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Short communication

Difficulties in the management of retinal capillary haemangiomas associated with von Hippel Lindau disease☆

M. Pastor-Montoro, N. Hurtado-Montalbán, J.A. Martínez-Morales, M.P. Villegas-Pérez*

Servicio de Oftalmología, Hospital General Universitario Reina Sofía, Murcia, Spain

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ABSTRACT

Clinical case: A 29-year-old female with bilateral retinal capillary haemangiomas (RCH). A genetic analysis was carried out due to the suspicion of von Hippel–Lindau (VHL) disease, with negative results on 2 occasions. There was progression of the RCH in the left eye, leading to a macular epiretinal membrane. The patient was treated with laser, intravitreal ranibizumab, and vitrectomy. Finally, a third genetic test detected a *de novo* mutation in the VHL gene, and led to the genetic diagnosis.
Discussion: VHL syndrome causes a complex ocular disease with a difficult diagnosis that requires early treatment of the RCH in order to modify its visual prognosis.

Dificultades en el manejo de los hemangiomas capilares retinianos asociados a enfermedad de von Hippel-Lindau

Palabras clave:
Hemangiomas capilares retinianos
Enfermedad de von Hippel Lindau
Estudio genético
Fotocoagulación láser

RESUMEN

Caso clínico: Mujer de 29 años con hemangiomas capilares retinianos (HCR) bilaterales. Ante la sospecha clínica de enfermedad de von Hippel Lindau (VHL), se realizan estudios genéticos que son negativos en 2 ocasiones. Se produce progresión de los HCR del ojo izquierdo, con aparición de membrana epimacular, que son tratados con láser, ranibizumab intravítreo y vitrectomía. Finalmente, el tercer estudio genético detecta una mutación *de novo* en el gen VHL que permite confirmar el diagnóstico.

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* *Corresponding author.*
E-mail address: pastormontoro@gmail.com (M. Pastor-Montoro).

Discusión: El síndrome de VHL causa una enfermedad ocular compleja y de difícil diagnóstico que requiere tratamiento precoz de los HCR para modificar el pronóstico visual.

Introduction

The von Hippel–Lindau disease (VHL), described in the early 20th century,[1] is rather infrequent (1 out of 36,000 live births) and usually expresses in the second decade of life.[1,2] It is generally due to mutations in the VHL gene located in the short arm of chromosome 3(p25-6) and is transmitted through dominant autosomal inheritance with nearly complete penetrance, although *de novo* mutations have been described in 20% of cases.[2,3] It is characterized by the formation of benign and malign tumors, including retina and central nervous system hemangioblastomas, renal clear cell carcinoma, pheochromocytomas, neuroendocrine pancreatic tumors, endolymphatic sac tumors and cysts in various organs. Frequently, retinal capillary hemangiomas (RCH) are the first expression of the disease and appear in 49–62% of cases.[2]

Clinical case

Female, 29, Caucasian from Turkey, who consulted in January 2008 due to photophobia. Familial history includes the mother with cerebral vascular lesions. Best corrected visual acuity (BCVA) was of 1 in right eye (RE) and 0.9 in left eye (LE).

RE ocular fundus showed an RCH having 1 papillary diameter within an afferent and another efferent vessel in the peripheral superotemporal retina as well as other small RCH in the temporal equator and superior nasal areas. The LE exhibited epimacular membrane (EMM), several small RCH and one having 2 papillary diameters, with dilated afferent and efferent vessels in the superotemporal peripheral retina with localized lipidic exudation (Fig. 1). Fluorescein angiography confirmed the RCH diagnostic with marked early hyperfluorescence fluorescence in arterial phase as well as dilated and tortuous vessels (Fig. 2).

On the basis of the above findings, a clinical diagnosis of VHL was made and accordingly nuclear magnetic resonance of the brain and spinal cord were requested, together with abdominal echography and determination of catecholamines in 24-h urine that did not show other alterations except ocular RCH. Genetic study was requested on 2 occasions and was carried out at the Carlos III National Center of Oncological Research of Madrid, without identifying VHL gene mutations.

In November 2009, the patient became pregnant and EMM was observed to progress with macular retinal thickening and signs of traction (Fig. 3). For this reason, LE RCH was treated with diode laser. After labor, BCVA of the LE was 0.5, and peripapillary, temporal superior and nasal superior exudation was observed, with vascular dilatation and extraction due to vitreoretinal proliferation (Fig. 4). Accordingly, posterior vitrectomy was performed with EMM peeling, internal limiting membrane rhexis, and laser, trans-scleral cryotherapy and intravitreal injection of ranibizumab (Fig. 5). New RCH continued to appear after surgery, requiring additional laser treatment and 4 intravitreal injections of ranibizumab.

In January 2013 a new genetic study from the same Center was requested which detected a mutation in the VHL gene, *i.e.*, a *de novo* deletion of 151 nucleotides in exon 1, which enabled the genetic diagnostic of the disease. Subsequently, the patient became pregnant again, during which time a new increase in the number of LE RCH was observed but without changes in LE BCVA. It was decided to treat postpartum with laser and 2 intravitreal injections of ranibizumab.

In 2015, the patient exhibited tractional retina detachment in LE treated with cerclage, posterior vitrectomy, peeling of pre-retinal glial membranes, injection of gas (C_3F_8) and ranibizumab. At the time of writing, the patient remains stable with a visual acuity of 0.1. One of her daughters exhibits the same genetic mutation.

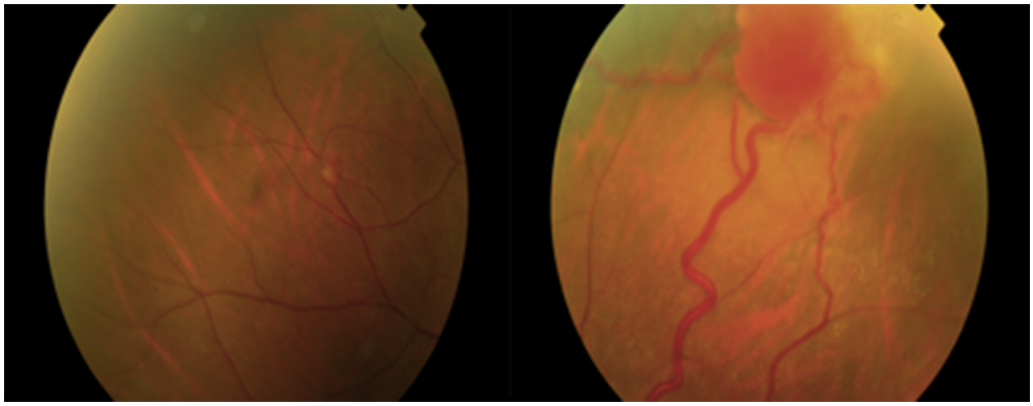

Fig. 1 – Peripheral superotemporal retinograph of both eyes showing retinal vascular tumors with nutrition vessels similar to capillary hemangioma.