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CASE REPORT

PERIOPERATIVE MEDICINE

Topiramate induced angle-closure glaucoma in a healthy female: a case report

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ABSTRACT

Topiramate-induced angle-closure glaucoma (ACG) is rare. This case report details an instance of secondary ACG in a young, relatively healthy female following the administration of topiramate for migraine prophylaxis. Topiramate, an antiepileptic drug, is approved in the United States for the management of seizures, prevention of migraine headaches, and in combination with phentermine, for chronic weight management therapy in adults. Clinical suspicion for topiramate-induced ACG should be high in patients presenting with the appearance of its signs and symptoms within several weeks of therapy initiation. Acute ACG is an ophthalmic emergency that can result in irreversible blindness if not promptly identified, and appropriately treated. The treatment consists of immediate discontinuation of the medication and administration of cycloplegic agents, intra-ocular pressure lowering agents, and topical and oral steroids. Prescribing physicians should identify any risk factors for the condition in patient history and weigh the benefits and risks of initiating the medication. Patients should be made aware of the possible side effects associated with the drug to make informed decisions.

Abbreviations: ACG: angle-closure glaucoma, AE: adverse event, IOP: intraocular pressure, GABA: gamma-aminobutyric acid,

Keywords: Glaucoma; Intra-Ocular Pressure; Migraine; Ophthalmic Emergency; Topiramate

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1. INTRODUCTION

Topiramate (Topamax®) received FDA approval in 1996 for treating epilepsy as monotherapy or adjunctive therapy.¹ Topiramate is a sulfamate-substituted monosaccharide, commonly used for epilepsy, migraine prophylaxis, and weight loss. This medication works by inhibiting carbonic anhydrase, inhibiting sodium channels, enhancing potassium channels, stimulating postsynaptic gamma-aminobutyric acid (GABA)

receptors, among many other mechanisms of action.¹ Although generally well-tolerated, it has been linked to rare but severe ocular side effects, including secondary angle-closure glaucoma (ACG).

ACG is the rapid increase in intraocular pressure (IOP) due to closure of the anterior chamber angle leading to obstruction of the aqueous outflow.² ACG commonly presents with acute onset of eye pain, redness, blurry vision, halos around lights, headache, nausea, vomiting,

and increased risk of blindness. 2,3,4 ACG can be primary or secondary based on the mechanism of anterior chamber obstruction. As opposed to primary ACG, which is caused by a pupillary block of the iris causing angle closure.. topiramate causes secondary ACG by choroidal effusion putting pressure on the vitreous body and compressing the lens-iris diaphragm.⁵ Usually a unilateral occurrence, a case of topiramate associated acute bilateral secondary angle closure glaucoma has been reported.² A report on patient demographics and characteristics of reported adverse events (AEs) for topiramate and other antiepileptics lists decreased sweating, renal calculus and renal hypercalciuria as the top three adverse events with abnormal vision as a distant, 34th among them. The incidence of adverse events with topiramate was 15.6 percent.² Early diagnosis and management of the serious ocular events like angle closure glaucoma is essential to prevent permanent damage.

2. CASE REPORT

This report is about a 39-year-old, relatively healthy Caucasian female with no significant medical history except for Bertolotti syndrome, chronic back pain, and episodic migraines, who presented for evaluation of acute onset of bilateral blurry vision, severe eye pain and pressure, and headache. The patient reports starting on topiramate 25 mg daily about 2 weeks prior for migraine prophylaxis. This patient has an extensive past history of multiple ocular pathologies in the left eye, including multiple episodes of retinal edema, cystoid macular degeneration of retina, and histoplasma capsulatum retinitis. She denied any family history of glaucoma. In addition to the newly prescribed topiramate, she was also taking over-the-counter Excedrin Migraine as needed. Past surgical history included bilateral tubal ligation, tonsillectomy, and adenoidectomy.

2.1. Investigations

The patient underwent a comprehensive eye examination, including visual acuity, external examinations, slit-lamp examination, IOP measurement, gonioscopy, fundoscopy.

Upon examination, visual acuity was reduced bilaterally to 20/400 at distance. Intraocular pressures were mildly elevated at 20 mmHg in the right eye and 21 mmHg in the left eye. Pupils were both 4mm, round and reactive without obvious afferent pupillary defect. Slit lamp examination revealed shallow peripheral anterior chamber in both eyes but no conjunctival injection. Gonioscopy showed angle closure for 360 degrees in both eyes. Fundoscopic exam revealed peripapillary atrophy of the left optic nerve, histo spot in central macula of left eye, and chorio-retinal scarring in the left

eye, but no papilledema or swollen optic nerve in either eye.

2.2. Differential diagnosis

The differential diagnosis included primary angle closure glaucoma, secondary angle closure glaucoma due to other causes, uveitis, and acute myopia. Based on clinical presentation and patient history, the diagnosis of bilateral topiramate-induced angle closure was made.

