Topiramate –Induced Unilateral Ptosis

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Abstract

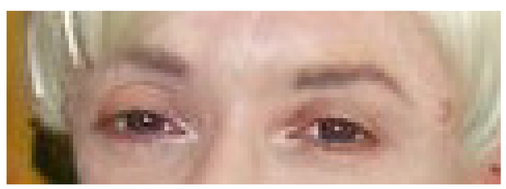
Topiramate is an anti-epileptic drug (AED) used to treat idiopathic generalized seizures either as monotherapy or in combination with other AEDs. It is also prescribed, at lower doses, for the prevention of migraines. The precise mechanism of topiramate has not been fully elucidated. We describe a rare finding of an ocular side effect induced by topiramate use. This is a case of a 43-year-old transgender man who presented with unilateral ptosis of the right eye. Ptosis was noted after four years of topiramate therapy, prescribed as prophylaxis against migraines. This case presents a unique ocular side effect that is not included on the drug label insert, nor described in the National Institute of Heath's medication profile of topiramate. There are currently no case reports of unilateral ptosis caused by the use of topiramate. Experience with this case has demonstrated that immediate discontinuation of the drug can restore eyelid function within one week.

Introduction

Topiramate is a sulfamate-substituted derivative of the naturally occurring monosaccharide, D-fructose. It is approved for use in more than 80 countries for use as monotherapy in refractory partial onset seizures and newly diagnosed epilepsy in adults, as well as adjunctive therapy for refractory partial onset seizures, primary generalized tonic-clonic seizures, and Lennox-Gastaut syndrome. Topiramate is also used in adults as prophylaxis against migraines.[1] Other off-label uses include weight reduction management and alcohol dependence management.

Topiramate is efficacious in migraine prevention. In multicenter randomized, double-blinded, placebo-controlled trains, topiramate reduced migraine periods in patients suffering from episodic and chronic migraines.[2] However, sulfonamides and its derivatives have been implicated in causing transient myopia, and acute angular closure glaucoma (AACG). Case reports of such adverse ocular effects have been found in the literature as far back as July 2001.[3] Acute myopia and secondary angle closure glaucoma is now the first side effect listed under Warnings and Precautions on Topamax's® drug label insert.

Figure 1: Unilateral Ptosis of the Right Eyelid



The patient with unilateral right eyelid ptosis.
Picture courtesy of Dr. J. Spiegel.

Case Report

A 43-year-old transgender man presented in July 2010 for the purpose of receiving cosmetic botulinum injections. The patient noted that for the past six weeks he had increasing difficulty lifting his right eyelid and observed that it did not open to the same extent as his left eye. The patient described having to struggle to open his right eye and described it as feeling "weighted down". The patient denied having any immediate symptoms associated with his previous botulinum injection in December 2009.

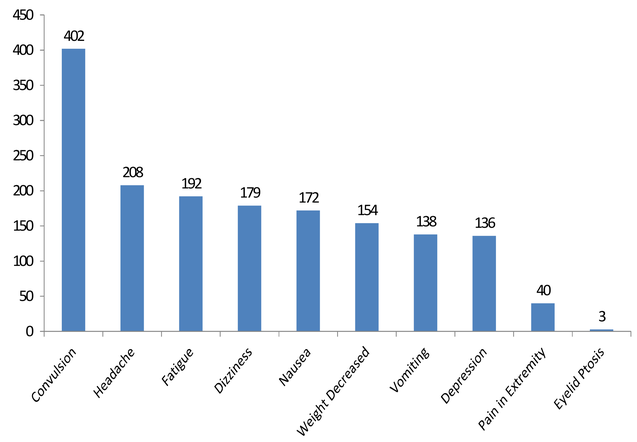
There was no previous clinical history of vision or eye symptoms. Upon examination, it was found that the right eye appeared to have slight exophthalmia compared to the left eye and palpation revealed a slightly firmer feeling right eye compared to the left. The patient had scars behind the ears and on the face from prior rhytidectomy surgery. The remaining physical findings were normal. The patient's medication list included Topamax®, Advair®, Klonopin®, Xanax®, and Cyclobenzaprine®.

The patient was advised against receiving botulinum injections at that appointment due to the fact that eyelid ptosis is a documented adverse effect of cosmetic botulinum injections. The patient was recommended for a head CT scan and chest radiograph, and was referred to an ophthalmologist.

