Comment

A lipogranulomatous reaction due to necrosis of orbital fat is sometimes seen in orbital myositis. However, primary granulomatous inflammation of the extraocular muscles, though recognised, is extremely rare.[10] Such painless myositis may represent a localised manifestation of sarcoidosis.[11] Interestingly, idiopathic orbital inflammatory disease has been referred to in the past as 'non-specific granuloma of the orbit',[12] which is correct in the macroscopic sense, characterising a non-neoplastic space-occupying lesion.

Treatment of the condition with systemic steroids results in rapid resolution of the inflammation. Premature withdrawal may result in recurrence. The underlying cause, however, of this rare sporadic disorder remains an enigma.

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Sir,

Polyhexamethylene biguanide (0.02%) alone is not adequate for treating chronic *Acanthameoba* keratitis

The use of polyhexamethylene biguanide (PHMB), a cysticidal drug with minimal ocular surface toxicity, was reported by Larkins *et al.*[1] in 1992 for the treatment of *Acanthamoeba* keratitis. Its effectiveness in killing trophozoites and cysts of *Acanthamoeba* has been documented by *in vitro* sensitivity testing.[1,2] Currently, most authors recommended multi-drug therapy, often in combination with PHMB, for the treatment of *Acanthamoeba* keratitis.[2] The use of multiple drugs, however, increases the risk of ocular surface toxicity. We therefore prospectively evaluated the safety and efficacy of monotherapy with topical PHMB 0.02% in the treatment of chronic *Acanthamoeba* keratitis. In the three patients reported, monotherapy with topical PHMB 0.02% resulted in persistent infection. The use of combination therapy, with the addition of propamidine and neomycin, eradicated the corneal infection and subsequent surgery resulted in good visual recovery.

Case report

The three patients with culture-proven *Acanthamoeba* keratitis presented 12, 15 and 8 months after onset of symptoms with pre-treatment visual acuities of hand movement, 1/60 and 3/60 respectively. The results of *in vitro* sensitivity testing are summarised in Table 1. All three patients with *Acanthamoeba* keratitis were treated initially with only topical PHMB 0.02%. The dosing schedule was one drop every hour, round the clock in the first week, two hourly between 0800 and 2400 hours for the next week and then gradually reducing, based on the clinical response. Although clinical signs and symptoms initially improved, the condition subsequently worsened with positive culture results from corneal re-scrapings in all patients.

Propamidine and neomycin were added to the therapeutic regimen, resulting in resolution of infection in all patients. The eyes were clinically uninflamed and there were no clinical signs suggestive of continuing infection. The combined treatment was continued for a total of 6 months even though the infection seemed clinically to have settled well long before the cessation of treatment. Subsequent surgery for the corneal opacity (cases 1, 2, 3), glaucoma (cases 1, 2) and cataract (cases 1,

Table 1. In vitro *sensitivity patterns of two isolates of* Acanthamoeba *from cases 1 and 2*

	Minimum cysticidal concentration (μg/ml)	
Drugs	Case 1	Case 2
Propamidine	125	3.9
Neomycin	> 500	–
Paromomycin	> 500	250
Hexamidine	–	0.49
Chlorhexidine	–	3.9
PHMB	7.8	1.9

PHMB, polyhexamethylene biguanide.

2) resulted in visual improvement in the three patients. Cultures of the excised corneal tissues did not reveal the presence of *Acanthamoeba* in any patient. Cataract formation in cases 1 and 2 could have resulted from chronic intraocular inflammation, as these patients had the longest duration of disease.

Comment

The reason for loss of response to PHMB in our patients is not clear. *In vitro* susceptibility testing revealed a low minimum inhibitory concentration for PHMB, compared with propamidine and neomycin, in the two isolates studied (Table 1). The lack of correlation between *in vitro* and *in vivo* effectiveness of PHMB in *Acanthamoeba* keratitis has been reported earlier.[2] The organism isolated in case 1 was resistant to neomycin, and it is unlikely that neomycin contributed to the therapeutic effect in our patients. In an earlier study, approximately 50% of patients treated with a combination of propamidine and neomycin were not medically cured.[3] It is therefore likely that combination therapy, including PHMB, effected the clinical cure in our cases.[1,4]

In our patients, it is possible that PHMB therapy reduced the pathogen load in the superficial corneal layers. However, with amelioration of inflammation and epithelial healing, further penetration of the drug could have been affected, resulting in recrudescence of infection from organisms in the deeper layers. Since PHMB is a polymeric biguanide, the large molecular size may result in poor corneal stromal penetration, although this has not been proven.[5] The persistence of viable cysts in the corneal button, following penetrating keratoplasty for resolved *Acanthamoeba* keratitis (after monotherapy with topical PHMB 0.02%), has been reported by Tseng *et al*.[6] in one patient. Debridement of epithelium to increase the stromal penetration of topical therapy has been suggested to improve treatment efficacy.[7] There are, however, very few data relating to the corneal penetration of compounds used to treat *Acanthamoeba* keratitis.[2] We hypothesise that the combination of PHMB with other epitheliotoxic anti-amoebic drugs such as neomycin could have increased the penetration and efficacy of PHMB in our patients. Combination therapy was successful in eradicating the keratitis in our patients, as shown by the failure to culture *Acanthamoeba* from the excised corneal buttons.

Reducing the frequency and number of topical drugs used is also a difficult decision in chronic infections such as *Acanthamoeba* keratitis, since the organism can encyst under unfavourable conditions. Confocal microscopy can help the clinician identify, *in vivo*, the persistence of trophozoites and cysts of *Acanthamoeba* in the cornea.[8] This would allow a more rational approach to the reduction and cessation of toxic anti-amoebic therapy, reducing the risk of drug toxicity while protecting against recurrence of infection.

In conclusion, our experience indicates that monotherapy with topical PHMB 0.02% should be avoided in chronic *Acanthamoeba* keratitis. Such infections are best treated using a multi-drug regimen consisting of PHMB or chlorhexidine,[9] propamidine or hexamidine, and neomycin. Since information on the ability of various drug combinations to eradicate *Acanthamoeba* from the cornea is still accruing, we suggest that excised corneal tissue in such eyes must be submitted for microbiological examination to evaluate treatment efficacy.

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