Unexpected outcome (positive or negative) including adverse drug reactions

Topiramate-induced refractive change and angle closure glaucoma and its ultrasound biomicroscopy findings

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Summary

Topiramate, a sulpha-based medication used in the treatment of migraine, has been documented as causing choroidal effusions, transient myopia and acute secondary angle closure glaucoma. We would like to report a case demonstrating these adverse effects and underscore the utility of ultrasound biomicroscopy in diagnosis and management.

BACKGROUND

Topiramate is a sulpha-based medication used in the treatment of migraine, epilepsy and numerous other off-label conditions (such as bipolar disorder, neuropathic pain, depression and weight loss). Adverse reactions have been reported in up to 3% of patients¹ and the occurrence of choroidal effusions, transient myopia and bilateral secondary angle closure glaucoma has been previously documented in the literature.^{2–5} Ultrasound biomicroscopy (UBM), which provides high-frequency detailed imaging of the anterior and middle segment structures of the eye, is a valuable technology in the diagnosis and management of these adverse effects.

CASE PRESENTATION

A 36-year-old woman with no ocular history and medical history significant for migraine presented with 2 days of bilateral red, painful eyes and acute onset of vision loss. She had been initiated on topiramate 25 mg daily 7 days prior. Examination was significant for myopic shift, with best-corrected visual acuity of 20/30 with -6.00 to 0.50×95 right (OD) and 20/40 with -5.50 to 1.50×75 left (OS). (Refraction 1 year prior was plano OD and -1.00×80 OS.) Intraocular pressures (IOPs) measured via Goldman tonometry were 24 OD and 25 OS. On anterior segment examination, bilateral conjunctival chemosis was present with narrow angles on slit-lamp examination. Gonioscopy revealed appositional angle closure bilaterally. Optic nerve examination revealed 0.2 cups bilaterally without disc haemorrhages. Indirect ophthalmoscopy revealed choroidal effusions bilaterally, which was confirmed by B-scan ultrasonography. UBM revealed bilateral supraciliary effusions (figures 1 and 2).

TREATMENT

Topiramate was immediately discontinued. Topical atropine 1% was initiated two times per day for 7 days, together with oral prednisone 60 mg, tapered rapidly over 1 week.

OUTCOME AND FOLLOW-UP

Within 24 h, the patient noted decreased head and eye pain. Best-corrected visual acuity improved to 20/25 with

-3.00 s OD and 20/30 with -3.75 to 1.00×90 OS. IOPs were 10 OD and 12 OS. Conjunctival chemosis had improved. On gonioscopy, the angle was 30° , and the iris inserted into the ciliary body band in all four quadrants bilaterally. Peripheral anterior synechia were absent. Within 2 weeks, the patient returned to baseline, off all medications. UBM was never repeated given the return of refraction to baseline and improvement of the angle on clinical examination.

DISCUSSION

Topiramate-induced angle closure is usually bilateral and occurs in the absence of pupillary block. It is due to cilio-choroidal effusions causing anterior rotation of the ciliary body and anterior displacement of the lens-iris diaphragm, occluding the angle.⁶ It has been theorised that topiramate (or other sulpha medications) can disrupt the ocular blood brain barrier through an inflammatory mechanism, causing an increase in the protein content of the cerebrospinal fluid. When large amounts of protein leak into the ciliochoroidal extravascular space, the osmotic pressure difference allows for choroidal expansion. The

Figure 1 Ultrasound biomicroscopy of the right eye showing appositional closure of nasal angle with supraciliary effusion.

Figure 2 Ultrasound biomicroscopy of the left eye illustrating occluded angle with supraciliary effusion of nasal angle.

enlargement of the choroid displaces the lens-iris diaphragm forward.⁷ This anterior rotation of anatomic structures induces a myopic shift, causing bilateral blurring of vision. In addition, ciliary body swelling allows for relaxation of the zonules, causing thickening of the lens. This also contributes to the forward displacement of anterior segment structures.

UBM is a valuable tool in diagnosis of this condition as it is able to provide high-resolution (35 mHz) imaging of middle and anterior chamber anatomy and the angle. Gonioscopy can only be used to identify the closure of the angle and although B-scan can occasionally identify posterior segment or ciliary body structures creating forward pressure, the 10 mHz probe does not provide adequate visualisation of the anterior chamber. UBM is the optimal technology for visualising the anterior chamber structures and their relative anatomy and positioning. It is the only one of these three modalities that can confirm the presence of secondary angle closure and diagnose the aetiology as choroidal effusions.⁸ We therefore recommend that any suspected cases of topiramate or other sulpha medication-induced secondary angle closure be evaluated using UBM.

The ability to differentiate between varying aetiologies of angle closure glaucoma is crucial to initiating appropriate management; in this case, confirmation of diagnosis via UBM directed therapy. Treatment begins with the immediate discontinuation of the offending agent (topiramate or other sulpha medication) and the subsequent administration of ocular hypotensives and cycloplegic agents. Importantly, cycloplegics function to tighten the zonules and displace the lens-iris diaphragm posteriorly. Miotics such as pilocarpine, the gold standard for the treatment of primary angle closure glaucoma, are actually contraindicated in the case of choroidal effusions—contraction of the ciliary body can cause additional zonular relaxation and further forward displacement the lens-iris diaphragm.⁹ Oral steroids, mannitol, choroidal drainage and laser peripheral iridoplasty have also been described in

the treatment of acute angle closure.^{1–10} However, in secondary angle closure due to choroidal effusions, miotics and laser iridectomy are not indicated, as pupillary block is not the underlying pathophysiology.¹⁰

Finally, sulpha-based medications other than topiramate have been known to cause similar phenomena and effected patients may experience cross-reactivity to these other medications.⁹ Therefore, the confirmation of topiramate-induced choroidal effusions should serve as a warning—even in those patients without appositional angle closure—to avoid both the offending agent and all sulpha-based medications in the future.

Learning points

- ▶ Topiramate, a sulpha-based medication used in the treatment of migraine, has been documented as causing choroidal effusions, transient myopia and acute secondary angle closure glaucoma.
- ▶ Ultrasound biomicroscopy is a valuable tool in diagnosis and management of topiramate-induced refractive change and angle closure glaucoma.
- ▶ The treatment of angle closure and choroidal effusions secondary to topiramate differs from the treatment of primary angle closure glaucoma, as miotics such as pilocarpine are contraindicated.
- ▶ Patients who experience acute angle closure glaucoma secondary to topiramate should avoid it as well as all sulpha-based medications in the future.

Competing interests None.

Patient consent Obtained.

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