Case Report

Central Serous Chorioretinopathy Development following Cessation of Terbinafine Treatment

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Keywords
Terbinafine · Antifungal treatment · Central serous chorioretinopathy

Abstract
This report describes a case of central serous chorioretinopathy (CSCR) occurring following cessation of terbinafine treatment. A 51-year-old man presented for a routine ophthalmic examination. He was treated with oral terbinafine for onychomycosis up to 3 months before the presentation. Spectral-domain optical coherence tomography (OCT) showed extrafoveal subretinal fluid in both eyes with small underlying pigment epithelial detachments. There were no additional relevant findings in the patient history or ocular examination. A diagnosis of CSCR was made. After 10 weeks without treatment, OCT demonstrated almost complete resolution of subretinal fluid in both eyes. The exact key ingredients of the perfect storm leading to CSCR in young, healthy individuals are still unknown. Here, we describe, to our knowledge, the first documented case, where the appearance of CSCR was apparently triggered by cessation of antifungal treatment. This unusual case may provoke further research that will bring us closer to understanding the mechanism behind the appearance of CSCR. It may also widen the scope of the routine anamnesis when dealing with patients newly diagnosed with this enigmatic condition.

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Introduction

Central serous chorioretinopathy (CSCR) predominantly affects young males. Clinically, CSCR manifests with one or more defined areas of serous retinal detachment in the posterior pole of the eye, in the absence of other ocular pathologies such as inflammation. Vision might be affected to a variable degree [1]. Optical coherence tomography (OCT) findings typically include limited areas of subretinal fluid, pigment epithelium detachments, choroidal thickening, and pigmentedary changes in areas previously affected by subretinal fluid (gutter).

The exact etiopathogenesis of this condition remains unclear. Dysfunction of the RPE and choriocapillaris are thought to play a role. Increasing evidence points to the involvement of glucocorticoids and mineralocorticoids in the pathogenesis of the condition [2–7]. Here, we describe an occurrence of CSCR following cessation of terbinafine treatment.

Case Presentation

A 51-year-old man presented for a routine ophthalmic examination. He denied any visual disturbance, pain, floaters, or photopsia. His past medical history was significant for the use of oral terbinafine treatment for onychomycosis up to 3 months before presentation. Terbinafine was administrated orally at a single daily dose of 250 mg for 4 months. He denied concurrent use of any medication in any form, specifically excluding the use of corticosteroids. His past ocular history included refractive surgery for myopia more than 20 years ago. His axial length measurements supported previous axial myopia (25.78 mm and 26.14 mm in the right and left eyes, accordingly). Best-corrected visual acuity on presentation was 0.9 in both eyes. Slit-lamp ocular examination was essentially within normal limits except for findings of extrafoveal subretinal fluid in both eyes that were confirmed by OCT (shown in Fig. 1a, c for left and right eyes, respectively).

In addition, OCT revealed small underlying pigment epithelium detachments and choroidal thickening. No pachyvessels were identified in the choroid. After 10 weeks of follow-up without treatment, the visual acuity remained excellent, while OCT showed nearly complete resolution of subretinal fluid in both eyes (shown in Fig. 1b, d for left and right eyes, respectively).

Discussion

We describe a transient appearance of CSCR following cessation of antifungal treatment with terbinafine. CSCR resolution with terbinafine treatment was previously reported [8].

Significant evidence points to the involvement of endogenous and exogenous corticosteroids in CSCR pathogenesis. Prospective studies have found exogenous use of glucocorticoids to be associated with CSCR development [3]. Adrenocortical glucocorticoids and sex steroids were found to be elevated in CSCR patients [4, 5].

RPE standing potential was found to be increased in humans treated with glucocorticoids [6]. In bovine and porcine RPE cell cultures, glucocorticoid exposure reduced transepithelial membrane potential, short circuit current, and transepithelial resistance [6].

Glucocorticoid-mediated activation of the mineralocorticoid receptor (MR) was reported in CSCR [7]. Retinal MR activation has been shown to cause upregulation of specific retinal electrolyte channels, leading to the accumulation of subretinal fluid [2].

