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CASE REPORT - BRAIN TUMORS

Vanishing diffuse leptomeningeal contrast enhancement in an infant with choroid plexus papilloma

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Abstract
Choroid plexus tumors (CPT) can present in the baseline magnetic resonance imaging (MRI) with lesions compatible with leptomeningeal dissemination. Therapeutic strategy in this condition is controversial. We present a case of an infant with CPP and significant diffuse leptomeningeal contrast enhancement at diagnosis, which spontaneously resolved after removal of the primary tumor. In these challenging cases, several aspects, such as histopathological/molecular diagnosis and close radiological follow-up, should be taken into account to avoid unnecessary treatments.

Keywords Brain tumor · Pediatric · Choroid plexus papilloma · Leptomeningeal enhancement

Introduction

Choroid plexus tumors (CPT) are rare intraventricular tumors that arise from the neuroepithelial lining of the choroid plexus. They account for 1–4% of all pediatric brain neoplasms [16, 19]. Based on the revised 2016 WHO classification, these tumors are stratified as choroid plexus papilloma (CPP, WHO Grade I), atypical choroid plexus papilloma (aCPP, WHO Grade II), and choroid plexus carcinoma (CPC, WHO Grade III) [5]. aCPPs are intermediate lesions formally recognized in 2007, and their most important distinguishing features are increased mitotic activity and a higher probability of recurrence compared with grade I CPPs [5, 10, 19]. However, in cases of children under 3 years of age, this increased mitotic activity, which leads to the diagnosis of aCPP, is not necessarily associated with a higher rate of recurrence [14]. CPP usually presents as a focal tumor with no radiologic signs of dissemination. Therapy for this entity involves exclusively surgical resection of the lesion. On the other hand, CPC therapeutic approach includes surgery, chemotherapy, and radiation therapy if patient's age permits [19]. Rarely, CPP can present in the magnetic resonance imaging (MRI) with lesions compatible with disease dissemination. Appropriate therapy for this condition is more challenging and several aspects should be taken into account to tailor appropriate therapy. In this report, we present the case of an infant who was found to have a lateral ventricular CPP and significant diffuse leptomeningeal contrast enhancement at diagnosis, which spontaneously resolved 1 month after removal of the primary tumor.

Case description

A previously healthy 4-month-old male infant presented to the emergency department with a history of progressively increasing head circumference, vomiting, and abrupt development of setting-sun eyes. Pregnancy had been uneventful and third trimester ultrasound did not identify any fetal abnormality.

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Physical examination revealed macrocephaly with prominent anterior fontanel and suture diastasis. Brain MRI showed a 44 × 59 × 31 mm, intraventricular, polylobulated contrast-enhancing mass extending from the right lateral ventricle through the foramen of Monro into the third ventricle, with evidence of hydrocephalus (Fig. 1a). Diffuse abnormal contrast enhancement was present into the right Silvian fissure, basal cisterns, and cerebellar folia (Fig. 1b). MRI of the spine showed significant leptomeningeal enhancement along the spinal cord (Fig. 1c).

The patient was subsequently taken to the operating room (OR). An external ventricular drainage was placed; thereafter, a right frontal craniotomy with subsequent complete tumor removal was achieved through a transcortical approach. Intraoperatively, it was noted that the tumor was a highly vascularized, well-delineated cauliflower-like intraventricular mass arising from the ventricular choroid plexus. The blood supply from the choroidal vessels was posteroinferior to the bulk of the tumor. The mass was removed piecemeal after the vascular pedicle was identified and coagulated. Postoperative MRI obtained within 24-h post-surgery demonstrated a gross-total resection of the tumor, with no postoperative complications (Fig. 2a).

Histological examination was compatible with a CPT. Most of the tumor was constituted by monolayer cells with mild atypia but no pleomorphism. Some areas showed pseudostratification, but no solid tumor formation. Focal areas of necrosis were present. There were two mitoses per 10 high power fields (HPFs). The Ki-67 proliferation index was variable, with most of the tumor being < 1% but increasing up to 20% in areas with more cell density. No overexpression of the p53 protein was found by inmunohistochemistry. At our institution, this tumor was classified as an aCPP (WHO Grade II). We sent it to an external review and a biology evaluation of this tumor was performed by DNA methylation profile. It was compatible with CPT subclass pediatric A (cluster I) [15]. Somatic *TP53* mutation was ruled out. Because mitotic activity was not markedly increased and criteria for aCPP were not yet met, as external reviewers suggested, we finally diagnosed the tumor as a CPP (WHO Grade I).

