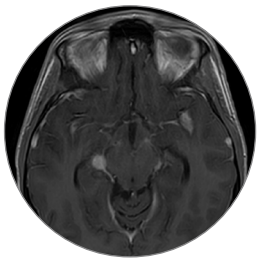

Radiological findings of a disseminated pilocytic astrocytoma in a Colombian teenager

Hallazgos radiológicos de un astrocitoma pilocítico diseminado, en una adolescente colombiana

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Summary

Pilocytic astrocytoma (PA) is the most common Central Nervous System (CNS) tumor in the pediatric population. It is regarded as a Circumscribed Glioma, due to its benign course. PA is a well-circumscribed, typically cystic lesion with a hyper-intense mural nodule. It shows a slow rate of growth and low cellularity. PA arises mostly in the cerebellum, optic pathway and hypothalamic/chiasmatic region. We report an unusual case of PA dissemination from the posterior fossa to the spinal canal in a 16 year old teenager.

Resumen

El astrocitoma pilocítico (AP) es el tumor más común del sistema nervioso central (SNC) en la población pediátrica. Es considerado un glioma circunscrito debido a su curso benigno. Aparece como una lesión bien determinada, típicamente quística, con un nódulo mural hiperintenso. Tiene una lenta tasa de crecimiento y baja celularidad. El AP se origina principalmente en el cerebelo, la vía óptica y la región hipotalámica/quiasmática. Se presenta un caso inusual de diseminación de un AP de fosa posterior al canal espinal en una adolescente de 16 años.

Introduction

Pilocytic astrocytoma (PA) is a grade I tumor, according to the World Health Organization (WHO) classification of central nervous system (CNS) tumors, which means that it is relatively benign and has a 10-year survival of more than 90% (1). It is the most common pediatric brain and cerebellar tumor (2-4). It is characterized by painless growth and can occur at any age, but it is most common in the first two decades of life. It accounts for 17.6% of primary brain tumors in childhood and 33.2% of gliomas in the first 14 years of life. AP has no significant gender predilection and usually has an excellent outcome (4, 5).

This tumor can occur anywhere in the neuraxis, but most lesions arise near the midline. In children it appears especially in the cerebellum, the v a ptic, the hypothalamic/chiasmatic region and in the posterior fossa, but it can also be found in the ventricles, cerebral hemispheres and thymus (2, 4-6). The location in the spinal cord is less frequent and in this site they present with nonspecific symptoms (4). These neoplasms are slow-growing tumors, with low cellularity, low mitotic activity, and rarely metastasize (6). The peak behavior of AP cannot be predicted, but high mitotic activity in 10 high power fields has been associated with a more aggressive outcome. Rarely, a spiky AP may show dissemination in the neuraxis even without alarming histology. However, progression through it does not necessarily indicate a poor prognosis; in fact, these deposits can be completely asymptomatic and are usually associated with long-term survival (4).

These tumors are highly vascularized and technically well-circumscribed solid-chiastic lesions. Most patients can be cured by complete surgical resection, except those in whom this procedure is not feasible (6).

Clinical features

There is a wide variety of clinical presentations of AP depending on the location of the tumor and it generally has a prolonged and insidious clinical course (7). Symptoms generated by increased intracranial pressure are a common complaint in patients affected by this type of tumor. They may also present with focal neurological deficits. Headache, macrocephaly and endocrinopathy are common. Patients with tumors in the visual field, suffer visual loss or field defect and proptosis. Seizures are unusual

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because the cerebral cortex is rarely affected. AP in the cerebellum causes headache, nausea, vomiting, ataxia, cranial nerve deficits, clumsiness, gait disturbance, blurred vision, diplopia and neck pain (1, 4, 7). The location in the brainstem is predominantly dorsal and exophytic in the pontocerebellar angle, and usually causes signs of brainstem dysfunction or hydrocephalus (4).

Imaging

On computed tomography (CT), most PA are well demarcated, with smooth margins and an oval or round shape (6). This tumor is very heterogeneous and one can observe areas of intensely enhancing soft tissue density combined with chemostatic areas. Although they enhance intensely, even with a ring-shaped pattern, a finding most commonly found in highly malignant astrocytomas, it is not a high-grade neoplasm (2, 4). It may show calcifications resembling speckles (6). Hemorrhage or multiple cystic masses are not typical imaging characteristics of these neoplasms (4).

