Figure 1 Temporal artery biopsy showing thickened vessel walls (a) and giant cells (b).

worked up for GCA to reduce the risks of blindness and potentially fatal problems.

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Sir, Sterile corneal ulcer with ring infiltrate and hypopyon after recurrent erosions

Recurrent corneal erosions (RCE) is a common condition in which the patient typically suffers from episodes of sudden eye pain, usually upon first awakening, accompanied by redness, photophobia, and tearing. The majority of patients have a history of previous corneal trauma, or evidence of anterior basement membrane dystrophy. The underlying pathogenesis appears to be a reduced adhesion of the epithelium owing to deficient epithelial basement membrane, absence of hemidesmosomes, and loss of anchoring fibrils.¹

The natural history of this condition is benign, involving recurrent episodes of epithelial breakdown usually healing uneventfully. There is a plethora of available treatments for this condition, reflecting their variable success rate and ranging from simple measurements such as lubrication and eye padding, use of an ointment at night to more invasive approaches such as epithelial/basement membrane debridement, anterior stromal puncture, and phototherapeutic keratectomy.¹ Complications have been occasionally reported, involving mainly anterior uveitis or corneal stromal scarring. We report a case of severe sterile corneal ulcer with ring infiltrate and associated hypopyon in a patient with previous history of RCE.

Case report

An 80-year-old female patient presented with a right corneal central ulcer, a surrounding incomplete ring infiltrate, and a 1 mm hypopyon. There was a history of RCE over the preceding year after an initial superficial fingernail corneal injury. Initial management was with topical antibiotics and lubricating ointment, as well as a bandage contact lens for a period of 4 weeks. She had

Figure 1 Corneal ulcer with central epithelial defect, surrounding incomplete ring infiltrate, and associated hypopyon.

had two episodes of a corneal ulcer with an associated small infiltrate over the last 4 months. These were both culture negative and were treated successfully with topical ofloxacin, and subsequently, lubricating drops and ointment. Topical anaesthetic or topical NSAIDs had not been used in the clinical course. The patient was in good general health. She presented in our emergency department with a third episode of a right corneal ulcer. Visual acuity was counting fingers only in the right eye and 6/60 in left eye (due to a history of traumatic optic neuropathy as a child). Slit-lamp examination revealed a large central corneal ulcer with a 3×4 mm central epithelial defect, a surrounding, marked, incomplete ring infiltrate, and a 1 mm hypopyon (Figure 1). Corneal cultures on routine culture media, as well as epithelial biopsy taken for *acanthamoeba*, were negative. Corneal sensation was also normal and serology for HSV-1 and -2 infections was negative. She was managed with intensive hourly topical ofloxacin 0.3% and cycloplegics three times daily. After 1 week of treatment, the appearance of the corneal ulcer was progressive with a larger epithelial defect and more extensive infiltrate. New scrapings taken for common bacterial pathogens, *acanthamoeba*, as well as fungi were negative once again. As there was no response to the treatment and the corneal thinning was progressive, a corneal biopsy was performed, which showed a nonspecific destructive keratitis without isolating any specific microorganism. The diagnosis of a sterile corneal ulcer and infiltrate was established. Treatment with topical dexamethasone 0.1% preservative-free drops and chloramphenicol 0.5% preservative-free drops, both of them four times daily, was commenced. After 3 days, the inflammatory reaction started to subside and within 2 weeks the corneal ulcer was completely epithelialised, the corneal infiltrate had

almost disappeared, and the hypopyon resolved. There remained subepithelial scars and central corneal stromal irregularities. During the follow-up period, the eye remained quiet, with no new episodes of epithelial breakdowns.

