Treatment of Atopic Eyelid Disease Using Topical Tacrolimus Following Corticosteroid Discontinuation in a Patient With Open-Angle Glaucoma

George D. Kymionis, MD, PhD, Miltiadis K. Tsilimbaris, MD, PhD, Olga E. Iliaki, MD, PhD, Emmanuelle Christodoulakis, MD, Charalambos S. Siganos, MD, PhD, and Ioannis G. Pallikaris, MD, PhD

Purpose: To report a case of atopic eyelid disease treatment using topical tacrolimus in a patient with open-angle glaucoma following corticosteroid discontinuation.

Design: Interventional case report.

Methods: A 59-year-old white man with a history of treated open-angle glaucoma (latanoprost 0.005%) was referred to our department for atopic eyelid disease. The patient had received previous treatment with topical corticosteroid ointments (hydrocortisone acetate 1%/dexamethasone 0.1% ointments) that, even though they were effective in controlling atopic eyelid disease, were complicated by markedly elevated intraocular pressure (IOP) (steroid responder). Topical steroids were discontinued while other treatment modalities (such as eyelid hygiene, artificial tears, topical antihistamine drugs, topical mast cell stabilizers, or topical/oral antibiotics) were proven ineffective.

Results: Topical tacrolimus 0.03% ointment (Protopic; Fujisawa, Dublin, Ireland) was applied to the eyelid skin twice daily. An improvement of eyelid inflammation was observed while eczematous skin lesions and erosions were resolved within 15 days. After 6 months of continued topical tacrolimus treatment, there was no evidence of atopic dermatitis recurrence. During this period IOP remained controlled without any evidence of deregulation.

Conclusions: Treatment of atopic eyelid disease with topical tacrolimus, following corticosteroid discontinuation in a steroid responder patient with open-angle glaucoma, seems to be an effective alternative treatment to corticosteroids without the risk of IOP increase.

Key Words: atopic eyelid disease, corticosteroids, glaucoma, tacrolimus

(*Cornea* 2004;23:828–830)

Atopic dermatitis (AD) is a common chronic relapsing inflammatory skin disorder that is characterized by eczematous skin lesions with pruritus. Ocular complications include eyelid (hyperemia, eczema, trichiasis, ectropion), conjunctival (atopic keratoconjuctivitis, conjuctival papillary formation, chemosis, hyperemia, symblepharon), limbus (trantas dots), corneal (superficial punctate keratopathy, epithelial defect, keratoconus, peripheral neovascularization), and tear film abnormalities.[1]

Antibiotics, corticosteroids, antihistamines, and less commonly immunosuppressive drugs comprise the treatment modalities for atopic dermatitis. Application of topical steroids to the affected area is usually sufficient for the majority of cases. However, their chronic use may be associated with significant side effects at the application site. Skin atrophy and other undesirable effects are frequently seen after long-term corticosteroid treatment. In addition, long-term application of topical corticosteroids to the eyelids for atopic dermatitis has been correlated with the development of glaucoma.[2,3]

In this case report, we describe our successful experience with topical tacrolimus treatment of atopic eyelid disease in a patient with open-angle glaucoma following corticosteroid discontinuation.

CASE REPORT

A 59-year-old man was referred to our department for the treatment of atopic eyelid disease. The patient had a history of glaucoma, which was well controlled with medications (latanoprost 0.005% once a day), and atopic eyelid disease for the last couple of years. The only effective treatment of the atopic eyelid disease was topical application of corticosteroids (hydrocortisone acetate 1%/dexamethasone 0.1% ointments),

Received for publication November 17, 2003; revision received February 18, 2004; accepted February 18, 2004.

From the University of Crete, School of Health Sciences, Division of Medicine, Department of Ophthalmology, Crete, Greece.

The authors have no financial or proprietary interest in any materials or methods described herein.

Dr. George Kymionis is supported by a grant from Bardinogiannis Foundation, Athens, Greece.

