



Case report

Corneal ulceration and episcleritis associated with Wiskott–Aldrich syndrome

Bruce M. Zagelbaum^a, Danielle C. Kalberer^{b,*}, Barry S. Pinchoff^a^a Department of Ophthalmology, Hofstra Northwell School of Medicine, 500 Hofstra Blvd, Hempstead, NY 11549, United States^b Department of Optometry, Northport Veterans Affairs Medical Center, 79 Middleville Rd, Northport, NY 11768, United States

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ABSTRACT

Purpose: To present anterior segment ophthalmic manifestations of Wiskott–Aldrich syndrome (WAS), a rare X-linked primary immune-deficiency.**Observations:** A 15-year old male with WAS presented with multiple corneal ulcers of the left eye. Once resolved, this was followed by separate episodes of episcleritis in the left eye and corneal infiltrates of the right eye. Successful treatment included topical antibiotics and anti-inflammatories.**Conclusions:** Ocular manifestations of WAS, due to secondary infection and inflammation, may be severe. This case report emphasizes the importance of prompt ophthalmic evaluation and treatment of these patients.© 2016 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

Wiskott–Aldrich syndrome (WAS) is an X-linked recessive primary immunodeficiency. This rare condition is characterized by an increased risk of recurrent infection, thrombocytopenia and eczema, which begins in infancy.¹ Our case report involves a 15-year-old male with WAS who presented initially with multiple corneal ulcers followed by separate episodes of corneal infiltrates and episcleritis.

2. Case report

A 15-year-old Caucasian male presented with progressive redness and pain of the left eye for 5 days. His pediatrician prescribed moxifloxacin ophthalmic solution and oral Augmentin one day prior to presentation. Past ocular history was unremarkable. Medical history was significant for WAS. The patient was concurrently being managed by an otolaryngologist for chronic sinus infections and undergoing iron infusion therapy for iron-deficiency anemia.

Uncorrected visual acuity was 20/25 in the right eye and 20/25 in the left. On slit lamp examination, mixed anterior and posterior blepharitis was present in both eyes with mild flaking on the patient's lashes. No telangiectatic vessels were noted. The right cornea showed a small inferior pannus with non-injected conjunctiva. The conjunctiva of the left eye showed diffuse injection. The left cornea displayed 5 areas of ulceration of which 3 were located superiorly and 2 inferiorly (Fig. 1). All ulcers stained with fluorescein. Both anterior chambers were quiet. The patient was diagnosed with corneal ulcers of the left eye, most likely due to an increased susceptibility and abnormal immune reaction to the common pathogen *Staphylococcus aureus* associated with chronic blepharitis.

Treatment consisted of continuing topical moxifloxacin and oral Augmentin as previously prescribed by the pediatrician. Topical prednisolone acetate and ciprofloxacin ophthalmic ointment at night were added. An extensive discussion took place with the patient and his mother regarding lid hygiene practices. The regimen to be used included warm compresses morning and night with good lid hygiene.

At the follow-up visit, the corneal ulcers had decreased in size with pinpoint staining along with quiet conjunctiva. Topical moxifloxacin and prednisolone acetate were tapered and the ciprofloxacin ointment was continued. At 1 week follow-up, the ulcers were significantly improved; however, peripheral corneal thinning was evident. As the corneal thinning was attributed to the topical

* Corresponding author.

E-mail addresses: eyesports@gmail.com (B.M. Zagelbaum), Danielle.kalberer@gmail.com (D.C. Kalberer), bpinchoff@gmail.com (B.S. Pinchoff).

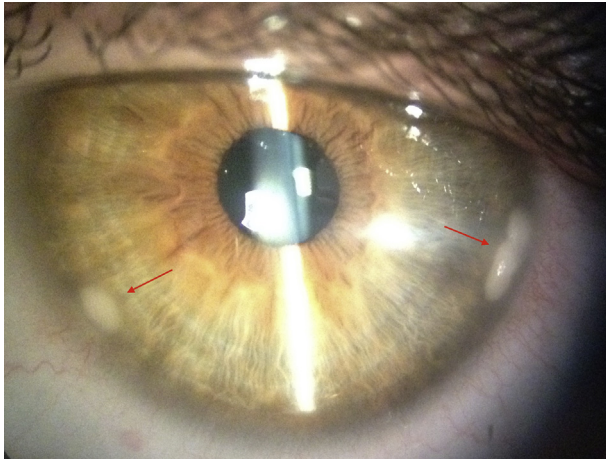


Fig. 1. Two inferior corneal ulcerations (arrows).

steroid, prednisolone acetate was discontinued and no further thinning recurred on follow-up exams.

Two months later, the patient presented with redness and discomfort in the left eye of one days duration. The conjunctiva of the left eye showed grade 2 sectoral injection temporally. Corneal scars were present in the left eye with no staining. The right eye remained quiet. The patient was diagnosed with episcleritis of the left eye. Treatment consisted of prednisolone acetate ophthalmic suspension twice a day; a lower dose due to the previous corneal thinning noted. At follow-up 4 days later, the left eye's condition had not improved and prednisolone acetate was increased to 1 drop four times daily. Subsequent follow-up showed that the condition was markedly improved and the medication was tapered over the course of two weeks with no recurrence.