Comment

Complications of RCE are infrequent, including mainly anterior uveitis and residual stromal scarring. Corneal stromal infiltrates are a rare complication. They usually present with an epithelial defect and a clinical picture resembling bacterial keratitis. In our case, the clinical picture was of a severe infectious keratitis, with a ring infiltrate resembling *acanthamoeba* keratitis, and a hypopyon. Corneal cultures and biopsies taken were negative. Ionides *et al*² reported that the bacterial isolation rate in their series of 11 patients with RCE was 16%, which was considerably less than the 44% recovery rate from their series of cases of suspected microbial keratitis unrelated to RCE, which was investigated during the same period. In this study, it is noted, as in our case, that the severity of the clinical signs did not correlate with the culture result. In contrast, Luchs *et al*³ reported five patients who developed an infiltrate associated with epithelial erosion where bacteria were isolated from four of the five eyes. Prolonged use of bandage contact lenses and topical corticosteroids may predispose to bacterial corneal ulcers.¹

Sterile corneal infiltrates are known to develop in a variety of situations, for example, in contact lens wearers, in association with Staphylococcal blepharitis, in viral infections or in systemic immunologically mediated diseases such as rheumatoid arthritis. Topical anaesthetic abuse is also associated with ring infiltrates, as well as topical NSAIDs can rarely lead to corneal melt. In patients with RCE, it seems that the epithelial breakdown plays an important role in triggering the inflammatory reaction. Epithelial injury produces a leukocyte chemotactic factor, attracting inflammatory cells to corneal stroma, which could result in sterile infiltrates, or even ring infiltrates similar in appearance to the Wessley ring seen in herpetic infections. Resolution of such infiltrates is usually rapid and complete.^{2,4} However, in our case significant stromal scarring limited the final visual acuity. The addition of topical corticosteroids in severe cases seems to shorten the disease period and hasten resolution.^{2,4}

In conclusion, corneal infiltrates are an uncommon complication of RCE. Their appearance could mimic a bacterial keratitis, or even, as in our case, an *acanthamoeba* keratitis. As it may be difficult to reliably distinguish an infected case from a sterile

infiltrate clinically, the safe approach is to always culture the lesions and treat them as potentially infective cases, until proven otherwise. Topical corticosteroids under the coverage of broad-spectrum antibiotics can be given in patients with severe disease and negative cultures to hasten resolution.

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Sir,
Highlighting the methodology

We read with interest the article of Tsang CSL *et al*¹ in which they compared the visual field and optic nerve head changes in normotensive patients with obstructive sleep apnoea (OSA) to age- and sex-matched controls without OSA. Unfortunately, we feel that some aspects of their analysis could have led the authors to invalid conclusions.

Comparing eyes in the two groups, the authors found statistically significant differences ($P < 0.01$) in both visual field (VF) indices using unpaired *t*-tests. However, as most patients have contributed both eyes to the analysis, eye-specific outcomes cannot be considered independent. Failure to account for this dependence results in standard errors that are too small and *P*-values

that are too significant.² For this reason alone, the author's conclusions must be considered questionable. Further, the authors despite having identified deviations from normality in the distribution of both VF indices in the OSA patients have used a test that assumes normality. One approach that addresses both the non-normality and the dependence in the data would be to construct bootstrap confidence intervals (CIs)^{3,4} for the difference in means allowing for clustering at the subject level. The authors have repeatedly used the term CI but none have been reported. From the figures shown, there does not appear to be a large difference in either VF index between the two groups and no estimates of this difference have been provided. Reporting the differences in means with CIs would have demonstrated whether any observed differences are clinically relevant.

There are also inaccuracies in the description of the study design methodology. The term 'incidence' of suspicious disc change is referred to in the title and in the text, whereas in fact the study investigates prevalence. This distinction in terminology is important and should not be confused. Furthermore, the term case-control study should be reserved for studies where subjects are selected on the basis of outcome and not exposure (as in this case, ie, presence/absence of OSA).

In summary, this paper demonstrates that collaborations between statisticians and other researchers are vital in order to avoid preventable mistakes that can render the results of otherwise well-conducted studies uninterpretable.

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