CASE REPORT

Pediatric cerebellar hemangioblastoma as a manifestation of von Hippel-Lindau disease: a clinic case

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ABSTRACT

von Hippel-Lindau disease is a familial neoplastic syndrome caused by genetic mutations in the vHL tumor suppressor gene located on chromosome 3 (3p25-3p26). It is an autosomal dominant and multiorgan disorder characterized by the formation of benign and malignant tumors and cysts in various systems. The most common tumors in this disease are central nervous system haemangioblastomas, which affect up to 80% of patients and can cause significant morbidity and mortality due to mass effects on nearby structures. This study is a case report of a 12-year-old patient who was admitted for endocranial hypertension, and magnetic resonance imaging revealed a tumor in the posterior fossa. The patient underwent surgical treatment, and pathological examination revealed the tumor to be a haemangioblastoma. This case illustrates an early presentation of von Hippel-Lindau disease. This rare disease may be related to a phenomenon known as genetic anticipation.

Keywords: von Hippel-Lindau disease; Hemangioblastoma (Source: MeSH)

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Hemangioblastoma cerebeloso pediátrico como manifestación de la enfermedad de von Hippel-Lindau: un caso clínico

RESUMEN

La enfermedad de von Hippel-Lindau es un síndrome neoplásico familiar autosómico dominante, multiorgánico, que es causado por mutaciones genéticas del gen supresor de tumores *vHL* ubicado en el brazo corto del cromosoma 3 (3p25-3p26). Se caracteriza por la formación de tumores benignos y malignos, así como quistes en varios sistemas. Los hemangioblastomas del sistema nervioso central son los tumores más comunes en la enfermedad de la enfermedad de von Hippel-Lindau y afectan al 60% a 80% de todos los pacientes. En su gran mayoría los tumores son benignos, pero son una causa importante de morbilidad y mortalidad debido al efecto de masa en las estructuras cercanas. Nuestro estudio presenta un caso clínico de un paciente de 12 años, quien fue admitido por hipertensión endocraneana. La resonancia magnética reveló un tumor en la fosa posterior del cerebro, llevando a un tratamiento quirúrgico. La evaluación anatomopatológica identificó el tumor como un hemangioblastoma. Este caso ilustra una presentación temprana de la enfermedad de von Hippel-Lindau, que es infrecuente y podría estar relacionada con un fenómeno conocido como anticipación genética.hemangioblastoma.

Palabras clave: Enfermedad de von Hippel-Lindau; Hemangioblastoma (Fuente: DeCS)

INTRODUCTION

von Hippel-Lindau disease (vHL), named after the initial descriptions by Eugene von Hippel in 1904 and Arvid Lindau in 1927, is based on observations of retinal and cerebellar hemangioblastomas (1, 2). This autosomal dominant, multiorgan, familial neoplastic syndrome is caused by mutations in the tumor suppressor gene *vHL*, located on the short arm of chromosome 3 (3p25-26) (3-5). Dysfunction of this pathway leads to sustained

expression of pro-tumorigenic molecules such as vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), and erythropoietin (3-5).

Although there are no population estimates of vHL disease in Latin America or Peru, the closest population estimate is in Denmark, where the prevalence of vHL was estimated to be 1 in 46,900 persons, and the incidence of births with vHL was 1 in 27,300 live births (6). This disease is characterized by the presence of a range of tumors and cysts, such as retinal, cerebellar, and medullary hemangioblastoma, renal carcinoma, renal and pancreatic cysts, pheochromocytoma, endolymphatic sac tumors, cysts in the epididymis and uterine broad ligament (1, 7-9). In addition, hemangioblastomas involving the brain, spinal cord, and retina, along with clear cell renal cell carcinoma (RCC), pheochromocytomas, paragangliomas, and pancreatic neuroendocrine tumors (PNETs), are among the tumors most commonly associated with vHL (1, 7-9).

