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Case Report

From Hair Loss to Vision Loss: Minoxidil-Associated CRVO in a Young Female

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Keywords
Minoxidil · Rogaine · Medication · Adverse effect · Central retinal vein occlusion · Retinal vein occlusion · Young · Risk factors

Abstract
Introduction: Central retinal vein occlusion (CRVO) is a common retinal vascular disorder that is most often seen in older adults and individuals with vascular risk factors. ***Case Presentation:*** We report a case of CRVO with cystoid macular edema (CME) in a young, otherwise healthy patient taking minoxidil for hair loss. The patient had no known vascular risk factors, and a comprehensive coagulability workup was negative. The CRVO with CME resolved without intervention upon cessation of minoxidil. ***Conclusion:*** Possible mechanisms for minoxidil-associated retinal vascular disorders are explored. Thorough medication histories and the consideration of possible adverse drug events in patients without traditional risk factors are recommended.

Introduction

Central retinal vein occlusion (CRVO) is characterized by the obstruction of the central retinal vein, resulting in retinal vascular insufficiency and vision loss from ischemia or CME. It is a common vision threatening condition among middle-aged to older adults with prevalence in the range of 0.1–0.9% [1–3], whereas it is only rarely seen in younger populations (≤35 years of age) [4]. CRVO is strongly associated with systemic vascular disease including cardiovascular and cerebrovascular disease, likely due to shared vascular risk factors such as

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hypertension, diabetes, and dyslipidemia [3, 5]. In younger patients, CRVO is more commonly associated with non-traditional risk factors including hormonal contraception or recent pregnancy, coagulopathy, and autoimmune or rheumatologic conditions [6].

Untreated CRVO rarely improves spontaneously and often deteriorates [7]. In the acute phase, CRVO leads to visual reduction due to macular hypoxia and CME, while prolonged occlusion results in ischemia and secondary neovascularization. Visual acuity typically worsens over time, and in approximately a third of cases nonischemic CRVO converts to the more serious ischemic form [7]. Intravitreal anti-vascular endothelial growth factor (VEGF) is the most common first-line treatment [8–10]. The following report presents a unique case of apparent minoxidil-induced CRVO in a young, otherwise healthy patient without any known risk factors, which resolved spontaneously upon medication cessation. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000537911).

Case Presentation

A 34-year-old female was referred for a right-sided nonischemic CRVO (Fig. 1). Visual acuity on initial presentation was 20/25 + 1 in the affected eye, with minimal CME and no optic disc drusen observed. She was otherwise healthy, without vascular risk factors. The patient's detailed medical history was unremarkable for hypertension, hyperlipidemia, or diabetes; she had a normal BMI and was a non-smoker. She did not use the oral contraceptive pill. Medication history was remarkable for oral minoxidil (0.5 mg nightly), taken for hair loss for 1 year preceding presentation with CRVO. A comprehensive hypercoagulability workup revealed no causative factor, with normal or negative results for polycythemia vera, multiple myeloma, antiphospholipid syndrome, Leiden factor V, activated protein C resistance, hyperhomocysteinemia, protein C and protein S deficiency, antithrombin III mutation, prothrombin mutation, as well as syphilis, and sarcoidosis (online suppl. Table 1). Given the absence of other causative factors, an adverse drug reaction to minoxidil was suspected. Minoxidil was therefore discontinued at the initial visit. The patient opted for expectant management. CME volume increased at 2-week follow-up, then gradually improved beginning at 4 weeks (Fig. 2). Complete resolution of CRVO manifestation and return of 20/20 visual acuity were observed at 7 weeks and sustained at 10 weeks follow-up.

Discussion

We present a unique case of a 34-year-old otherwise healthy woman who developed CRVO while taking minoxidil for hair loss. A complete workup revealed no other potential causative agent. She was managed conservatively with discontinuation of minoxidil and close follow-up, leading to complete resolution of the CRVO and restoration of visual acuity and retinal anatomy. While the exact pathophysiological mechanisms underlying CRVO in this patient remain unclear, the temporal association with the use of minoxidil suggests a potential role for the medication in its development.

Minoxidil is an arteriolar vasodilator initially developed as an antihypertensive agent, which was found to cause hypertrichosis and is now used for the treatment of a variety of hair loss conditions [11]. Minoxidil is known to have off-target effects when taken orally [12] and may have contributed to the development of CRVO by altering retinal circulation. Though not well studied, minoxidil is not thought to directly alter coagulability or increase the risk of large vessel thrombosis and occlusion [13, 14]. However, minoxidil has been demonstrated in

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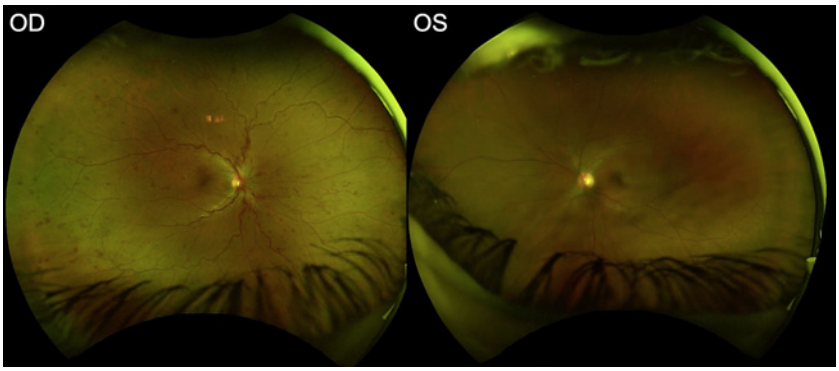

Fig. 1. Fundus images at initial presentation demonstrate right-sided CRVO.

animal studies to significantly reduce retinal microcirculation [15]. There is also a reported case of fetal malformation with abnormal capillary angiogenesis associated with minoxidil use [16]. Minoxidil is known to induce VEGF in multiple cell types within the hair follicle [17, 18]. Off-target induction of VEGF may alter angiogenic signaling in the retina, resulting in capillary rearrangement. This may lead to compromised vascular supply to the retinal vessels, thereby increasing the risk of thrombosis. Therefore, oral minoxidil may have the off-target effect of reducing retinal microcirculation, potentially leading to vascular occlusion, as in the present case.

