Outcomes of topiramate induced secondary bilateral angle closure glaucoma management – Case series

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Abstract

Purpose : *To describe a case series of bilateral acute angle-closure glaucoma due to use of topiramate therapy*

Cases report: *Three cases were presented with blurred vision, severe nausea and headache after initiation of topiramate oral intake due to migraine and weight loss. Best corrected visual acuity were markedly reduce with very high Intraocular pressure in both eyes of three cases. Bilateral conjunctival chemosis, shallow anterior chamber and mild to moderate corneal edema were observed. Topiramate therapy was discontinued. Topical therapy was initiated in both eyes with Prednisolone, cycloplegic and anti glaucoma medications.*

Results: *Pain was reduced with improvement of visual acuity after starting of treatment. Intraocular pressure was also reduced to normal level after 2- 7 days. No residual effects were found in any cases.*

Conclusion: *Topiramate therapy may be associated with myopic shift with secondary bilateral angle closure glaucoma due to ciliochoroidal effusion. So patient must be counseled and monitored for development of angle closure to prevent permanent loss of vision.*

Keywords: *Topiramate, Angle-closure Glaucoma, gonioscopy, ultrasound biomicroscopy, anterior segment optical coherence tomography, Ciliochoroidal effusion.*

Introduction

Topiramate, a sulfamate derivative drug, is primarily used in the treatment of epilepsy, however, it has also demonstrated efficacy in the treatment of migraine, depression, bipolar disorders, neuropathic pain, posttraumatic stress disorder, postherpetic neuropathy, idiopathic intracranial hypertension, and as "off-label application" it has been used for weight loss, adjunctive therapy for alcoholism and nicotine cessation[1,2].

The ocular adverse reaction consists of peripheral ciliochoroidal effusion with ciliary body edema and anterior rotation of the ciliary body. There is an anterior shifting of the lens iris diaphragm shallowing the anterior chamber in the periphery causing the acute angle closure glaucoma without pupillary block. The exact mechanism of the ciliochoroidal effusion is unknown. It is believed to be an idiosyncratic adverse reaction to the drug[3].

The most common complication to be ciliochoroidal effusion syndrome. The conditions that fall under this umbrella include transient topiramate-induced myopic shift and topiramate induced angle closure. Patients with topiramate

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induced angle closure typically present with bilateral blurry vision, headache, nausea and ocular pain[4]. The current standard of treatment is to stop topiramate immediately, and treat with a combination of topical ocular hypotensive agents, cycloplegics, topical and systemic steroids. Recent evidence suggests that intravenous methylprednisone is used very effectively to control intraocular pressure in cases of topiramate induced angle closure refractive to these conventional treatments[4,5].

The incidence of permanent vision loss in topiramate associated bilateral acute angle closure glaucoma has been reported to be 8.1%[6]. Topiramate-induced angle closure may present in a variety of ways; in terms of duration, dose and clinical picture, visual and anatomical outcomes[5,6]. Delayed recognition may result in iris atrophy and cataract[7].

We report a series of three cases of topiramate induced angle closure glaucoma highlighting the importance of increasing the awareness of this rare, idiosyncratic adverse effect of topiramate and the need for timely intervention to avoid irreversible visual loss.

Case series

Case 1

A 38 year old man took a single dose of 50 mg topiramate four days prior to presentation which was prescribed for weight loss. Distance corrected vision was right: count fingers; left: 6/36. A new myopic shift of 2.50 D was noted. Both corneas were oedematous, angles were completely closed on gonioscopy and intraocular pressures measured 62 mmHg bilaterally. Suspicious of topiramate induced angle closure, the patient was treated with timolol 0.5%/brimonidine 0.2%, prednisolone 1.0% six times daily, atropine 1.0% drops three times daily and a 1 g/kg dose of intravenous mannitol. Optic discs were pink with cup–disc ratios of 0.4, peripheral choroidal effusions were seen and confirmed on a Bscan. Oral acetazolamide 250 mg four times daily were also started. By after 6 hours, his intraocular pressures dropped to 28 mmHg bilaterally. He was discharged with intraocular pressures of 22 mmHg bilaterally on oral acetazolamide 250 mg four times daily and topical treatment as above. In the following day, intraocular pressures were 11 mmHg (right) and 15 mmHg (left). Gradually over several weeks, his myopic shift resolved and his distance vision normalised to 6/6 in each eye.

