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Topiramate-induced bilateral acute angle-closure attack

Christina Pattinger · Teresa Rauchegger · Barbara Teuchner

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Summary
Background Topiramate, a sulfonamide-derived drug, is not only approved as an anticonvulsant but also for migraine prophylaxis. Ocular side effects are rare.
Case presentation The case of a 25-year-old woman with bilateral topiramate-induced angle-closure attack is presented. Clinical findings included elevated intraocular pressure, reduced anterior chamber depth, iridotrabecular contact, thickening of the lens, forward displacement of the iris–lens diaphragm, myopic shift and uveal effusion. Non-invasive techniques such as anterior segment optical coherence tomography (AS-OCT) and B-scan ultrasonography were used to confirm the diagnosis. Under discontinuation of topiramate, aqueous suppressants, cycloplegia and corticosteroids, symptoms and findings were reversible.
Conclusion and importance The aim is to raise awareness of possible side effects of topiramate among ophthalmologists and neurologists in order to avoid permanent visual impairment due to delayed diagnosis and treatment.

Keywords Topiramate · Acute angle closure · Myopic shift · Uveal effusion · Migraine · Intraocular pressure

Topiramat-induzierter beidseitiger akuter Winkelblock

Zusammenfassung
Hintergrund Das Sulfonamidderivat Topiramat ist ein Antiepileptikum, das auch zur Migräneprophylaxe zugelassen ist. Okuläre Nebenwirkungen sind selten.
Fallpräsentation Wir präsentieren den Fall einer 25-jährigen Frau mit Topiramat-induziertem beidseitigem Winkelblock. Die klinische Untersuchung zeigte einen erhöhten Augeninnendruck, eine verringerte Vorderkammertiefe, einen iridotrabekulären Kontakt, eine Verdickung der Linse, eine Vorverlagerung des Iris-Linsen-Diaphragmas, eine Myopisierung und eine uveale Effusion. Nichtinvasive Techniken wie die optische Kohärenztomographie des Vorderabschnitts (AS-OCT) und die B-Scan-Sonographie wurden zur Bestätigung der Diagnose eingesetzt. Nach Absetzen von Topiramat und Durchführung einer antiglaukomatösen Therapie, Zykloplegie und Kortikosteroidbehandlung bildeten sich Symptome und Befunde zurück.
Schlussfolgerung Ziel dieses Fallberichts ist es, Augenärzt:innen und Neurolog:innen für die möglichen Nebenwirkungen von Topiramat zu sensibilisieren, um eine dauerhafte Seheinschränkung aufgrund einer verspäteten Diagnose und Behandlung zu vermeiden.

Schlüsselwörter Topiramat · Akuter Winkelblock · Myopisierung · Uveale Effusion · Migräne · Erhöhter Augendruck

Introduction

Topiramate (Topamax®) is an antiepileptic drug, also used as a therapeutic option for obesity, alcohol dependence, bipolar personality disorders and migraine prophylaxis. Adverse reactions are rare. Systemic side effects include fatigue, paresthesia, confusion and memory issues. The best-known ocular side effect is ciliochoroidal effusion, leading to acute angle closure and myopic shift, occurring in three per 100,000 patients taking topiramate [1]. Other symptoms include diplopia, uveitis, retinal or neuro-ophthalmic complications [1, 2].

C. Pattinger · T. Rauchegger (✉) · B. Teuchner
Department of Ophthalmology and Optometry, Medical University of Innsbruck, Innsbruck, Austria
teresa.rauchegger@i-med.ac.at

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A case of bilateral topiramate-induced acute angle closure diagnosed using multimodal imaging is reported in order to raise awareness among ophthalmologists and neurologists. It is crucial not to misinterpret the symptoms as migraine-related conditions.

Case report

A 25-year-old woman presented to the emergency department complaining of a 1-day history of bilateral blurred vision and ocular discomfort. Beside the need for glasses with –1.50 diopters in both eyes, there was no history of ocular diseases. The patient's medical history revealed migraine headache, which is why she had been started on topiramate 25 mg as prophylactic therapy 1 week prior to presentation. Since the previous day, the dose had been doubled according to the neurologist's prescription.

