

Topiramate-induced bilateral acute angle closure glaucoma and myopic shift

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ABSTRACT

Topiramate (TPM) shows idiosyncratic adverse reaction of peripheral ciliochoroidal effusion leading to acute angle closure glaucoma (AACG), which should be diagnosed and managed at the earliest to prevent irreversible visual loss. We report, a case of TPM-induced bilateral AACG and myopic shift, which was reversed by omitting TPM and administering antiglaucoma medications.

Keywords: Topiramate, Acute angle closure glaucoma, Ciliochoroidal effusion, Young mania rating scale

INTRODUCTION

Topiramate (TPM) is a sulfonamide derivative used as oral medication for treatment of epilepsy. It is a new potent antiepileptic drug with antiepileptic activity mediated by multiple mechanisms, e.g., hyperpolarization of K⁺ current, enhances postsynaptic GABA A – receptors and also limited activation of the AMPA-kainite-subtype(s) of glutamate receptor. TPM also reduces voltage-gated Na⁺ currents in cerebellar granule cells and may act on the inactivated state of the channel.¹ It is used as an add-on therapy for generalized and partial seizures that are resistant to the other antiepileptic drugs and as a mood stabilizer for patients with bipolar disorders.² It was originally considered as an oral hypoglycemic agent, but recently it has gained

importance as off-label treatment of neurological and psychiatric disorders e.g., bipolar disorders, post-traumatic stress disorders, de-addiction for alcoholism and nicotine, post-herpetic neuralgia, migraine and idiopathic intracranial hypertension. TPM has not yet been studied systematically as primarily weight loss agent, but it has been associated with a decrease in appetite and weight loss in patients with epilepsy and bipolar disorder.³ The most common side-effects are somnolence, fatigue, weight loss, and renal calculi, which is likely to be due to inhibition of carbonic anhydrase. There are few case reports of acute angle closure glaucoma (AACG) presumably associated with TPM.^{4,5} The mechanism proposed can be analyzed in view of the existing literature i.e. pharmacodynamics of the TPM; specificity in relation to eye; histopathology of eye; normal mechanism of

production of aqueous humor; structure involved in the eye uveoscleral junction; response in relation to sulphonamide,⁶⁻⁸ carbonic anhydrase inhibitor and role of prostaglandins or leukotrienes. TPM may cause peripheral ciliochoroidal effusion with ciliary body edema and anterior rotation which shifts lens-iris diaphragm anteriorly, thus shallowing anterior chamber at the periphery and causing AACG without pupillary block. The exact mechanism of the ciliochoroidal effusion is unknown, and it is believed to be an idiosyncratic adverse drug reaction or secondary AACG related to the ciliary body detachment.⁹⁻¹¹

CASE REPORT

Mrs. X aged 37 years, married female reported in the outdoor patient unit, Department of Psychiatry, Govt. Medical College, Rajindra Hospital, Patiala with the complaints of garrulous talking, overspending, over-familiarity, over-religiosity, euphoric in mood, decreased need for sleep, increased appetite, and sexuality for the last 1 month, which were gradual in onset. During the last 10 years, there were three episodes of depression and two episodes of mania. The last episode of mania occurred 1 year ago, which was precipitated when she suddenly inherited maternal uncle's house and received 1 lakh rupees in cash. There was significant social and occupational work impairment during these episodes, and symptoms were not due to any other medical, substance or psychiatric illness. She took divalproex sodium 1500 mg/day and lorazepam 4 mg/day for 8 months under the supervision of the psychiatrist and recovered from an episode of mania. She stopped the medications without consultation and remained symptoms free for about 4 months. On mental status examination, she was conscious, distractible, though oriented to time, place, and person. Eye to eye contact was made and rapport established with difficulty, mood was euphoric; affect appropriate to the mood content, with flight of ideas, delusion of grandiosity "worth." Judgment was poor, insight to illness and reality contact was broken. According to the International Classification of Disease: classification of mental and behavioral disorders: diagnostic criteria for research (ICD-10), she was diagnosed as a case of F 31.20 bipolar affective disorder, current episode mania with mood-congruent psychotic symptoms. She was started with divalproex sodium 1500 mg/day, olanzapine 10 mg/day and lorazepam 4 mg/day at bedtime. Her baseline young mania rating scale (YMRS) score was 39 and clinical global impression (CGI)-S score 6. After 2 weeks, the scores on YMRS and CGI-I were 19 and 2, respectively; indicating much improvement (more than 50% reduction), but efficacy index of 4, means side-effects outweigh therapeutic benefits. After olanzapine, there was an increase in the body mass index of the patient from normal level of 24 to 28 i.e. an indicating overweight. She was given TPM 25 mg/day to reduce the metabolic side-effect of the olanzapine, but within 2 weeks, patient noticed blurring of vision and pain in both eyes. There was no past history of any drug allergy or other medical history of bronchial asthma,