Hemangioblastomas, although generally benign, occur spontaneously in 75-80% of cases between the ages of 30 and 60 (1, 5, 10). The remaining cases are associated with the disease. The areas most commonly affected by these tumors include the cerebellum, with an incidence ranging from 16% to 69%, the brainstem (5% to 22%), the spinal cord (13% to 53%), the cauda equina (11%), and the supratentorial region (1% to 7%) (1, 5, 10). The morbidity and mortality of these patients are mainly due to the mass effect produced by the cystic lesion, edema, and its location. These tumors usually have multiple periods of tumor growth separated by periods of growth arrest, and many of the untreated tumors may remain the same size for several years (5, 10, 11).

To detect central nervous system hemangioblastomas, contrast-enhanced MRI is the radiologic examination of choice, in which contrast-enhancing lesions are seen on T1-weighted images. Macroscopically, these tumors appear as red vascular masses within a thin capsule (1, 5, 12, 13). In addition, surgical resection of hemangioblastomas in patients with vHL is generally curative and offers durable results. Neurological symptoms, rapid tumor growth, or a critical tumor and/or cyst size are key indications for surgery (1, 12, 14, 15).

The management of tumors associated with vHL disease requires a multidisciplinary approach, and advances in genetic testing have led to early diagnosis of the syndrome. The present study aims to present a clinical case of von Hippel-Lindau disease.

CLINICAL CASE

A 12-year-old male patient, the son of a mother diagnosed with vHL disease, presented to the hospital after 20 days of symptoms consisting of headache, nausea, vomiting, and loss of balance. At the hospital in her region, a non-contrast brain tomographic study was performed, showing a cystic intracerebellar expansive process, collapsing the IV ventricle and generating obstructive hydrocephalus. For this reason, a peritoneal ventricular shunt was performed.

Subsequently, he was referred to a specialized and more complex institution to treat the cerebellar lesion. On arrival, the neurological examination showed the patient awake and alert, with a functioning ventriculoperitoneal shunt, gait instability, and the ability to mobilize his limbs. A brain MRI with contrast showed a cystic lesion in the right cerebellar hemisphere, extending beyond the midline, with a contrast-enhancing nodule in its wall (see Figure 1).

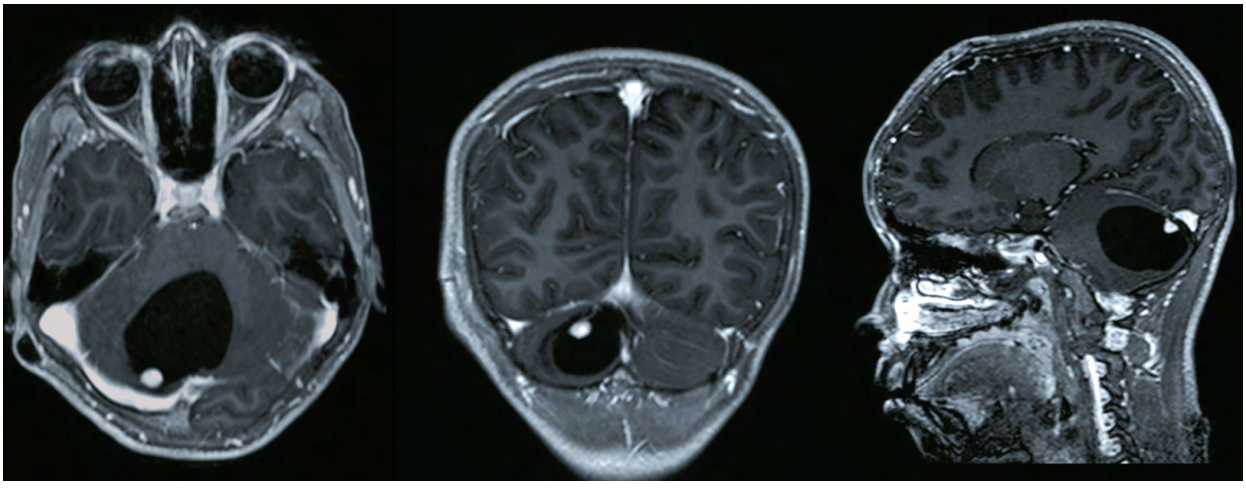

Figure 1. Contrast-enhanced T1-weighted magnetic resonance image in axial, coronal and sagittal views.

