

LETTERS TO THE EDITOR

Local interferon alfa-2b for ocular cicatricial pemphigoid

EDITOR.—Ocular cicatricial pemphigoid (OCP) is a relatively uncommon, chronic, fibrotic, progressive, bilateral, potentially blinding disease of the ocular surface.¹ The finding in most cases of antibodies binding the basement membrane of conjunctival epithelial cells indicates an immune pathogenesis. Currently, systemic immunotherapy is required to achieve remissions of active OCP,² risking significant morbidity and potential mortality. Our usual treatment is a combination of corticosteroids with either methotrexate, 10–30 mg per week, or cyclophosphamide, 1–3 mg/kg per day. Side effects of steroids include osteoporosis, infection, weight gain, and myopathy, while immunosuppression increases the risk of leucopenia, malignancy and internal organ toxicity.

Interferon alfa-2 (IFN α) may offer significant advantages over current treatments for OCP, since it has effects which may be active against both the immune³ and the fibrotic^{4,5} components of the disease. The apparent ability of IFN α to reduce the permeability of microvascular endothelium might also be beneficial.⁶

CASES

We have administered IFN alfa-2b (Schering-Plough, Kenilworth, NJ, USA) by subconjunctival injection to five patients suffering from OCP. All patients had active conjunctival inflammation with symblepharon formation in the treated eye and were poor candidates for systemic immunosuppression because they were either too old and infirm (patients 1 and 2) or they had been unable to tolerate it (patients 3–5). Interferon alfa-2b was given in doses of 1.5×10^6 IU twice weekly for 3 weeks then weekly for another 3 weeks for a mean total dose of 12.8 (range 9–16) $\times 10^6$ IU. After topical anaesthetic had been given, the drug was injected in a volume of 0.2 ml beneath the posterior bulbar conjunctiva, preferably in an area uninvolved by symblepharon. Only the eye that displayed the more advanced disease was treated in each patient, the other eye serving as a control.

Table 1 shows the results of a pretreatment conjunctival biopsy and the pre- and post-treatment (most recent) OCP scores⁷ for each patient. This OCP grading scheme, devised by us, takes into account inflammation, acuity, and the sequelae of both dryness and fibrosis. Patients 1 and 2 had OCP related to topical glaucoma medication⁸ which had already been

discontinued. The scores of the treated eyes were unchanged in two patients and improved in three. Interestingly, no progression was found in untreated eyes. All patients reported a gradual easing of their symptoms of chronic ocular discomfort in the treated eye during the months after treatment. No significant adverse events were found, nor has any patient required subsequent treatment in either eye apart from occasional topical steroid preparations.

COMMENT

The mechanism of action of IFN α against OCP is uncertain. The lack of progression in untreated eyes may be simply because the disease was less active in that eye, as it was in each of our cases, but it also raises the possibility of an effect of IFN α on the systemic immune response. This would be consistent with ability of IFN α to downregulate class II MHC antigen expression³ resulting in a reduced antigen load visible to immune surveillance mechanisms. The greater effect in the treated eye, however, suggests that local factors, such as its antifibrotic effect, might also be important.

When combined with the data from a previous study,⁹ these results show that subconjunctival IFN α as we administered it appears to be relatively safe in humans. Systemic problems are very unlikely at this low dose, as are local side effects. Although systemic IFN α has occasionally been associated with the development of autoimmune disease, no such ocular association has ever been described. Similarly, we have not found any evidence of retinal vascular disease in our patients.

While these results are encouraging with respect to efficacy, the number of patients is too small to allow any firm conclusions to be drawn. We recommend that interferon alfa be used for OCP only in the context of a prospective clinical study.

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Unilateral pellucid marginal degeneration in an elderly patient

EDITOR.—Pellucid marginal degeneration (PMD) of the cornea is a disorder characterised by bilateral, clear, inferior, peripheral corneal thinning.^{1,2} It is usually diagnosed between 20 and 40 years of age.¹ I present the unusual case of unilateral pellucid marginal degeneration in a 60-year-old patient.

CASE REPORT

A 60-year-old black man reported normal vision in both eyes as a child. Around the age of 30 he noted progressive blurring in his right eye, which he attributed to mild blunt trauma he suffered to his eye around that time. No ocular surgery or treatment was performed after the trauma. His vision gradually worsened in the right eye. At no time was the eye inflamed. He denied any problems in his left eye. His medical history was notable for atherosclerotic cardiovascular disease, asthma, and hypertension. He denies arthritis and seasonal allergy. There is no family history of eye disease, including keratoconus or corneal dystrophy.

