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Research Article

Severe Anterior Segment Toxicity Associated to Long-Term Use of Topical Trifluridine

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Keywords

- Anterior segment
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Abstract

Objective: To report a case of severe anterior segment toxicity associated to long –term use of trifluridine (3FT).

Results: A 71 year-old male with history of long –term use of trifluridine (3FT), a non selective antiviral drug, for a presumed herpetic keratitis. The clinical features and course of conjunctival and corneal toxicity and anterior segment ischemic changes are described. Anterior chamber lavage, pars plana vitrectomy, lensectomy, Baerveldt glaucoma implantation and intravitreal bevacizumab injection were performed in the right eye. One week after the surgical procedures in the right eye, best-corrected visual acuity was 20/200 with a +9.00 aphakic correction. Laboratory investigations, cultures, PCR and stains were all negative or within normal limits. The same surgical plan was executed in the left eye thereafter.

Conclusions: To our knowledge this is the fourth reported case of toxic ocular changes not explainable other than by the chronic use of topical trifluridine. Emphasis is made on reducing the incidence of potentially disastrous adverse effects with the use of selective topical antiviral drugs.

INTRODUCTION

Antiviral topical medications appear to be one of the antimicrobial agents most commonly associated with local ophthalmic complications [1]. Their use is associated to medication-induced epithelial keratitis, punctal stenosis and canalicular stenosis in patients who have had chronic follicular conjunctivitis and conjunctival cicatrization related to the same drug [1]. Its long term use has alsobeen postulated to cause conjunctival and anterior segment ischemia [2,3].

METHODS

A case report of a 71 year-old male who presented to our institute with bilateral keratitis and uveitis, after longstanding topical trifluridine(3FT) therapy for nine months for a presumed herpetic keratitis. He presented with bilateral epithelial defects, generalized corneal edema, pallor and chemosis of the bulbar conjunctiva, anterior uveitis, and uncontrolled ocular hypertension. He had no significant ophthalmic history other than narrow angle glaucoma controlled on medical therapy. Corneal cultures were found be negative. He subsequently developed spontaneous bilateral hyphemas, leading him to hand motions vision in both eyes (Figure 1). The hyphema of his right eye was removed through anterior chamber lavage, and a pars plana vitrectomy and lensectomy were performed to examine the posterior pole and assess a possible pan-ischemic event. Baerveldt glaucoma implantation and intravitreal bevacizumab injection were used at the end of the procedure.

RESULTS

One week after the surgical procedures in the right eye, his best-corrected visual acuity improved to 20/200 with a +9.00 aphakic correction and a bandage contact lens. His left eye had persistent hyphema, uncontrolled glaucoma and a persistent corneal epithelial defect, and the same surgical plan

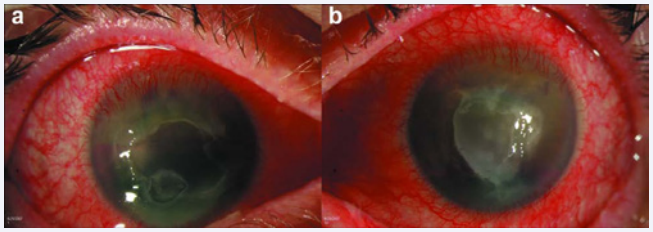

Figure 1 Parts a and b. Severe anterior segment toxicity both eyes. a, Ciliary injection, epithelial defect, corneal edema, and hyphema in the right eye. b, Ciliary injection, epithelial defect, corneal edema and hyphema in the left eye.

