Topical Cyclosporine in Severe Steroid-Dependent Phlyctenular Keratoconjunctivitis Associated with Ocular Rosacea

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ABSTRACT

Introduction: Phlyctenular keratoconjunctivitis is an uncommon and often misdiagnosed ocular immunological disorder, secondary to ocular or systemic illness, that usually responds well to topical steroids. In a few cases, it can be refractory or steroid dependent, hindering treatment.

Case Report: A healthy 12-year-old dark skin female without prior ocular or systemic disease presented in our department with a corneal ulcer and centripetal corneal neovascularization in the left eye and phlyctenules in both eyes, without blepharitis. Testing for different possible inciting agents, such as *Chlamydia* and tuberculosis, was negative. During follow-up, the patient presented episodes of chalazia and facial pustules and the diagnosis of bilateral phlyctenular keratoconjunctivitis secondary to recurrent ocular rosacea was presumed. As soon as the corneal ulcer was completely healed, the patient started topical corticosteroid treatment with clinical improvement. After several failed attempts of steroids tapering, topical cyclosporine was added to therapy, enabling corticosteroid discontinuation.

Discussion: Phlyctenular keratoconjunctivitis is frequently caused by a hypersensitivity reaction to microorganisms, such as *Staphylococcus* species and *Mycobacterium tuberculosis*, but it can be also associated with ocular rosacea without evidence of other inciting agents. The progression of phlyctenulosis to severe complications, as corneal scarring or even perforation, can compromise visual acuity at an early age. Thus, for the successful management of this disease it is important to find and treat any inciting agent. Even with adequate treatment with steroids, side effects of long-term therapy to control recurrent ocular inflammation grants topical cyclosporine an important role in disease management.

Keywords: rosacea, children, phlyctenular keratoconjunctivitis, cyclosporine

CASE REPORT

A healthy 12-year-old dark skin female without history of prior ocular or any relevant systemic disease presented in our emergency department with photophobia associated with hyperemic and painful left eye for 6 weeks. Ophthalmological examination revealed best corrected visual acuity (BCVA) of 20/20 in right eye (OD) and 20/30 in the left eye (OS). Slit-lamp examination of OS showed conjunctival hyperemia, a paracentral corneal ulcer, without relevant findings in OD. No signs of blepharitis bilaterally. Fundoscopy of both eyes was unremarkable with no vitreous inflammation and seemingly healthy retinae bilaterally.

Gram stain and culture of a conjunctival swab was unremarkable. The patient was treated with topical moxifloxacin (q.i.d.), ciprofloxacin ointment (q.d.) and artificial tears (q.2h.), successfully restoring corneal integrity.

Four weeks later, she presented with new symptoms and slit-lamp examination revealed a new stromal ulcer and centripetal corneal neovascularization in OS, and conjunctival hyperemia and phlyctenules in both eyes. (Figure 1) At this phase, the examination of the eyelid margin revealed signs of posterior blepharitis, including meibomitis. The patient was treated with topical moxifloxacin (q.i.d.), oral doxycycline (100mg q.d.) and artificial tears (q.2h.). As soon as the corneal ulcer was completely healed, the patient started topical dexamethasone eye drops (q.i.d.) and a low dose of oral prednisolone (20 mg/day).

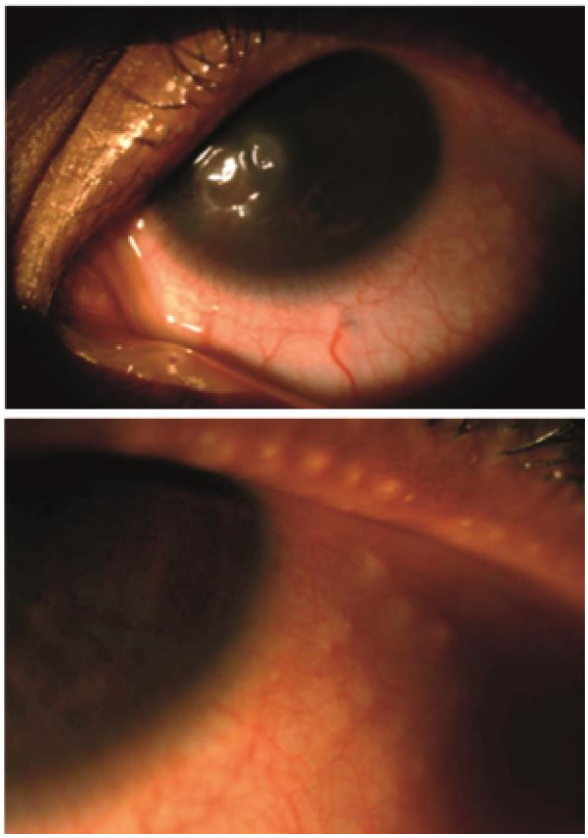

Figure 1 - Slit-lamp photograph of the left eye reveals conjunctival hyperemia, corneal ulcer associated with corneal neovascularization approaching visual axis (A) and temporal conjunctival phlyctenules (B).

Testing for C*hlamydia trachomatis* and M*ycobacterium tuberculosis* was negative, as it was immune disease investigation. During follow-up, the patient presented episodes of chalazia and facial pustules, so eyelid hygiene and warm compresses were added to the treatment (Figure 2). At this point, the diagnosis of bilateral phlyctenular keratoconjunctivitis (PK) secondary to recurrent ocular rosacea was presumed.

