Grand Rounds
A 53-year-old woman with a severe headache, bilateral eye pain, blurred vision, and photophobia

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History
A 53-year-old woman presented to our emergency department with a severe headache, bilateral eye pain, blurred vision and photophobia. She started oral topiramate 25 mg daily for migraine prophylaxis the evening before. Symptoms immediately started upon awakening, and she was brought to our emergency department. She reported a history of allergy to corticosteroids and gastric intolerance to oral non-steroidal anti-inflammatory drugs (NSAIDs).

Examination
On arrival, her visual acuity was counting fingers in both eyes. Intraocular pressure (IOP) measured 45 mm Hg in the right eye and 49 mm Hg in the left eye by applanation tonometry. She had fixed pupils, conjunctival chemosis and injection, moderate corneal edema, markedly shallow anterior chambers with 360° iridocorneal touch peripherally and a 4.00 D myopic shift in both eyes. Gonioscopy revealed closed angles bilaterally with a flat iris configuration. The cup/disc ratio was 0.2 in both eyes.

Ancillary Testing
B-scan ultrasonography showed uveal effusions in both eyes and ultrasound biomicroscopy showed ciliary body swelling and anterior displacement of the lens-iris diaphragm (Figure 1).

Treatment
She was treated with intravenous mannitol (100 g in 500 ml), oral acetazolamide (500 mg), and topical brimonidine tartrate 0.2%, timolol maleate 0.5%, and prednisolone acetate 1% in both eyes. Ninety minutes after mannitol administration, the IOP was 31 mm Hg in the right eye and 33 mm Hg in the left eye. Four hours later she was discharged with a prescription for topical brimonidine tartrate 0.2% twice daily, timolol maleate 0.5% twice daily, and prednisolone acetate 1% four times daily in both eyes. She was experiencing no major discomfort. The IOP on discharge was 27 mm Hg in the right eye and 29 mm Hg in the left.

Four days later visual acuity had improved to 20/30 in both eyes. The IOP was 16 mm Hg in the right eye and 17 mm Hg in the left, and the anterior chambers were deeper, with gonioscopy showing angle structures bilaterally. B-scan and ultrasound biomicroscopy revealed improvement of the uveal effusions and ciliary body swelling, respectively (Figure 2). Nine days after the episode the visual acuity returned to 20/20 in both eyes, the IOP was 13 mm Hg in the right eye and 14 mm Hg in the left eye, and the uveal effusion and ciliary body swelling had resolved completely (Figures 3–4).

Differential Diagnosis
Primary angle-closure glaucoma (PACG) with pupillary block is the most common form of PACG and occurs in eyes in which apposition of the iris pupil against the crystalline lens or intraocular lens impedes the passage of aqueous humor from the posterior chamber to the anterior chamber. When the pressure in the posterior chamber surpasses that in the anterior chamber, the peripheral iris is pushed forward (iris bombé), occluding the iridocorneal angle. The frequency of PACG increases with age and is 2–4 times more common in women. In our case, pupillary block was absent.

Secondary angle-closure glaucoma with pupillary block may be associated with the following etiologies:

Published August 28, 2011.
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doi:10.5693/djo.03.2011.05.002
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The authors received no public or private financial support and have no conflicts to disclose.
The presence of posterior synechiae following ocular inflammation (eg, uveitis), trauma, or posterior lens implantation

- Use of miotics, which relax the zonules, producing a forward shift of the lens-iris diaphragm
- Cataract surgery with anterior chamber lens implantation (when iridectomy is not patent)
- Surgical aphakia, where the block is due to the apposition of the anterior hyaloid face to the iris pupil
- Pars plana vitrectomy with intravitreal silicone oil or gas

In our case there were no posterior synechiae, and the history was negative for use of miotics and eye surgery.

