

Case report

Cefixime-induced angle closure and transient myopic shift in a healthy individual; A case report

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ABSTRACT

Purpose: To report a case of Acute bilateral angle closure and Myopia following oral Cefixime therapy for pharyngitis.

Observation: A 49-year-old man presented to the clinic with a history of aggravating ocular pain and blurry vision in both eyes from 5 days ago. He was under treatment with oral Cefixime 400 mg twice a day for acute bacterial pharyngitis since last week. His refractive error was -3.75 and -4.25 diopters in the right and left eye respectively. Intraocular pressure (IOP) was 32 mm Hg in the right eye and 40 mm Hg in the left eye. Slit lamp examination and gonioscopy showed shallow anterior chamber with 360° appositional angle closure. Ultrasound biomicroscopy revealed shallow anterior chamber, narrow angle, supraciliary effusion and anterior rotation of ciliary body in both eyes. With diagnosis of drug-induced acute angle closure, oral Cefixime was discontinued and eye drops Betamethasone every 4 hours, Cosopt and Brimonidine twice a day, and Atropine 1% twice a day were started. Few days after starting treatment all ocular symptoms and signs were resolved.

Conclusions and importance: Systemic Cefixime can induce acute angle closure disease with myopic shift and elevated IOP secondary to supraciliary effusion and ciliary body rotation.

Introduction

Cefixime is one of the widely used antibiotics worldwide since its FDA approval in 1989.¹ Its main mechanism of action is inhibiting the cell wall synthesis in bacteria. Cefixime is usually prescribed for uncomplicated urinary tract infections, otitis media, pharyngitis and tonsillitis, acute exacerbations of chronic bronchitis, and Gonorrhea (cervical/urethral).^{2,3} Systemic complications of Cefixime include but not limited to diarrhea, dyspepsia, nausea and rarely urticaria and Stevens-Johnson syndrome.⁴ To the best of our knowledge, acute angle closure disease and acute myopia secondary to oral Cefixime have not been reported so far.

Case report

49-year-old man presented to our clinic on April 2019 with ocular pain and blurry vision from 1 week ago. The past ocular and systemic diseases were all negative. He has been using Cefixime 400 mg capsule (CEFIXIME 400MG CAP, Farabi Pharmaceutical Company, Iran) twice a day from 1 week ago due to acute bacterial pharyngitis. On ocular

examination, best corrected visual acuity (BCVA) of the right and left eyes were 20/30 and 20/20 respectively. The refractive error was -3.75 and -4.25 diopters in the right and left eye respectively. He had never had a visual problem to use corrective glasses. Intraocular pressure measured by Goldmann applanation tonometer was 32 mm Hg in the right eye and 40 mm Hg in the left eye.

Slit lamp examination in both eyes showed chemosis, mild cortical cataract and shallow anterior chamber (AC). In gonioscopy, there was 360° appositional angle closure. Funduscopic examination showed pink and sharp optic disc with Cup/disc ratio of 0.4 in both eyes. Based on the history of the patient and ocular examinations, diagnosis of secondary acute angle closure disease induced by systemic medications was made. Ultrasound biomicroscopy was then performed which showed shallow anterior chamber, narrow angle, supraciliary effusion and anterior rotation of the ciliary body in both eyes. (Fig. 1). By considering the pathophysiology of the disease, oral Cefixime was discontinued and oral prednisolone 50 mg/day (PREDNISOLONE-FORT 50MG TAB, Abur-aihan Pharmaceutical Company, Iran), eye drop Betamethasone (BETAMETHASONE DP 0.1% 5ML OPH DROP, Daroupakhsh Pharmaceutical Company, Iran) every 4 hours, eye drop Cosopt (COSOPT Drop,

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Ophthalmic 2/0.05%, 5 ml, Behestan Pharmaceutical Company, Iran) and Brimonidine (BRIMONIDINE DP 0.2% OPH DROP, Daroupanksh Pharmaceutical Company, Iran) twice a day and eye drop Atropine Sulfate 1% (Atrin 1% OPH DROP, Sinadarou Labs Company, Iran) twice a day were prescribed.