Reprints: George D. Kymionis, MD, PhD, University Of Crete, School of Health Sciences, Division of Medicine, Department of Ophthalmology, 71110 Heraklion, Crete, Greece (e-mail: kymionis@med.uoc.gr).

which deregulated the intraocular pressure (steroid responder). Corticosteroid discontinuation was suggested to the patient when eyelid hygiene, artificial tears, topical antihistamine drugs, topical mast cell stabilizers, and topical/oral antibiotics proved ineffective.

The patient presented at the initial examination with eyelid and ocular surface discomfort and eyelid redness (Fig. 1). Uncorrected visual acuity was 20/25 (improved with pinhole to 20/20) in both eyes. Examination showed erythematous eyelid skin with scaling, indurations, and skin erosions in both eyes. The patient had additional atopic keratoconjuctivitis with diffuse conjunctival injection and superficial punctate keratopathy.

Topical tacrolimus 0.03% ointment (Protopic; Fujisawa, Dublin, Ireland) was applied to the eyelid skin twice daily. An improvement of eyelid inflammation was observed while eczematous skin lesions and erosions were resolved within 15 days. In parallel, an improvement in conjunctival injection was found within 3 weeks of therapy (Fig. 2). There was no evidence of infection, skin atrophy, or other adverse effects related to tacrolimus application during the follow-up period. IOP was closely followed up with no evidence of increase. Six months later the patient was asymptomatic with no evidence of inflammation or IOP deregulation.

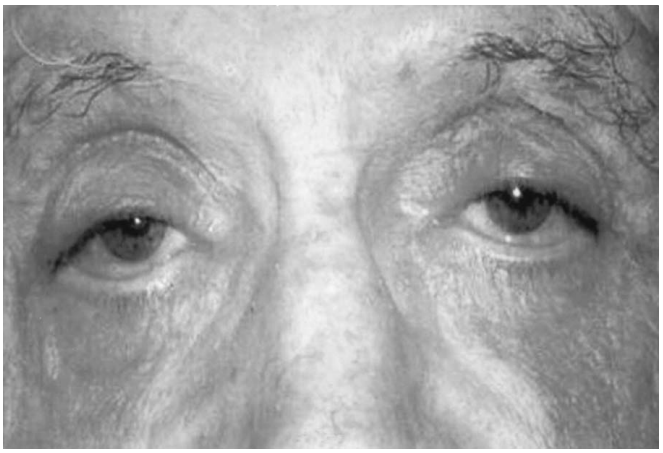

FIGURE 1. Before topical tacrolimus application, an increased eyelid skin thickness, erythema, crusting, and conjunctival injection were observed.

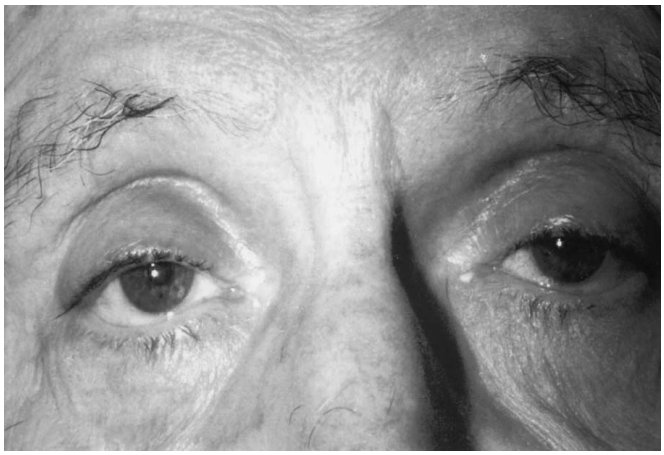

FIGURE 2. Three weeks after tacrolimus treatment, we noticed a reduction in eyelid and conjunctival inflammatory alterations with an improvement in subjective symptoms of the patient.

DISCUSSION

Tacrolimus was first isolated in 1984, and its immunosuppressant properties were first described in 1987.[4] Like cyclosporin, tacrolimus binds to a cytoplasmic immunophilin, and their complex inhibits the activity of the calcium-dependent phosphatase, known as calcineurin, but in contrast with cyclosporin, tacrolimus exhibits activity when applied topically. Large multicenter randomized vehicle-controlled studies in adults and children have shown that tacrolimus ointment is effective and safe in the treament of AD and has been proved to be safe for topical use. The incidence rates for potential side effects, such as skin infections (viral infections including herpes), have not proved to be higher that in the general AD population, and reduced levels of staphylococcal colonization has been reported after prolonged treatment.

