ECRONICON OPEN ACCESS

EC OPHTHALMOLOGY
Case Report

Hypertensive Retinopathy Cause by Pheochromocytoma in a Young Female Initially Diagnosed as Infectious Neuroretinitis

Jose A Roca[1,2,3]*, Nathaly V Huaman[1] and Caleb Llacctarimay[4]

[1]*Oftalmologos Contreras, Lima, Perú*

[2]*Universidad Peruana Cayetano Heredia, Lima, Peru*

[3]*Universidad Nacional Federico Villarreal, Lima, Peru*

[4]*Hospital Nacional Sergio E. Bernales, Lima, Perú*

***Corresponding Author:** Jose A Roca, Oftalmologos Contreras and Universidad Peruana Cayetano Heredia and Universidad Nacional Federico Villarreal, Lima, Perú.

Received: November 03, 2022; **Published:** December 12, 2022

Abstract

Purpose: To describe a case of hypertensive retinopathy associated to pheochromocytoma in a 13-year-old female initially treated for infectious neuroretinitis.

Methods: An observational case report. The multimodal images are shown and a review of the literature is done.

Results: We present the multimodal images and results of a 13-year-old female with initial diagnosis of neuroretinitis, that ended having hypertensive retinopathy cause by pheochromocytoma.

Conclusion: Pheochromocytoma, although infrequently at younger age, could cause hypertensive retinopathy that may resemble, initially, neuroretinitis.

Keywords: *Hypertensive Retinopathy; Pheochromocytoma; Neuroretinitis; Macular-Star*

Introduction

Pheochromocytoma is an adrenal medulla catecholamine-secreting tumor which may cause malignant arterial hypertension (MH), defined as extremely high blood pressure with diastolic blood pressure above 130 mmHg at the time of diagnosis and hypertensive retinopathy grades III or IV in the Keith´s classification. Malignant hypertension may cause hypertensive retinopathy, hypertensive encephalopathy (manifested as severe headache, vomiting, visual disturbances, seizures or even coma), and is associated with a double probability of mortality from cardiovascular events as evidenced by the Beaver Dam Eye Study [1].

We report the case of an adolescent with bilateral malignant hypertensive retinopathy, who was diagnosed with pheochromocytoma, an uncommon finding at this age group.

Case Report

A 13-year-old female from Lima, came to consultation derived from the neurology department with bitemporal headache (one or two episodes per month, that lasted more than 4 hours each one), photophobia, phonophobia, nausea, and blurred vision. Elevated systemic blood pressure was not reported neither was taken, at the time of consultation. She presented a history of occipital infarction (with negative etiological studies) and a diagnosis of migraine. No significant family history. At initial examination, uncorrected visual acuity was 20/70 in the right eye and 20/200 in the left eye, normal intraocular pressure (IOP) in both eyes. Anterior segment within normal limits. Tyndall or flare were not present, neither into the anterior chamber, nor in the anterior vitreous cavity. No RAPD. Fundus examination showed increase vascular tortuosity, cotton-wool spots, macular edema with intraretinal exudate (star-shaped pattern), retinal flame hemorrhages at the nerve fiber layer, focal arteriolar narrowing and some papillary swelling (Figure 1). Color vision was preserved.

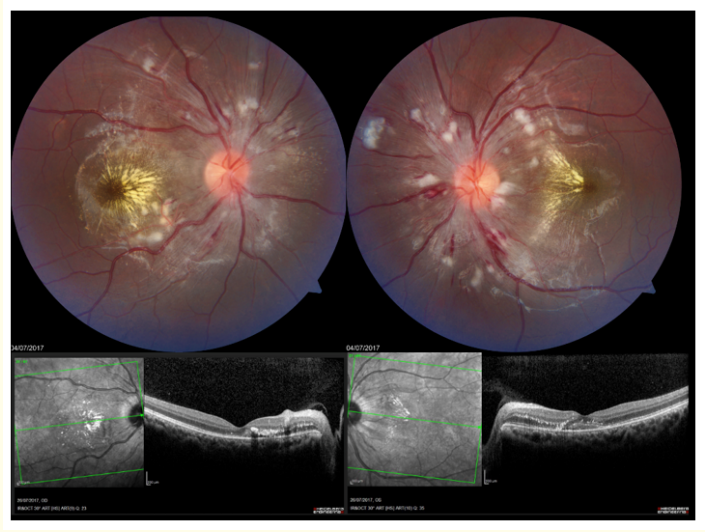

Figure 1: *a. Fundus picture of a 13-year-old adolescent with headache, macular star and papillary edema in both eyes (more predominant in the left eye). b. Optical coherence tomography showing macular edema and exudative lipid deposits in the outer plexiform layer.*

Based on the clinical findings (disc edema, exudative macular star, vascular tortuosity), lab test were solicitated, and presumed bilateral neuroretinitis diagnosis was made; treatment with azithromycin 500 mg and prednisone 50 mg/day was started.