On magnetic resonance imaging (MRI), the solid component of PA can be homogeneous or heterogeneous. It may be seen with medium or low signal on T1-weighted images or with high signal on T2/FLAIR-weighted images, compared to gray matter. The surrounding vasogenic edema is much less extensive than in higher grade glial neoplasms, due to the low mitotic activity of the tumor (6, 7). Between 50% and 70% of the cases show a chiasmatic mass with a mural nodule that enhances with contrast medium; and the other 30% show a chiasmatic mass with a non-enhancing central zone, or a predominantly solid mass with a minimal chiasmatic zone. It is important to clarify that the cyst wall may or may not show enhancement and the relief of the cyst wall may or may not indicate the presence of the tumor (4, 7).

Non necrotic solid tumors are less common and represent approximately 10% of the cases (7).

The appearance of AP in the visual acuity is different, depending on whether the patient has neurofibromatosis type 1 (NF1) or not. It usually appears as a fusiform or tortuous enlargement of the ptic nerve. Patients with NF1 and AP usually have a nonchiasmatic presentation, mainly affecting the ptic nerve, without dissemination along the ptic vein. In patients with AP in the v a ptica, not associated with NF1, the cyst-like manifestation predominates, mainly involving the ptic chiasm and spreading extraptically (4).

Treatment and prognosis

Because of the rare metastasis rate of AP, there is currently no standard treatment and the results of long-term therapies are not fully known. This tumor usually responds well to treatment with excision, local radiotherapy, brachytherapy and/or chemotherapy for inoperable lesions (3, 5). When it has a favorable localization and the standard treatment, total surgical resection, is performed, survival rates approach 80-100%. However, the prognosis is variable when it is located in critical sites such as the ptic chiasm, the hypothalamic region and the brainstem (2, 5, 8).

Radiotherapy may delay tumor progression, if given at the time of subtotal resection or at the onset of progressive disease; but it may cause deleterious effects on the developing neuraxis, such as anaplastic transformation of the tumor. In cases of recurrent, disseminated, progressive or unresectable recurrent AP, chemotherapy can be used to avoid or delay radiotherapy in younger patients, with good long-term survival. However, these tumors usually do not respond to treatment with carboplatin and vincristine. Therefore, an alternative treatment using temozolomide should be employed (5, 8).

It has been hypothesized that malignant transformation, cellular anaplasia, surgical manipulation or natural history contribute to tumor dissemination. The occurrence of metastatic disease is a rare event, estimated to occur in less than 5-10% of cases (6, 8). Low-grade astrocytomas in the vicinity of cerebrospinal fluid (CSF) ventricles or cisterns are more likely to spread than tumors in other regions (8).

AP, in rare cases, may have widespread dissemination, and such metastatic dissemination may occur without associated increased mortality (2).

Case report

Female patient, 16 years old, resident of a rural area of Colombia. She consulted at the age of 14 years for intense headache of 4 months duration, associated with dizziness, blurred vision and multiple emetic episodes. On physical examination, the patient had bitemporal campimetric visual impairment and impaired coordination of the lower extremities. On CT of the brain there was an infratentorial mass with obstructive hydrocephalus. Brain MRI revealed a lesion with apparent origin in the fourth ventricle and extension towards the right pontocerebellar angle. (Figure 1). At 7 days, a ventriculostomy of the third ventricle was performed with improvement of the hydrocephalus both clinically and radiological findings.

After one month, the patient underwent surgery to remove the lesion. A semi-solid tumor was found infiltrating the right cerebellar hemisphere, the lower cranial nerves and complex VII-VIII, as well as infiltration of the left cerebellar hemisphere. The pathology corresponded to grade I pilocytic astrocytoma, with positive immunohistochemical test for PFGA, synatopophysin, positive S-100, low KI-67.

Two years later, the patient consulted again for weight loss, bitemporal headache, nausea, multiple emetic episodes and weakness in the left leg. However, the neurological examination was normal. A new MRI with contrast medium was performed of the entire neuroaxis, which showed pachymeningeal enhancement and irregularity of the cisterns of the base, infiltration of the left cerebellopontine angle with extension to the internal auditory canal and supratentorial cisterns such as the one surrounding the middle cerebral artery bilaterally (Figures 2, 3 and 4). In addition, leptomeningeal dissemination was found surrounding the medullary cord and metastasis in drip towards the distal end of the thecal sac (Figure 5).

