

Scleral Compromise in Hereditary Porphyria Cutanea Tarda

Eugenia Andrea Paez Soria¹, Federico Andres Cremona¹, Francisco Lucero Saá¹, Pablo Chiaradía¹

¹Department of Ophthalmology, Hospital de Clínicas "José de San Martín", University of Buenos Aires, Buenos Aires, Argentina

Abstract

Purpose: To report a case of bilateral scleral compromise in a male patient with hereditary porphyria cutanea tarda (PCT).

Methods: Case report.

Results: A 57-year-old male was referred to the Cornea Service at Hospital de Clinicas in Buenos Aires for bilateral scleral thinning. He claimed ocular discomfort and photophobia. Slit-lamp biomicroscopy revealed an oval area of deep scleral thinning without uveal prolapse, adjacent to a conjunctival hyperemic zone in the interpalpebral area, 2 mm temporal to the limbus in the right eye. The left eye presented with a conjunctivalized scleral thinning in the interpalpebral area, 2 mm temporal to the limbus. Physical examination revealed facial hyperpigmentation and hypertrichosis and multiple hypopigmented scars in hands and nails. His family history was positive for PCT. The diagnosis was made by urine porphyrin test and genetic molecular testing. In an attempt to reduce ocular and systemic levels of porphyrins, the patient was treated with oral hydroxychloroquine and repeated phlebotomies, altogether with specially designed glasses to avoid local exposure to sunlight.

Conclusions: Scleral involvement is a rare manifestation of PCT. An adequate treatment, including interdisciplinary management may ameliorate ocular signs and symptoms.

Keywords: Eye protective devices, Porphyria, Porphyria cutanea tarda, Porphyria cutanea tarda/diagnosis, Scleral diseases

Address for correspondence: Eugenia Andrea Paez Soria, Beruti 2839 8 "D", Buenos Aires, C1425BBG, Argentina.

E-mail: eugepaezsoria@gmail.com

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INTRODUCTION

Porphyria cutanea tarda (PCT) is the most common type of porphyria worldwide. It can be acquired (type I) or hereditary (type II). The disease is originated by the deficiency of uroporphyrinogen decarboxylase, an enzyme responsible for heme biosynthesis. This causes an accumulation of photosensitive intermediaries such as uroporphyrinogen and is associated with injuries in sun-exposed skin and other tissues.¹ Eye involvement is rare, although there are reports of ocular manifestations such as pterygium, ectropion, symblepharon,² cicatrizing conjunctivitis,³ scleral thinning, and corneal melt.⁴ We report a case of bilateral scleral thinning in a male patient with hereditary genetically verified PCT.

CASE REPORT

A 57-year-old male was referred to the Cornea Service at Hospital de Clinicas in Buenos Aires for bilateral scleral thinning. Anamnesis revealed that the patient had been diagnosed with PCT at the age of 4. Despite having been previously treated with hydroxychloroquine, the patient denied any improvements in the disease, presumably due to poor adherence to treatment. His family history was positive, as his father had suffered from the same disease. He claimed ocular discomfort and photophobia. Ocular examination showed a corrected visual acuity of counting fingers in the right eye and 20/20 in the left eye. Slit-lamp biomicroscopy revealed an oval area of deep scleral thinning without uveal

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prolapse, adjacent to a conjunctival hyperemic zone in the interpalpebral area, 2 mm temporal to the limbus [Figure 1a] in the right eye. The left eye presented with a conjunctivalized scleral thinning in the interpalpebral area, 2 mm temporal to the limbus [Figure 1b]. Fundus examination showed a macular scar due to myopic maculopathy in the right eye and a myopic fundus in the left eye.

Physical examination yielded facial hyperpigmentation and hypertrichosis [Figure 2] and multiple hypopigmented scars in hands and nails [Figure 3]. The patient did not have any active skin lesions. No signs of rheumatoid arthritis or other collagen vascular disease were found.

A 24-h urine test was performed, showing total porphyrins of 5803 ug (normal values: up to 250 ug/24 h).

In order to find a possible mutation in the urodecarboxylase enzyme gene, a genetic test was carried out. Two mutations were detected in the direct sequencing of the urodecarboxylase

gene: a point mutation p.M324R in exon 10 and another one of splicing c.942 + 1G>A in intron 9, both responsible for porphyria.

Dermatology and hematology services in our hospital were consulted. The patient was prescribed treatment with hydroxychloroquine 200 mg twice a week and sun protection to avoid skin injuries. Blood samples were taken to analyze liver function, iron concentration, and possible triggers of the disease such as hepatitis C virus (HCV) infections. A phlebotomy was performed with the aim of lowering circulating porphyrin concentrations.