Best corrected visual acuity (BCVA) after 1 week was 20/40 and 20/30 in the right eye and left eye respectively, IOP remained within normal limits (18 mmHg OD /20 mmHg OI), azithromycin was maintained and oral prednisone was progressively reduced. After 3 weeks, BCVA was 20/40 both eyes, IOP stable; treatment was continue with topical nepafenac (1 drop tid) and prednisolone 1% (1 drop bid). There was also significant improvement in the fundus, which can be seen in figure 2. During the ophthalmological follow up visit, systemic arterial pressure was not taken.

After 10 months, at the endocrinology service, systemic high blood pressure was evidenced on two occasions (164/121 mmHg and 184/121 mmHg), in addition headache and hirsutism. No evidence of tremor, exophthalmos, goiter, diaphoresis, palpitations or weight

C-reactive protein	2.7 mg/L	
Erythrocyte sedimentation rate	20 mm/h	
Typhoid/parathyfoid/brucella	Negative	
Anticardiolipin (IgG/IgM)	Negative	
Bartonella henselae (IgG/IgM)	Negative	
RBC	5´010,100	
Leukocytes	16,500	VN 1500 - 6,000
Eosinophils	Normal	VN 1,500 - 4,500
Basophils	Normal	
Bastons	Normal	
Segmented	14,684	
Lymphocytes	1,155	
Monocytes	Normal	
Hemoglobin	14.8	
Hematocrit	43%	

Table 1

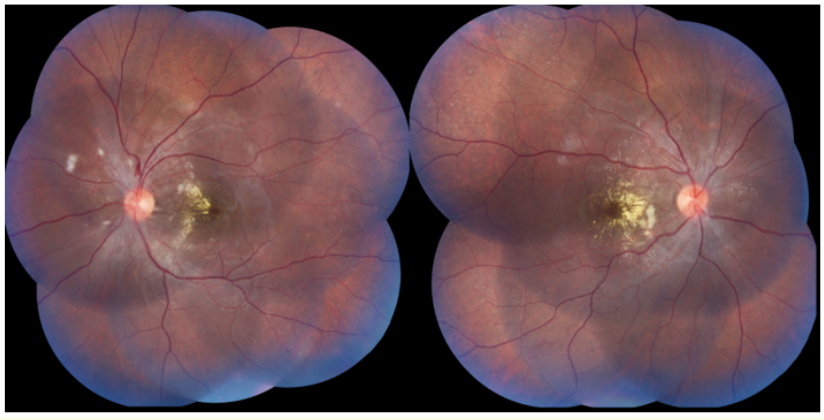

Figure 2: *Fundus picture after 3 weeks.*

loss. Thus, the diagnosis of malignant arterial hypertension was considered and the patient was referred to the emergency room due to arterial hypertension, to rule out a secondary cause.

As an inpatient, metanephrine tests was requested: catecholamines 7.53 (NV: 0.05 to 1.00 mg/24h), urine cortisol: 114.30 ug/24h (NV: 50 to 190 ug/24h), vanylmandelic acid/24 hours: 34.50 (NV: 0 to 4 mg/24h), thyroid hormones within normal limits, methine/creatinine ratio 12.55 (NV: 0 to 0.60), urine creatinine in 24 hours: 0.6 (NV: 1.0 - 2.0).

Abdominal magnetic resonance imaging (MRI) showed a heterogeneous solid lesion, dependent on the left adrenal gland, that confirmed the diagnosis of pheochromocytoma with definitive surgical adrenalectomy indication.

Although our initial diagnostic approach was an infectious neuroretinitis, according to the new evidence and clinical evolution we concluded that the changes in the fundus were due to malignant hypertensive retinopathy secondary to pheochromocytoma. Two years after adrenalectomy, BCVA improve to 20/20 in both eyes, fundus findings resolve, as well as OCT macular edema.