The patient presented to the clinic in February 2011 with right eye ptosis that he described as worse than his previous visit. He denied vision changes but remarked that there was pain with eye movement. Physical examination again revealed a slightly proptotic right eye. The patient's CT scan of the head only revealed a mild amount of soft-tissue density at the inferior aspect of the left maxillary sinus which was interpreted as may be related to periodontal disease. Since the July visit, the patient had been examined by two ophthalmologists at two different institutions. Both recommended ptosis repair surgery.

In April 2011, it was hypothesized that the ptosis could potentially be attributed to topiramate. The patient was advised to discontinue use. Right eye proptosis improved within one week of stopping the medication and he regained normal movement of the right eye over the following month. In a May 2011 visit to the clinic, examination of the patient revealed intact and symmetric extraocular movements and no proptosis.

Figure 2: Self-Reported Adverse Effects Attributed to Topiramate Use in Women 1998-2012



Source: ehealthme.com (http://www.ehealthme.com/drug-interactions-side-effects/Topiramate-7448216) June 22, 2012

Discussion

An extensive list of adverse effects has been attributed to topiramate. While cognitive impairment is chief among them, ocular effects have been well documented. Although ocular impairments have mainly centered on acute myopia and AACG, ptosis has only been listed as an infrequent adverse reaction in past clinical studies without any case reports.[4] Myopia is severe with reports of myopia up to -8.75 D. The pathophysiology can be predominantly attributed to cilio-choroidal effusion.[5] Swelling of the choroid and ciliary body displaces these structures forward, closing the angle of the anterior chamber, resulting in AACG. The vast majority of cases have been bilateral.[6] In the present patient, ptosis was unilateral. Secondary angle closure glaucoma has been reported in pediatric patients as well as adults. Unlike with CNS impairments, there is a clear female gender predominance amongst patients affected by ocular events.[7]

Frequent adverse CNS effects cited are impaired concentration, confusion, dizziness, fatigue, paresthesia, somnolence, and abnormal thinking.[8] Similar adverse effects were found in obese patients taking topiramate as a means of weight loss. CNS disturbances in this population included difficulty in memory, difficulty in concentration / attention, nervousness, anxiety, and depression.[9] Other adverse reactions and effects may include nephrolithiasis, metabolic acidosis, gastrointestinal symptoms (constipation, diarrhea, dysphagia), cardiovascular symptoms (bradycardia, palpitations), and fetal teratogenicity (increased risk of cleft palate or cleft lip).

The onset of AACG ranges from within hours to 49 days from the initiation of therapy, with a mean of 7 days. Eighty-five percent of cases occurred in the first 2 weeks of treatment with topiramate.[10] There does not appear to be a dosage relationship with the onset of acute myopia or AACG as reported cases of glaucoma has ranged from less than therapeutic doses to over 100 mg. Currently, there is a prevailing belief that ocular side effects are idiosyncratic.[11] Discontinuation of topiramate can resolve AACG without medical intervention if recognized early. Pressure usually normalizes in a period of hours. Some patients did require antiglaucoma medication or laser / surgical iridectomies. Permanent loss of vision has also been reported.[12]

In contrast, this patient did not present with unilateral ptosis until four years after the initiation of therapy. Neither myopia nor AACG were experienced. Unilateral ptosis persisted for nine months with only a slight progression in severity while other concomitant ocular defects did not occur. The patient was referred to two different ophthalmologists, both who separately recommended that surgical ptosis repair as the only treatment option for this patient. This case highlights the importance of thoroughly scrutinizing each medication for all possible adverse reactions. Although eyelid ptosis was not listed as a potential side effect on topiramate's drug label insert, nor listed on the National Institute of Health's medication profile of topiramate, 0.14% of individuals did self-report experiencing eyelid ptosis with topiramate use on the website, *ehealth.com*.[13] Despite the low incidence, the possibility of such a reaction occurring coupled with the fact that ocular side effects predominantly affected female patients provided an important clue to the etiology of this patient's ptosis. The patient regained full function of the right eyelid within one week of drug seizure and did not require medication or surgical therapy.

Conclusion

Management of topiramate-associated ptosis requires patients to stop using topiramate immediately. Experience with this case suggests conservative treatment as an effective means to regain eyelid function. Unlike AACG which has a rapid onset, patients must be made aware that the onset of ptosis is gradual and may not appear for several years after topiramate use is begun. Ophthalmologists will have to be aware of this complication, as they may be one of the first ones to see such symptoms in patients.

Based on our knowledge, this is the first reported case of topiramate-induced unilateral ptosis. This case highlights areas in need of further research, primarily the mechanism underlying topiramate related to ptosis, predilection for females, and genetic and environmental correlates of topiramate-associated ocular impairment.

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