

Trichothiodystrophy: a case report of childhood glaucoma associated with non-acquired systemic disease

Tricotiodistrofia: relato de caso de glaucoma infantil associado a doença sistêmica não adquirida

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ABSTRACT | Trichothiodystrophy belongs to a group of rare genetic diseases characterized by DNA repair anomalies. Ocular manifestations can occur in 50% of cases, including cataract, refractive errors, strabismus, microcornea, microphthalmia, dry eye, and pigmentary macular changes. We report a case of childhood glaucoma in a patient with trichothiodystrophy who underwent trabeculectomy in the left eye. To our knowledge, this is the first clinical report of childhood glaucoma associated with trichothiodystrophy.

Keywords: Trichothiodystrophy syndromes; Glaucoma; Xeroderma pigmentosum; DNA repair-deficiency disorders; Ocular manifestations; Humans; Case reports

RESUMO | A tricotiodistrofia pertence a um grupo de doenças genéticas raras caracterizadas por anomalias da reparação do DNA. Manifestações oculares podem ocorrer em 50% dos casos, incluindo catarata, erros refrativos, estrabismo, microcórnea, microftalmia, olho seco e alterações maculares pigmentares. Relatamos um caso de glaucoma infantil em um paciente com tricotiodistrofia submetido à trabeculectomia no olho esquerdo. No nosso conhecimento, este é o primeiro caso descrito de glaucoma infantil associado à tricotiodistrofia.

Descritores: Síndromes de tricotiodistrofia; Glaucoma; Xeroderma pigmentoso; Distúrbios no reparo do DNA; Manifestações oculares; Humanos; Relatos de casos

INTRODUCTION

Childhood glaucoma is an uncommon disorder characterized by two of the following symptoms: intraocular pressure (IOP) higher than 21 mmHg, progressive optic disc cupping, characteristic corneal findings, progressive myopia, increased ocular axial length, or reproducible visual field defects⁽¹⁻⁵⁾. Childhood glaucoma associated with non-acquired systemic disease corresponds to approximately 11% of childhood glaucoma cases⁽²⁾.

Trichothiodystrophy (TTD) is an autosomal recessive disorder⁽⁴⁻⁷⁾, with a reported incidence of 1.2/1,000,000 births in a Western European population⁽⁴⁾. Although ocular manifestations have been described previously^(7,8), to our knowledge, this is the first clinical report of childhood glaucoma associated with trichothiodystrophy.

CASE REPORT

A 6-year-old male child was referred for ophthalmological examination by our hospital's dermatology section, to help with syndromic diagnosis. He presented malar erythema associated with telangiectasia (Figure 1A) from birth. His mother reported the absence of cilia and toenails at birth, and very sparse hair, which started growing 2 years later. General physical examination revealed uncharacteristic facies, slight low ear implantation with normal stature, and weight development. Hair, cilia, and nails were normal at this presentation. He presented two café-au-lait spots on his skin.

There were no ocular or visual complaints. Past and familial ocular histories were unremarkable. His mother denied systemic and ocular medication use. Routine ophthalmological evaluation presented a best-corrected

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visual acuity of 20/30 in his right eye (RE) and 20/20 in his left eye (LE). IOP measurements obtained with the Goldmann tonometer were elevated in both eyes (RE: 31 mmHg/LE: 44 mmHg). Biomicroscopy was unremarkable bilaterally, and corneal diameter was 12 mm in both eyes.

Upon gonioscopy of both eyes, all structures of the cameral angle were visualized up to the ciliary body band and showed normal development, without iris

strands or peripheral synechiae. Fundoscopy showed a 0.9 × 0.9 cup-to-disc ratio, with nasal deviation of the retinal vessels in the RE (Figure 1B). In the LE, a pink-colored optic disc was observed, with a 0.6 × 0.6 cup-to-disc ratio and normal emergence of the retinal vessels (Figure 1C). No retinal lesions were visible in either eye.