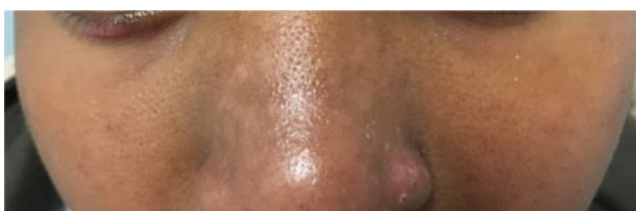

Figure 2 - Chalazion in the lower eyelid of the right eye and facial pustules.

Two months later, conjunctival and corneal phlyctenules improved with regression of the neovessels but a left paracentral corneal opacity remained, leading to

vision impairment in OS, with 20/40 BCVA (20/20 in OD).

After several failed attempts of steroids tapering (Figure 3), the addition of topical cyclosporine 0.05% (q.i.d.) for 3 months to the therapy enabled topical steroid discontinuation, in order to avoid side effects of its long-term use, such as cataract and intraocular pressure rise (Figure 4).

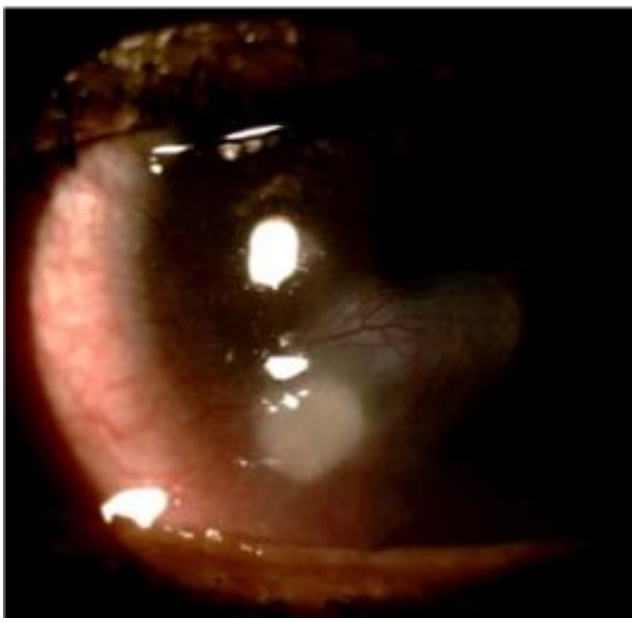

Figure 3 - Relapsing episodes with inflamed left corneal phlyctenule, associated with a trail of superficial vascularization from the inferior limbus.

Figure 4 - Clinical stabilization: complete regression and resolution of corneal phlyctenules and corneal neovascularization with a paracentral corneal scarring in OS.

After that, topical cyclosporine 0.05% (b.i.d.) was maintained for more than 12 months, along with eyelid hygiene and preservative-free lubricant eye drops, and the patient remained in remission.

DISCUSSION

Phlyctenular keratoconjunctivitis is a rare local corneal and conjunctival inflammation, presumed to be a type IV cell-mediated hypersensitivity to microbial antigens, with bilateral presentation in approximately 40% of the patients.[1] It occurs primarily in children and adolescents under 18 years old with higher prevalence in females and it is typically caused by *Staphylococcus* species and *Mycobacterium tuberculosis*.[2] The most common findings in PK are inferior superficial punctate keratopathy, corneal and conjunctival phlyctenules. These two types of phlyctenules can be distinguished mainly by the location and severity of the symptoms. Although both can be located at the limbus, corneal phlyctenules frequently migrate to cornea and progress to corneal ulceration and posterior neovascularization.[3] In severe cases, they can progress to corneal scarring/opacities, thinning and even perforation.

Less frequently, phlyctenulosis can be associated with blepharitis, meibomian gland dysfunction, recurrent hordeola/chalazia, telangiectasias of the lid margin, and aqueous tear film insufficiency suggesting a possible causative role of ocular rosacea in PK.[3–5] In fact, ocular rosacea occurs in more than 50% of the patients with this disease.[7]

Typically, rosacea is harder to identify in dark skin individuals, especially because important signs such as facial flushing and erythema are obscured.[6] It is also difficult to recognize in children because dermatologic findings are frequently absent.[7] Interestingly, up to 90% of pediatric patients already have corneal involvement before the diagnosis of ocular rosacea is made, emphasizing how intricate this diagnosis can be.[8] In this particular case, the recognition of the ocular signs, and some months later the dermatologic findings was fundamental for the diagnosis of PK secondary to ocular rosacea. Early recognition of earlier ocular signs of this condition and prompt, aggressive treatment is essential to improve patient outcomes by preventing extensive corneal scarring and opacification.

Although in mild to moderate cases, especially in the presence of staphylococcal or rosacea related blepharitis, treatment with eyelid hygiene and oral antibiotics drugs, like doxycycline or erythromycin, is usually enough to control the inflammation.[7] Topical steroids are considered the mainstay of treatment in cases of severe disease with corneal ulcers and neovascularization.[9] Unfortunately, in a few patients, the chronic inflammatory nature of rosacea, with intermittent recurrences, renders it a steroid-dependent disorder or refractory to steroid therapy tapering. In order to prevent potential adverse effects of steroid long-term use, topical or even systemic immunosuppressive drugs, as cyclosporine and tacrolimus, have been used with success.[1,9–11] The literature reports an adequate control of ocular inflammation with topical cyclosporine (0.2% and 2%)[9,11] with minimal side effects, in more complex cases.[1,9] Topical cyclosporine 0.05% has also shown to be more effective than artificial tears in the rosacea-associated eyelid disease and corneal changes.[12] Our case illustrates well how aggressive this disease can be and supports the use of a lower concentration of topical cyclosporin (0.05%) in the successful management of recurrent ocular inflammation in childhood ocular rosacea with severe steroid-dependent PK.

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Conflicts of interest: none.