One week after the episode of episcleritis resolved, the patient presented with a painful red right eye of 2 days duration. Vision remained unchanged. The conjunctiva of the right eye showed diffuse injection more concentrated nasally. The right cornea displayed 2 areas of infiltration supero-nasally (Fig. 2). Slit lamp examination of the left eye was unremarkable. Both anterior chambers were quiet. Treatment consisted of prednisolone acetate ophthalmic suspension and moxifloxacin solution both four times

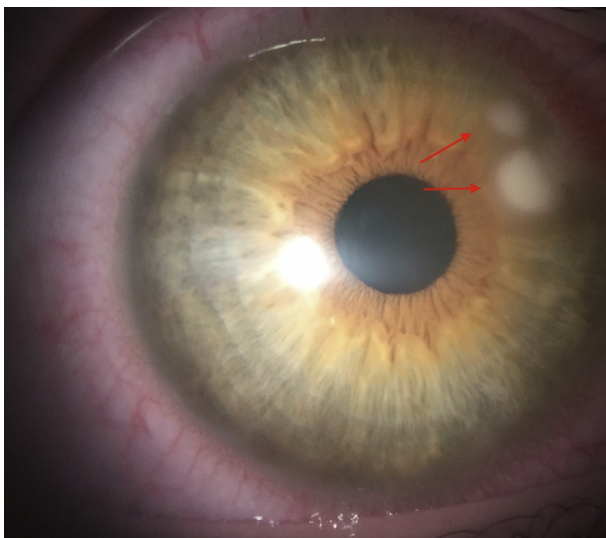


Fig. 2. Two supero-nasal corneal infiltrates (arrows).

daily to the right eye. At follow-up 4 days later, the condition showed only slight improvement and the patient was asked to continue on the same medication course. At subsequent follow-up, 5 days later, the condition was markedly improved; the medications were tapered with no recurrence of the condition.

3. Discussion

WAS is a rare, X-linked primary immune deficiency due to mutations of the WAS gene in hematopoietic cells.¹ The classic triad of eczema, thrombocytopenia and immunodeficiency is often observed. The average incidence of WAS is approximately 4 cases per million boys.² Historically, patients suffering from this condition have a poor prognosis and survival beyond the second decade is uncommon.³ Due to poor survival rate and rarity of the condition, reports of WAS ophthalmic manifestations have been infrequent. As treatments, including splenectomy, bone marrow transplantation and gene therapy continue to improve prognosis, less life-threatening complications have come to light.

Previously reported ophthalmic manifestations result from the immune-compromised and the hemorrhagic state caused by WAS. These include blepharoconjunctivitis, keratitis, corneal ulceration, subconjunctival hemorrhage, and papilledema.⁴ Karampatakis et al., in 2011 reported a case of scleritis and iritis in an 18-year old Caucasian male with WAS.⁴ Guss et al., in 1982 presented three cases with WAS-related episcleritis, marginal keratitis and chronic blepharitis. One such case involved a 13-year old male who suffered from a single bacterial corneal ulcer adjacent to marginal keratitis. The ulcer was cultured and the organism was identified as *Hemophilus aegyptius*, while a culture of the eyelids revealed various strains of staphylococcus. According to Guss, WAS patients, who commonly suffer from eczema, should be kept on a long-term lid hygiene regimen, including vigorous lid scrubs, due to the increased risk of bacterial infection and resultant blephar-conjunctivitis.⁴ Podos also attributed noted cases of conjunctivitis and ulcerative keratitis to the presence of eczema of the eyelids.⁵ Podos, in 1969, noted that ophthalmic molluscum contagiosum and herpes simplex infections were common in patients with WAS in addition to or in conjunction with previously noted blephar-conjunctivitis. He also noted that the two most common bacterial pathogens related to ocular manifestations were *Staphylococcus* and *Hemophilus influenzae* which is consistent with that reported by Guss.⁵

Whereas previous, older cases used culturing to help manage treatment modalities, we felt that with the advent of fourth generation fluoroquinolones, culturing would not have changed our initial management. Had the patient not responded to our initial management, however, culturing would have been entertained.

4. Conclusion

Our patient had separate episodes of ocular manifestations which included corneal ulceration, corneal infiltration and episcleritis associated with WAS. Treatment with topical antibiotics, and topical anti-inflammatories was successful in this case.

Chronic blepharitis and its sequelae are multifactorial in nature and attributed to direct infection with staphylococcus, and inflammatory or allergic reaction to exotoxin.⁶ While similar presentations can occur in immune-competent individuals, we believe patients with WAS are at increased risk due to exaggeration of both causative factors. We hypothesize that our patient's ocular manifestations were due to both increased propensity for infection due to immune compromise and also abnormal responses to *staphylococcus aureus* exotoxins, byproducts of the common eyelid pathogen.

With eczema, or atopic dermatitis, being one third of the triad of disorders leading to WAS diagnosis, we must consider its role in creating an altered ocular surface environment. Our patient did have associated ocular signs including blepharitis with flaking on his lashes. In a study of keratoconjunctivitis associated with meibomian gland dysfunction, those patients with underlying dermatitis or atopic conditions showed the most severe ocular signs.⁷

Whereas multiple proteins are secreted by *staphylococcus aureus*, alpha-toxin has been identified as the most pathogenic. This protein has known cytolytic properties and has been shown to initiate the classical and alternate complement pathways, initiating inflammatory reactions.⁸ The cytolytic effect on the cornea can lead to the creation of membrane-damaging pores, increasing ulceration risk. The exotoxin increases incidence of inflammatory response activation, which in the cornea involves infiltration of white blood cells. In addition, episcleritis is caused by an infiltration of mononuclear leukocytes from superficial blood vessels.³

This report is one of few attestations to the need for ophthalmologic management of patients with WAS; this consists of eradication of chronic infectious agents and management of chronic inflammation.

Patient consent

The patient and legal guardian provided written consent for publication of personal information including medical record details and photographs.

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Conflict of interest

None. The authors have no financial disclosures.

Authorship

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

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