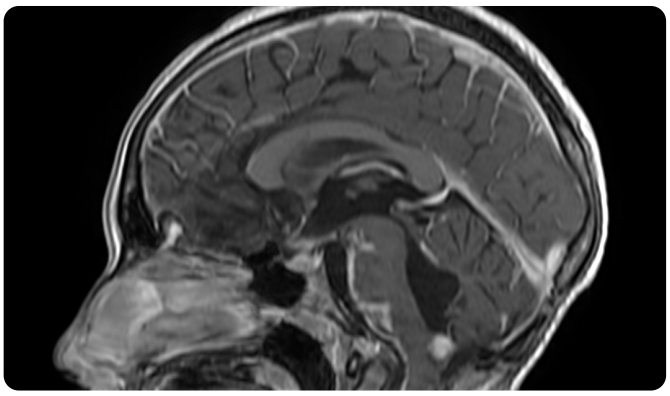

Figure 1. MRI sagittal sequence with T1 information and contrast medium in the medial line: diffuse enhancement of the perimesencephalic and prepontine cisterns and along the bulbar-medullary junction. A contrast-enhancing nodule is seen in the obex.

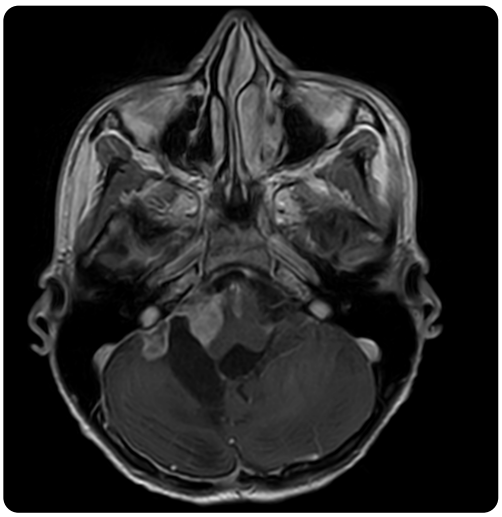

Figure 2. Axial sequence with T1-weighted information after contrast medium administration in posterior fossa: extraaxial enhancement, predominantly affecting the right pontocerebellar angle and pachymeningeal relapse secondary to tumor infiltration. Postoperative changes in the medial aspect of the cerebellar hemisphere of the same side.

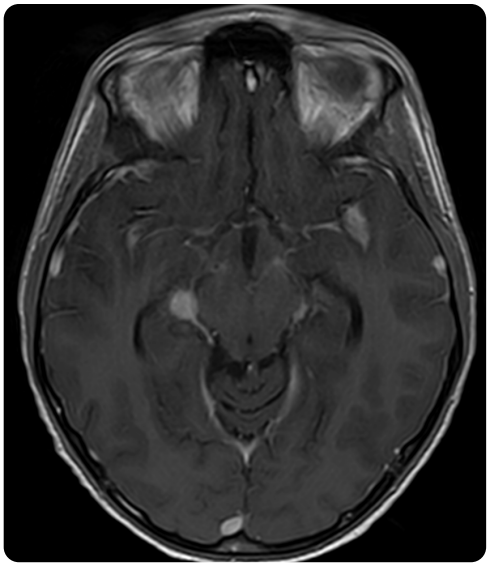

Figure 3. Axial sequence with T1 information and contrast medium: in the depth of the left insula and in the Sylvian fissure: nodular and extraaxial enhancement, secondary to tumor involvement.

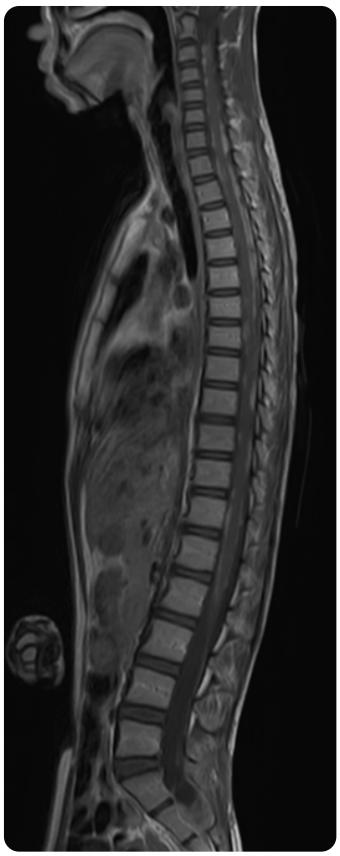

Figure 4. MRI sagittal spine sequence with T1 information with contrast medium: leptomeningeal enhancement surrounding the spinal cord in a circumferential manner, with nodular shape, which involves the cervical, dorsal and lumbar segments.