hay fever, skin rash, etc. The laboratory investigations for complete blood count, urine test, fasting blood sugar, liver function test, renal function test, thyroid function test, electrocardiogram, and ultrasound for abdomen were normal. Her unaided visual acuity was 20/200 both eyes, but best corrected visual acuity was 20/50 for both eyes with $-4.0D$ sphere/ $-0.75D$ cylinder $\times 35^\circ$ for the right eye and $-4.5D$ sphere/ $-0.50D$ cylinder $\times 90^\circ$ for the left eye. On applanation tonometry, intraocular pressure (IOP) was 50 mmHg and 56 mmHg for right and left eye, respectively. On slit-lamp examination of both eyes, conjunctiva showed mild chemosis and injection along with ciliary flush and corneas were edematous with diffused stromal haze. The anterior chambers were very shallow without iridocorneal touch or any signs of inflammation (Figure 1) and pupils were sluggishly reacting. A-scan showed anterior chamber depth of 1.9 mm both eyes and B-scan showed no evidence of choroidal effusion. Gonioscopy of both eyes showed 360° appositional closure (Figure 2).

Anterior segment optical coherence tomography (ASOCT) showed appositional closure of angles (Figure 3).

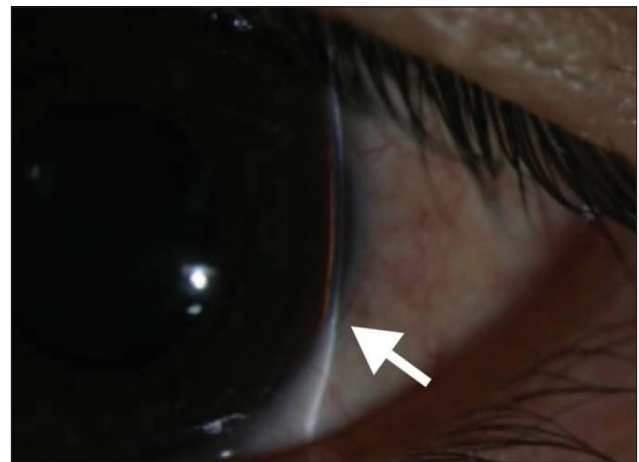


Figure 1: Slit lamp examination showing shallow anterior chamber at the periphery.

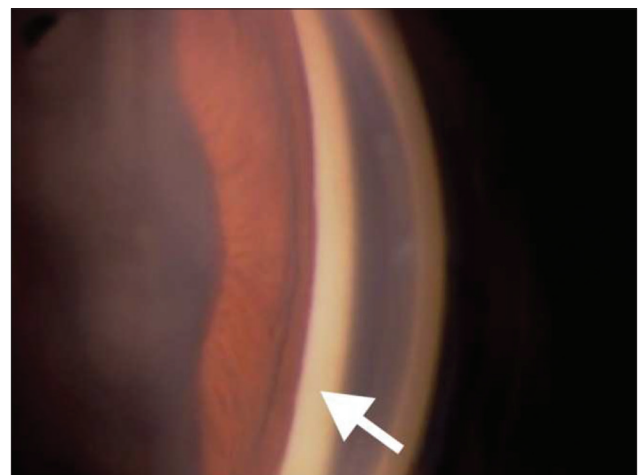


Figure 2: Gonioscopic examination showing closed angle (nasal).

