

Case Report

Acute allergic reaction caused by topical azithromycin eye drops: A report of two cases



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Abstract

Azithromycin 1.5% ophthalmic solution (Azyter[®], Thea Pharmaceuticals, Newcastle, UK) is an effective and well-tolerated option for the treatment of bacterial conjunctivitis and blepharitis, and has the advantage of a shorter treatment duration than other topical antibiotics. No acute allergic reaction has yet been reported in response to topical azithromycin eye drops. Here, we report two cases with unusual acute-type allergic reaction to topical azithromycin eye drops. A 63-year-old female patient and 67-year-old male patient treated for blepharitis with topical azithromycin 1.5% eye drops presented with epiphora, eyelid edema, chemosis, conjunctival injection, hyperemia, intensive papillary reaction, and rhinitis within 30 min of instillation. Upon cessation of the topical medication and administration of antiallergic therapy, both patients immediately showed dramatic improvement. Acute-type allergic reaction to topical azithromycin eye drops may be a rare side effect, but ophthalmologists should keep this possibility in mind and inform the patients about its potential occurrence.

Keywords: Allergy, Drug hypersensitivity, Macrolide antibiotic, Topical azithromycin, Type I hypersensitivity

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Introduction

Macrolide antibiotics have a number of advantages, including effective bacteriostatic and bactericidal actions, good intracellular penetration, rapid tissue distribution, prolonged post-antibiotic effects, and additional anti-inflammatory and immunomodulatory functions.^{1,2} Macrolides are usually well tolerated and have a low incidence of allergic side effects (0.4–3%).³ Because of their efficacy and safety benefits, these antibiotics are widely used in the treatment of systemic and local infections, including those of eye.

Topical azithromycin 1.5% ophthalmic solution (Azyter[®], Thea Pharmaceuticals, Newcastle, UK), a second-generation

macrolide belonging to the azalide group, shows broad-spectrum activity against gram-positive, gram-negative, and atypical (e.g., *Chlamydia trachomatis*) bacteria. The clinical efficacy of topical azithromycin 1.5% eye drops has been demonstrated in patients with bacterial conjunctivitis and blepharitis, and these patients also experience a shorter treatment duration than is observed in patients treated with other topical antibiotics.^{4–8}

Topical administration of azithromycin is usually well tolerated.⁴ One case of allergic contact dermatitis has been reported in the literature,⁹ but no acute allergic reactions have yet been reported following application of eye drops containing azithromycin. Here, we report an unusual

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acute-type allergic reaction to topical azithromycin eye drops in two patients.

Case report

The first case was a 63-year-old female who was admitted to our ophthalmology clinic in March 2016 with redness in the eyelid margins, crusting of the lashes, and an itching and burning sensation. Her best corrected visual acuity (BCVA) was 20/20 in the right and left eyes, and her intraocular pressure (IOP) was 14/16 mmHg. A funduscopy examination revealed retinal pigment epithelial changes in the macula. Slit lamp examination showed chronic posterior and staphylococcal anterior blepharitis, stage 3 Meibomian gland dysfunction, grade 3 corneal fluorescein staining according to the Oxford grading scale, a break-up time (BUT) of 4/4 seconds, and stage 2 nuclear sclerosis. Her Schirmer test result was 5/7 mm. The patient was diagnosed with blepharitis and treated with topical azithromycin (1.5% ophthalmic solution), preservative-free dexamethasone topical eye drops, preservative-free artificial tear eye drops, and warm compresses.

The second case was a 67-year-old male, who was admitted in May 2016 with itching, photophobia, and redness in both eyes. He had been diagnosed with rosacea, Meibomian gland dysfunction, and non-Sjogren dry eye syndrome, which had been treated for the previous four months with lid scrubs, topical cyclosporine, and artificial tear eye drops. An ophthalmologic examination indicated the presence of acute anterior staphylococcal blepharitis. Topical azithromycin (1.5% ophthalmic solution), preservative-free dexamethasone topical eye drops, and warm compresses were prescribed for the treatment of his blepharitis.



(a)



(b)

Fig. 1. On ophthalmologic examination of a 63-year-old female patient (a), eyelid hyperemia, edema, and epiphora were recorded. On ophthalmologic examination of a 67-year-old male patient (b), eyelid edema and epiphora with fluorescein were recorded.

