Mycobacterium chelonae infection of a corneal graft

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SUMMARY We present a case of *Mycobacterium chelonae* infection in a corneal graft. The chronic ulceration and stromal infiltration followed a well defined course and eventually responded to topical amikacin, though a further graft was required. Previous cases of keratitis due to the *M. fortuitum* complex are reviewed.

There is currently much topical interest in bacterial infections of the cornea associated with the use of extended wear soft contact lenses.¹ We report a case of a well defined keratitis in a corneal graft due to a very unusual organism, and associated with the wear of a Sauflon 85% soft contact lens.

Case report

In 1976 a 57 year old Caucasian woman with Fuchs's endothelial dystrophy and lens opacities underwent a left intracapsular cataract extraction. She was fitted with an extended wear contact lens (Sauflon 85%), but this was discontinued after two episodes of suppurative keratitis due to *Staphylococcus aureus*. In 1979 a left penetrating keratoplasty was performed because of stromal scarring and bullous keratopathy, and six months later another contact lens (Sauflon 85%) was fitted to correct her aphakia.

In May 1984 a stromal infiltrate was noted. It was within the graft next to the graft-host junction at 5 o'clock. She was treated with topical Betnesol-N (betamethasone and neomycin) once daily and chloramphenicol thrice daily, but one week later it had increased in size with thickening of the stroma and corneal oedema affecting the lower half of the graft. Corneal scrapings were taken for culture but were unfortunately lost in transit. Over the next two months more infiltrates appeared within the graft. These were white, fluffy, and stellate in appearance. It was thought that the cornea had decompensated owing to graft rejection and because she had little useful vision in the other eye (owing to a branch vein occlusion), a further penetrating keratoplasty was

performed in July 1984 with young donor material. A Stein intraocular lens was inserted at the same time.

Postoperatively the graft was clear and she was receiving topical dexamethasone three times a day. Six weeks later she presented with pain and redness of the left eye. She had a 1.5 mm ulcer at 9 o'clock on the graft-host junction, with several stromal infiltrates. There were cells in the anterior chamber but no hypopyon, and the intraocular pressure was raised on digital examination. She was admitted to hospital and corneal scrapings were taken for microscopy and culture, but no organisms were detected. She was treated with subconjunctival methicillin 125 mg and gentamicin 20 mg and topical methicillin and neosporin hourly. Additionally she received topical dexamethasone six times daily and oral acetazolamide 250 mg four times daily. After four days there was only limited improvement, and, in order to ensure that infection with pneumococcus or other streptococci was covered, the antibiotics were changed to topical penicillin hourly, chloramphenicol four times daily, and Polyfax ointment (containing polymyxin B and bacitracin) at night. Oral indomethacin 50 mg three times daily and ascorbic acid 500 mg three times daily were added in order to reduce the inflammation and to promote healing. The ulcer decreased in size, and she was allowed home one week later on this treatment, the penicillin being reduced to four times daily.

Two weeks later she was readmitted with a recurrence of pain in the left eye. On examination the ulcer had increased in size and there were several new infiltrates around the graft-host junction and a hypopyon. Corneal scrapings again revealed no organisms. She was treated with subconjunctival gentamicin 20 mg and cephaloridine 125 mg, topical

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Fig. 1. Slit-lamp photograph of the left eye showing ulceration temporal to the conjunctival bridge flap and areas of stromal infiltration.

penicillin, and neosporin hourly and polyfax ointment at night. She continued with oral indomethacin 50 mg three times daily and ascorbic acid 500 mg three times daily. Later, oral tetracycline 250 mg four times daily was added. After 10 days there was no significant improvement, and a conjunctival bridge flap was fashioned to cover the area of ulceration, which was now approximately 2 mm in diameter. Further corneal scrapings were taken and inoculated into thioglycollate broth, and 11 days later an organism was isolated which was

initially reported as *Nocardia* sp. At this stage the eye was red with an area of ulceration temporal to the conjunctival flap. Smaller areas of ulceration with stromal infiltration were present along the graft-host junction between 12 and 5 o'clock (Fig. 1).

Two weeks later the organism initially reported as *Nocardia* sp. was identified by the reference laboratory as *Mycobacterium chelonae* sensitive to ethionamide and gentamicin but resistant to streptomycin, isoniazid, rifampicin, ethambutol, capreomycin, cycloserine, and pyrazinamide. All antibiotics were stopped for 72 hours and further corneal scrapings were taken. Ziehl-Neelsen staining revealed large numbers of acid-alcohol fast bacilli. (Fig. 2). There was no evidence of systemic mycobacterial infection, and a full blood count and chest radiograph were normal. Treatment with topical gentamicin six times daily and dexamethasone twice daily was begun and continued for two months. Initially the cornea cleared, but then several new areas of stromal infiltration appeared with two areas of ulceration (Fig. 3). Further corneal scrapings were taken for microscopy and culture. Again *M. chelonae* was isolated, and this isolate was found to be resistant to gentamicin in addition to the antibiotics previously tested. The organism was also tested against amikacin and found to be resistant. However, treatment was changed to topical amikacin four times daily and erythromycin ointment at night on the advice of Professor D. B. Jones (personal communication). Over the next month the ulcers

Fig. 2. Photomicrograph of corneal scrapings with Ziehl-Neelsen staining showing acid-alcohol fast bacilli (arrows).