The ophthalmological treatment was based on reducing inflammation caused by circulating porphyrins and preventing solar exposure of the interpalpebral sclera. We designed special glasses with lower, upper, temporary, and nasal coverage to protect against exposure to ultraviolet (UV) light. Topical treatment with artificial teardrops and loteprednol etabonate 0.5% qid was indicated to reduce the inflammatory effect of accumulated porphyrins in exposed ocular tissue. The

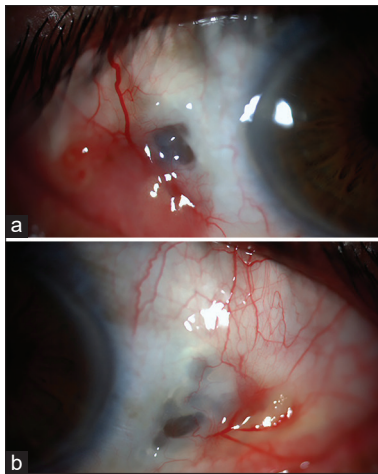


Figure 1: (a) Right eye shows an oval area of deep scleral thinning without uveal prolapse, adjacent to conjunctival hyperemic zone in the interpalpebral area. (b) Left eye shows an area of conjunctivalized thinned scleral in the interpalpebral area



Figure 2: Hyperpigmentation and hypertrichosis on the face



Figure 3: Multiples hypopigmented scars on the skin dorsum hand

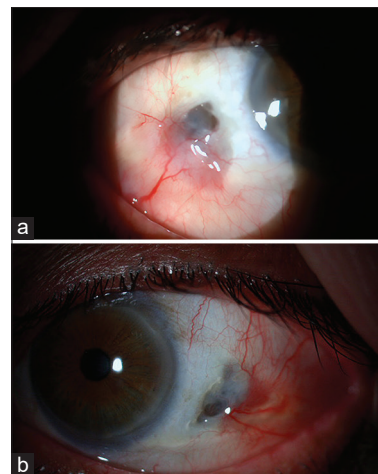


Figure 4: (a and b) Improvement of scleral lesions in both eyes at the last follow-up visit

possibility of a scleral patch graft was discussed as soon as the porphyrins values became normal.

After 1 year of follow-up, oral treatment with hydroxychloroquine and ten cycles of phlebotomy, the patient showed some improvements. Slit-lamp biomicroscopy revealed a decrease in the size and depth of the scleral lesions, as well as a reduction of conjunctival hyperemia adjacent to the lesion in the right eye [Figure 4]. A new 24-h urine test was performed, showing total porphyrins of 3384ug/24 h, a concentration that is still high. Since the disease improved with medical treatment, no surgery was required. The patient will continue with the treatment to lower the values of porphyrins in the blood. The disease-triggering factor has not been found yet.

DISCUSSION

Porphyrias are categorized into the two groups of erythropoietic or hepatic based on the defects of specific enzymes in the heme synthesis pathway. The exact diagnosis is based on measurement of defective enzyme, or the accumulated precursors in heme synthesis.⁵ PCT is a hepatic porphyria that consists of a deficient uroporphyrinogen decarboxylase activity. PCT can be sporadic (type 1) or hereditary (type 2). Hereditary PCT is characterized by enzyme deficiency in all tissues while in acquired PCT, the deficiency is isolated to the liver and may be precipitated by triggering factors such as alcohol, iron, estrogen, smoking, HCV, human immunodeficiency virus, polychlorinated hydrocarbons, hemodialysis, chronic renal failure, and hereditary hemochromatosis.⁶

Patients with PCT predominantly develop cutaneous manifestations. Dermatology manifestation can be bullae,

blisters, sores, and vesicles. The bullae contain porphyrin-rich serous or serosanguinous fluid and rupture easily. These injuries become crusted and tend to heal with areas of hypo- or hyperpigmentation or sclerodermatous change. Skin manifestations involve sun-exposed areas (face, hands, forearms, and lower legs). Furthermore, patients with PCT present hirsutism and hyperpigmentation.⁷

Ocular compromise is uncommon in PCT; however, it can manifest as lid scarring, ectropion,⁸ pinguecula, pterygium,² cicatrizing conjunctivitis,³ scleral necrosis and thinning, and corneal perforation.⁴ Only a few cases of scleral involvement have been reported [Table 1].

Increased concentration of uroporphyrinogen in tissues and the exposure of porphyrins to UV light cause an inflammatory reaction.¹⁵ The biological effects of oxygen radicals, mast cell-derived mediators, and anaphylatoxin, generated as a consequence of complement activation may account for the damage of the sunlight-exposed tissues.¹⁶ This could be the explanation for the usual location of eye injuries in the interpallebral fissure.

