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Effectiveness of 0.05% Cyclosporine in the Treatment of Subepithelial Infiltrates Related with Adenoviral Keratoconjunctivitis

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Introduction

Adenoviral keratoconjunctivitis (AK) has a wide spectrum of duration and clinical manifestations. Conjunctival infection with adenovirus is the most common external ocular infection worldwide and is highly contagious, sometimes appearing in epidemics [1]. After an incubation period of 2 to 14 days, symptoms of tearing and itching along with findings of conjunctival edema and hyperemia with or without conjunctival pseudomembranes can appear in 1 eye, and then in the fellow eye a few days later [2].

Individual serotypes typically cause specific types of disease; thus, epidemic keratoconjunctivitis is usually due to serotypes 8, 19, and 37, follicular conjunctivitis to serotypes 3, 4 and 7 [3].

Keratitis that follows approximately 10 days after the onset of the follicular conjunctivitis, may present with the formation of Subepithelial Corneal Infiltrates (SEIs) usually bilaterally and often asymmetric [4].

CsA is a well-known immunosuppressant that has been used in the prevention of transplant rejection for decades. It is an immunomodulator that specifically inhibits $CD4^+$ T-lymphocyte proliferation through the inhibition of interleukin-2 receptor expression and other T cell–dependent inflammatory mechanisms. CsA also has inhibitory effects on eosinophil and mast cell activation and the release of granule proteins, inflammatory mediators, and cytokines. Topical CsA has been used successfully in the treatment of Mooren ulcers, ulcerative keratitis associated with rheumatoid arthritis, Thygeson's punctate keratitis, Keratoconjunctivitis Sicca (KCS), Vernal Keratoconjunctivitis (VKC), Atopic Keratoconjunctivitis (AKC), ligneous conjunctivitis and high-risk penetrating keratoplasty [5].

Case

A 30 year-old man who did not have any prior eye discomfort, was referred to hospital with complaints of blurred vision, foreign-body sensation, irritation and photophobia in his left eye. He was on topical moxifloxacin HCl (Vigamox®), topical fusidic acid (Fucithalmic®) and topical ketorolac tromethamine 0.5% (Acular LS®) treatment. Because of the increase in the white spots on the cornea, the patient was referred to our clinic.

On examination, his best corrected vision was 20/20 in both eyes; intraocular pressures were within normal limits. According to slit-lamp examination, the right eye was normal but in the left eye dense corneal subepithelial deposits and conjunctival ciliary injections and chemosis were seen (Figure 1). Fundus examination was normal in both eyes. The medication of the patient was rearranged. Topical antibiotics and topical ketorolac tromethamine 0.5% eye drops were discontinued. Topical 0.05% cyclosporine (Restasis®) 3 times a day was started.

On the 4th day of the treatment, all symptoms were improved including blurred vision, foreign-body sensation, irritation, and photophobia. Corneal subepithelial deposits had disappeared; conjunctival ciliary injection and chemosis both were decreased (Figure 2). His medication was continued.

On the 7th day of the treatment no subepithelial deposits, no conjunctival ciliary injection and no chemosis were seen (Figure 3). All medications were stopped on the 14th day. From now on the has't has any complaints about his eyes.

Discussion

AK may cause serious sight-threatening complications related with dense subepithelial deposits. These subepithelial deposits may be permanent and result in visual impairment.

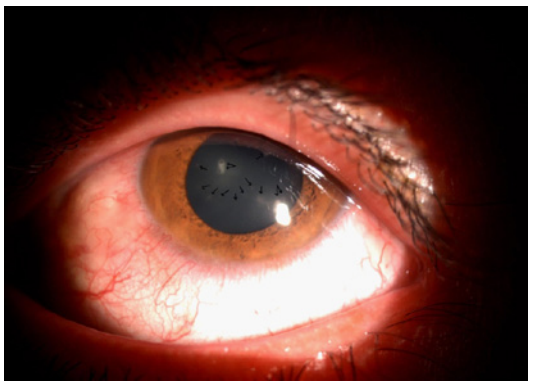

Figure 1: Dense corneal subepithelial deposits and conjunctival ciliary injections and chemosis were seen.

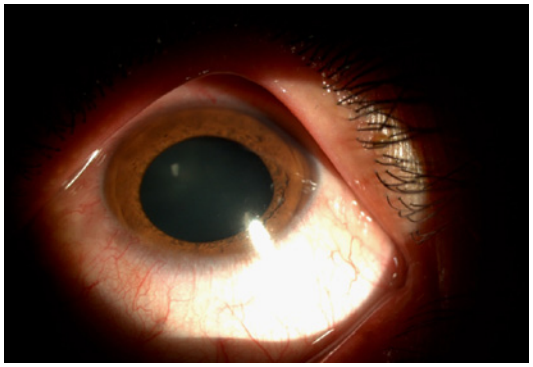

Figure 2: Corneal subepithelial deposits had disappeared and conjunctival ciliary injection and chemosis were decreased.

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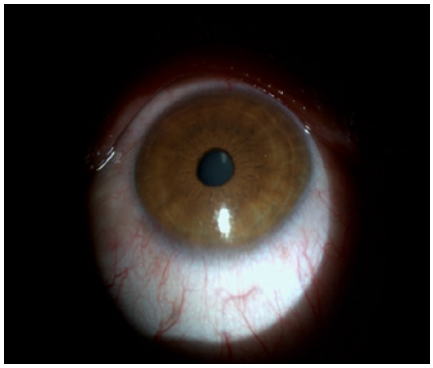

Figure 3: No subepithelial deposits, no conjunctival ciliary injection and no chemosis were seen.

Although AK is not blinding, SEI in the visual axis may cause serious reduction of visual acuity. SEIs may show persistancy for months to years.

SEIs caused by adenoviral infection are a common chronic ocular condition that typically presents with significant patient symptomatology [3]. Long-term topical steroid use is usually effective but may be associated with side effects. Laibson et al. showed that topical corticostreoid treatment was proven to prevent SEI [6].

Okumus et al. showed promising results with 0.5% CsA in steroid resistant cases [7]. In addition, 2% and 0.5% CsA in a mouse model have been shown to reduce the formation of SEI [8]. In a retrospective study, seven patients with corneal SEIs unresponsive to steroids were treated with CsA. Because of the side effects of corticosteroids in adenoviral keratoconjunctivitis, instead of corticosteroids, it was reported that CsA could be used [9].

Topical CsA has proved useful for subjective improvement of patients with post-adenoviral infiltrates in the retrospective case series by Levinger et al. [10] However, in this series, no improvement in visual acuity was observed. In addition to Hillenkamp et al. [4] found topical CsA didn't prove useful for decreasing the incidence of post-adenoviral infiltrates.

Finally, the evidence from this single case is insufficient for proposing the recommendation that topical CsA should be the first line of treatment of post-adenoviral infiltrates. In order to prevent the long-term complications of corticosteroids, topical CsA can be used instead of steroids. We believe that this treatment may benefit many patients with corneal infiltrates related AK around the world. This interesting hypothesis should be proven through a randomised clinical trial of topical CsA versus topical corticotherapy for post-adenoviral infiltrates.

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