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Acute serous and hemorrhagic choroidal effusion associated with topical dorzolamide therapy

Abdulla Shaheen [a], Sara Schultis [a], Maria Magraner [a], Zelia M. Correa [a,b], Nicolas A. Yannuzzi [a], David S. Greenfield [a,*]

[a] Department of Ophthalmology, Bascom Palmer Eye Institute, Miller School of Medicine, University of Miami, Miami, FL, USA
[b] Sylvester Comprehensive Cancer Center, And Interdisciplinary Stem Cell Institute, Miller School of Medicine, University of Miami, Miami, FL, USA

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ABSTRACT

Purpose: To report a case of acute onset unilateral hemorrhagic and serous choroidal effusion associated with dorzolamide administration and antiplatelet use that recurred in a patient who experienced a dorzolamide-induced choroidal effusion ten years prior to presentation.

Observations: A 78-year-old male with a history of POAG in both eyes presented with sudden onset decreased vision and flashes of light in the left eye two days after escalating from timolol maleate 0.5% twice daily in both eyes to fixed combination dorzolamide-timolol 22.3–6.8 mg/mL twice daily in both eyes. Systemic medication included daily aspirin 81 mg for primary prevention of cardiovascular disease. Dilated fundus examination and B-scan ultrasound of the left eye revealed a hemorrhagic choroidal effusion in the nasal retinal periphery and low lying serous choroidal effusion in the temporal periphery. Complete resolution of the choroidal detachment was achieved in four days following prompt cessation of dorzolamide, and treatment with topical prednisolone acetate 1% four times daily and atropine 1% two times daily.

Conclusions and importance: Topical dorzolamide may induce an idiosyncratic reaction leading to serous and hemorrhagic choroidal effusion, which can be exacerbated by antiplatelet use. Prompt recognition and management of drug-induced choroidal effusion can lead to improved visual outcomes and prevent long-term sequelae.

1. Introduction

Dorzolamide, a sulfonamide-derived carbonic anhydrase inhibitor (CAI), is a commonly used medication to lower intraocular pressure in patients with glaucoma and ocular hypertension. The mechanism of action involves suppression of aqueous humor production by inhibition of carbonic anhydrase isoenzyme II found on the ciliary body epithelium which reduces bicarbonate ion formation, thus reducing fluid transport. While topical CAIs are generally safe and effective, localized ocular adverse reactions may occur which include stinging, corneal superficial punctate epitheliopathy, and metallic taste disturbance. In contrast, oral CAIs are commonly associated with systemic side effects such as fatigue, depression, paresthesia, gastrointestinal distress, hypokalemia, aplastic anemia, and nephrolithiasis. Previous studies have reported sporadic ocular adverse effects with systemic CAI administration including ciliary body edema and choroidal effusion.[1,2] However, such cases associated with topical CAI use are rare. Herein, we report a case of acute onset unilateral hemorrhagic and serous choroidal effusion associated with dorzolamide administration and antiplatelet use that recurred in a patient who experienced a dorzolamide-induced choroidal effusion ten years prior to presentation.

2. Case report

A 78-year-old Caucasian male with primary open angle glaucoma (POAG) in both eyes and pseudophakia in the left eye presented with sudden onset decreased vision and flashes of light in the left eye over the course of 2 days. The patient was using netarsudil 0.02% daily in the left eye and had recently escalated from timolol maleate 0.5% twice daily in both eyes to fixed combination dorzolamide-timolol 22.3–6.8 mg/mL twice daily in both eyes for uncontrolled intraocular pressure (IOP) noted two days prior to presentation. There were numerous past adverse reactions to anti-glaucoma medication including latanoprostene bunod 0.024% (iridocyclitis), brimonidine tartrate 0.2% (ocular hyperemia),

* Corresponding author. Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, 7101 Fairway Dr, Palm Beach Gardens, FL, 33418, USA.
E-mail address: d.greenfield@med.miami.edu (D.S. Greenfield).