Secondary angle-closure glaucoma without pupillary block can be due to anterior pulling mechanisms or posterior pushing mechanisms. Anterior pulling mechanisms include peripheral anterior synechiae, neovascular glaucoma, iridocorneal endothelial syndrome, aniridia, and epithelial downgrowth. Posterior pushing mechanisms include malignant glaucoma, suprachoroidal hemorrhage, cysts and tumor of the ciliary body or iris, swelling and anterior rotation of the ciliary body and choroidal effusion.

PACG without pupillary block is usually due to a plateau iris configuration. Ultrasound biomicroscopy demonstrates anterior rotation of the ciliary body and ciliary processes that push the peripheral iris close to the angle wall.

Diagnosis and Discussion

In this case, ultrasound biomicroscopy and B-mode echography as well as the patient’s history made the diagnosis of secondary angle closure glaucoma without pupillary block due to intake oral topiramate (Figures 1–4).

Topiramate, a widely used anti-epileptic sulfamate-derived drug, has recently gained widespread use for migraine prophylaxis. It is also used to manage depression and neuropathic pain; off-label use as a weight-reduction and bipolar disorder agent has also become more widespread. Uveal effusion and secondary angle-closure glaucoma associated with topiramate use was first reported in July 2001 by Banta et al. Since then several case reports have shown evidence of ciliary process inflammation and forward displacement of the lens-iris diaphragm with secondary angle closure and myopia related to topiramate therapy. Almost always bilateral, angle-closure glaucoma has been reported in patients with ages varying from 3 to 70 years and with doses from 50 mg or less to 100 mg or more. Onset may occur within hours; the majority of cases present in the first two weeks of therapy. Other reported ocular effects include scleritis, blepharospasm, myokymia, ocu- logyric crisis, nystagmus, and diplopia associated with dosages of at least 200 to 400 mg per day. Topiramate is quickly absorbed after oral use, has a half-life of 24 hours and is rapidly excreted in urine. The exact mechanism of action is unknown, but research has shown that the drug blocks sodium channels, hyperpolarizes potassium currents, activates some subtypes of the GABA-A receptors and weakly inhibits carbonic anhydrase. Ultrasound technology has shown that angle-closure glaucoma can be induced when edema of the ciliary body

![Image](image-url)
leads to relaxation of the lens zonules, allowing the lens to thicken.\textsuperscript{7,8} Suprachoroidal effusion, frequently present, and simultaneous anterolateral rotation of the ciliary body leads to anterior displacement of the iris-lens diaphragm, resulting in induced myopia and secondary anterior chamber shallowing with consequent angle closure.

Uveal effusions as well as acute myopia have been reported in association with several sulfa-derived drugs,
including acetazolamide, indapamide, chlorothiazide, promethazine, spironolactone and antibacterial sulfa preparations.\textsuperscript{7,9–13}

Treatment of this condition requires IOP-lowering drugs and discontinuation of the sulfa-derived drug. Topical atropine 1\% may lower IOP by causing retraction of the ciliary process thereby reducing lens thickness.\textsuperscript{14} Methylprednisolone, possibly because of its stabilizing effect of the blood-retina barrier, may accelerate the resolution of the choroidal effusion.\textsuperscript{8} Miotics are contraindicated in these cases since they induce contraction, mainly of the longitudinal portion of the ciliary muscle, which in turn can lead to further anterior displacement of the lens-iris diaphragm and increased angle narrowing.\textsuperscript{7,10,15} Peripheral iridotomies are also ineffective because this entity occurs without pupillary block.\textsuperscript{2,16} In our case, topiramate was discontinued and hypotensive medication and topical prednisone 1\% were administered; we did not administer an oral corticosteroid since the patient had a history of corticosteroid allergy. Her condition resolved rapidly, probably because she had had a single, low dose (25 mg) of topiramate.

Her allergy to corticosteroid shows some idiosyncrasy for adverse reactions to drugs. Although there have been reports of bilateral angle-closure glaucoma after oral acetazolamide apparently by the same mechanism, we chose to administer the hypotensive agent to our patient since these cases have not been reported after a single dose of acetazolamide but only after a sensitizing dose in the past or repeated dosing.

References