At presentation, visual acuity examined by Snellen chart was 20/250 on the right eye (OD) and 2/250 on the left eye (OS) corrected with the patient's glasses (–1.5D). Auto-refractometer revealed a–6.50 diopter myopic shift in the right and –5.50 diopters in the left eye. Best-corrected visual acuity (BCVA) improved to 20/32 OD and 20/25 OS. Intraocular pressure (IOP) was elevated to 40 mm Hg OD and 38 mm Hg OS.

Pupils were mid-dilated and reactive to light. Bilateral anterior segment examination showed mild corneal oedema and a very shallow anterior chamber. Gonioscopy showed 360-degree angle closure, which was confirmed by anterior segment optical coherence tomography (AS-OCT), showing iridotrabecular contact of 360 degrees. Other AS-OCT findings included an anterior chamber depth (ACD) of 1.68 mm, a thickened lens and forward displacement of the iris–lens diaphragm (Fig. 1). Fundoscopy showed normal optic disc, macular and retina, although accurate assessment of the periphery in miosis was virtually impossible. B-scan ultrasound detected increased choroidal thickness and suprachoroidal effusion.

Based on the patient's history, topiramate-induced bilateral acute angle-closure attack was suspected and the patient was hospitalized. Topiramate use was stopped immediately and treatment with topical antiglaucomatous eyedrops (dorzolamide 2% + timolol 0.5%) and systemic IOP lowering medications (acetazolamide, mannitol), topical steroids and cycloplegics was started. Additionally, intravenous steroid was administered on 2 consecutive days.

After 24 h, IOP decreased to 18 mm Hg, and after 48 h to 12 mm Hg on both eyes. After 4 days, slit lamp examination showed a clear cornea and deepened an-

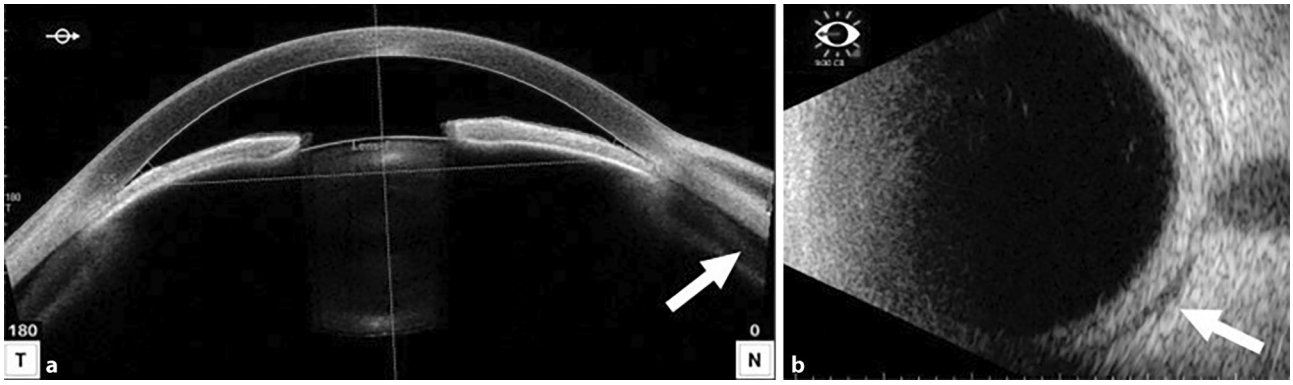

Fig. 1 **a** Anterior segment optical coherence tomography of the right eye revealing a shallow anterior chamber (anterior chamber depth, 1.68 mm) with a closed angle. *Arrow* shows ciliochoroidal effusion. **b** B-scan of the right eye showing suprachoroidal effusion