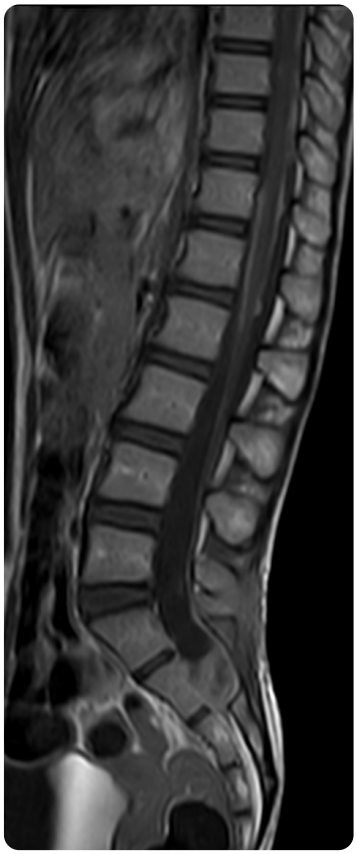

Figure 5. Sagittal lumbar spine MRI with T1 information and with contrast medium: enhancement with contrast medium as “drop metastasis” and towards the distal end of the thecal sac, due to diffuse tumor dissemination. There is no involvement of the vertebral bodies.

Surgery was performed again to characterize the lesion in SI-S2, with the finding of a semisolid mass in the sacral roots. Partial resection was performed and the pathology showed cells of glial aspect, arranged in lines, with eosinophilic granular bodies, with rounded nuclei and clear cytoplasm, without mitotic activity or proliferation of vascular endothelium or necrosis, so it was considered a low-grade pilocytic astrocytoma.

Given the complexity of the case, the patient presented to the staff of a hospital in the United States, where it was concluded that it was a disseminated oligodendroglial-like leptomeningeal tumor of infancy (DOLT, disseminated oligodendroglial-like leptomeningeal tumor), and she was started on palliative treatment for low-grade tumors.

She was started on vincristine/carboplatin in August 2017, received peak chemotherapy in November 2017, and began maintenance therapy. She was subsequently referred to neurology for lower limb weakness and hyperreflexia, with preserved sensation and muscle strength 3-4/5, so they considered it was due to spinal cord tumor involvement, rather than vincristine toxicity. Another MRI was performed in December 2017, which showed extensive leptomeningeal dissemination with a nodular mass-like lesion adjacent to the obex and circumferential compromise of the medulla, as well as a pseudonodular lesion towards the distal aspect of the thecal sac at S2.

Discussion

Although the appearance of metastasis is infrequent in PA (6), after a clinical, pathological and imaging correlation, the case presented is considered a leptomeningeal dissemination of this tumor.

The patient was in the first two decades of life, the usual age of presentation of these tumors. In addition, the location of the tumor in this case is one of the most frequent in PA (2).

In subsequent imaging studies it was observed that initially complete resection of the tumor was not achieved, due to its location, which is one of the objectives in the treatment of these tumors, in order to achieve an excellent prognosis. If an incomplete resection is performed, it is possible that the tumor grows again and even spreads through the ventricular system and the cisterns (6). Although the pathological findings did not indicate the pilomyxoid variant, the patient exhibited visual symptoms, suggesting involvement of the chiasm, the site of localization of this variant (1). It is important to mention that the patient's tumor had an apparent origin in the fourth ventricle, a site where low-grade astrocytomas are more likely to spread (8).

Tumors located in the hypothalamic/chiasmatic region in which complete surgical resection is not performed have a less favorable progression-free survival and overall survival. In addition, PAs showing leptomeningeal dissemination have worse outcomes (1).

After surgery, PA can be treated with radiotherapy, especially in the face of incomplete resection. Chemotherapy is administered when the tumor progresses, especially if surgery could not be performed (1). The patient in this case did not receive radiotherapy after surgery, because it was considered to be a DOLT tumor.

In addition, she was treated with carboplatin and vincristine, without response. It is now known that APs do not respond to these drugs (8). Pathologically, the most frequent differential diagnoses of AP include relatively circumscribed, mostly low-grade tumors: ganglioglioma (GG), disembryoplastic neuroepithelial tumor (DNET), rosette-forming glioneuronal tumor of the fourth ventricle (RFGNT) and a grade II tumor according to the WHO classification: pleomorphic xanthoastrocytoma (PXA) (1).

Likewise, AP may mimic DNET with its typical oligodendroglial-like appearance, but the presence of glomeruloid vessels and the enhanced imaging appearance point to the correct diagnosis. AP may also have a diffuse, featureless appearance, showing a predominantly oligodendroglial or astrocytic appearance, without its typical biphasic pattern. In addition, it may undergo acute hemorrhage, show necrosis and/or microvascular proliferation. These findings are more challenging in the supratentorial compartment, especially in adult patients, in whom they would not easily induce consideration of AP but rather diffuse glioma. Additionally, AP can closely mimic oligodendroglioma from which it can be morphologically distinguished on the basis of its solid growth pattern and the presence of bipolar cells with Rosenthal fibers and/or eosinophilic granular bodies (1).