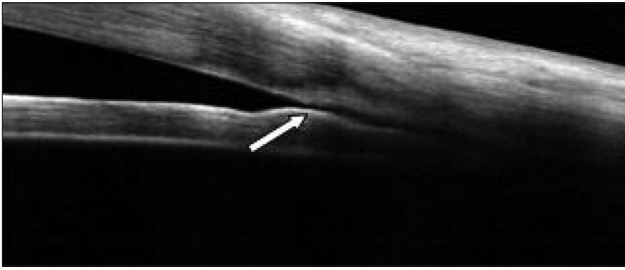


Figure 3: ASOCT showing appositional closure of angle.

Fundus of both eyes was unremarkable with normal optic disc and healthy rim tissue with the cup to disc ratio of (0.2-0.3). The diagnosis of bilateral secondary AACG due to TPM was made. IOP spikes were lowered down with intravenous mannitol, topical aqueous suppressants, cycloplegics, and oral hyperosmotics. After 2 days, patient was comfortable with partial resolution of symptoms. Anterior chamber remained shallow with resolution of corneal edema and decreased IOP. After 1 week, unaided vision acuity was recorded 20/20 for both eyes and cycloplegic retinoscopy revealed $-0.75D$ sphere right eye and $-0.5D$ sphere left eye. IOP was 14 mmHg and 16 mmHg for right and left eye, respectively; anterior chambers became deep and corneas clear. After normalization, IOP gonioscopy revealed bilateral open angles and several small bilateral peripheral anterior synechiae. The treatment of glaucoma was gradually tapered off and completely stopped within about next 15 days, and no further rechallenge test with TPM was given considering higher risk/benefit ratio as it involved potentially sight threatening complication with permanent loss of vision. The possibilities of other drugs causing angle closure glaucoma were unlikely as they continued during the course of treatment and TPM was the only drug which was stopped, leading to attenuation of symptoms.

DISCUSSION

TPM has been approved for seizure disorders, and there has been increasing interest in its weight reducing properties, which can be used in patients on atypical antipsychotics e.g. clozapine, olanzapine, etc.³ There have been reports by Rhee et al., 2006 of ocular complications due to TPM causing permanent loss of visual acuity seen in 7 cases.¹² TPM can cause AACG and mimics primary AACG. A careful inquiry by ophthalmologists of current and past medications is critical in the evaluation of angle closure glaucoma. Most cases of TPM-associated angle-closure glaucoma are present within the first 2 weeks of treatment as was seen in our case, but reactions have been reported within hours of the first dose or as long as 7 weeks after the onset of therapy.¹¹ The mechanism of AACG is thought to be idiosyncratic reaction leading to ciliochoroidal effusion and forward displacement of lens iris diaphragm, which can be confirmed on B-Scan. This can also occur in otherwise normal eye as seen in our case, where there was no ciliochoroidal effusion seen on

B-Scan. This complication can be treated by stopping the drug and controlling the IOP aggressively. Miotics and iridotomies are of no use in this entity because there is no pupillary block. Cycloplegics can help deepening the anterior chamber, relaxes ciliary body and tightens the zonules, thus keeping the iris-lens diaphragm in check. Systemic steroids can be used to decrease ciliary body edema caused by inflammation. Rhee et al., 2006 suggested that cases, which do not respond to conventional therapy require systemic corticosteroids and hyperosmolar agents for early recovery and remission to avoid surgical intervention.¹²

CONCLUSION

TPM may lead to idiosyncratic drug reaction with ocular symptoms ranging from myopic shift to secondary angle-closure glaucoma due to ciliochoroidal effusions or in an otherwise normal eye. Patients on TPM should be warned, and physicians should be aware of possibilities of developing this potentially sight threatening complication with prompt withdrawal of the drug and by instituting cycloplegics and steroids for early remission.

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