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Title: Acetazolamide-Induced Bilateral Ciliochoroidal Effusion Syndrome in Plateau Iris Configuration

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Abstract

Purpose. Our purpose is to describe a 60-year-old male, who has plateau iris configuration and developed bilateral ciliochoroidal effusion syndrome after ingestion of acetazolamide.

Observations. Our case was a research participant in a multi-center clinical study (ClinicalTrials.gov NCT01677507). During the course of this study, he was treated with a single dose of acetazolamide (500 mg), and seven days later treated with latanoprost one drop daily at bedtime both eyes for seven days, and then was administered another dose of acetazolamide (500 mg). Several hours later he complained of blurred vision in the distance and mild headache. On examination, he had a myopic shift, intraocular pressures of 36 mmHg in right eye and 35 mmHg in left eye, shallow anterior chambers both eyes, and occluded angles by gonioscopy both eyes. An echographic exam confirmed the bilateral ciliochoroidal effusion syndrome. He was treated by no further dosing of acetazolamide and started on timolol, atropine and prednisolone. Two weeks later, the bilateral choroidal effusion and acute angle closure were resolved. Repeat echography showed plateau iris configuration.

Conclusions and Importance. To the best of our knowledge, drug-induced bilateral ciliochoroidal effusion syndrome has not been reported with acetazolamide in plateau iris configuration.

Key words: Acetazolamide; Ciliochoroidal effusion; Plateau iris; Ultrasound Biomicroscopy; Drug reaction; Angle closure
Introduction

Sulfonamide derivatives have been reported to be associated with an idiosyncratic inflammation in the uveal tissues that result in choroidal effusion and ciliary body edema. Such tissue edema can cause forward displacement of the lens-ciliary body-iris complex, shallow anterior chamber and angle closure, elevated IOP and myopia shift [1-3]. The clinical consequences of this idiosyncratic reaction in uveal tissues was termed as ciliochoroidal effusion syndrome in 2002 when ophthalmologists were trying to illustrate the pathomechanism of topiramate-induced myopic shift and acute angle closure [4]. The ciliochoroidal effusion syndrome can occur days or weeks after drug administration [3] and the definitive treatment is to discontinue the causative medication. Early case reports about bilateral choroidal effusion and acute angle closure were most commonly associated with the use of topiramate [2]. There have been a few bilateral cases reported after acetazolamide following monocular cataract surgery [3, 5-8]. We present a case of bilateral ciliochoroidal effusion syndrome after exposure to acetazolamide in a subject with plateau iris configuration, normal lens, and without any surgery.

Case report

We report a research subject who was part of a clinical research study (ClinicalTrials.gov NCT01677507). The patient provided written consent for publication of this report. A 60-year-old male, with previous healthy eyes, was participating in multi-center clinical study. As part of the protocol, he was exposed to 500 mg of acetazolamide. One week later, he started taking latanoprost in each eye daily at bedtime for seven days. Afterwards, he was administrated another dose of acetazolamide, and several hours later he noted blurred vision and headache. He reported no history of any adverse effect from any sulfonamide agent. Systemic medications included over the counter supplements.

His initial examination before the first acetazolamide administration showed uncorrected visual acuity of 20/15 in the right eye and 20/15-1 in the left eye. His right IOP was 14 mmHg and left IOP was 11 mmHg. His anterior chamber was deep and quiet in both eyes. His iris showed central transillumination defects and lens had trace nuclear sclerosis in both eyes. Fundus exam were both normal with vertical cup-to-disc ratios of 0.1. Gonioscopy showed open angle in all quadrants with mild pigment in trabecular meshwork and no classic “double hump” sign.

After his second ingestion of acetazolamide, his visual acuity decreased to 20/25 in the right eye with manifest refraction to 20/15 with minus 0.50 sphere diopters, and 20/15 in the left eye. His IOPs were 36 mmHg in right eye and 35 mmHg in left eye. He had very shallow anterior chambers with iris touch in the peripheral cornea and iris draping over the lens in both eyes. Gonioscopy showed occluded angle both eyes. Fundus exam showed no choroidal folds. Physical examination of his body showed no rash, and he denied urticaria and any breathing difficulties.