The corneal thickness was RE: 590 μm and LE: 585 μm. Axial length was normal (RE: 23.58 mm; LE: 23.03 mm). Optical coherence tomography indicated a reduction of

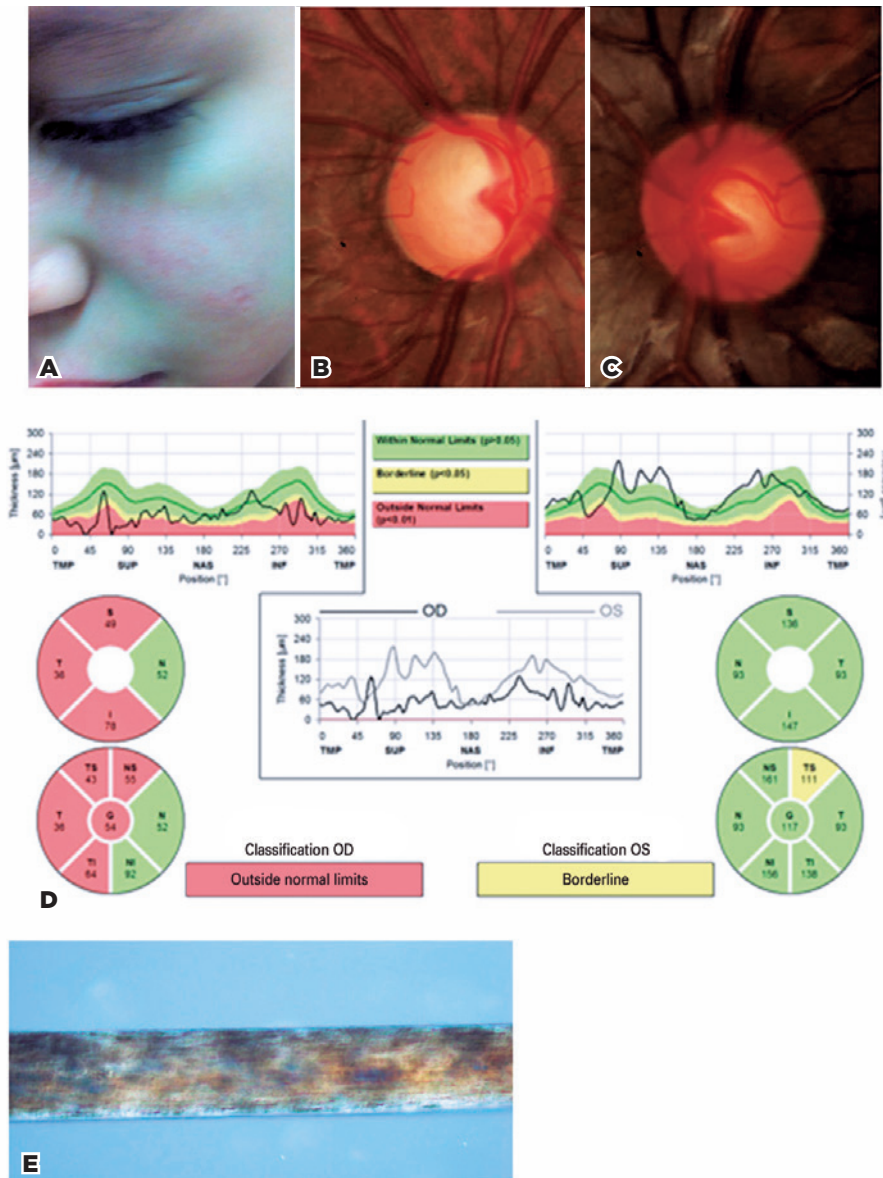


Figure 1. A) Malar erythema with telangiectasia. B) Right eye retinography: A 0.9 × 0.9 cup-to-disc ratio is visible on the right eye. C) Left eye retinography: pink optic disc with a 0.6 × 0.6 cup-to-disc ratio and normal emergence of the retinal vessels. D) Retinal fiber layer from the optic disc optical coherence tomography examination of both eyes: right eye with absolute defects on the temporal superior, superior, and inferior quadrants. His left eye contained a borderline defect on the superior temporal quadrant. E) Light microscopy hair examination: characteristic tiger tail banding is visible.

the peripapillary fiber layer thickness in the superior, temporal, and inferior quadrants in OD (Quality score: 23) and a borderline defect on the superior temporal sector in OS (Quality score: 18). Visual field testing was unreliable for both eyes because of a lack of cooperation (Figure 1D).

A skin biopsy on the erythematous facial lesions (Figure 1A) revealed they were chronic actinic lesions. No etiological diagnosis was determined at this point.

The patient was initially medicated with topical timolol maleate and dorzolamide in both eyes. Latanoprost was further added, but IOP remained at 24 mmHg RE and 18 mmHg LE. Because of advanced glaucomatous damage in RE, a mitomycin-augmented trabeculectomy was indicated. There were no surgical complications, and the first postoperative days were uneventful. He developed seidel on the 18th postoperative day associated with conjunctival wound dehiscence. Suture revision was performed the next week; however, wound dehiscence and conjunctival thinning was observed again 3 weeks later. On second observation under general anesthesia, we found melting of the scleral flap; thus, a scleral patch and conjunctival advancement was necessary (Figure 2A and B). No further complications were observed. The hypotony was controlled successfully and IOP stabilized at 15 mmHg RE.