The patient's symptoms improved significantly after surgery and no focal neurological deficits were observed. A CSF sample collected by lumbar puncture 2 weeks after surgery was negative for malignant cells. Based on the histologic diagnosis, the age of the patient, and prior similar cases published in the literature, we decided to observe with no further therapy. MRI performed 4 weeks after surgery did not demonstrate residual disease in the primary site and moreover showed almost complete resolution of the diffuse leptomeningeal gadolinium enhancement (Fig. 2b, c). Two months after the initial surgery, new signs of hydrocephalus developed. Therefore, the patient was taken back to the OR for a programmable ventricular-peritoneal shunt placement. One year after diagnosis, the patient remains asymptomatic with normal neurologic development. Follow-up MRI of both the brain and whole spine continues to demonstrate no recurrence or new areas of abnormal contrast enhancement.

Discussion

CPTs, particularly CPCs, have the capacity to spread along CSF into the leptomeningeal compartment and can reach any part of the subarachnoid space, both at diagnosis and relapse [2, 3, 7]. There are several reports in adult patients of distant metastases present either at the time of diagnosis or occurring months to years after initial resection [1]. In contrast, there are very few published cases that demonstrate similar findings in children. The incidence of metastases arising from CPP has been reported in 5% of patients at diagnosis [19]. Although in

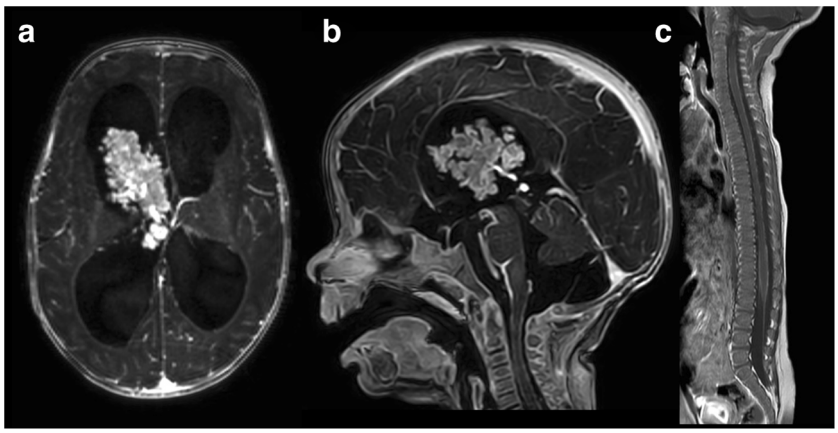

Fig. 1 Brain and spinal MRI at diagnosis. **a** Axial TFE with gadolinium shows a lobulated mass with strong enhancement in the lateral ventricle, with close relationship with the choroid plexus and extension into the III ventricle. Hydrocephalus. **b** Sagittal TFE with gadolinium. Diffuse leptomeningeal enhancement in the vermis and on the surface of the brainstem can be seen. **c** Sagittal FSE with gadolinium of the spine shows extension of the leptomeningeal enhancement on the whole spinal cord