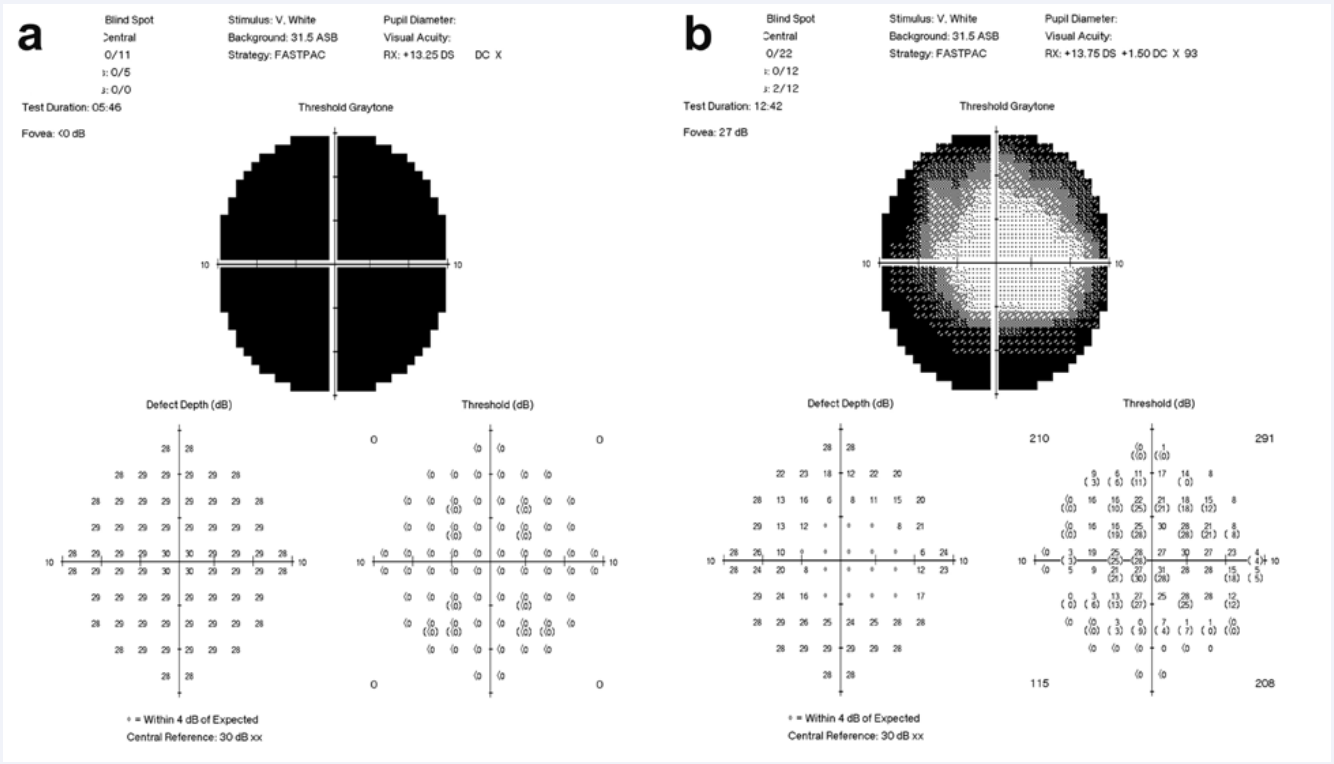

Figure 2 Parts a and b. Significant central visual loss. a, Left eye, complete visual loss in a central 10-2 threshold test. b, Right eye, severe constriction of the central field.

was executed thereafter. Laboratory investigation included a complete blood count with differential, complete metabolic panel, HLA-B27 antigen, sedimentation rate, C-reactive protein, antinuclear antibodies, antineutrophil cytoplasmic antibodies, rheumatoid factor, angiotensin-1 converting enzyme, human immunodeficiency virus antibody detection, rapid plasma reaginin and fluorescent treponemal antibody absorption test, which were all within normal limits or negative. Cultures, PCR and stains from vitreous and anterior chamber taps were negative.

DISCUSSION

We present a case of a 71 year old male treated with trifluridine for a long term (nine months) period due to a presumed bilateral herpetic keratitis. He presented to the clinic with ocular signs of conjunctival and corneal epithelial toxicity and some other signs of conjunctival ischemia (pallor and chemosis) and anterior segment inflammation (uveitis) related to the chronic use of trifluridine. Some days later, he developed more severe signs and symptoms that would be consistent with augmented anterior segment toxicity and possible ischemia.

Antiviral topical medications are antimicrobial agents commonly associated with local ophthalmic complications [1]. Their use is associated to medication-induced epithelial keratitis, punctal stenosis, canalicular stenosis, chronic follicular conjunctivitis, and conjunctival cicatrization [1]. Other adverse effects include conjunctival injection, stromal edema and haze, mild iritis and its long term use has been postulated to cause conjunctival and anterior segment ischemia [2,3]. Three cases of severe Anterior Segment Toxicity (ASI) directly associated with the chronic use of trifluridine have been reported in the literature [2-4].

Idoxuridine, trifluridine, and vidarabine act as thymidine analogs and inhibit DNA polymerase, forming defective viral DNA [5]. Their use is associated with ocular surface toxicity explainable by their nonselective action on infected and noninfected host cell DNA molecules [6].

None of the previously known systemic or ocular factors to develop ASI were present in our case as demonstrated by the laboratory investigations [7]. Therefore we could attribute the severe anterior segment toxic signs to the chronic use of 3FT. Although the bilateral presentation argues against an infectious herpetic etiology, cases of anterior segment ischemia associated chronic vasculitis related to herpes simplex keratouveitis have been reported and this phenomenon could not be ruled out without a conjunctival biopsy [8].We did not perform anterior segment fluorangiography as an objective test of ischemia due to the poor visualization of the iris and anterior segment. However, we do report clinical signs that are often unequivocal of anterior segment ischemia.

This is the fourth reported case of severe anterior segment toxicity and anterior segment ischemic changes not explainable other than by the long-term use of trifluridine. The incidence of these potentially disastrous conditions could be further reduced with the use of selective topical antiviral drugs targeted against infected cells, as ganciclovir and acyclovir [6,9].

Based on the ICJME, all authors had: 1) substantial contributions to conception and design, acquisition of data, or

analysis and interpretation of data; 2) drafting the article or revising it critically for important intellectual content; and 3) final approval of the version to be published.

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