On examination, best corrected visual acuity was 20/200 in the right eye and 20/20 in the left with $-10.75 +7.25 \times 180$ right and $-0.25 +0.75 \times 180$ left. Laser interferometry revealed 20/40 potential acuity right. There was no afferent pupillary defect. Motility was normal, but there was a 15 dioptre exotropia in the right eye. Confrontation visual fields were intact in both eyes. Slit-lamp examination was remarkable for a narrow band of corneal thinning inferiorly in the right eye with central bulging above the thinned zone and an area of normal thickness between the thinned section and the limbus (Fig 1). Faint vertical stromal striae were present in the right eye. No iron lines, lipid deposition, or vascularisation were present in the cornea in the right eye. The left cornea appeared normal, without any trace of iron line, striae,

Table 1 Pathology and response to treatment with subconjunctival interferon alfa-2b in each patient with ocular cicatricial pemphigoid (OCP)

Patient No	Age, sex	Conjunctival biopsy			OCP scores		Duration of follow up (months)
		Squamous metaplasia	Lymphocytic infiltration	Ig binding	Pre T, C	Post T, C	
1	84, F	Yes	Yes	No	22, 14	16, 14	30
2	89, M	Yes	Yes	No	16, 14	16, 14	6
3	77, M	Yes	Yes	Yes	18, 16	18, 14	30
4	65, F	Yes	Yes	Yes	18, 16	12, 12	23
5	63, F	Yes	Yes	Yes	18, 14	16, 11	10

Ig = immunoglobulin; T = treated eye; C = control eye.

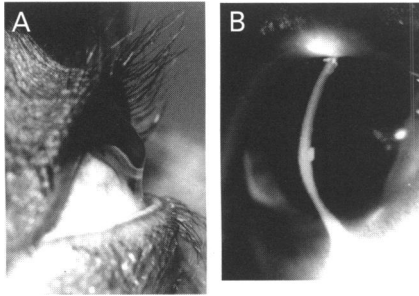


Figure 1 (A) Photograph of right eye showing corneal protrusion. (B) Slit-lamp photograph of same eye showing band of clear corneal thinning 1–2 mm above limbus.

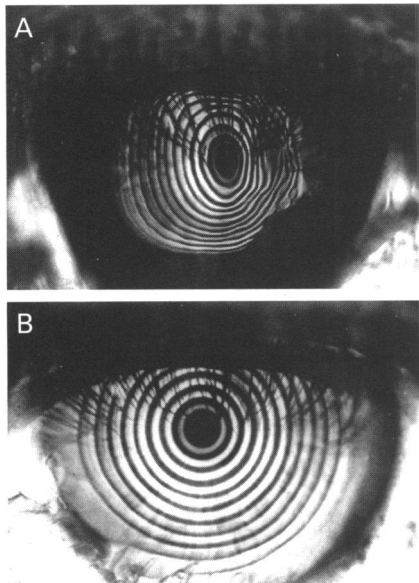


Figure 2 (A) Corneoscope photograph of right eye demonstrating marked, against the rule astigmatism. (B) Corneoscope photograph of left eye demonstrating sphericity.

thinning, or abnormal protrusion. The dilated fundus examination was unremarkable in both eyes. Intraocular pressures were 10 and 15 mm Hg right and left eye, respectively, by pneumotometry. Keratometry was 40.75 by 53.5 × 180 right eye and 42.5 by 42.50 left eye. Corneoscope photographs revealed marked against the rule astigmatism in the right eye and no apparent corneal astigmatism in the left (Fig 2).

COMMENT

This patient was noted to have corneal findings in the right eye consistent with PMD including a clear, narrow band of corneal thinning above the inferior limbus with maximal anterior displacement and apparently normal thickness cornea above this thinned band. Corneal topography shows fairly regular against the rule astigmatism. These findings are all present only in the right eye. The left eye shows no evidence of degeneration and is without astigmatism by keratometry and corneoscopy. Other possible causes of the peripheral corneal thinning observed in the right eye include Tierren's degeneration, Mooren's ulcer, rheumatoid corneal thinning, keratoconus, and keratoglobus.

This case can be distinguished from Tierren's degeneration by the absence of vascular invasion or lipid infiltration. The lack of corneal ulceration or systemic connective tissue disease makes Mooren's ulcer or rheumatoid aetiologies unlikely. This case differs from keratoconus in that the maximal

protrusion occurs above the area of thinning, whereas in keratoconus the maximal protrusion occurs in the thinned area. Also, the iron lines typical of keratoconus are absent here. In keratoglobus thinning and protrusion occur over the entire cornea rather than in one area as in this case.

The unilateral presentation in this case is unusual, for PMD is considered a bilateral condition.^{1,2} Although bilateral conditions often present asymmetrically in degree or time, the left eye in this case shows no signs of corneal involvement 30 years after the first eye became symptomatic and past the age that PMD typically is diagnosed. Cases of unilateral PMD associated with other corneal thinning disorders such as keratoconus in the opposite eye have been reported,^{3,4} but this is the first case of isolated unilateral PMD in an elderly patient.