Cross-sectional images often demonstrate the classic appearance of a chemostatic mass with an enhancing mural nodule (2, 7). Surrounding vasogenic edema rarely appears, and this feature provides a valuable clue to the correct diagnosis. Accurate interpretation of imaging studies plays an essential role in directing the management of these tumors, particularly when they arise in the clinical pathology of patients with NF1 (2). APs may have histologic and imaging features of higher grade neoplasms, such as macrovascular proliferation, infiltration of surrounding tissues and structures, intratumoral hemorrhage, intense enhancement of postcontrast images, and leptomeningeal spread. In addition, it is important to know the multiple clinical and radiological manifestations of this tumor, since the diagnosis of PA is often initially suggested on the basis of an imaging study (7). In imaging, the differential diagnosis in children is ependymoma and medulloblastoma. Ependymomas have more calcifications (50%) and extend laterally to the cerebellopontine angles, while medulloblastomas tend to spread through the cerebrospinal fluid spaces into the brain and spine (7).

Previously reported cases of leptomeningeal dissemination took a minimum of 3 years and a maximum of 6 years from presentation for dissemination to occur; however, two cases were documented in 2005 in which dissemination occurred in less than 1 year, indicating aggressive disease, with pathologic findings of glomeruloid microvascular proliferation and high mitosis rates. Another study in 2012 reported a median time to identification of disseminated disease of 12 months after initial diagnosis (5, 8). In the patient in this case, dissemination occurred within 2 years and pathologic findings showed no signs suggestive of aggressiveness.

In documented cases of disseminated AP disease, the most common demographic and clinical factors were subtotal resection of the primary tumor, young age and extensive dissemination at presentation (5).

A case was reported in which, although dissemination, and especially metastasis of the PA at initial presentation is rare, a complete evaluation of the neuraxis at diagnosis would have been useful. It is also true that most patients will have stable disease after initial treatment, unlike the clinical case presented here (3). Finally, the importance of the routine use of MRI with gadolinium to identify more cases of disseminated AP disease is emphasized, due to the fact that because it is an infrequent presentation, its patterns of dissemination, prognosis and treatment are poorly defined (5).

References

1. Collins VP, Jones DTW, Giannini C. Pilocytic astrocytoma: pathology, molecular mechanisms and markers. Acta Neuropathol [Internet]. 2015 Jun 20 [citado: 2018 sep. 5];129(6):775-88. Disponible en: http://www.ncbi.nlm.nih.gov/pubmed/25792358
2. Correlation P. From the Archives of the AFIP Pilocytic Astrocytoma. Radiologic-OBJECTIVES. 2004;1693-708.
3. Yecies D, Fisher PG, Cheshier S, Edwards M, Grant G. Long-term outcomes of primarily metastatic juvenile pilocytic astrocytoma in children. J Neurosurg pediatr. 2018;21(1):49-53. doi: 10.3171/2017.7.PEDS17168 .
4. Louis DN, Ohgaki H, Wiestier OD, Cavenee WK, Ellison DW, Figarella-branger D, et al. The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary. Acta Neuropathol. 2016;131(6):803-20. doi: 10.1007/s00401-016-1545-1 .
5. Bian SX, McAleer MF, Vats TS, Mahajan A, Grosshans DR. Pilocytic astrocytoma with leptomeningeal dissemination. Child's Nerv Syst [Internet]. 2013 [citado: 2018 sep. 5];29(3):441-50. Disponible en: http://www.ncbi.nlm.nih.gov/pubmed/23207974
6. Docampo J, González N, Muñoz A, Bruno C, Morales C. Astrocitoma pilocítico. Formas de presentación. Rev Argentina Radiol. 2014;78(2):68-81.
7. Chourmouzi D, Papadopoulou E, Konstantinidis M, et al. Manifestations of pilocytic astrocytoma: a pictorial review. Insights Imaging. 2014;5(3):387-402. doi: 10.1007/s13244-014-0328-2
8. Aryan HE, Meltzer HS, Lu DC, Ozgur BM, Levy ML, Bruce DA. Management of pilocytic astrocytoma with diffuse leptomeningeal spread: two cases and review of the literature. Child's Nerv Syst [Internet]. 2005 [citado: 2018 sep 5];21(6):477-81. Disponible en: http://www.ncbi.nlm.nih.gov/pubmed/15378329

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