Case 2

A 42 year old woman presented acutely with blurry vision bilaterally, followed by headache and nausea. She had been on topiramate the week prior to presentation for the prevention of migraines. On examination, she had reduced distance vision of right 6/120, left 6/48. Both anterior chambers were shallow and quiet. Gonioscopy revealed 360 degrees closed angles bilaterally with fixed, mid-dilated pupils and intraocular pressures of 72 mmHg, 70 mmHg, right and left, respectively. Over concerns regarding TiAC, topiramate was stopped immediately. She was started on oral acetazolamide 500 mg, timolol 0.5%/brimonidine 0.2%, and prednisolone 1.0% topical drops. She was trialled on intravenous mannitol 1 g/kg but intraocular pressures remained elevated (right 66 mmHg, left 60 mmHg) post-infusion. She was then given two doses of 500 mg intravenous methylprednisolone with a good reduction of intraocular pressures the following morning (right 34 mmHg, left 31 mmHg) and was symptomatically better. Her B-scan showed ciliary effusions bilaterally. The third dose of intravenous methylprednisolone returned her intraocular pressures to normal. She was discharged on oral prednisone in conjunction with topical prednisolone 1.0%, timolol 0.5%/brominidine 0.2% and atropine 1.0% eye drops. Treatment was tapered over the course of a month with final acuities of 6/9 corrected in both eyes.

Case 3

A 33-year-old woman presented to her ophthalmologist 2 days after sudden onset of pain, redness and decreased vision in both eyes. She was a known case of migraine and was on oral topiramate 50 mg daily for 9 days, prior to the onset of ocular symptoms. Her intraocular

pressure (IOP) recorded was 50 mmHg in the right eye and 38 mmHg in the left eye, which lead to the diagnosis of acute primary angle closure. She was treated with intravenous mannitol, oral acetazolamide, topical 2% pilocarpine, brimodine and topical prednisolone. On presentation, nearly 72 hours after onset of symptoms, visual acuity was a finger count at 1 meter and 2 meters in the right and left eye respectively. Manifest refraction could not be estimated due to central corneal oedema. Slit-lamp examination showed bilateral conjunctival congestion, corneal oedema with Descemet's folds, shallow anterior chambers with irido-corneal touch, mid-dilated and sluggishly reacting pupils. The IOP was 28 mmHg in the right eye and 18 mmHg in left eye. Bilaterally, no angle structures were identified even with indentation gonioscopy. Ultrasound biomicroscopy revealed nearly flat anterior chamber with supra-choroidal effusion and anterior rotation of ciliary processes in both eyes. As a result, a diagnosis of secondary angle closure was made. Topiramate and pilocarpine were discontinued; and topical prednisolone was continued in addition to atropine 1% which normalized the IOP with re-formation of the anterior chamber and clearing of corneal oedema. Gonioscopy revealed bilaterally open angles without any peripheral anterior synechiae. Slit-lamp examination showed pigment dispersion on corneal endothelium, sectoral atrophy of iris and cataract changes. Best corrected distant visual acuity was 6/6p in both eyes. The IOP was 10 mmHg in both eyes without any anti-glaucoma medication.

Fig-01: Secondary acute angle closure on anterior segment optical coherence tomography due to topiramate therapy.

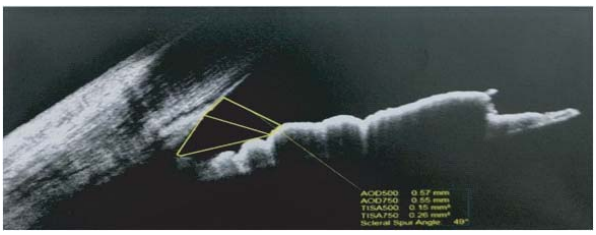

Fig-02: Anterior segment optical coherence tomography showing resolving phase of angle closure due to topiramate therapy

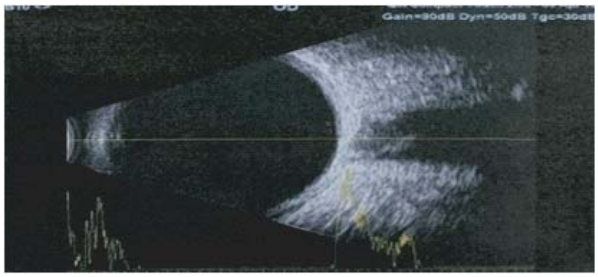

Fig-03: Bscan ultrasonography showing ciliochoroidal effusion

Discussion

Topiramate associated acute angle closure can mimic pupillary block angle closure, and clinical differentiation between the two is very important. Secondary acute angle closure, related to topiramate, occurs without papillary block and can also affect eyes with open angles[8]. The mechanism understood to date, underlying the myopia and secondary angle closure, is choroidal effusion and forward rotation of the iris-lens diaphragm[9]. Unlike papillary block, this condition is not aborted with laser peripheral iridotomy. Diagnostic clues in the clinical examination include history of topiramate use, bilateral presentation and preservation of pupillary reaction.

The principal step in appropriate management is making a correct diagnosis. We believe that a prompt diagnosis and treatment at the time of the patient's presentation to the emergency department might have allowed faster resolution of the episode of angle closure in our cases. The ocular adverse reaction consists of peripheral ciliochoroidal effusion with ciliary body edema

and anterior rotation of the ciliary body. There is an anterior shifting of the lens iris diaphragm shallowing the anterior chamber in the periphery, causing the angle closure glaucoma without pupillary block.