Terbinafine blocks ergosterol production and potently inhibits the activity of several enzymes necessary for the conversion of cholesterol to adrenocortical steroid hormones [9]. An Addisonian crisis following treatment with terbinafine was previously described, pointing
toward an anti-steroid effect of terbinafine [10]. The effect of other antifungal medications such as ketoconazole on CSCR has been previously explored as well; however, data have been inconsistent [11–13]. Meyerle et al. [13] reported on 5 patients with CSCR treated for 4 weeks with ketoconazole 600 mg/day. While plasma cortisol levels were lower at 4 weeks and 8 weeks from treatment onset, BCVA remained stable at 4 weeks and 8 weeks, and PED dimensions were stable at 4 weeks and decreased at 8 weeks, suggesting a possible delayed response. Golshani et al. [11] reported on the efficacy of ketoconazole 200 mg/day in 15 patients with CSCR. Another 15 patients with CSCR served as controls. After 4 weeks of treatment, the treatment and control groups demonstrated no significant change in BCVA or pigment epithelial detachment thickness. In a recent study by Chantarasorn et al. [12], the efficacy of ketoconazole 400 or 600 mg per day was evaluated in 21 patients and compared to 20 patients who served as controls. Ketoconazole shortened the time to resolution (7 vs. 16 weeks; \( p < 0.01 \)) and reduced the need for rescue laser treatment (23.8\% vs. 50\%; \( p = 0.01 \)).

Both terbinafine and ketoconazole play a role in steroidogenesis inhibition [9]. We suggest that terbinafine treatment might lower serum glucocorticoid levels, thereby inhibiting activation of MR on RPE cells, ultimately reducing the accumulation of subretinal fluid in CSCR.

In our case, possible depletion of systemic steroids following prolonged terbinafine administration might have created a compensatory upregulation of MRs in the RPE/choriocapillaris. Cessation of terbinafine treatment might have resulted in a rebound phenomenon, increasing the steroid end-organ effect.

Alternatively, the patient might have been suffering from subclinical CSCR suppressed by terbinafine, and when treatment was stopped, the CSCR worsened. In this respect, the presence of flat irregular pigmented epithelium detachments and focal RPE mottling may imply sustained disease duration. Therefore, we cannot preclude the possibility that CSCR was evident prior to terbinafine cessation. The latter is even more plausible in the presence of

Fig. 1. CSCR development following cessation of terbinafine. SD-OCT images of left (a) and right (c) eyes demonstrating CSCR formation 3 months after cessation of terbinafine treatment. SD-OCT images of left (b) and right (d) eyes after 10 weeks of follow-up with no treatment, demonstrating fluid resorption. CSCR, central serous chorioretinopathy; SD-OCT, spectral-domain optical coherent tomography.
extrafoveal involvement, decreasing patients’ awareness of vision reduction stemming from the condition.

**Conclusion**

Previous anecdotal clinical and laboratory evidence indicates a possible beneficial role of terbinafine in CSCR. We speculate that the appearance of CSCR in our case might be related to cessation of terbinafine treatment.

This case sheds light on the interplay between terbinafine treatment and CSCR progression and urges further research to establish its underlying mechanisms. It may also widen the scope of the routine anamnesis when dealing with patients who are newly diagnosed with this enigmatic condition.

**Statement of Ethics**

This retrospective review of patient data did not require ethical approval in accordance with local guidelines. All procedures followed were in accordance with ethical standards and the Helsinki Declaration. This report does not contain any personal information that could lead to the identification of the patient. Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

**Conflict of Interest Statement**

The authors have no conflicts of interest to declare.

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**Author Contributions**

Or Shmueli was involved in data acquisition and manuscript drafting. Edward Averbukh and Itay Nitzan contributed to critical revision of the manuscript.

**Data Availability Statement**

All data generated or analyzed during this study are included in this article, and further inquiries can be directed to the corresponding author.

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