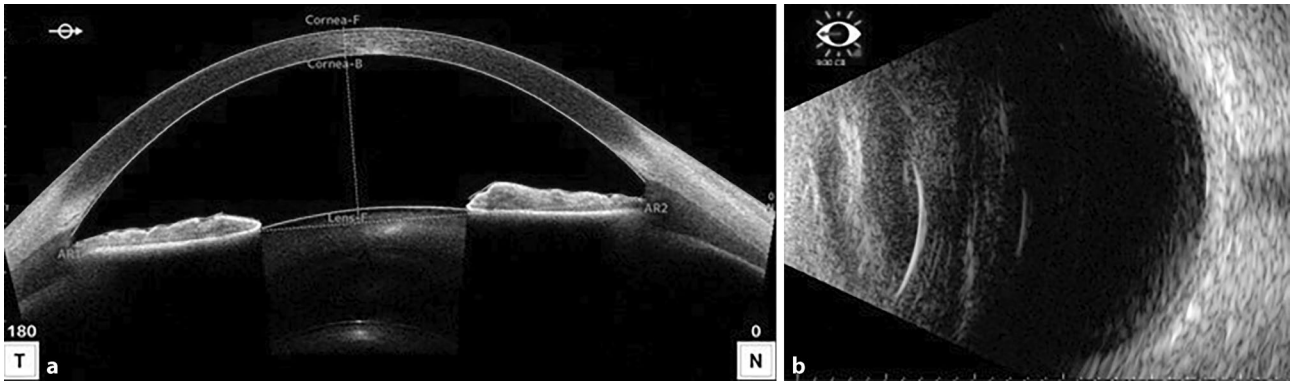

Fig. 2 Anterior segment optical coherence tomography (**a**) and B-scan (**b**) of the right eye on the fifth day after discontinuation of topiramate and initiation of hypotensive, cycloplegic and anti-inflammatory therapy

terior chamber with opened angles (Fig. 2). At 2-week follow-up, the myopic shift was reversed and BCVA was 20/20 with an IOP of 11 mm Hg in both eyes.

Discussion

The first description of topiramate-induced secondary acute angle closure was published in 2001 [3]. Although several case reports followed, the mechanism is not fully understood. An idiosyncratic reaction is hypothesized with uveal effusion as the key mechanism [1, 3–5]. Stimulation of prostaglandin E2 and blockage of sodium channels lead to increased permeability of the ciliochoroidal vasculature. Ciliary body oedema induces forward displacement of the iris–lens diaphragm resulting in a shallow anterior chamber and myopic shift [2, 4, 6, 7]. Inflammation may also contribute, as uveitis-related cases are reported in the literature [5, 8].

Topiramate-induced secondary acute angle closure usually affects young female patients (less than 40 years of age) within the first 2 weeks of treatment [1, 2]. This might suggest that women are at increased risk, but a plausible explanation is that women have a higher incidence for migraines with topiramate as prophylactic treatment option [1].

Treatment of topiramate-induced acute angle closure consists of discontinuation of the causal drug, lowering IOP, cycloplegia and corticosteroids [8]. Topical aqueous suppressants (beta-blockers, alpha-adrenergics) are recommended.

One should consider whether hyperosmotic agents (mannitol) are preferable to acetazolamide, since acetazolamide, like topiramate, is a sulfa-derived drug and is suggested to exacerbate the symptoms [4]. The development of uveal effusion with subsequent acute angle closure has been documented to be associated with many sulphonamide-containing drugs. Mancino et al., for example, reported a case of bilateral angle closure with extensive choroidal effusion following administration of oral acetazolamide immediately after routine cataract surgery [9]. However, in case reports similar to this report, systemic acetazolamide is frequently administered to control high IOP in patients with topiramate-induced angle-closure attacks, suggesting that idiosyncratic reactions to one sulfonamide drug may not be worsened by concomitant use of a second drug of the same class [9].

However, there is general agreement in the literature that topical cycloplegics are recommended to retract the ciliary body in order to reopen the iridocorneal angle [7]. As pupillary block is not the causal mechanism for angle closure, iridectomy is ineffective and cholinergic agents, such as pilocarpine, are contraindicated and may even aggravate the condition [6].