Long-term application of topical corticosteroids to the eyelids for atopic dermatitis has been correlated with the development of glaucoma, and more than 90% of patients with primary open-angle glaucoma respond with greater than 6 mm Hg elevation of IOP after receiving a 4-week course of steroids (dexamethasone 0.1%).[5,6] Risk factors include preexisting primary open-angle glaucoma, a family history of glaucoma, high myopia, diabetes mellitus, and history of connective tissue disease (especially rheumatoid arthritis).[6] The proposed mechanism of corticosteroid-induced glaucoma includes morphologic and functional changes in the trabecular meshwork system.[7] It has been suggested that induced alterations to the trabecular meshwork cells (where high concentration of steroid-specific receptors are found) from corticosteroids can lead to changes in the extracellular matrix, with the accumulation of amorphous granular material beneath the endothelial lining of the canal of Schlemm, thickened trabecular beams, and decreased intertrabecular spaces, all of which may lead to an increased resistance to aqueous flow and an elevated IOP.

To our knowledge, there are two studies regarding the application of tacrolimus in patients with atopic eyelid disease with encouraging results.[8,9] Rikkers et al[9] found that application of topical tacrolimus on eyelid skin may be effec-

tive for treatment of severe atopic dermatitis of the eyelids refractory to topical corticosteroids and may have secondary benefits for atopic keratoconjuctivitis. In our study, we found that treatment of atopic eyelid disease in a steroid-responder patient with open-angle glaucoma could improve the symptoms of atopic eyelid disease without the risk of IOP deregulation.

In conclusion, topical tacrolimus application, following corticosteroid discontinuation in a steroid-responder patient with open-angle glaucoma, seems to be an effective alternative treatment without the risk of IOP increase. Further follow-up and additional cases must be reviewed to draw final conclusions about the efficacy of this therapeutic approach for atopic eyelid disease in steroid-responder patients with open-angle glaucoma.

ACKNOWLEDGMENT

The authors would like to thank Ms Vasilia Maniadi for technical assistance with the photographs in this manuscript.

REFERENCES

1. Tuft SJ, Kemeny M, Dart JKG, et al. Clinical features of atopic keratoconjuctivitis. *Ophthalmology*. 1991;98:150–157.
2. Akduman L, Kolker AE, Black DL, et al. Treatment of persistent glaucoma secondary to periocular corticosteroids. *Am J Ophthalmol*. 1996; 122:275–277.
3. Vie R. Glaucoma and amaurosis associated with long-term application of topical corticosteroids to the eyelids. *Acta Derm Venereol*. 1980;60:541–542.
4. Kino T, Hatanaka H, Miyata S, et al. FK-506, a novel immunosuppressant isolated from a Streptomyces II: immunosuppressive effect of FK-506 in vitro. *J Antibiot (Tokyo)*. 1987;XL:1256–1265.
5. Akduman L, Kolker AE, Black DL, et al. Treatment of persistent glaucoma secondary to periocular corticosteroids. *Am J Ophthalmol*. 1996; 122:275–277.
6. Clark AF. Steroids, ocular hypertension, and glaucoma. *J Glaucoma*. 1995;4:354–369.
7. Hernandez MR, Wenk EJ, Weinstein BI. Glucocorticoid target cells in human outflow pathway: autopsy and surgical specimens. *Invest Ophthalmol Vis Sci*. 1983;24:1612–1616.
8. Mayer K, Reinhard T, Reis A, et al. 0.1% FK 506-Salbe—Eine neue therapeutische option bei der atopichen blepharitis. Klinische Studie an 14 Patienten. *Klin Monatsbl Augenheilkd*. 2001;218:733–736.
9. Rikkers SM, Holland GN, Drayton GE, et al. Topical tacrolimus treatment of atopic eyelid disease. *Am J Ophthalmol*. 2003;135:297–302.