Concurrent dermatological investigation led to examination of the hair under light microscopy, which revealed characteristic tiger tail banding highly suggestive of trichothiodystrophy (Figure 1E). A diagnosis of secondary glaucoma associated with trichothiodystrophy was thus established.

Two years after surgery, IOP is 15 mmHg RE without drugs and 16 mmHg LE, with latanoprost, timolol maleate,

and dorzolamide. Visual acuity and optic disc cupping remain stable in both eyes.

DISCUSSION

Incidental findings of elevated IOP, raised cup-to-disc ratio for the optic nerve in both eyes, and characteristic defects in the nerve fiber layer optical coherence tomography, along with normal gonioscopy, axial length, corneal diameter, and anterior segment examination led us to the potential diagnoses of primary juvenile glaucoma, secondary glaucoma associated with systemic diseases, and corticosteroid-induced glaucoma. The latter was excluded on the basis of the absence of corticosteroid use.

The hallmark of trichothiodystrophy is congenital hair dysplasia characterized by hair deficient in sulfur and cystine content, as well as an alternating light banding pattern (tiger tail banding) when visualized microscopically, associated with multisystemic abnormalities⁽⁸⁾. The spectrum of clinical manifestations is broad, with some patients presenting only mild hair and nail changes, but commonly consists of photosensitivity, ichthyosis, brittle hair, intellectual impairment, short stature, and predisposition to infectious diseases⁽⁸⁾.

The diagnosis is established on the basis of observation of the characteristic microscopic changes of the hair. Genetic changes typically include mutations in DNA repair genes xeroderma pigmentosum type B, xeroderma pigmentosum D, or trichothiodystrophy group A (TTDA) (also involved in xeroderma pigmentosum pathogenesis), as well as in TTDN1, a gene of unknown function⁽⁶⁻⁸⁾. Our patient's presentation with malar rash associated with telangiectasia present from birth, photosensitivity, and a history of nail and hair changes led to the consideration of genetic photodermatoses, namely, Bloom syndrome, which was excluded after normal comparative genomic hybridization testing. Further investigation revealed, through hair microscopy analysis, a characteristic tiger tail banding pattern, which is highly suggestive of trichothiodystrophy. The absence of mental impairment, short stature, and repeated infections led us to believe that this could be a milder case of trichothiodystrophy⁽⁹⁾.

Regarding postoperative scleral flap melting, we believe that although mitomycin is indicated frequently in pediatric trabeculectomy surgeries, this complication possibly arose because of a synergistic effect between the antimetabolite action of mitomycin and a trichothiodystrophy-related DNA repair anomaly, unknown when surgery was indicated. Although no records of scleral flap

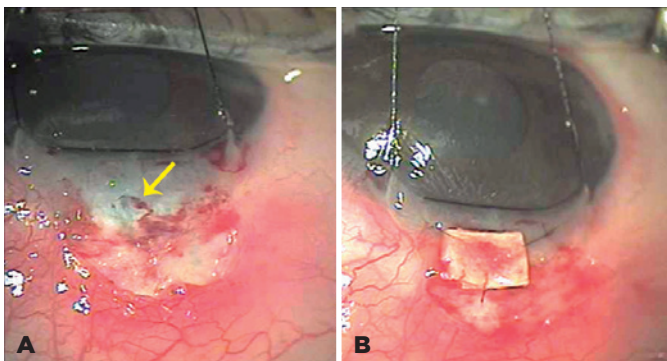


Figure 2. A) An area of scleral flap melting, identified by the yellow arrow, was found upon observation under general anesthesia. B) A scleral patch was sutured in the melted area.

melting associated with systemic diseases are reported in the literature, in our opinion, prior knowledge of the diagnosis would have contraindicated mitomycin use⁽¹⁰⁾.

To the best of our knowledge, this is the first case of childhood glaucoma associated with trichothiodystrophy. We conducted a search in the MEDLINE/PUBMED, EBSCO, EMBASE, Ophthalmic Literature, and Zentralblatt für die gesamte Ophthalmologie und ihre Grenzgebiete databases, which produced zero results.

Thorough investigation is important to establish the diagnosis of this disorder, and, when glaucoma surgery is indicated, we believe that mitomycin use should be carefully evaluated.

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