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Amikacin may be drug of choice in *Nocardia* keratitis

EDITOR.—While *Nocardia* infections usually follow a self limiting course, rapid extension of the primary focus and dissemination have been reported in immunosuppressed patients.¹ Owing to the more frequent use of immunosuppressive drugs, *Nocardia* infections are diagnosed with increasing frequency.² Case reports have recently encouraged the use of topical amikacin in *Nocardia* keratitis.³ We present another patient with this condition treated successfully with topical amikacin.

CASE REPORT

A 31-year-old man noticed a foreign body sensation in the right eye after drilling into the ceiling of a decayed building. He presented to a local ophthalmologist, who removed two metal fragments from the right cornea. Although a treatment with norfloxacin eye-drops, subconjunctival corticosteroid, and antibiotic injections was initiated, symptoms were progressively aggravated. Three weeks later, a central corneal infiltrate had developed. Oral fluconazole, 200 mg a day, and topical kanamycin ointment were added to the treatment.

Five weeks later, the patient presented to the university eye clinic. The uncorrected visual acuity (UCVA) was 20/200 in the right and 20/20 in the left eye. Slit-lamp examination of the right cornea disclosed a central, subepithelial infiltrate with two satellite lesions (Fig 1). A corneal scraping was performed immediately. The Gram stain revealed Gram positive coccoid elements. Presuming keratomycosis, the patient was put on topical amphotericin 0.5% hourly. Two weeks later, the UCVA of the right eye had diminished to hand movement as a result of expansion of the lesion. Material from a second scraping was examined in 10% potas-

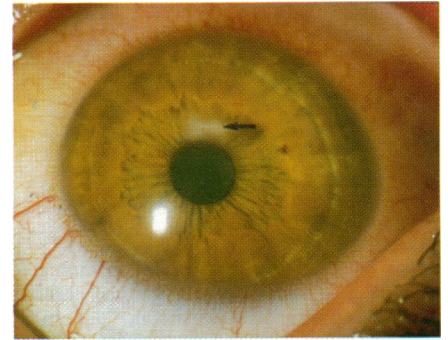


Figure 1 Slit-lamp photograph, showing the central corneal infiltrate (arrow). Two satellites can be discerned. The corresponding visual acuity was 20/200.

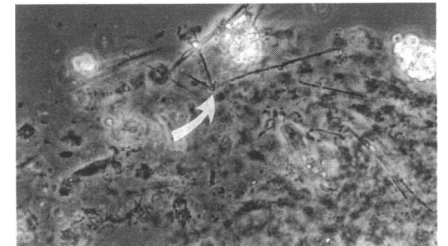


Figure 2 Light microscopy of corneal scraping material in potassium hydroxide solution: *Nocardia* organisms appear as rectangular branching rods (arrow) surrounded by corneal debris.

sium hydroxide solution by light microscopy (Fig 2). Long rectangular elements were discerned between stromal debris. Meanwhile, culture of material from the first scraping revealed *Nocardia* species. Further subclassification was impossible owing to scarcity of material and slow growth of the organism. Subsequently, the patient was put on topical amikacin 5% every 2 hours and amphotericin 0.5% five times a day.

Two months later, scar tissue was observed in the subepithelial corneal stroma and best corrected visual acuity had recovered to 20/25.

COMMENT

Exogenous ocular inoculation by *Nocardia* species usually affects the cornea. An intact immune response is critical for the eradication of *Nocardia* infections. Topical steroids were reported to aggravate the disintegration of corneal tissue.⁴

Nocardia keratitis can result in permanent reduction of visual acuity due to corneal scarring. Unfortunately, an exact differentiation between yeast-like fungi, diphtheroids, *Nocardia*, and non-tuberculous mycobacteria is not possible by light microscopy. Culture often fails to isolate the organism and antibiotic sensitivity test results do not correlate with the clinical response in keratitis.⁵ However, early detection and treatment of *Nocardia* are critical for a satisfactory outcome.

Sulphonamides have been used as first choice therapy in *Nocardia* keratitis in the past, but results have been controversial.⁴ Better clinical responses of *Nocardia* keratitis have been reported with topical trimethoprim-sulphamethoxazole,⁶ but susceptibility tests suggested a 92.5% resistance of *Nocardia asteroides* to trimethoprim-sulphamethoxazole.²

Amikacin is the treatment of choice in human disseminated nocardiosis.² In vitro susceptibility tests failed to detect resistance of *Nocardia* to amikacin.² Although paratotoxicity of topical amikacin 10% has been observed