Note: Cystic lesion in the right cerebellar hemisphere slightly crossing the midline with a contrast-enhancing mural nodule is evidenced. Also, the reservoir of the peritoneal ventricular shunt system can be visualized, which is functional.

The first surgery performed was a ventriculoperitoneal shunt for surgical treatment of obstructive hydrocephalus. Subsequently, surgical treatment for the tumor lesion was performed using a right suboccipital craniotomy and excision of the lesion via transulcoscopy. Intraoperatively and macroscopically, a red nodular lesion with a thin, difficult-to-resect transparent cystic capsule was evidenced. Therefore, tumor resection was performed, plane closure was performed, and the patient was subsequently transferred to the intensive care unit. The histological sections of the tumor can be seen in Figure 2..

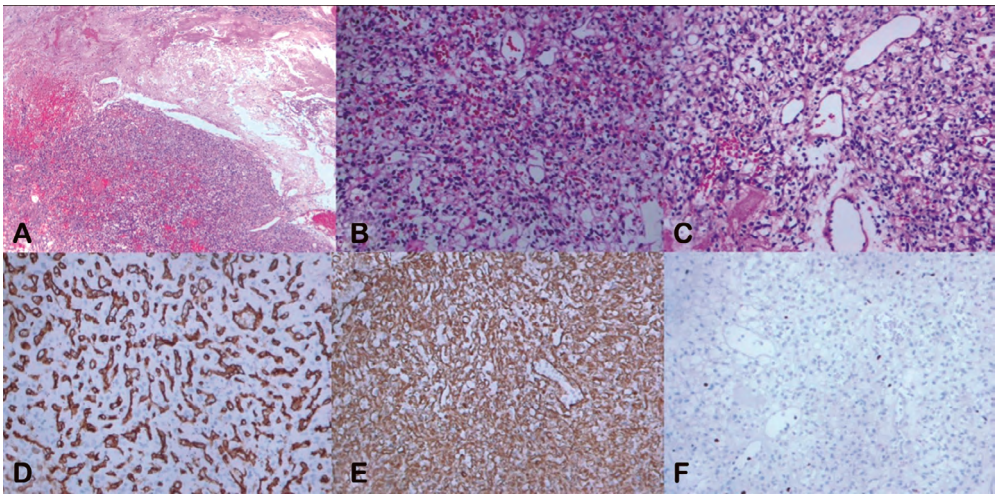

Figure 2. Histologic sections of the tumor.

Note: **A**. Tumor tissue is well demarcated by the adjacent cerebellar parenchyma in the upper right corner (Hematoxylin and eosin, 10X). **B**. The neoplasm shows vascular hyperplasia, mainly capillaries with hypertrophic endothelial cells (Hematoxylin and eosin, 20X). **C**. Tumor tissue, with abundant stromal cells showing clear cytoplasm with mild nuclear pleomorphism (hematoxylin and eosin, 40X). **D**. Immunohistochemical staining for CD34, highlighting the abundant vasculature within a hemangioblastoma (40X). **E**. Diffuse immunostaining for Vimentin, characteristic of hemangioblastoma (20X). F. Cell proliferation is less than 2%, as shown by immunohistochemical staining for Ki-67 (40X).

The anatomopathological diagnosis was Hemangioblastoma, capillary variant grade I, according to the World Health Organization (WHO) classification. The patient was discharged on the tenth postoperative day (see Figure 3), awake, alert, with no signs of infection in the operative wounds, and with mobility in his extremities. The Karnofsky Scale at discharge was 90. There was no worsening of the clinical picture after hemangioblastoma surgery.

