Multimodal etiology of drug induced angle closure with topical glaucoma therapy

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ABSTRACT

Purpose: We present a case of acute onset of bilateral choroidal effusions leading to angle closure glaucoma attributed to multiple mechanism of actions causing ciliary body and aqueous flow disruption in the setting of topical glaucoma therapy with latanoprost, brimonidine 0.2%, and Brinzolamide 0.1%.

Observation: The patient presented with ocular hypertension in the setting of bilateral choroidal effusions, leading to angle closure without pupillary block. After cessation of the glaucoma drops and starting steroids and cycloplegics, the patient’s symptoms resolved.

Conclusions and importance: This case report highlights the various physiological mechanisms of action that can induce angle closure glaucoma from commonly used topical medications for glaucoma treatment. Thus, a keen awareness is warranted of this idiosyncratic reaction in order to avoid morbidity and long term vision loss.

1. Introduction

Drug induced bilateral angle closure is a well reported phenomenon, especially with sulphamate-substituted compounds, such as topiramate, hydrochlorothiazide, and acetazolamide . Topical brinzolamide, a carbonic anhydride inhibitor, brimonidine, alpha 2 adrenergic receptor agonist, and latanaprost, a prostaglandin analog, are routinely used for the treatment of glaucoma. This case presents a patient with bilateral angle closure, who improves rapidly after cessation of all glaucoma drop therapy. We seek to identify various mechanisms of action of each glaucoma drug taken by our patient that may have lead and compounded to the development of angle closure.

2. Case presentation

A 78 year old female presented to the ophthalmology clinic with acute vision loss and headache. Her past ocular history was significant for pseudophakia OU, dry macular degeneration and open angle glaucoma, for which she had chronically used latanaprost 0.005% QHS OU, and recently prescribed Simbrinza™ (Brimonidine 0.1%/Brinzolamide 0.1%) BID OU. Her medical history was significant for COPD. On examination, her visual acuity was 20/400 OD and 20/400 OS. Pupils were equally reactive and without a relative afferent pupillary defect.

Her IOP was 24 OD and 23 OS. Slit lamp exam showed a quiet anterior chamber but shallow peripherally. Indentation gonioscopy revealed closed angles OU. UBM demonstrated irido-corneal apposition in the setting of 360° choroidal effusions OU (Fig. 1). A manifest refraction revealed a 3 diopter myopic shift. The diagnosis of bilateral secondary acute angle closure secondary to choroidal effusions from brinzolamide was made. As a result, Simbrinza™ was discontinued and brimonidine 0.15% TID OU was added to control her IOP, as well as topical homatropine BID OU.

The following day the patient’s VA had worsened to CF OD and 20/400 OS although IOP improved to 9 OD and 7 OS. There was now 2+ anterior chamber cell OU. The choroidal effusions had enlarged and were now extending over the temporal macula OU (see Fig. 2). Brimonidine and latanoprost were discontinued and the patient was prescribed prednisolone 1% QID OU in addition to her cycloplegia. The patient continued to show improvement over five days as the choroidal effusions resolved and her vision returned to baseline. Examination revealed a deep and quiet anterior chamber with angles open to scleral spur 360° OU. Her latanoprost was restarted and the patient maintained an adequate IOP.

3. Discussion

Our patient presented with acute angle closure, without pupillary
block, in the setting of large choroidal effusions after recently starting a combination of brinzolamide and brimonidine. The differential diagnosis for bilateral choroidal effusions include melanoma, metastasis, hypertensive choroidopathy, chronic hypotony, VKH, aqueous misdirection, posterior scleritis, or posterior uveitis. However, none of these conditions were present in our patient.

We initially hypothesized the choroidal effusions were due to brinzolamide, as it is a carbonic anhydrase inhibitor that shares the same sulfamate moiety as topiramate and acetazolamide, and therefore, has the potential to cause this idiosyncratic reaction. However, the patient had worsening choroidal effusions and subsequently developed anterior uveitis when brimonidine was continued alone. Nevertheless, brinzolamide may still have a residual effect on this idiosyncratic reaction since it had only been stopped for 24 hours, given it has a longer washout period.

Drug-induced uveitis due to brimonidine has been well established but choroidal effusions have not been reported previously. Previous reports have reported other non-sulfamate moiety containing drugs causing secondary bilateral angle closure. Multiple hypothesis have been postulated as to the cause of this idiosyncratic reaction including dysregulation of aqueous flow and inflammation in the ciliary body, which could have been potentiated by the uveitis caused by brimonidine in our patient. Interestingly, the IOP dropped significantly prior to the resolution of choroidal effusions, thought likely due to ciliary body shutdown in the presence of uveitis.