On the next day, the ocular symptoms were improved with 20% reduction in IOP and myopia in both eyes. After 5 days of starting medications, myopic shift, elevated IOP and supraciliary effusion were resolved completely in both eyes. Also refractive error reached to -0.5 diopter with BCVA of 20/20 in both eyes. In gonioscopy, angle was open in all quadrants with no signs of synechia formation.

Discussion

Cefixime is a third generation cephalosporin with chemical formula of $C_{16}H_{15}N_5O_7S_2 \cdot 3H_2O$ and molecular weight of 507.50 g/mol. It is a broad spectrum antibiotic active against gram-positive and gram-negative bacteria. This antibiotic is widely used in systemic infections but its use in the field of ophthalmology is very limited. In the European Union, intracameral Cefixime is utilized during the cataract surgery as a prophylaxis of postoperative endophthalmitis.⁵ There are no recognized ocular side effects related to Cefixime except for rare mild inflammation of ocular surface.⁶

This is the first report of acute angle closure disease and acute myopia following the systemic use of Cefixime for acute pharyngitis. His past medical history was unremarkable for any specific diseases including hypertension and cardiovascular diseases. Additionally, he declared no history of any significant ocular diseases. Cefixime was the only drug that he had consumed in past few months. Hereby, induced myopic shift and supraciliary effusion was mainly contributed to Cefixime consumption. Although it seems that people with undetected narrow iridocorneal angle, hyperopia and positive family history of angle closure are more susceptible to this idiosyncratic reaction,^{7,8} but in our case, none of the factors mentioned above were observed. Few days after suspension of Cefixime and starting topical Cycloplegic, Cosopt and Brimonidine and oral prednisolone, all ocular manifestations were resolved.

Overall, systemic medications can induce acute rise of IOP or

glaucoma by 2 different mechanisms: the first is acute angle closure attack by pupillary block mechanism secondary to the anticholinergic or adrenergic properties of the drug. The second mechanism is non-pupillary block angle closure that occurs because of supraciliary or suprachoroidal effusion, anterior rotation of ciliary body and lenticular swelling. The first mechanism usually occurs on those cases with anatomical predisposition such as shallow anterior chamber, small anterior chamber volume and narrow or occludable angle. In our case, all the clinical and imaging findings were in favor of the second mechanism as a cause of the disease. The most common group of drugs with the potential to stimulate myopia and glaucoma attack is Sulfa-based drugs. Medications containing sulfa component include antibiotics (e.g. Trimethoprim-sulfamethoxazole, Sulfadiazine, Sulfisoxazole, Dapsone, and Topical sulfa antibiotics), Rheumatologic drugs (e.g. Sulfasalazine, Probenecid, and Celecoxib), Sulfonylurea, Diuretics (e.g. Acetazolamide, Furosemide, Hydrochlorothiazide) and other drugs such as Sumatriptan, Topiramate, Sotalol and Zonisamide.^{7,9} Additionally, some studies reported the same probable role for prostaglandin E2, Isotretinoin and Cefalium.¹⁰⁻¹² By correct diagnosis, early treatment and discontinuing the responsible drug, all ocular findings will be reversible.¹³ For the management of the secondary angle closure, topical cycloplegics (mostly topical 1% atropine or Homatropin), topical and systemic steroids as well as aqueous suppressant (e.g. drop Beta blocker, adrenergic agents and Carbonic anhydrase inhibitors) are prescribed. Unfortunately, many of these cases are wrongly diagnosed as primary angle closure attack and YAG laser PI is performed. There are some clinical points which help to differentiate between these two mechanisms such as simultaneous bilateral involvement and significant myopic shift which is induced mostly by systemic medications.

In conclusion, systemic Cefixime can cause ciliochoroidal effusion, increased IOP, angle closure glaucoma and induced myopia. Although this complication has not been reported before but physicians should be aware of this rare side effect.