In agreement with this hypothesis, topical minoxidil has been previously implicated in retinal vascular diseases in otherwise healthy young patients. These case studies reported (1) a 21-year-old male with a 3-year history of topical 5% minoxidil for hair loss, manifesting with retinal artery occlusion upon clinical examination [19], and (2) a 42-year-old male with a 1-year history of topical 5% minoxidil at two-fold normal dose for hair loss, manifesting with NAION [20]. In these cases, reduced retinal microcirculation may have caused compromised vascular supply to the retinal arteries, increasing thrombosis risk, or vascular supply to the optic nerve, respectively. Similar to the present case, a detailed workup revealed no traditional predisposing factors for the respective diseases, suggesting minoxidil may have been the causative agent.

Central serous chorioretinopathy has also been reported in association with topical minoxidil use [21, 22]. This is proposed to occur through increased choroidal and retinal vascular vessel permeability secondary to increased sympathetic activity, increased VEGF, and potential direct effects on ion and fluid balance [21, 22]. Similarly, increased vascular permeability may have contributed to CME in the present case. Higher doses and longer duration of topical minoxidil were implicated in patients with non-arteritic anterior ischemic optic neuropathy [20] and central serous chorioretinopathy [21], and gradual spontaneous recovery was observed in all cases following dose lowering or drug cessation.

Despite resolution of CRVO upon cessation of minoxidil (positive dechallenge) suggesting a possible causative relationship, we cannot exclude that CRVO may have resolved without medication cessation. Younger patients with CRVO require less intervention on average, and spontaneous resolution can occur [6, 23]. It is also possible that underlying hormonal imbalances that may have contributed to female pattern hair loss in this patient also played a role in the development of CRVO. This mechanism was thought to explain CRVO pathophysiology in a young woman with polycystic ovarian syndrome [24]. However, high androgen levels appear to be associated with retinal artery, but not vein, occlusion [25]. Moreover, the patient in the present case had isolated hair loss without other signs and symptoms of endocrine pathology.

This case highlights an atypical presentation of CRVO in a young healthy patient without known vascular risk factors taking minoxidil for hair loss. CRVO in this age-group is uncommon.

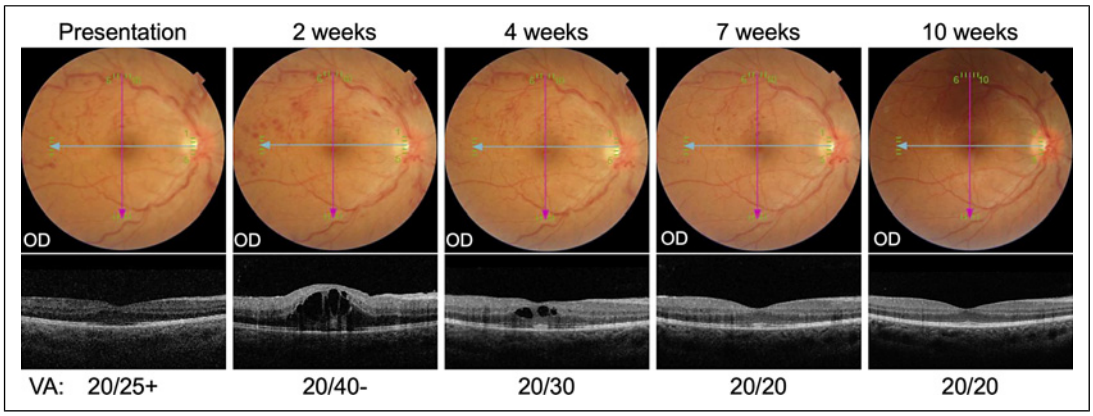

Fig. 2. Fundus images and optical coherence tomography (OCT) demonstrating temporal course of CRVO and CME.

When it does occur, it is more often associated with non-traditional risk factors, and in some cases no cause can be found [6]. Though further evidence is needed to confirm the relationship between minoxidil and retinal vascular pathology, previous reports support this association, and pre-clinical models provide a plausible mechanism through altered microvascular circulation. Given the relative likelihood of uncovering risk factors with impact on systemic health, a comprehensive workup is recommended in young patients with CRVO [6, 26]. This case emphasizes the importance of thorough medication histories and the consideration of ADEs in the evaluation and management of CRVO, particularly in young patients without traditional risk factors.

Statement of Ethics

Written informed consent was obtained from the patient for publication of the details of their medical case and accompanying images. Research ethics approval was not required for this paper as per University of Toronto Research Ethics Board. The study complies with the guidelines for human studies and was conducted in accordance with the World Health Organization Declaration of Helsinki.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Lauren Pickel contributed to conception and design, preparation of the manuscript, and final approval of the manuscript. Patrick Xiang Ji and Amr Abdelazim contributed to the preparation and final approval of the manuscript. Nirojini Sivachandran contributed to conception and design, data collection, critical revisions, and final approval of the manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material files. Further inquiries can be directed to the corresponding author.

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