Lastly, the concomitant use of latanoprost in our patient may also have compounded to the rapid enlargement of choroidal effusions. Latanoprost increases aqueous flow into uveo-scleral outflow pathway and could disrupt blood-aqueous barrier in pseudophakic eyes. Previous case report, have shown topical latanoprost as a culprit for choroidal effusions.

Ultimately, the drugs causing this reaction lead to a similar clinical course - the development of choroidal effusions with forward rotation of ciliary processes-iris-lens complex, leading to angle closure without pupillary block and acute myopic shift.

The discontinuation of all glaucoma drops, with the addition of prednisolone and a cycloplegic, led to the rapid resolution of the anterior chamber cell and choroidal effusions. The use of brimonidine in our patient met 7 out of 7 criteria established by Naranjo et al. in order to determine causality of a drug to the reported adverse event. However, a re-challenge with Simbrinza, brimonide or brinzolamide alone was not performed, in order to avoid further morbidity to our patient. This case report highlights multiple mechanisms by which routine glaucoma drops (latanoprost, brinzolamide, and brimonidine) may compound and lead to drug induced bilateral acute angle closure. Physicians must be highly aware of this idiosyncratic reaction and stop all inciting medications to promptly treat the patient.

**Patient consent**

This report does not contain any personal identifying information.

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**Authorship**

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

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**Abbreviations**

- IOP: Intraocular Pressure
- OU: Oculus Uterque - Both eyes
- QHS: Quaque hora somni - Every night
- COPD: Chronic Obstructive Pulmonary Disease
- OD: Oculus Dexter
- OS: Oculus Sinister
- UBM: Ultrasound biomicroscopy
- Va: Visual Acuity
- CF: Count Fingers
- QID: Four times a day
- TID: Three times a day
- BID: Two times a day
- VKH: Vogt-Koyanagi-Harada Disease

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**Fig. 1.** UBM OD, demonstrating irido-corneal apposition in the setting of suprachoroidal fluid (white arrows) with resultant anterior rotation of ciliary processes and closed angle (arrowhead). The curved arrows indicate a shallow peripheral anterior chamber.

**Fig. 2.** Optos fundus photo OD demonstrating temporal choroidal effusion extending into the macula and peripheral nasal choroidal effusions.
Declaration of competing interest

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References

1. Murphy R, Rakir B, O’Brien C, et al. Drug induced bilateral secondary angle-closure glaucoma: a Literature Synthesis. J Glaucoma. 2016;25. e99-e105.
2. Lester M. Brinzolamide ophthalmic suspension: a review of its pharmacology and use in the treatment of open angle glaucoma and ocular hypertension. Clin Ophthalmol. 2008;2(3):517–523.
3. Byles D, Frith P, Salmon J. Anterior uveitis as a side effect of topical brimonidine. Am J Ophthalmol. 2000;130(3):287–291.
4. Nguyen E, Azar F, Papalkar D, McCluskey P. Brimonidine-induced anterior uveitis and conjunctivitis: clinical and histologic features. J Glaucoma. 2008;17(1):40–42.
5. Hsu Cheng-Ru, Chen Yi-Hao, Tai Ming-Cheng, Lu Da-Wen. Sumatriptan-induced angle-closure glaucoma. Medicine. 2017;96. 10.1097/MD.0000000000006953.
6. Chen EL, Kang KB. Acute onset of blurry vision in a young man. JAMA Ophthalmol. 2019 Aug 22. https://doi.org/10.1001/jamaophthalmol.2019.3058.
7. Pirmohamed M, Naishitt DJ, Gordon F, et al. The danger hypothesis - potential role in idiosyncratic drug reactions. Toxicology. 2002;181:55–63.
8. Miyake, et al. Latanoprost accelerates disruption of blood-aqueous barrier and the incidence of angiographic cystoid macular edema in early postoperative pseudophakias. Arch Ophthalmol. 1999;117:24–30.
9. Rowe, et al. Ciliochoroidal effusion induced by topical latanoprost in a patient with Sturge-Weber syndrome. Am J Ophthalmol. 1997;124:683–685. Sakai et al. Jpn J Ophthalmol 2002;46:553-555.
10. Naranjo C, Busto D, Sellers E, et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther. 1981;30:239–245.