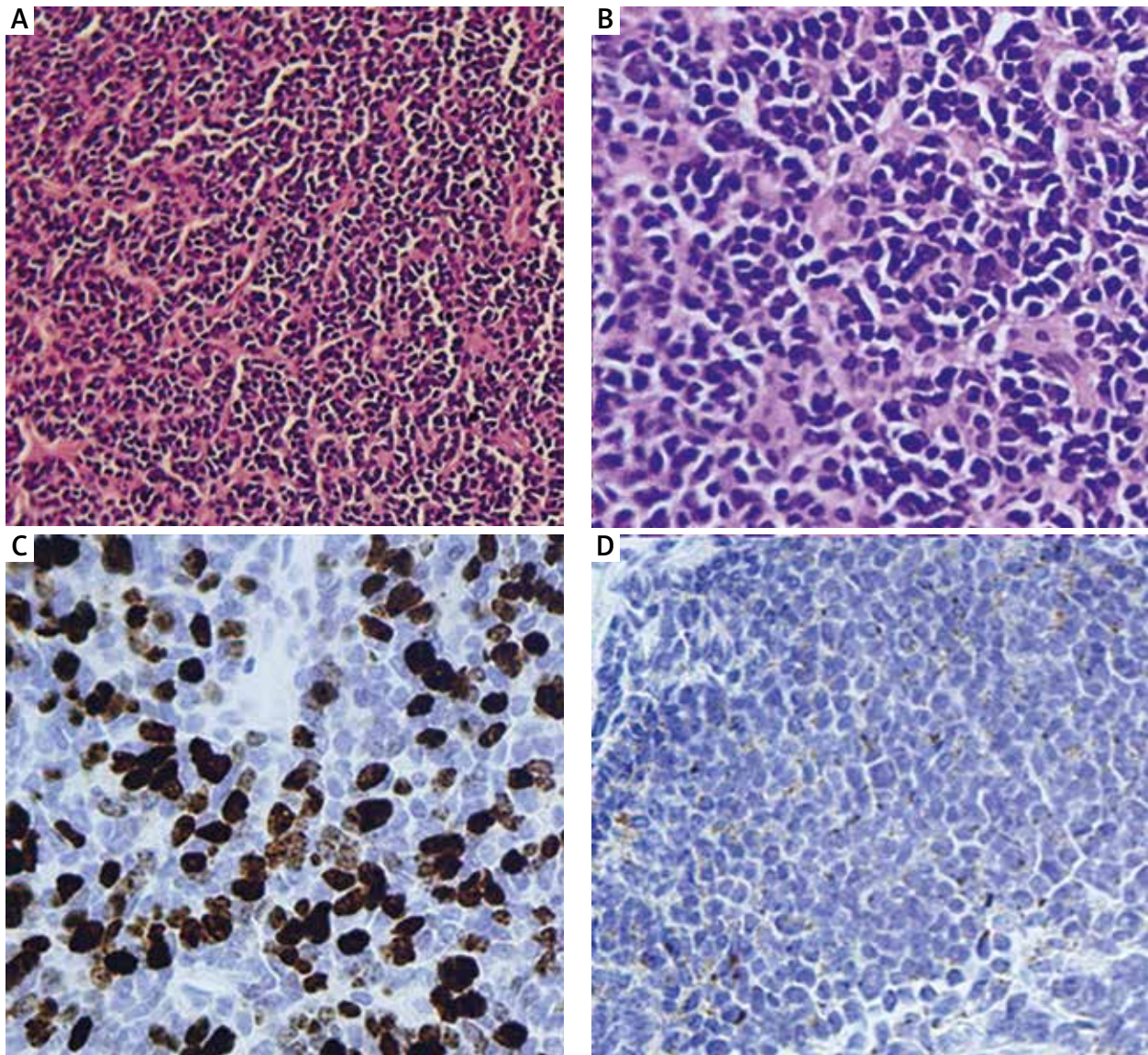


Fig. 2. A, B) Pathological characteristics of medulloblastoma showing carrot-shaped cell with monomorphic hyperchromatic nuclei and Homer Wright rosette appearance. C, D) Immunohistochemical analysis. Positive Ki-67 (C) and synaptophysin (D) staining of tumor cells

Discussion

Medulloblastoma lesion has a nonspecific clinical and radiographic presentation and exhibits a varied behavior depending on its location. Histopathology, immunohistochemistry and radiological features are critical in the diagnosis of MB [25, 26].