Echography exam with high frequency (50 MHz) ultrasound biomicroscopy (UBM) showed bilateral shallow anterior chambers with anterior chamber depth (ACD) measurements of 1.68 mm in right eye and 1.63 mm in left eye (Figure 1A). Other UBM findings included 360 degrees of anterior rotation of the ciliary body with angle closure and ciliochoroidal detachment in both eyes (Figure 1B). B-scan findings
included 360 degrees shallow choroidal effusions in the posterior segment, with the highest elevation being nasally were found in both eyes (Figure 1C).

Based on the history, clinical exam and ultrasound findings, the diagnosis of ciliochoroidal effusion syndrome with myopic shift and acute angle closure after acetazolamide was determined. The treatment included no further use of acetazolamide and latanoprost, and withdrawal from the clinical study. To manage his IOP and choroidal effusions, timolol 0.5% one drop bid, prednisolone 1% one drop qid and atropine 1% one drop bid were prescribed to both eyes.

After two weeks, all of the clinical findings and his symptoms resolved. His visual acuity was 20/15 in right and 20/20 in left. His IOPs were 12 mmHg in right and 11 mmHg in left. His anterior chambers were comparable to his baseline examination and were deep and quiet in both eyes. His ACD was deeper (Figure 1D) with measurements of 2.16 mm in right and 2.3 mm in left. Repeat UBM showed plateau iris configuration with anterior rotation of the ciliary body and minimal ciliary sulcus in both eyes (Figure 1E), with open angle and resolution of the ciliochoroidal detachment. The B scan also showed resolution of the shallow posterior choroidal effusion in both eyes (Figure 1F).

Discussion

Ciliochoroidal effusion syndrome has been documented as a side effect of sulfonamide derivatives such as topiramate, hydrochlorothiazide, acetazolamide and other medications [1, 9, 10]. However, the pathogenesis underlying this idiosyncratic reaction of the uveal tissues is still unknown [3, 5, 9]. Acetazolamide is one of sulfonamide-based agents which acts as carbonic anhydrase inhibitor (CAI) and is commonly used to reduce elevated IOP in patients with acute angle closure attack or after cataract surgery [3]. Early cases about acetazolamide-induced ciliochoroidal effusion syndrome were reported presenting all after cataract surgery. Mancino et al [3] reported a case of bilateral angle-closure glaucoma (ACG) with extensive choroidal effusion following administration of oral acetazolamide immediately after routine cataract extraction and intraocular lens implantation. Malagola et al [5] reported another case of bilateral acute ACG with massive choroidal effusion, posterior retinal folds and papillary edema following administration of oral acetazolamide immediately after cataract surgery.

Our case is distinct from these previously reported cases with the demonstration of plateau iris configuration (PIC) by UBM after resolution of the ciliochoroidal effusion. Clinically, there is still no precise definition of PIC. Based on the UBM images, we propose a taxonomy of PIC into typical and atypical anatomy based on the angle, iris root insertion, ciliary process orientation, and ciliary sulcus (Table). For typical PIC (Figure 2B), a peripheral narrow angle is present with a clear iris root angulation, anterior ciliary process rotation, and absent or narrow ciliary sulcus. While in atypical PIC (Figure 2C), there is an open angle with the iris root inserted on top of the ciliary process, anterior ciliary process rotation, and absent ciliary sulcus, which is hallmark of PIC [11]. Our case represents atypical PIC anatomy.

PIC has been initially described as an anatomical variant of iris structure in which the peripheral iris root angulates sharply forward and then centrally but the iris plane is flat and the anterior chamber is assumed to be not shallow axially [11]. Additional features include an anteriorly directed ciliary body, an absent or narrow
ciliary sulcus, and irido-angle contact [12]. On gonioscopy, it can be challenging to identify PIC, but the classical “double hump” sign is a clue to the presence of PIC [13]. As in our case, UBM is frequently used to clarify this configuration and is a valuable tool for PIC diagnosis [14].

We speculate that in PIC anatomy where there is a very narrow or absent ciliary sulcus, the sulfa-associated swelling of anteriorly rotated ciliary processes impinges directly on the iris root with forward displacement of the iris. With the congested uveal tissues of the iris diaphragm and ciliary body, there is forward movement of the lens that contributes axial shallowing of the anterior chamber. At the same time, ciliary body swelling allows for relaxation of the lens zonules causing lens thickening and the development of myopia [4]. Studies are in progress to determine the quantitative biometry measurements of the ciliary sulcus, ciliary processes, and inter-plicata distance in PIC cases versus controls. Such measurements will allow us to model dynamic changes in uveal tissues and anterior segment imaging to understand the potential role of PIC in acute angle closure from drug-induced ciliochoroidal effusion.