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and systemic acetazolamide and methazolamide (gastrointestinal upset). Systemic medications consisted of daily aspirin 81 mg for primary prevention of cardiovascular disease, and hydrochlorothiazide 12.5 mg, and telmisartan 20 mg (for hypertension). On examination the IOP was 9 mmHg in the right eye and 8 mmHg in the left eye. Visual acuity was 20/25–1 OD and 20/20–2 OS corrected (−1.50 SphD OD and plano OS). No myopic shift was noted. Slit lamp examination demonstrated mild nuclear sclerosis OD, a posterior chamber intraocular lens OS, and absence of intraocular inflammation in both eyes. The anterior chambers were deep, angles were open to grade 4 in both eyes. Fundus exam was unremarkable OD. Funduscopic examination OS revealed moderate glaucomatous optic disc cupping, and lobular choroidal detachment in the nasal fundus periphery (Fig. 1). B-scan ultrasound showed a hemorrhagic choroidal effusion in the nasal periphery, and a low lying serous choroidal effusion in the temporal periphery with no retinal detachment or solid lesions present (Fig. 2). Fluorescein angiography with transit in the left eye showed no evidence of a peripheral choroidal neovascular membrane.

The patient was treated with topical prednisone acetate 1% four times daily and atropine sulfate 1% twice daily in the left eye, and cessation of dorzolamide-timolol. Rapid improvement in symptoms, and complete resolution of the choroidal effusion was noted with repeat B scan ultrasonography after four days of therapy. Additional historical information was solicited from the patient and suggested a prior episode of a dorzolamide-induced choroidal effusion in the left eye that occurred 10 years prior to presentation and promptly resolved with cessation of therapy. This was subsequently confirmed after a comprehensive review of medical records obtained from an outside physician. The patient had normal coagulation tests and no personal or family history of blood dyscrasias or eye trauma. The left eye had undergone uncomplicated cataract extraction 18 years prior to presentation; axial length measurements were unavailable.

3. Discussion

The differential diagnosis of choroidal effusion without recent intraocular surgery is broad and includes choroidal melanoma, choroidal metastasis, choroidal hemangioma, central serous chorioretinopathy, idiopathic uveal effusion syndrome, choroiditis, Vogt-Koyanagi-Harada disease, posterior scleritis, central serous retinopathy, hypertension, paraneoplastic syndrome, and peripheral angiomatous retinal gliotic lesions. This case highlights unique and atypical features including a spontaneous choroidal hemorrhage that developed after only two doses of topical CAI administration. Coban et al. reported a case of an 82-year-old patient on warfarin who developed a hemorrhagic choroidal detachment one day after starting a combined preparation of 0.5% timolol maleate and 0.004% travoprost for POAG.[3] Another relevant fact is that our patient had a similar episode of acute-onset dorzolamide-induced choroidal effusion 10 years earlier, thereby confirming this event as a drug-induced idiosynchratic reaction. Such occurrences are characterized by rapid onset uveal edema and inflammation following drug administration, and rapid resolution after cessation of treatment and anti-inflammatory therapy.

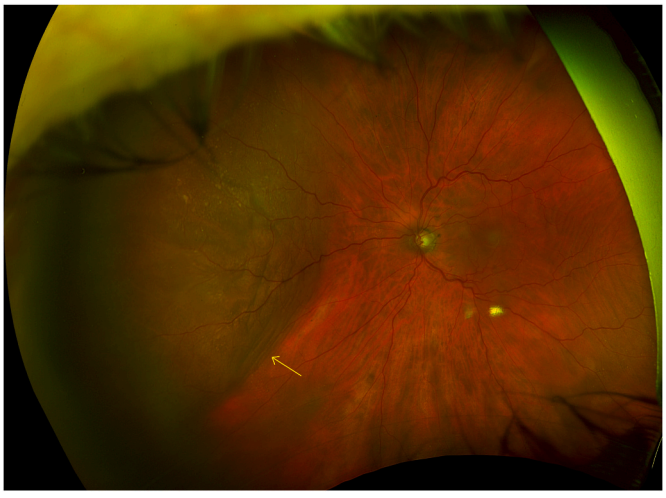

Fig. 1. Wide field fundus photograph of the left eye demonstrates a localized orange-red elevation in the nasal retinal periphery (arrow) consistent with a hemorrhagic choroidal effusion. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