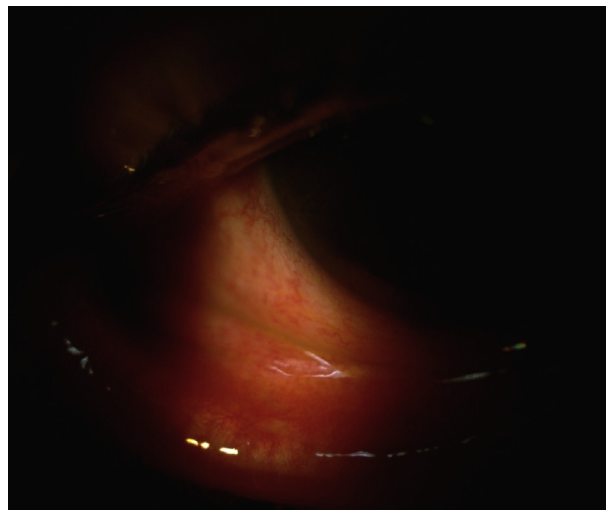


Fig. 2. Chemosis and conjunctival hyperemia was evident on slit lamp examination of a 67-year-old male patient.

Both patients reported sneezing, itching, nasal congestion, rhinorrhea, eyelid edema, and itchy, red, and watery eyes within 30 min after instillation of the topical azithromycin drops; these symptoms lasted 3–4 hours. The 67-year-old male patient was admitted urgently to our clinic after instillation of the second dose. Ophthalmologic examinations of both patients revealed eyelid edema, chemosis, conjunctival injection and hyperemia, excessive papillary reaction, epiphora, and rhinitis (Fig. 1).

Slit lamp examinations also confirmed the chemosis and conjunctival hyperemia (Fig. 2). The female patient did not take the second dose, but the allergic conjunctivitis was still present the next day. The azithromycin use was stopped in both patients, and topical and systemic antiallergic treatment was initiated. Antiallergic treatment protocol was preservative-free dexamethasone topical eye drops five times a day, olopatadine 0.1% topical eye drops two times a day, and oral desloratadin 5 mg once a day for five days. The symptoms of acute allergic reaction quickly subsided.

There was no history for atopy or drug allergy in both patients and in their families.

Two months after these allergic reactions, both patients had a skin prick test with azithromycin at the allergy immunology clinic. The first case tested negative to azithromycin in a concentration 1/10, but the results of full-strength skin test were positive with a wheal and flare size of 5 and 15, respectively. In the second case, skin prick test with azithromycin was also negative; and wheal and flare size was 5 and 20 on full strength concentration of azithromycin, respectively. All tests were run in duplicate, with an unremarkable saline control and a histamine control that measured wheal and flare size of 5/15.

Both patients have given written consent for the inclusion of their photographs in this report.

Discussion

This paper is the first report of an azithromycin eye drop preparation causing acute allergic reactions. Hypersensitivity reactions of the immune system are traditionally classified into four types. Type 1, or immediate hypersensitivity

reactions, usually occurs in 30–60 min after contact with the allergen and are mediated by immunoglobulin E (IgE). Type 1 hypersensitivity reactions manifest as urticaria and eczema in the skin, conjunctivitis and chemosis in the eye, and rhinitis in the nasopharynx, and these reactions can range clinically from rhinorrhea to asthma and anaphylactic shock.^{3,10}

Azithromycin shows the immunomodulatory and anti-inflammatory action typical of a second-generation macrolide. It also exerts bacteriostatic and bactericidal effects by binding to the 50S ribosomal subunit of bacteria, thereby preventing peptide translocation, and subsequent protein synthesis.¹¹

Allergy to systemic macrolides like azithromycin, and especially IgE-mediated immediate hypersensitivity reactions, are extremely rare. Azithromycin is accepted as a well-tolerated and effective single dose drug in all age groups; however, the rapid increase in its use has increased the number of reported adverse reactions.^{9,12} A macrolide allergy diagnosis cannot be predicted or confirmed by allergy tests like skin tests (skin prick tests, intradermal tests, patch tests, etc.), *in vitro* tests (the lymphocyte transformation test, basophil histamine release test, etc.), or oral provocation tests.¹³

The present report indicates that topical azithromycin treatment may cause unpredictable type 1 hypersensitivity reactions that can create patient anxiety and dissatisfaction. For this reason, the patient must be informed prior to azithromycin administration about the possible side effects of the drug and of the potential for allergic reactions to other macrolide group antibiotics.

In conclusion, acute allergic reaction may be a rare side effect of topical azithromycin eye drop application. Ophthalmologists should therefore be aware of the allergic potential of topical azithromycin eye drop treatments and, as a precaution, should monitor their patients during the first administration of the drug.

Patient's consent to publication

Patients presented in this case report have given written consent for the inclusion of their photographs in this report.

Conflict of interest

The authors declared that there is no conflict of interest.

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