Although CPA lymphoma was considered a probable diagnosis, such tumors are extremely infrequent at this site [10, 27]. Primary central nervous system lymphoma is an extra-nodal non-Hodgkin lymphoma representing approximately 1% [27] of all intracranial tumors [10, 26, 27].

Unlike children, adult MBs are more likely to be hemispheric than midline, with cystic formation, poorly defined margins, irregular enhancement, extension through fourth ventricle foramina and presentation as a CPA lesion [21, 23, 28, 29]. Even in children, MBs are rarely found in the CPA. Furthermore, the exact histogenesis of MB is still unclear,

but recent theories suggested that these tumors may arise from the exophytically growing pattern of pluripotential cells or remnants of the external granular layer of cerebellar hemisphere [23, 26, 30] or may grow to occupy the CPA through a lateral extension from the fourth ventricle [31]. MB have to be considered in the differential diagnosis of CPA tumors. However, there are no radiographic features to differentiate MBs from other tumors in the CPA [30–32]. The differential diagnosis of CPA MB may be a challenge, and is based on the clinical, radiological and histopathological examination. The most frequent differential diagnosis is made with CPA lymphomas, schwannoma, and meningioma. The two most common soft tissue masses in the IAC and CPA are schwannomas and meningiomas. Distinguishing these tumors carries particular importance [33], as they have certain surgical and histological prognostic implications. Some authors propose that signs of brainstem and cerebellar dysfunction and the early onset

of symptoms may point toward the diagnosis of an intra-axial lesion, rather than of an extra-axial one, such as vestibular schwannomas [30]. Vestibular schwannomas, and meningiomas are the two most frequent lesions and account for approximately 90% of all CPA tumors [2–4]. Acoustic neuromas, or Schwannomas, originate from the Schwann cell in the peripheral portion of superior and inferior vestibular nerves, and also from the cochlear nerve, and are usually round or oval masses epicentered upon IAC and extending to the cerebellopontine cistern because of the anterior limit, with an “ice cream cone sign” as a distinguishing feature. In addition, schwannomas classically exhibit a characteristic MRI signal pattern consisting in a slight hypointensity in T1-weighted images and an increased signal in T2-weighted images, but MRI findings of Schwannomas can also be heterogeneous [7] due to cyst formation [4], or recurrent spontaneous bleeding. Conversely, meningiomas are usually hemispheric, semilunar masses with a broad petrous or tentorial base, with obtuse angles towards the dura and dura tails, and are usually eccentric to the internal auditory canal [4, 16]. However, meningiomas with IAC extension can appear identical to schwannomas on MRI imaging. Lymphomas invading the CPA have no specific imaging features; they are usually iso-hypointense to gray matter on T2-weighted images [27]. Further, infrequently lymphomas are multiple, associated with patchy gadolinium enhancement on T1-weighted images, necrotic or hemorrhagic in immunocompetent patients, and on rare occasions can invade or erode the IAC. Interestingly, based on MRI, steroid pulse can help in diagnosis and rapid remission [1].

Based on MRI, the appearance of MB is variable and nonspecific [14, 34–36], with no pathognomonic features [22], and is classically defined by iso- to hypointensity on T1-weighted images relative to cortex and heterogeneous hyper- or isointensity on T2-weighted images as the most common characteristics.

We report a case of multicentric disease involving the bilateral CPA and cerebellar hemisphere. The lesion in our patient presented with atypical MR image features of medulloblastoma.

According to recent reports, the current standard of care for medulloblastoma is aggressive surgical resection with normal CSF flow restoration followed by craniospinal irradiation, and chemotherapy [15, 28, 37]. Nevertheless, a few studies have shown that the role of tumor resection and chemotherapy in overall survival for adult MB remains controversial [5, 11, 17, 37–41].

Only a few cases of CPA MB have been described in the literature to date. We herein report the first case of bilateral CPA medulloblastoma.

Conclusions

Cerebellopontine angle medulloblastomas in adults and children are extremely infrequent. Medulloblastoma is a primitive neuroectodermal tumor of the cerebellum with a dismal prognosis and nonspecific clinical symptoms and radiological features, and is seldom considered in the preoperative differential diagnosis. Due to the rarity of

these tumors, a conclusive radiological pattern and therapeutic recommendations are currently not standardized. However, pathologists are able to accurately diagnose MB through a review of the histopathology.

The authors declare no conflict of interest.

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