Fig. 3. Slit-lamp photograph of the left eye showing new areas of ulceration and stromal infiltration.

healed and the infiltrates cleared leaving a scarred, irregular cornea (Fig. 4).

She was continued on topical amikacin four times daily and dexamethasone twice daily for a full six months, and there was no recurrence of the ulceration or infiltrates. A further penetrating keratoplasty was performed in September 1985. Histology of the excised button showed a thickened epithelium with a chronic inflammatory infiltrate beneath Bowman's membrane. No granulomata were seen, but after staining with Ziehl-Neelsen stain a single acid-fast bacillus was found. She received amikacin four times daily for two months post-operatively. Eight months later she had a visual acuity of 6/18 with a clear graft (Fig. 5).

Discussion

In 1959 Runyon² classified the atypical mycobacteria

Fig. 4. Slit-lamp photograph of the left eye showing the healed but scarred and irregular cornea.

into four groups based on the pigmentation of colonies after exposure to light or darkness and their rate of growth on culture media. Group 4 contains the rapidly growing mycobacteria, including two species which are pathogenic to man, namely *M. fortuitum* and *M. chelonae*, which are often referred to collectively as the *M. fortuitum* complex. Owing to taxonomic confusion it is likely that *M. chelonae* has often been misidentified as *M. fortuitum* in the past. Therefore it may be reasonable to consider the reported cases of keratitis caused by these two organisms together as a single clinical entity.

Turner and Stinson described the first case of *M. fortuitum* keratitis in 1965.³ Since then a further 15 cases⁴⁻¹³ due to *M. fortuitum* and *M. chelonae* have been reported in the American literature. We believe that the present case is the first to be reported in the United Kingdom.

Keratitis follows corneal trauma after a latent period of two to eight weeks. In two reports^{10,13} there is a suggestion that contaminated ophthalmic instruments were responsible, though no organisms were cultured from them. The clinical appearance is similar to fungal keratitis, and in eight out of 17 cases (47%) this was the initial clinical diagnosis. An epithelial defect is associated with a white stromal infiltrate, often with satellite lesions and stromal radiations. Lazar *et al.*¹⁰ observed four early cases and described the 'cracked windshield' appearance of the cornea. The reaction in the anterior chamber varies from a few cells to a hypopyon. Posterior segment involvement has not been described. There was a long delay between presentation and diagnosis except in the three cases where the organism was suspected. During this period there was usually

Fig. 5. Slit-lamp photograph of the left eye following the third penetrating keratoplasty.

intensive treatment with topical corticosteroids and a variety of antibiotics. The initial microbiological diagnosis was nocardia in six out of 17 cases (35%). This was probably because *M. fortuitum* and *M. chelonae* grow rapidly on ordinary culture media producing colonies in only three to four days, and because they may be easily decolourised on Ziehl-Neelsen staining. Moreover, if examined only by Gram stain, they may be dismissed as 'diphtheroids,' as happened in the case reported by Levenson and Harrison.⁴ The course of the disease is long and indolent, resolving in up to 13 months, usually leaving corneal scarring.

In 1970 Turner⁸ reviewed the first eight reported cases of ocular disease due to atypical mycobacteria including six cases of keratitis due to *M. fortuitum*. He also reported experimental studies which shed light on the pathogenesis of the condition. Rabbit eyes were inoculated with a suspension of *M. fortuitum* under various conditions. A progressive keratitis was not induced by inoculation into healthy corneas, but could be when the host defences were altered. This was accomplished by the use of topical corticosteroids, subconjunctival methylprednisolone, or intravenous cyclophosphamide. The presence of liquid petrolatum seemed to increase the virulence of the organism, suggesting that ointments should not be used in the treatment of infections caused by *M. fortuitum*.

Our case fits a well defined background for this type of keratitis but it is interesting to speculate on the possible source and time of infection. One possibility is that the organism was acquired on the occasion of the second penetrating keratoplasty. The progress of the infection may well have been assisted by the postoperative topical steroids. The period of six weeks between the graft and the development of the keratitis would fit well with the latent period of previous cases. Another possibility is that the organism was already present in the host cornea at the time of surgery and was responsible for the unusual stromal infiltrate that appeared in May 1984. If this is so, the organism may have been acquired as a complication of the use of the extended wear contact lens. These are well known to predispose to infectious keratitis from other more common bacteria.

M. chelonae is resistant to most antituberculosis agents. In the present case the organism was initially reported as sensitive to gentamicin but later became resistant, a fact which probably accounts for the initial improvement and subsequent relapse of the keratitis. Amikacin appears to be more effective both

in vitro and in vivo, and it is notable that the three cases treated with this drug responded relatively quickly, though one recurred on cessation of treatment.¹²

The following recommendations are made. There should be a high index of suspicion for *M. fortuitum* complex in any unusual keratitis, particularly those following corneal trauma and with multiple infiltrates underlying the ulceration. Staining for acid-fast bacilli should be performed, and suitable culture media for mycobacteria should be used routinely in such cases. Once the diagnosis is established, topical amikacin is probably the treatment of choice. This should be continued for a long period and well after the keratitis has resolved. If grafting is required, it should be carried out under appropriate antibiotic cover.

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