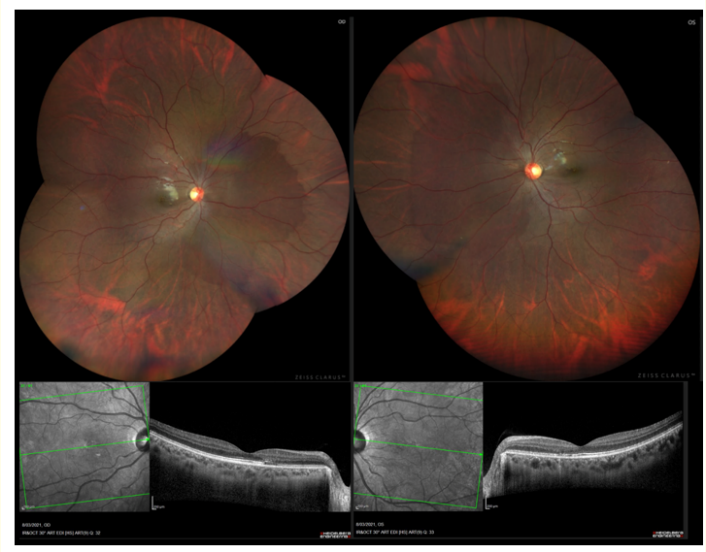

Figure 3: *Fundus picture and macular OCT after adrenalectomy.*

Discussion

Pheochromocytomas are catecholamine-secreting tumors that arise from the chromaffin cells of the adrenal medulla. Pheochromocytoma incidence rate is estimated at 0.3 cases per million inhabitants per year, being rare in childhood (in a series of 748 patients with pheochromocytoma only 13% occurred during childhood) [2].

Among hypertensive children, the incidence of surgically confirmed catecholamine secretory pheochromocytoma varied from 0.8 to 1.7 percent [3-5].

Approximately two-thirds of pheochromocytomas in children have no family history of disease [6] and even in patients with apparently sporadic pheochromocytoma, up to 56% will have unsuspected germline pathogenic variants of the RET, VHL, SDHD, SDHB, SDHC, SDHAF2 or SDHA genes, as well as TMEM127 or MAX [7].

Thus, compared to adults, these tumors in children are more likely to be familial, multicenter, or malignant [8,9]. Hence, the current recommendation is that all children with this disorder, regardless of family history, undergo genetic testing [10].

Signs and symptoms of pheochromocytomas are caused by hypersecretion of norepinephrine, epinephrine, and dopamine from the tumor, although some of the sympathetic hyperactivity may be mediated by the central nervous system.

The classic triad of symptoms in these disorders consists of episodic headache, sweating and tachycardia, usually accompanied by paroxysmal or sustained hypertension. However, only 50% of patients have one or more of these three classic symptoms, especially in children [11].

The clinical presentation usually is varied, it could be asymptomatic or with low hypertension when is associated with multiple endocrine neoplasia type 2 [12] and could have normal blood pressure and normal catecholamine tests when is associated to von Hippel-Lindau disease [13].

Malignant hypertension resulting from pheochromocytoma may include manifestations of hypertensive encephalopathy such as severe headache, vomiting, visual disturbances, convulsions or even coma. Blurred vision, papilledema and hypertensive retinopathy, as an initial presentation are extremely rare. Unrecognized pheochromocytoma can lead to death as a result of hypertensive crisis, myocardial infarction, or arrhythmia. Therefore, fundus examination should be considered in cases of severe or prolonged headache [14].

Normal blood pressure at the time of ophthalmological examination does not exclude the diagnosis of pheochromocytoma in patients with apparent optic neuritis; the presence of bilateral macular star should lead to blood pressure control, and a carefully rule out of pheochromocytoma [15,16].

When pheochromocytoma is suspected (due to suggestive signs/symptoms or due to family history), diagnosis is confirmed by biochemical tests of metanephrines and catecholamines 24-hour urinary fractionated test (or metanephrines fractionated in plasma), followed by the location of the tumor with computed tomography (CT-scan) or magnetic resonance imaging (MRI).

Patients with pheochromocytoma usually have normal results on routine laboratory tests, including complete blood count, electrolytes, blood urea nitrogen, creatinine, and urinalysis. Globular sedimentation rate or C-reactive protein may be elevated, reflecting elevated catecholamine levels. Approximately 40 percent of adult patients have hyperglycemia because catecholamines are insulin counter-regulatory hormones. Hyperglycemia is less common in children with pheochromocytoma [17]. Optimal care for children with pheochromocytoma includes a multidisciplinary team approach in an experienced center.

Surgical resection is the main treatment. Up to half of these tumors in children are malignant, metastatic disease can be present at the initial diagnosis or manifest itself many years later so lifelong surveillance is necessary to detect recurrences and metastases. After surgical resection, our patient showed complete clinical recovery (visual acuity and fundus appearance), although similar evolution has been evidenced in other reports [18-20], the delay in the diagnosis may progress to optic atrophy, with partial or total blindness [15,21].

