WHAT IS YOUR DIAGNOSIS

IMAGING CLINICAL CASE

CASO CLÍNICO IMAGIOLÓGICO

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A 16-year-old, previously healthy female with unremarkable family history (including regarding tumoral pathology) was referred to the Ophthalmology Emergency Room due to sudden unilateral loss of left vision and was diagnosed with vitreous haemorrhage and hemangioblastoma of the retina in the upper temporal quadrant. No other signs or symptoms were evident. Vision was recovered after laser photocoagulation therapy.

During follow-up in the Ophthalmology consultation, the girl underwent brain and pelvic magnetic resonance imaging (MRI) to detect other lesions.

Brain MRI (Figure 1) showed several cerebellar hemangioblastomas spread through both cerebellar hemispheres (the largest with 7-mm diameter located in the left posterior inferior medial region) associated with left ocular wall thickening and a lesion in the right supraclavicular region, probably corresponding to parangangioma. In pelvic MRI (Figure 2), two cortical cysts (with 19-mm and 9-mm diameter) were detected in the right kidney, as well as a well-circumscribed, nodular, 9-mm lesion with low signal intensity in all sequences and several non-specific micronodules of suspected neoplastic nature in the left kidney.

Figure 1 - Brain MRI. T1-weighted, contrast-enhanced fat supressed showing cerebellar hemangioblastomas, the largest with 7-mm diameter and located in the left posterior inferior medial region

Figure 2 - Pelvic MRI. T1-weighted, contrast-enhanced fat supressed showing a 19-mm cortical cyst in the right kidney
After Pediatric Nephrology/Urology consultation, the study was complemented with a reno-pelvic computed tomography (CT) scan that revealed two cortical cysts in the right kidney and several solid nodular images in the left kidney (Figure 3). Plasma as well as urinary metanephrines and cortisol laboratory results were unaltered.

Based on imaging results, decision was made to perform a partial left nephrectomy to remove the largest left kidney lesion. Histological characterization revealed papillary renal cell carcinoma with clear-cell predominance.

The patient is currently also followed at the Neurosurgery consultation, remaining in surveillance and multidisciplinary follow-up including genetic evaluation.

**DISCUSSION**

Von Hippel-Lindau (VHL) disease is a rare, inherited, autosomal dominant syndrome of multiple neoplasms caused by germline mutations in the VHL tumor-suppressor gene. VHL diagnosis should be suspected when an individual with family history of VHL presents a disease-characteristic lesion, such as central nervous system (CNS) or retinal hemangioblastoma, renal cell carcinoma, pheochromocytoma, pancreatic cysts or endocrine tumors, or epididymal cystadenoma. In absence of family history of VHL, clinical diagnosis requires evidence of two tumors: two CNS and/or retinal hemangioblastomas or a CNS or retinal hemangioblastoma associated with renal cell carcinoma, pheochromocytoma, pancreatic cysts or endocrine tumor, or cystadenoma of the epididymis.

Imaging plays a role in VHL disease, through identification of abnormalities, follow-up, and screening of asymptomatic mutated gene carriers.

The disease can be categorized in types 1 and 2. Type 1 is characterized by retinal angiomatis, CNS hemangioblastomas, renal cell carcinomas, pancreatic cysts, and neuroendocrine tumors, whereas type 2 is characterized by pheochromocytomas, retinal angiomas, and CNS hemangioblastomas.

Identification of a germline mutation on VHL gene enables molecular diagnosis of the condition.

Patients are predisposed to the development of cysts and hypervascular neoplasms, the most common being hemangioblastomas of the CNS and retina, cysts and renal cell carcinomas, and pheochromocytomas.

This case highlights the importance of thoroughly analysing key findings in the first observation, establishing early VHL diagnosis and starting immediate treatment. Retinal angiomas or hamartomas should immediately prompt additional workup to exclude VHL disease.

In this patient, VHL molecular diagnosis was confirmed by detection of the c.326 C> G heterozygous variant in VHL gene.

During the course of disease, individuals typically manifest synchronous or metachronous neoplasms, located or not in the same organ. Although excision of hypervascular neoplasms carries hemorrhagic risks, lesion progression can potentially elicit complications that compromise patient’s quality of life and survival. Therapeutic decision is not obvious and relies on the balance between lesion progression risk and treatment.

The uncertain tumor location and onset in VHL disease warrants lifetime follow-up. Early lesion detection in patients and affected relatives based on genetic testing allows a more conservative therapeutic approach. Additionally, mutation identification enables to predict associated phenotype and adjust the follow-up protocol accordingly.

**DIAGNOSIS**

Von Hippel-Lindau disease

**ABSTRACT**

Here in is reported the case of a 16-year-old female diagnosed with vitreous haemorrhage and hemangioblastoma of the retina, referred to the Emergency Department due to sudden vision loss. Brain and pelvic magnetic resonance imaging showed cerebellar hemangioblastomas and renal nodular lesions of suspicious nature. The patient was submitted to partial left nephrectomy and histological examination revealed papillary renal cell carcinoma with clear-cell predominance. Clinical diagnosis of Von Hippel-Lindau (VHL) disease was confirmed by genetic study.
VHL disease is a hereditary, autosomal dominant syndrome of multiple neoplasms caused by germline mutations in VHL tumor-suppressor gene. Patients are predisposed to development of cysts and hypervascular neoplasms, the most common being hemangioblastomas of the central nervous system (CNS) and retina, cysts and renal cell carcinomas, and pheochromocytomas. VHL diagnosis should be suspected if an individual with family history of VHL presents with a characteristic disease lesion or, in absence of family history of VHL, with two CNS and/or retinal hemangioblastomas or a CNS/retinal hemangioblastoma associated with renal cell carcinoma, pheochromocytoma, pancreatic cysts or endocrine tumor, or epididymal cystadenoma. In VHL disease, imaging plays a key role in detection of abnormalities, follow-up, and screening of asymptomatic mutated gene carriers.

Keywords: Hemangioblastoma of the central nervous system; renal cell carcinoma hemovitreous; Von Hippel-Lindau

REFERENCES

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