The treatment of topiramate induced angle closure glaucoma is tailored to the severity of IOP elevation[10]. The first step is immediate discontinuation of topiramate. This step combined with topical hypotensive medications and cycloplegics is most often sufficient to reduce the IOP. In a large retrospective case series, the typical course of IOP normalization was reported to be within hours to days after cessation of topiramate and initiating of conventional IOP reducing therapy[11].

Laser peripheral iridotomy used in some cases reported in literature has not been uniformly effective in relieving the secondary angle closure and should be reserved for cases where the above treatment fails. Iridotomy may not be advisable as acute glaucoma is caused by uveal effusion without pupillary block; when performed, it can aggravate glaucoma by pushing forward iris and lens.

Miotics and iridotomies are of no use in this entity. Physicians prescribing topiramate need to be aware of this idiosyncratic reaction for the first 2 weeks or if an increase in the dose is needed. Suspect this entity when there is a myopic shift and acute angle closure glaucoma in a patient on topiramate.

There is a report of a case with lens-corneal touch that did not improve with topical and systemic treatment, they did a choroidal drainage with resolution of the acute angle closure glaucoma. In this case the patient was treated initially with pilocarpine that worsened the clinical picture. Miotics are not helpful in this entity[12]. Ecography and anterior segment optical coherence tomography helps us to rule out intraocular tumors or bilateral iris cyst in the periphery that could also produce a bilateral acute angle closure glaucoma.

There have been a number of theories as to the mechanism responsible for propagating topiramate induce angle closure. There is a pressure gradient driving aqueous flow from the posterior chamber to the anterior chamber and resistance is exerted on this system by the iris– lens diaphragm. Quigley et al.[13] suggested a mechanism for angle closure relating to choroidal expansion in which choroidal oedema exerts a retrolenticular pressure, thereby moving the lens forward in the eye and diminishing the depth of the anterior chamber. This alteration in fluid dynamics could increase the predisposition for angle closure. Applying this mechanism to topiramate induced angle closure, Issum et al.[14] attributed increased vascular permeability of the ciliochoroidal capillaries as the cause of ciliochoroidal effusion. This localised ciliary body oedema then causes anterior rotation of ciliary processes, thereby narrowing the ciliary sulcus and displacing the iris–lens diaphragm anteriorly, causing acute angle closure[15,16]. Additionally, oedema of ciliary processes reduces tension of zonular fibres, thereofore allowing the lens to assume a more spherical shape, inducing myopia[4,7,17].

To confirm the diagnosis of angle closure, ultrasound biomicroscopy is used to assess the anterior chamber angle and detect localized ciliary body oedema[18]. topiramate induced angle closure can often be confused with primary angle closure, highlighting the importance of a proper drug history and taking note of the myopic shift only demonstrated with topiramate induced angle closure, which improves after resolution of the ciliochoroidal effusions[13,14]. It is especially important to consider secondary causes of angle closure when encountering bilateral, simultaneously raised intraocular pressure. The standard of treatment starts with immediate cessation of topiramate, which alone is often enough to terminate the adverse event. Topical ocular antihypertensives are the next step in management, often a combination of beta-blockers and alpha agonists[17,19].

Cycloplegic agents are key in the management of

topiramate induced angle closure, although this is often counterintuitive due to their contraindication in treating primary angle closure. Cycloplegics, in this setting, act to tighten lenticular zonules, thereby exerting a posterior force on the lens–iris diaphragm to reverse the mechanism of angle closure. Cyclopentolate, with its intermediate duration of action, is frequently chosen for a mydriatic agent in topiramate induced angle closure, in anticipation of a rapid treatment response.Topical and systemic steroids are increasingly commonly used as current literature suggests there is an inflammatory component to ciliochoroidal effusion syndrome[12,14,15].

Typically topiramate-induced acute angle closure resolves without residual changes. However; Aminlari et al., reported resolution with bilateral peripheral anterior synechiae[17]. In our one case, iris changes probably resulted from persistent ischaemia. Sudden and persistent raised IOP can produce ischaemic changes in ocular structures. Raised IOP for 2 - 7 days can cause ischaemic changes and synechiae formation[9]. Iris stroma and ciliary body were the first structures to manifest ischaemic changes[19]. Iris sphincter muscle and its vascular supply were affected by sustained high IOP, resulting in ischaemia and then infraction of sectors of the iris[20]. The untreated raised IOP and sequel of ischaemia may have deleterious effects on the eye.

Conclusion

Topiramate induced angle closure is an idiosyncratic reaction and can occur in otherwise normal eyes with normal anterior chamber angles. Ocular examination before starting topiramate cannot identify eyes at risk. The internists should be aware of the documented side effects of topiramate, particularly when presented with simultaneous bilateral acute angle closure glaucoma. Neurologists initiating therapy with topiramate should also educate the patients of its potential side effects and the importance of reporting back immediately in case of any visual disturbance. Prompt cessation of therapy alone can result in the rapid resolution of most of these adverse effects, whereas failure to recognize can lead to permanent visual problems.

Disclosure

The authors have no financial or proprietary interest in a product, method, or material described herein.

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