Acanthamoebic keratitis diagnosed by paracentesis and biopsy and treated with propamidine

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SUMMARY A previously healthy 53-year-old man had keratitis of the right eye for six months, unresponsive to topical medical therapy. *Acanthamoeba* was grown from tissue obtained by corneal biopsy and from aqueous from an anterior chamber tap. The patient was treated with propamidine isethionate 0.1% drops and dibromopropamidine isethionate 0.15% ointment, and after two and a half months the ocular inflammation was continuing to resolve. This case supports a role for the diamidines in the treatment of acanthamoebic keratitis.

Acanthamoebic keratitis is a serious sight threatening condition. It can be difficult to diagnose and very difficult to treat. Despite an increasing number of reports ophthalmologists must base their knowledge of the condition on anecdotal reports of those cases which provide insight into the clinical problem. This report is of a man who had a persistent hypopyon from which the organism was recovered, and who responded to topical administration of propamidine isethionate and dibromopropamidine isethionate.

Acanthamoeba species have now been reported many times as having caused protracted keratitis unresponsive to medical therapy.¹⁻¹¹ Reports of successful medical treatment are few. Of these, one has been of treatment with a combination of propamidine isethionate drops 0.1%, dibromopropamidine isethionate 0.15% ointment, and neomycin drops¹² and another of treatment with topical miconazole 10 mg/ml, polymyxin-neomycin-gramicidin, and propamidine isethionate.¹³ The case reported here supports a role for diamidines in the medical management of acanthamoebic keratitis.

Case report

A healthy 53-year-old man was referred with right keratitis, unresponsive to treatment with topical prednisolone acetate 1% and acyclovir during the preceding month. He remembered no episodes of ocular trauma but had had an attack of keratitis four years previously which healed within two weeks of beginning topical antiviral therapy.

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On examination, visual acuity in the right eye was hand movements at 1 m, in the left eye 6/5. In the right eye there was a large central corneal epithelial defect overlying an area of stromal inflammation which extended to the corneal mid-periphery, where the opacification was denser (Fig. 1). Iris details could not be seen. Corneal scrapings grew *Staphylococcus epidermidis*, and topical treatment was continued with vidarabine ointment, prednisolone sodium phosphate 0.5%, and atropine 1% drops.

After five weeks the anterior segment inflammation had increased and a hypopyon was evident (Fig. 2). On several occasions during the next two months cultures for bacteria, fungi, and amoebae were negative, and the hypopyon persisted, accompanied by severe ocular pain. At the end of this time the

Fig. 1 Large central corneal epithelial defect overlying an area of stromal inflammation.

Fig. 2 Central keratitis with hypopyon.

Fig. 3 Central epithelial defect stained with rose Bengal.

corneal opacity was dense, but the corneal epithelial defect had begun to heal and was completely epithelialised three months after the patient's initial presentation.

For the next two months the condition remained unchanged. At the end of this time aqueous from an anterior chamber tap showed unusual eosinophils but no causative organism. One week later, and six months after the onset of the keratitis, corneal biopsy was performed, with repeat anterior chamber tap. *Acanthamoeba* grew from both specimens after five days, though none was seen in the histopathological sections of the corneal biopsy. Morphologically, the organism was similar to but not identical with *Acanthamoeba polyphaga*.

Because of the extent of anterior segment inflammation and the presence of amoebae in the aqueous humour, medical treatment was preferred to surgical excision and corneal grafting. Treatment was started with propamidine isethionate 0.1% drops two hourly, dibromopropamidine isethionate 0.15% ointment at night, prednisolone acetate 1% drops every two hours, and atropine 1% drops twice daily.

After three weeks there were signs of improvement, with less anterior segment inflammation, disappearance of the hypopyon, and clearing of the stromal infiltrate and oedema, allowing some view of the iris details. This improvement was maintained during the next month; but, with recurrence of a central epithelial defect (Fig. 3), treatment was reduced to propamidine isethionate 0.1% drops and prednisolone acetate 1% drops, each four times a day, and atropine 1% drops twice daily. The eye was padded. The epithelial defect healed within one week, but further reduction of propamidine isethionate 0.1% to twice daily resulted in a rapid increase in anterior segment inflammation.

Subsequently the patient received propamidine isethionate 0.1% drops four times a day and dibro-

mopropamidine isethionate 0.15% ointment at night for two months, then the drops only for a similar period. Further reduction of treatment resulted in increased inflammation, but this tendency decreased with time and ocular inflammation continued to resolve. The eye is now quite comfortable, but visual acuity remains hand movements at 1 m, owing to corneal opacity and cataract (Fig. 4).

Discussion

Two aspects of this case are unusual. Firstly, *acanthamoeba* was recovered from the anterior chamber and disaggregated corneal material but could not be seen in a biopsy conducted by personnel experienced in identifying the organism. Secondly, a favourable response to medical therapy was apparent. In other respects the case represents a common clinical problem: a clinical picture at presentation assumed due to herpes simplex virus and an

Fig. 4 Appearance of the cornea six months after commencement of medical therapy for *acanthamoebic* keratitis. The epithelium has healed, but extensive stromal opacity and vascularisation remain.

encouraging healing of an epithelial defect in response to topical steroids, but with stromal inflammation continuing despite further topical medication. In this situation corneal biopsy needs to be considered, and the results can be most helpful, as in this case.

Acanthamoeba is a small, free-living organism commonly found in soil, fresh water, and sea water, and cysts can occur in airborne dust. Of all free-living amoebae, only acanthamoeba and *Naegleria fowleri* are pathogenic in man.^{14,15} Two forms of the organism exist: cysts and trophozoites. The cysts are remarkably resistant to desiccation and heat, as well as to chemical disinfectants, but are killed by autoclaving or gas sterilisation.¹⁶ Both forms of the organism are also resistant to most antimicrobial agents,¹⁷⁻¹⁹ but cysts are more resistant than trophozoites and may persist in the cornea indefinitely, requiring prolonged topical therapy.²⁰

Although acanthamoebic keratitis is reported with increasing frequency, reports are anecdotal, and the outcome is often poor. There have been few indications as to what treatment might be expected to be effective, but the most promising has been with propamidine and dibromopropamidine isethionate.

Propamidine isethionate and dibromopropamidine isethionate are members of the diamidine group of drugs. They both have antibacterial and antifungal activity and have long been used for the treatment of blepharitis and conjunctivitis. Dibromopropamidine isethionate is available as a 0.15% ointment and is reported to be active against pyogenic cocci, *Staphylococcus aureus*, and Gram-negative organisms, including some strains of *Pseudomonas*.¹² Propamidine isethionate is available as 0.1% drops and has a reduced spectrum of antibacterial activity, being active against Gram-positive organisms, including staphylococci and *Streptococcus pyogenes*, but not against Gram-negative organisms.¹²

The diamidines are also toxic to a number of different protozoa, but their mechanism of action has not yet been established.²¹ Wright and colleagues¹² showed that propamidine and dibromopropamidine isethionate have acted in vitro against both cysts and trophozoites of acanthamoeba and that, clinically, there were no adverse reactions to these drugs during two months' treatment.

The case reported here further supports the place of propamidine and dibromopropamidine isethionate in the treatment of acanthamoebic keratitis and also emphasises the useful role of corneal biopsy in the diagnosis of this condition.

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