A unique observation of our patient is that he had concomitant exposure to latanoprost between two doses of acetazolamide, which makes it difficult to attribute the causative effect solely to acetazolamide. However, during the one week course of latanoprost, he reported no visual disturbance. His symptoms developed several hours after acetazolamide ingestion. Thus, the timing of the exposure to acetazolamide supports the role of this drug involved in ciliochoroidal effusion. There are a few reports of latanoprost-associated choroidal effusion syndrome. Sakai et al [15] reported a drug-induced ciliochoroidal effusion in a patient with Sturge-Weber syndrome. They postulated that interaction of the enhanced uveoscleral outflow with latanoprost adjunctive with elevated episcleral venous pressure may have caused the congestion of the aqueous humor in the supraciliary-choroidal space, resulting in the ciliochoroidal effusion. Alimgil and Benian [16] reported choroidal effusion and shallow anterior chamber after adjunctive therapy with latanoprost in a patient who had trabeculectomy for angle closure glaucoma. In contrast to these two cases, our patient has healthy eyes and we cannot conclude with certainty the role of latanoprost in the pathogenesis of choroidal effusion syndrome in our patient.

Conclusion

We propose a taxonomy classification of the anterior segment relevant to the angle, iris insertion, ciliary process orientation, and ciliary sulcus. This well-documented case of atypical PIC suggests a potential anatomical risk to develop acute angle closure in acetazolamide-induced ciliochoroidal effusion syndrome. Although these cases are rare, clinicians are encouraged to continue ultrasound imaging at the time of the episode and after resolution to determine if such anatomy is a possible factor underlying this adverse reaction.

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References


Figure Captions

Figure 1. Echography of ciliochoroidal effusion syndrome. Ultrasound biomicroscopy (UBM) showed shallow anterior chamber (A) and anterior rotation of the ciliary body with angle closure (B). B-scan demonstrated 360 degrees shallow choroidal effusions in the posterior segment (C). After treatment and resolution of ciliochoroidal effusion, repeat UBM showed deep anterior chamber and open angle (D).
and plateau iris configuration with anterior rotation of the ciliary body and absence of the ciliary sulcus (E). B-scan showed resolution of shallow posterior choroidal effusion (F).

Figure 2. Echography of different anterior angle anatomies. (A) Normal anatomy demonstrating an open angle, iris root insertion at the ciliary body-sclera junction, and open ciliary sulcus. (B) Typical plateau iris configuration (PIC) anatomy demonstrating clear iris root angulation with peripheral narrow angle, iris root insertion near the ciliary body-sclera junction, anterior rotation of the ciliary process, and narrow ciliary sulcus. (C) Atypical PIC anatomy demonstrating an open angle, iris root insertion on top of the ciliary process, anterior rotation of the ciliary process and absent ciliary sulcus, which is hallmark of PIC. (D) Plateau iris syndrome demonstrating peripheral angle closure with iris root insertion on the ciliary process, anterior rotation of the ciliary process, and absent ciliary sulcus.
Table. Spectrum of Anterior Angle Anatomy Defined by High Resolution Ultrasound Biomicroscopy

<table>
<thead>
<tr>
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<th>Normal</th>
<th>Typical PIC</th>
<th>Atypical PIC</th>
<th>PIS</th>
</tr>
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<tr>
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<td>Open</td>
<td>Narrow</td>
<td>Open</td>
<td>Closed</td>
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<tr>
<td></td>
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<td>Uvea tissue and ciliary process</td>
<td>Ciliary process</td>
<td>Uvea tissue and Ciliary process</td>
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<tr>
<td><strong>Iris Insertion</strong></td>
<td>Normal</td>
<td>Anterior rotation</td>
<td>Anterior rotation</td>
<td>Anterior rotation</td>
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<td>Absent</td>
<td>Absent</td>
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<tr>
<td><strong>Ciliary Process</strong></td>
<td>Normal</td>
<td>Anterior rotation</td>
<td>Anterior rotation</td>
<td>Anterior rotation</td>
</tr>
<tr>
<td><strong>Orientation</strong></td>
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<td>Absent</td>
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<tr>
<td><strong>Ciliary Sulcus</strong></td>
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<td>Absent</td>
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Abbreviations: PIC, plateau iris configuration; PIS, plateau iris syndrome