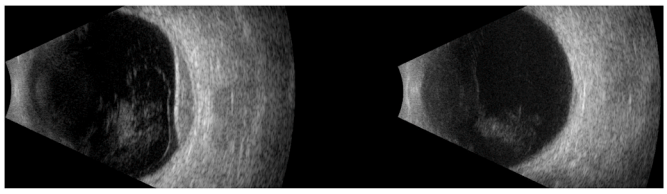

Fig. 2. B-scan ultrasonography image of the left eye shows a subretinal elevation in the nasal retinal periphery with moderate internal reflectivity (left panel) consistent with a hemorrhagic choroidal effusion and 4 days after presentation demonstrates resolution of the hemorrhage (right panel).

Authors have described rare cases of ciliochoroidal effusion in response to oral sulfonamides. Banta and colleagues described a case of bilateral acute angle-closure glaucoma after topiramate therapy with ciliary body effusion, myopic shift and anterior rotation of the lens-iris diaphragm.[4] Prior reports have described choroidal effusion in response to several classes of medications including oral acetazolamide therapy, anti-CD38 monoclonal antibodies (e.g. daratumumab), sulfonamide drugs (e.g. sulfamethoxazole-trimethoprim and zonisamide), anticonvulsants (e.g. topiramate), humanized single-chain antibody fragments (e.g. brolucizumab), and bisphosphonates.[5] Choroidal effusion is extremely rare after topical CAI administration. Goldberg et al. described a case of choroidal effusion in a 76-year-old female with no prior ocular surgery within 12 hours after starting dorzolamide therapy.[6] Davani et al. reported a similar case associated with dorzolamide.[2] Another unique feature in this case is that no choroidal effusion or ocular adverse reaction was observed in response to oral acetazolamide or methazolamide administration, however acute onset of choroidal effusion developed after topical dorzolamide therapy. This suggests that the underlying pathophysiology of sulfonamide-induced choroidal effusion may differ between topical and systemic carbonic anhydrase inhibitors.

Our patient developed a unilateral choroidal effusion despite using dorzolamide in both eyes. Vitreous penetration in the pseudophakic left eye was likely enhanced by the absence of the lens, which may serve as a partial barrier limiting drug dispersion to the vitreous cavity. Increased drug penetration in pseudophakia and aphakia was demonstrated by Kent et al. who examined vitreous levels of topically applied brimonidine tartrate 0.2% in humans and found greater concentrations in aphakic and pseudophakic eyes compared to phakic eyes.[7] We speculate that the use of systemic anti-platelet therapy may have contributed to the onset of choroidal hemorrhage. Our patient had no other associated risk factors such as ocular hypotony (defined as IOP of 5 mmHg or less), physical straining, inflammation, peripheral choroidal neovascular membrane, occult tumor, or recent intraocular surgery. Rapid resolution and excellent visual outcome were achieved with prompt recognition and intervention.

4. Conclusions

Our case displays a recurrent episode of idiosyncratic dorzolamide-induced acute choroidal effusion that occurred in the setting of normal IOP and did not develop in response to oral CAI administration with either acetazolamide or methazolamide. Anti-platelet therapy may

have contributed to the choroidal hemorrhage. Prompt recognition and management of drug-induced choroidal effusion can lead to improved visual outcomes and prevent long-term sequelae.

Patient consent

Consent to publish this case report was obtained from the patient. This report does not contain any personal information that could lead to the identification of the patient.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

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Declaration of competing interest

The authors have no relevant conflicts of interest to disclose with this manuscript.

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None.

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