Patient consent

This report does not contain any personal identifying information of the patient. Additionally, a written consent was obtained from the

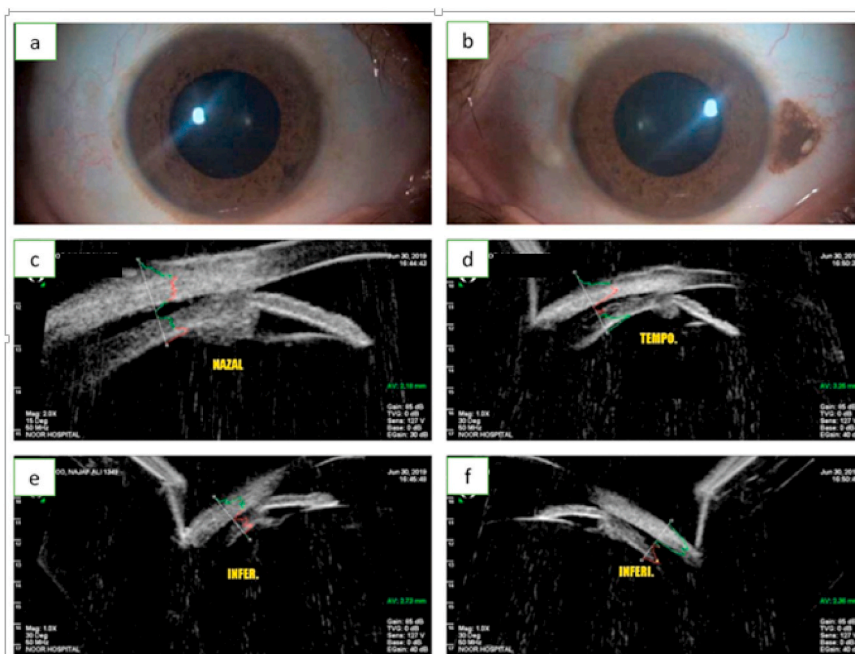


Fig. 1. a and b; slit photos shows shallow anterior chamber of the right and left eye respectively. c and d; ultrasound biomicroscopy shows supraciliary effusion of the right and left eye respectively. e and f; ultrasound biomicroscopy shows appositional angle closure and supraciliary effusion of the right and left eye respectively.

patient.

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

The authors have nothing to disclose.

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References

1. Smith GH. Oral cephalosporins in perspective. *Diap Ann Pharmacother.* 1990;24(1):45–51.
2. Faulkner RD, Yacobi A, Barone JS, Kaplan SA, Silber BM. Pharmacokinetic profile of cefixime in man. *Pediatr Infect Dis J.* 1987;6(10):963–970.
3. Siddiq S, Grainger J. The diagnosis and management of acute otitis media: American Academy of Pediatrics Guidelines. *Arch Dis Child Educ Pract.* 2013;100(4):193–197, 2015.
4. Thompson JW, Jacobs RF. Adverse effects of newer cephalosporins. An update. *Drug Saf.* 1993;9(2):132–142.
5. Group EES. Prophylaxis of postoperative endophthalmitis following cataract surgery: results of the ESCRS multicenter study and identification of risk factors. *J Cataract Refract Surg.* 2007;33(6):978–988.
6. American Academy of O. *Basic and Clinical Science Course.* 2016:20172016.
7. Razeghinejad M, Pro M, Katz L. Non-steroidal drug-induced glaucoma. *Eye.* 2011;25(8):971.
8. Ramos-Esteban J, Goldberg S, Danias J. Drug induced acute myopia with supraciliary choroidal effusion in a patient with Wegener's granulomatosis. *Br J Ophthalmol.* 2002;86(5):594–596.
9. Levy J, Yagev R, Petrova A, Lifshitz T. Topiramate-induced bilateral angle-closure glaucoma. *Can J Ophthalmol.* 2006;41(2):221–225.
10. Park Y-m, Lee T-E. Isotretinoin-induced angle closure and myopic shift. *J Glaucoma.* 2017;26(11):e252–e254.
11. Arana LA, Bach MB, Vedana G, Volkmann MA, Arana J. Cefalium-induced bilateral transient myopia, retinal folds, and focal choroidal delay. *Retin Cases Brief Rep.* 2018;12(2):118–121.
12. Nakajima T, Nakagami T, Kaneko S, Kawamura H, Watanabe I. Effects of prostaglandin E2 on intraocular pressure, anterior chamber depth and blood flow volume of the iris and the ciliary body in rabbit eyes. *Nippon Ganka Gakkai Zasshi.* 1992;96(4):455–461.
13. Fraunfelder F, Fraunfelder F. Adverse ocular drug reactions recently identified by the national registry of drug-induced ocular side effects. *Ophthalmology.* 2004;111(7):1275–1279.