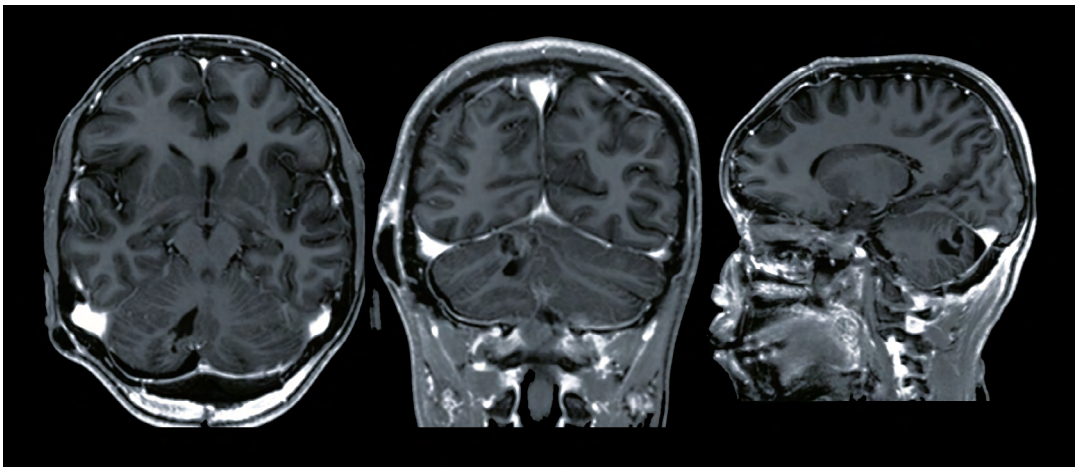

Figure 3. Contrast-enhanced magnetic resonance image 8 days after surgery, in three views: axial, coronal, and sagittal.

Note: There is evidence of resection of the contrast-enhancing mural nodular lesion, with the collapse of the cystic content without evidence of hydrocephalus.

DISCUSSION

Genetic anticipation is a genetic phenomenon that explains how certain hereditary diseases, such as vHL disease, can manifest at an earlier age and with greater severity in successive generations than in previous generations (4). This mechanism could cause the disease's earlier and possibly more severe presentation in the clinical case presented. Genetic anticipation suggests that the mutations responsible for the disease may undergo modifications across generations, affecting the expression and function of vHL disease-related genes (4).

On the other hand, in a study of 181 patients undergoing surgical resection of hemangioblastomas, total resection was achieved in the majority, while six patients required subtotal resection due to tumor adhesion to adjacent tissues or its large size (16). During the mean follow-up of 30.65 ±16.68 months, 146 had a favorable outcome with improved preoperative symptoms. In addition, twelve patients with sporadic hemangioblastomas had tumor recurrence, and ten patients with VHL-associated hemangioblastomas experienced distant progression. Six patients died perioperatively within 30 days (16).

Patients with vHL can present with a variety of clinical manifestations, including central nervous system hemangioblastomas, pheochromocytomas, clear cell renal cell carcinomas, renal and pancreatic cysts, pancreatic neuroendocrine tumors, and endolymphatic sac tumors (7)(10)(11)(12). Pheochromocytomas may be the only or initial manifestation in pediatric patients with vHL disease, with late manifestation in other organs (17).

The vHL disease is a pathology that deserves multidisciplinary treatment and management. The main complaints are due to the mass effect of hemangioblastomas, the most frequent localization at the cerebellar level. MRI with contrast is the method of choice for diagnosis, and surgical treatment with total resection is currently a safe and curative method with long-lasting effects.

Conclusion

This case highlights the importance of considering vHL in pediatric patients with hemangioblastomas, especially with relevant family history, and underlines the efficacy of surgical treatment in these cases. In addition, our study shows the need for a multidisciplinary approach in managing vHL, given its multiorgan nature and associated clinical manifestations.

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