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LETTER TO THE EDITOR

Topical 0.03% tacrolimus ointment in the management of ocular surface inflammation in chronic GVHD

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We present a case in which topical tacrolimus 0.03% was used successfully in the management of ocular surface inflammation from chronic GVHD. Dry eye is the most common complication of chronic GVHD, occurring in 40–76% of patients.[1] Inflammation of the ocular surface leads to aqueous deficiency and tear film instability; blindness could ensue from conjunctival cicatrization and corneal epithelial breakdown.[2] The mainstay of treatment for ocular surface GHVD consists of lubrication and topical steroid,[3] but the long-term use of the latter is limited by complications, such as cataract and glaucoma. Protopic (Tacrolimus 0.03%, Astellas Pharma, Tokyo, Japan) is a dermatological ointment approved by the US Food and Drug Administration for atopic eczema. Off-label ophthalmic use has emerged for eczematous eyelid disease, atopic keratoconjunctivitis and various other anterior segment inflammations with promising results.[3,4] Its twice-daily regimen, higher potency than commercially available calcineurin inhibitor (CYA 0.05%), lack of serious side effects and steroid sparing properties have made it ideal for at least short-term use when other modalities fail.

A 13-year-old Chinese boy was referred to the eye clinic in November 2008 with a 2-month history of bilateral intermittent redness and pain. He was a known case of Ph translocation-positive (Ph+) ALL diagnosed in July 2005. He was treated according to the ALL IC-BFM 2002 protocol. BM relapse in June 2007 prompted a PBSC transplant from his HLA-identical sister in November 2007. He then entered CR2. Review at 1 year showed complete donor chimerism and ongoing remission. Further PCR for BCR–ABL was negative. He developed chronic GVHD with pulmonary and gastrointestinal tract involvement, for which he was maintained with prednisolone 15 mg alternate daily and CYA 100 mg twice daily. His red eyes had been labeled before referral as infective conjunctivitis and treated with topical chloramphenicol without improvement. Initial corrected visual acuities were 20/40 for the right eye and 20/20 for the left eye. He was photophobic and actively tearing. Examination of the tarsal conjunctiva on eversion showed diffuse injection over the upper and lower lids bilaterally, with 50% fibrotic changes over the superior edges at each site. This was compatible with grade 3 ocular surface GVHD.[5] He developed corneal epithelial breakdown despite 1 week of intensive topical steroid, preservative-free lubrication, bandage contact lens and lacrimal punctal occlusion (Figure 1). His vision dropped to 20/100. Clinically dry eyes were confirmed by negative Schirmer wetting (0 and 1 mm). It was suspected that a combination of dry eyes and mechanical damage from tarsal fibrosis had led to the corneal epithelial breakdown. The off-label use of dermatological tacrolimus 0.03% twice daily was discussed and commenced on the ninth week from symptom onset (1 week after corneal complication). He responded with complete corneal healing after 1 week and moderate reduction in conjunctivitis (Figure 2). Review by pediatricians a week after the start of topical tacrolimus prompted the escalation of systemic immune suppression. Oral prednisolone was increased from 15 mg to 30 mg alternate daily, CYA was maintained at 100 mg twice daily and mycophenolate mofetil 500 mg twice daily was added. Examination at 1 month showed normal vision of 20/20 bilaterally. He was not photophobic. Corneal epithelial defects healed completely and conjunctivitis resolved with asymptomatic fibrous scarring. Topical tacrolimus and prednisolone were both stopped; his eyes were stable at 5 months on preservative-free lubricants and systemic immune suppression.

Reports on the efficacy of topical tacrolimus in ophthalmic diseases exist for both dermatological[3] and specially prepared ophthalmic ointments.[4] The most frequently reported side effect from the dermatological ointment was the blurring of vision caused by the viscous base, and a burning sensation, both of which were

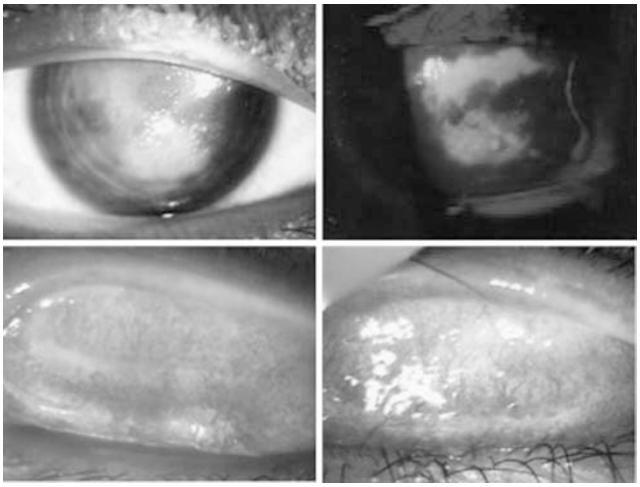

Figure 1 Right eye, pre-treatment. Upper left: corneal epithelial breakdown under normal light, stained with fluorescein. Upper right: corneal epithelial breakdown, stained with fluorescein under cobalt blue light. Lower left: right upper tarsal surface, showing diffuse injection and subconjunctival cicatrization. Lower right: left upper tarsal surface, showing diffuse injection and subconjunctival cicatrization.

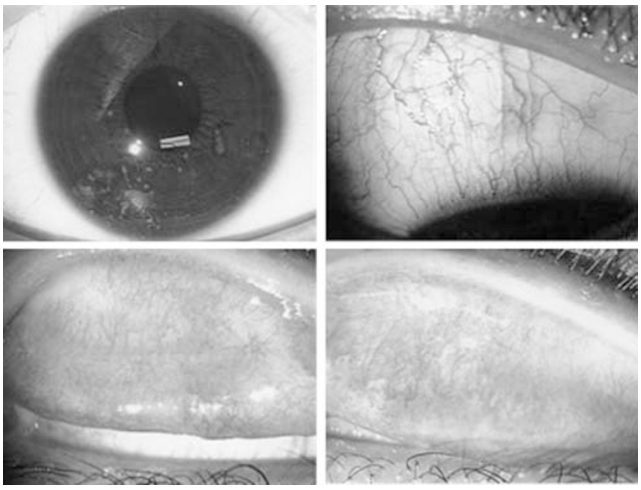

Figure 2 Right eye, at 1 month post-treatment. Upper left: normal cornea, no epithelial defect seen. Upper right: right superior bulbar conjunctiva, no sign of conjunctivitis. Lower left: right upper tarsal surface, Lower right: left upper tarsal surface, residual subconjunctival fibrotic tissue, minimal injection seen.

tolerated. Concerns are raised regarding the increased susceptibility to infection and skin malignancy as a result of local immunological suppression. The longest treatment duration for ocular use was 26 months in a 46-year-old man with peripheral ulcerative keratitis in whom no significant adverse effects were noted. Results from controlled long-term studies are, however, lacking.

Our case has illustrated the efficacy of topical tacrolimus in controlling ocular surface inflammation when conventional treatments have failed. Improvements were noticeable from the first week, a useful time period when decisions regarding the possible systemic immune suppression and its associated baseline evaluations are underway. The successful tapering of treatment after one month could be the effect of systemic immune suppression or the end to an exacerbated local inflammatory process. More data on the natural history of this condition are necessary to formulate the ideal treatment plan.

Conflict of interest

The authors declare no conflict of interest.

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