2.3. Treatment

Topiramate was discontinued immediately. The patient was treated with topical atropine 1%, topical dorzolamide 22.3 mg-timolol 6.8 mg/mL, topical prednisolone 1%, and systemic prednisone 10 mg. Atropine was discontinued after 24 hours.

2.4. Outcome and follow-up

At 1-week follow-up, the patient reported resolution of blurry vision and eye pain. Her visual acuity had returned to normal, and IOP was within normal limits (14 mmHg in the right eye and 15 mmHg in the left eye). A repeat gonioscopy showed open angles bilaterally. The patient was instructed to taper off steroids and discontinue Dorzolamide-Timolol.

3. DISCUSSION

The diagnosis of Topiramate-induced ACG requires clinical presentation, detailed patient history, and physical examination. Our patient presented with sudden onset of bilateral blurry vision, bilateral eye pain and pressure, and headache. Although consistent with ACG, there are other conditions that may present with the same symptoms. In addition, there are sporadic reports of patients experiencing ACG after 7, 4, 14 and 17 days after stopping topiramate. It has been postulated because of the persistent effect of topiramate after stopping this medication similar to when prescribed for migraine prophylaxis. 10 A report is also described in the literature of topiramate resulting in acute angle closure and severe panuveitis.² Detailed patient history played a big role in our case, as the patient's recent initiation of topiramate further raised our suspicion for drug related ACG. Finally, the examination findings confirmed the diagnosis of ACG with elevated IOP and closed angles on gonioscopy exam.

It is important to determine whether the angle closure is due to a primary or secondary process. Both present with similar signs and symptoms, including eye pain, headache, blurred vision, halos, nausea, vomiting, elevated IOP, angle closure on gonioscopy and others.^{3,5,6} Some risk factors that predispose people to

primary ACG include ages between 55 and 65, female gender, certain races (Southeast Asian, Chinese, and Eskimo), and family history of ACG or other ocular anatomic abnormalities. The patient is a young, relatively healthy female with no family history of ACG or other ocular abnormalities, making primary ACG less likely. In addition, physical examination did not show any evidence of pupillary block, the key mechanism of anterior chamber blockage in primary ACG, as the pupils were equal, round, and reactive without any afferent pupillary defect. It is to be noted that this patient had personal history of chronic ocular damage on the left eye due to histoplasmosis, which could predispose her to ACG.

Topiramate-induced ACG is rare, with incidence rate of approximately three cases per 100,000 people.^{2,6} Onset is acute as symptoms usually develop within 2 weeks of therapy initiation, consistent with our patient.⁶ Exact mechanism has not been fully understood, but topiramate is believed to increase permeability of the ciliochoroidal vasculature, leading to excess fluid and subsequent ciliochoroidal swelling.² This results in forward rotation of the ciliary body and anterior displacement of the iris-lens diaphragm, leading to acute myopia and angle closure.^{2,4,6}. In addition, the patient's response to cycloplegia agent points to a more likely to a secondary process. Cycloplegics such as atropine are effective treatment for secondary but not primary ACG,⁴ as they paralyze the ciliary body and cause posterior shift of lens-iris diaphragm and flattening of the lends, leading to angle opening.2 Other medications such as dorzolamide, a carbonic anhydrase inhibitor, and timolol, a nonselective beta-adrenergic antagonist, play a role in lowering the IOP by reducing aqueous humor production.⁵ Topical and systemic steroids are also helpful in reducing inflammation.²

This case highlights the importance of early recognition and treatment of secondary ACG and patient education when prescribing medications with serious side effects. When started on topiramate, our patient was carefully informed about the adverse effects and counseled on the red flag symptoms. The patient immediately sought specialist evaluation on the same day of onset, and the physician was able to obtain appropriate tests for a quick diagnosis. The patient's IOP measures on the initial visit were mildly elevated with no signs of serious ocular damage, suggesting that we were able to detect the condition at the very beginning of the disease process. Topiramate-induced ACG generally has a good prognosis with prompt recognition, immediate discontinuation of drug, and appropriate therapy.²

4. CONCLUSION

Topiramate-induced ACG is a rare but serious condition that can lead to irreversible blindness if not identified and treated in a timely manner. It is important for physicians to learn detailed patient history to identify any risk factors for ACG and weigh the benefits and risks when prescribing topiramate for off-label use of migraine prophylaxis. Patients need to be educated on the possible side effects so they can make informed decisions and should be advised to seek care for serious adverse effects.

5. Conflict of interest

No conflict of interest reported by any of the authors.

6. Consent of the patient

The consent of the patient was obtained to publish this report.

7, Authors contribution

All authors took part in Concept, conduction of the study work, consult, and manuscript editing

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