As an underlying inflammatory component is discussed in the development of topiramate-induced acute angle closure, some reports consider that topical or systemic steroids may be beneficial [7, 8].

Topiramate has an elimination half-life of 21 h [1], and after cessation of use and initiation of treatment, acute angle closure usually resolves within 1–2 days and the myopic shift within 1–2 weeks [10]. This corresponds to the author's experience.

Conclusion

In conclusion, this case report illustrates the case of acute angle closure associated with topiramate treatment in a young woman suffering from migraine. Bilateral secondary acute angle-closure attack caused by uveal effusion is a rare but severe side effect of topiramate therapy. This report emphasizes the importance of taking an accurate medical history in young patients with acute angle closure in order to recognize the underlying mechanism and to prevent confusion with migraine-associated symptoms. Otherwise, there may be a delay in diagnosis and subsequent complications due to incorrect treatment. Non-invasive techniques such as AS-OCT, ultrasound biomicroscopy (UBM) and B-scan ultrasonography are crucial for early diagnosis, correct treatment and adequate follow-up. With prompt appropriate treatment, all ocular symptoms are reversible.

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Declarations

Conflict of interest C. Pattinger, T. Rauchegger and B. Teuchner declare that they have no competing interests.

Ethical standards For this article no studies with human participants or animals were performed by any of the authors. All studies mentioned were in accordance with the ethical standards indicated in each case. For images or other information within the manuscript which identify patients, consent was obtained from them and/or their legal guardians.

References

1. Abtahi S-H, Abtahi, Fazel, et al. Topiramate and the vision: a systematic review. Clin Ophthalmol. 2012; https://doi.org/10.2147/OPTH.S27695.

2. Fraunfelder FW, Fraunfelder FT, Keates EU. Topiramate-associated acute, bilateral, secondary angle-closure glaucoma. Ophthalmology. 2004;111:109–11. https://doi.org/10.1016/j.ophtha.2003.04.004.
3. Banta JT, Hoffman K, Budenz DL, et al. Presumed topiramate-induced bilateral acute angle-closure glaucoma. Am J Ophthalmol. 2001;132:112–4. https://doi.org/10.1016/S0002-9394(01)01013-3.
4. Lan Y-W, Hsieh J-W. Bilateral acute angle closure glaucoma and myopic shift by topiramate-induced ciliochoroidal effusion: case report and literature review. Int Ophthalmol. 2018;38:2639–48. https://doi.org/10.1007/s10792-017-0740-y.
5. Goldberg J, Lau A, Fan B, et al. Is uveitis associated with topiramate use? A cumulative review. Clin Ophthalmol. 2016;10:1467–70. https://doi.org/10.2147/OPTH.S104847.
6. Van Issum C, Mavrakanas N, Schutz JS, et al. Topiramate-induced acute bilateral angle closure and myopia: pathophysiology and treatment controversies. Eur J Ophthalmol. 2011;21:404–9. https://doi.org/10.5301/EJO.2010.5979.
7. Ikeda N, Ikeda T, Nagata M, et al. Ciliochoroidal effusion syndrome induced by sulfa derivatives. Arch Ophthalmol. 2002;120:1775.
8. Rhee DJ, Ramos-Esteban JC, Nipper KS. Rapid resolution of topiramate-induced angle-closure glaucoma with methylprednisolone and mannitol. Am J Ophthalmol. 2006;141:1133–4. https://doi.org/10.1016/j.ajo.2006.01.021.
9. Mancino R, Varesi C, Cerulli A, et al. Acute bilateral angle-closure glaucoma and choroidal effusion associated with acetazolamide administration after cataract surgery. J Cataract Refract Surg. 2011;37:415–7. https://doi.org/10.1016/j.jcrs.2010.12.032.
10. Thambi L. Topiramate-associated secondary angle-closure glaucoma: a case series. Arch Ophthalmol. 2002;120:1108. https://doi.org/10.1001/archopht.120.8.1108.