In cases that do not respond well to medical therapy, with severe scleral thinning or perforation with prolapsed uveal tissue, surgical treatment has been described. Proposed techniques in the literature include heterologous scleral patch graft⁴ and amniotic membrane transplantation.¹⁴

We present a case of hereditary PCT, confirmed by genetic molecular testing and positive family history, with scleral compromise in the interpallebral fissure of both eyes. As no connective tissue disease was found, the findings were considered to be associated with PCT. Furthermore, the

Table 1: Reported cases of scleral compromise in porphyria cutanea tarda

Authors	Year of publication	Number of patients with PCT	Scleral manifestation	PCT type*	PCT diagnosis
Urrets-Zavalía <i>et al.</i> ⁹	1937	1	Conjunctivalized thinned scleral in the interpallebral area in both eyes	Does not specify	Clinical manifestations and porphyrin profiles
Barnes <i>et al.</i> ¹⁰	1952	7	Scleromalacia perforans Scleromalacia semiperforans	Does not specify	Does not specify
Sevel <i>et al.</i> ¹¹	1971	1	Scleroconjunctival adhesions and scleral collagen degeneration	Does not specify	Urine concentration of porphyrins
Chumbley <i>et al.</i> ¹²	1977	2	Scleral resorption and thinning with visible underlying uveal tissue	Acquired	Urine concentration of porphyrins
Salmon <i>et al.</i> ¹³	1990	3	Acute scleritis and thinning interpallebral sclera	Acquired	Clinical manifestations and porphyrin profiles
Zaborowski <i>et al.</i> ⁶	2004	1	Scleral inflammation and thinning with uveal show in the interpallebral fissures	Acquired	Clinical manifestations and urine porphyrins
Altıparmak <i>et al.</i> ¹⁴	2008	1	Scleral necrosis in the interpallebral area	Acquired	Clinical manifestations and urine porphyrins
Gogri <i>et al.</i> ⁴	2014	1	Scleral thinning with uveal show in the interpallebral fissures	Hereditary	Clinical manifestations in childhood and urine porphyrins. No genetic testing

*Type I acquired, Type II hereditary. PCT: Porphyria cutanea tarda

disease improved with systemic and topical treatment, special glasses (to avoid sunlight exposure) and phlebotomies, lowering the concentration of porphyrins. No surgical procedure was required. Even though it is considered to be rare, ocular compromise in PCT may occur and must be addressed adequately, with a multidisciplinary approach involving ophthalmologists, dermatologists, and hematologists.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Franzon VA, Mikilita ES, Camelo FH, Camargo R. Porphyria cutanea tarda in a HIV-positive patient. *An Bras Dermatol* 2016;91:520-3.
2. Hammer H, Korom I. Photodamage of the conjunctiva in patients with porphyria cutanea tarda. *Br J Ophthalmol* 1992;76:592-3.
3. Park AJ, Webster GF, Penne RB, Raber IM. Porphyria cutanea tarda presenting as cicatricial conjunctivitis. *Am J Ophthalmol* 2002;134:619-21.
4. Gogri PY, Misra NS, Misra S. Ocular manifestations in porphyria cutanea tarda. *BMJ Case Rep* 2014;2014. bcr2013010402. doi: 10.1136/bcr-2013-010402.
5. Meyer UA. Porphyria. In: Braunwald E, Issebacher KJ, Petersdorf RG, Wilson JD, Martin JB, Fauci AS, editors. *Harrison's Principles of Internal Medicine*. 13th ed., New York, NY: McGraw-Hill; 1994. p. 2073-9.
6. Zaborowski AG, Paulson GH, Peters AL. Sight threatening complications in porphyria cutanea tarda. *Eye (Lond)* 2004;18:949-50.
7. Besur S, Hou W, Schmeltzer P, Bonkovsky HL. Clinically important features of porphyrin and heme metabolism and the porphyrias. *Metabolites* 2014;4:977-1006.
8. Sober AJ, Grove AS Jr., Muhlbauer JE. Cicatricial ectropion and lacrimal obstruction associated with the sclerodermoid variant of porphyria cutanea tarda. *Am J Ophthalmol* 1981;91:396-400.
9. Urrets-Zavalía A, Allende IM, Oliva RO. [Escleromalacia observada en el curso de una porfirinuria crónica]. *Arch Oftal Buenos Aires* 1937;12:115. [Spanish].
10. Barnes HD, Boshoff PH. Ocular lesions in patients with porphyria. *AMA Arch Ophthalmol* 1952;48:567-80.
11. Sevel D, Burger D. Ocular involvement in cutaneous porphyria. A clinical and histological report. *Arch Ophthalmol* 1971;85:580-5.
12. Chumbley LC. Scleral involvement in symptomatic porphyria. *Am J Ophthalmol* 1977;84:729-33.
13. Salmon JF, Strauss PC, Todd G, Murray AD. Acute scleritis in porphyria cutanea tarda. *Am J Ophthalmol* 1990;109:400-6.
14. Altiparmak UE, Ofly Y, Kocaoglu FA, Katircioglu YA, Duman S. Ocular complications in 2 cases with porphyria. *Cornea* 2008;27:1093-6.
15. Sati A, Sangwan VS, Basu S. Porphyria: Varied ocular manifestations and management. *BMJ Case Rep* 2013;2013. bcr2013009496. doi: 10.1136/bcr-2013-009496.
16. Lim HW. Pathophysiology of cutaneous lesion in porphyrias. *Semin Hematol* 1989;26:114-9.