Conclusion

Pheochromocytoma, although infrequently at younger age, could cause hypertensive retinopathy that may resemble, initially, neuroretinitis.

Disclosure

The authors have no receive any kind of funding from any institution, including National Institutes of Health (NIH), Wellcome Trust, and Howard Hughes Medical Institute (HHMI). The authors manifest to have no proprietary interest. The authors manifest to have no conflict of interest. The patient has given a written consent to use the data and pictures to publish and share knowledge with colleagues.

Bibliography

1. Wong TY., *et al.* "Retinal microvascular abnormalities and 10-year cardiovascular mortality: a population-based case-control study". *Ophthalmology* 110.5 (2003): 933-940.

2. Pamporaki C., *et al.* "Characteristics of Pediatric vs Adult Pheochromocytomas and Paragangliomas". *The Journal of Clinical Endocrinology and Metabolism* 102.4 (2017): 1122-1132.

3. Januszewicz P., *et al.* "Pheochromocytoma in children: difficulties in diagnosis and localization". *Clinical and Experimental Hypertension* 12.4 (1990): 571-579.

4. Wyszyńska T., *et al.* "A single pediatric center experience with 1025 children with hypertension". *Acta Paediatrica* 81.3 (1992): 244-246.

5. Fonkalsrud EW. "Pheochromocytoma in childhood". *Progress in Pediatric Surgery* 26 (1991): 103-111.

6. Pham TH., *et al.* "Pheochromocytoma and paraganglioma in children: a review of medical and surgical management at a tertiary care center". *Pediatrics* 118.3 (2006): 1109-1117.

7. Neumann HP., *et al.* "Germ-line mutations in nonsyndromic pheochromocytoma". *The New England Journal of Medicine* 346.19 (2002): 1459-1466.

8. Neumann HPH., *et al.* "Pheochromocytoma and Paraganglioma". *The New England Journal of Medicine* 381.6 (2019): 552-565.

9. Neumann HP., *et al.* "Germ-line mutations in nonsyndromic pheochromocytoma". *The New England Journal of Medicine* 346.19 (2002): 1459-1466.

10. Waguespack SG., *et al.* "A current review of the etiology, diagnosis, and treatment of pediatric pheochromocytoma and paraganglioma". *The Journal of Clinical Endocrinology and Metabolism* 95.5 (2010): 2023-2037.

11. Baguet JP., *et al.* "Circumstances of discovery of phaeochromocytoma: a retrospective study of 41 consecutive patients". *European Journal of Endocrinology* 150.5 (2004): 681-686.

12. Pomares FJ., *et al.* "Differences between sporadic and multiple endocrine neoplasia type 2A phaeochromocytoma". *Clinical Endocrinology* 48.2 (1998): 195-200.

13. Walther MM., *et al.* "Clinical and genetic characterization of pheochromocytoma in von Hippel-Lindau families: comparison with sporadic pheochromocytoma gives insight into natural history of pheochromocytoma". *The Journal of Urology* 162.3-1 (1999): 659-664.

14. Rogers BM., *et al.* "Small intraretinal haemorrhage as the initial manifestation of pheochromocytoma". *Acta Ophthalmologica* 91.4 (2013): 385-387.

15. Gaines SR. "Ocular changes in pheochromocytoma, with a note on its mimicry of optic neuritis". *American Journal of Ophthalmology* 47.4 (1959): 471-487.

16. Berradi S., *et al.* "Phaeochromocytoma revealed by a stellate neuroretinitis". *The Lancet Diabetes and Endocrinology* 2.8 (2014): 676.

17. Lenders JW., *et al.* "Phaeochromocytoma". *Lancet* 366.9486 (2005): 665-675.

18. Breffeilh LA and Robinson JP. "The ocular manifestations of pheochromocytoma". *Southern Medical Journal* 58 (1965): 73-75.

19. Hervás Ontiveros A., *et al.* "Bilateral hypertensive retinopathy diagnostic of pheochromocytoma". *Archivos de la Sociedad Española de Oftalmología* 90.3 (2015): 148-149.

20. Petkou D., *et al.* "Severe bilateral hypertensive retinopathy and optic neuropathy in a patient with pheochromocytoma". *Klinische Monatsblätter für Augenheilkunde* 225.5 (2008): 500-503.

21. Tibbetts MD., *et al.* "Hypertensive retinopathy in a child caused by pheochromocytoma: identification after a failed school vision screening". *Journal of American Association for Pediatric Ophthalmology and Strabismus* 16.1 (2012): 97-99.

Volume 14 Issue 1 January 2023