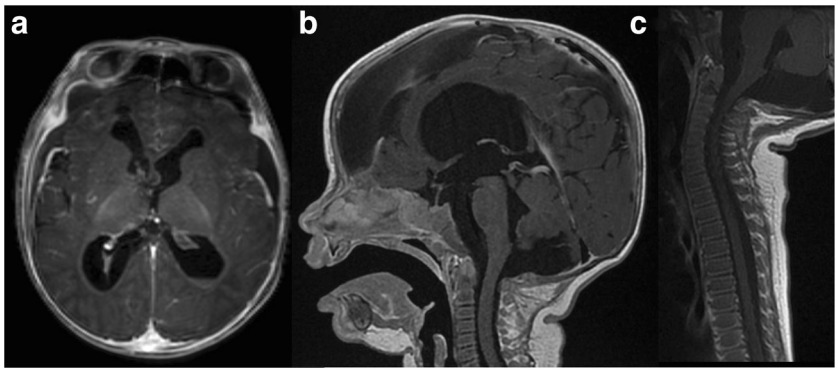

Fig. 2 Follow-up brain and spinal MRI, immediate postoperative (**a**) and at 1 month of follow-up (**b**, **c**). **a** Immediate postoperative MRI (24 h). Axial TFE with gadolinium shows removal of the mass with postsurgical changes in the foramen of Monro. **b** 1-month follow-up brain MRI. Sagittal TFE with gadolinium. There is almost complete resolution of the previous diffuse leptomeningeal enhancement. **c** 1-month follow-up spinal MRI. Sagittal FSE with gadolinium of the spine shows almost no leptomeningeal enhancement

some cases of disseminated disease, chemotherapy and radiation therapy (in patients older than 3–5 years of age) have been used with success, there are no standard treatment strategies for metastatic CPP.

Here we report a pediatric case of CPP presenting with diffuse leptomeningeal contrast enhancement at diagnosis, which spontaneously disappeared 4 weeks after resection of the primary tumor. There are a few cases described in adults [1] but, to our knowledge, only two similar pediatric cases have been previously reported in the literature. In these patients, leptomeningeal contrast enhancement vanished few months after surgery [11]. From neuropathologist's perspective, it is likely that otherwise benign plexus papillomas (either CPP or aCPP) with dissemination at disease presentation might have specific, and so far unknown, molecular alterations. Scala et al. [4, 18] proposed that this phenomenon could be the result of abnormal arachnoidal vessel permeability induced by hormonal factors secreted by the tumor, or of a real auto limited arachnoidal infiltration by a lining of neoplastic cells. However, we hypothesize another explanation for this observation. Due to high and abnormal vascularity identified in CPT, spontaneous tumoural bleedings may occur. In fact, there have been several reports of patients presenting with subarachnoid, subdural, and intraventricular or intraparenchymal hemorrhages from choroid plexus neoplasms [6, 8, 9]. One or multiple spontaneous tumoural bleed(s) could explain the images of leptomeningeal enhancement at baseline MRI and its resolution on subsequent MRI performed a few weeks later without any intervention. Subdural contrast enhancement on MRI after cranial surgery, especially after surgery to the posterior cranial fossa, has been widely reported [12, 17, 18]. The cause of this observation is still debated. Wiener et al. reported three patients who had temporary changes on MRI within 3 days after resection of posterior fossa tumors. The authors suggested that the presence of subarachnoid blood introduced by surgery caused meningeal irritation and enhancement on MRI [18]. As in the report of Wiener et al., our patient could have suffered a meningeal irritation due to a spontaneous tumoural bleed.

Finally, we want to emphasize the importance of complete brain and spine imaging at diagnosis in all pediatric brain tumors including benign CPPs [13, 20]. The histopathological/molecular diagnosis in CPT, the extent of resection, the presence or absence of images suspicious of metastases, and the presence of germline predisposition syndromes are the most important factors to determine the appropriate therapeutic scheme. DNA methylome analysis of these tumors could help to better stratify and tailor treatment of these patients, especially in most difficult cases due to their pathology grading diagnosis or clinical presentation [15, 21]. In this case, after extensive discussion among our team and the parents of the baby, we opted for a "wait and see" approach with a good outcome. In selected cases, this strategy should be considered in order to avoid unnecessary treatments and toxicities.

Patient consent

The patient guardians have consented to the submission of the case report for submission to the journal.

Compliance with ethical standards

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

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Comments

This is an interesting case report of a patient presenting with a choroid plexus tumor who also demonstrated diffuse leptomeningeal enhancement at presentation. The tumor was successfully resected. No adjuvant treatment was given. The leptomeningeal enhancement subsequently disappeared on follow-up MR imaging. The authors speculate that the enhancement may have been related to subclinical hemorrhage from the tumor. This case suggests that in the context of a low-grade choroid plexus, tumor diffuse leptomeningeal enhancement is not an indication for adjuvant therapy.

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