LETTERS TO THE JOURNAL

Sir,

Keratitis Due to the Fungus *Acremonium* (*Cephalosporium*)

The most common causes of fungal keratitis are *Candida* and *Aspergillus*.[1] *Aspergillus* species, especially *A. flavus* and *A. fumigatus*, are often associated with corneal ulcers and severe corneal diseases.[2,3] Although *Acremonium* has frequently been reported to cause keratitis and exogenous endophthalmitis in the southern part of the United States and India,[4–10] it has not previously been reported in the British Isles. Its histological appearance is unusual and sufficiently distinctive that once seen, it can be recognised on fixed tissue. The rarity of this fungus as a cause of mycotic keratitis, its insidious clinical course and its distinctive pathological appearance prompted this report.

Case Report

A 34-year-old white man attended the eye clinic at Falkirk and District Royal Infirmary with a year-long history of recurrent redness and epiphora of the right eye Six months before his presentation at the clinic he had climbed up a scaffold on a building site and accidentally scratched his eye with a saw which was lying on the scaffolding. Examination of the right eye revealed a lower corneal infiltrate with stromal oedema, a superficial area of fluorescein staining, uveitis and raised intraocular pressure. The left eye was normal. He was thought to have herpetic keratitis and was treated with Zovirax (Wellcome), Betnesol (Evans) and mydriatics. He initially responded well, but the eye flared up four times over the next few months, finally requiring inpatient treatment. At that time he was found to have a central corneal infiltrate affecting the endothelium rather than the epithelium and uveitis. He again responded well to antiviral treatment and steroids (trifluorothimidine and Eumovate N (Glaxo)). The eye flared up intermittently until January 1990 when he presented with a corneal abscess involving the lower third of the cornea, raised intraocular pressure, hypopyon and a large epithelial defect. Conjunctival scrapings were sent for microbiological examination on the clinical suspicion of a fungal infection, but did not yield any results. He was treated with co-trimoxazole drops hourly, topical Zovirax and Genticin (Nicholas). Over a 6 week interval the eye slowly healed but the lesion recurred shortly after the patient was discharged. In March 1990 he underwent emergency penetrating keratoplasty. Since then he has had no recurrence and the graft remains clear.

Pathological Findings. The corneal disc was 8 mm in diameter with a central 4 mm ulcerated area which had irregular borders and a creamy colour. The endothelial surface was roughened and scattered pigment was present.

Microscopic examination: The corneal epithelium was absent axially, with stromal erosion to about 50% of normal thickness. Amorphous basophilic debris lay between the lamellae. A mild to moderate inflammatory infiltrate composed of polymorphonuclear leucocytes and a few lymphocytes was present in the mid stroma. A granulomatous inflammatory reaction surrounded and eroded Descemet's membrane (Fig. 1a). Remnants of the endothelium persisted at the periphery of the specimen. Extensive septate hyphae were present in the posterior inflammatory membrane percolating into the stroma up to Bowman's layer on the routine haematoxylin and eosin stain and were highlighted by special stains for fungi (periodic acid Schiff and Grocott's methanamine silver).

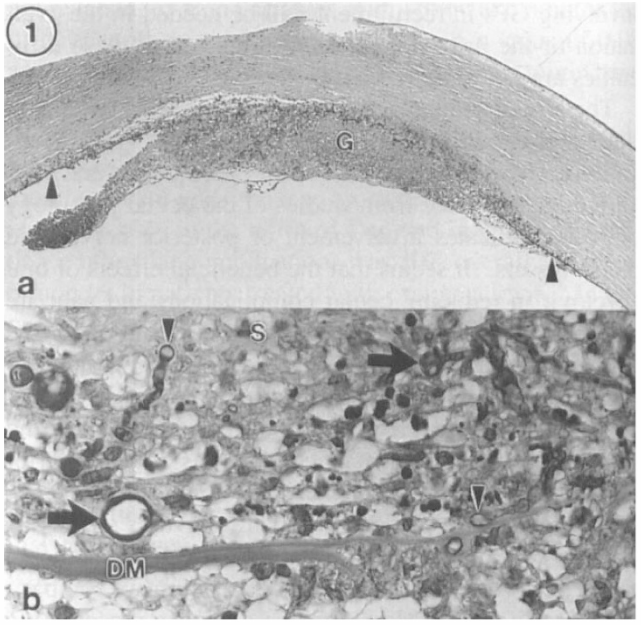

Fig. 1. *(a) Photomicrograph of the affected cornea shows an ulcer reaching the mid stroma and a posterior mycotic granuloma (G). The latter destroyed Descemet's membrane (arrowheads). (PAS, ×350) (b) Detail of the posterior stroma (S) and the granuloma. Numerous septate fungi with small (arrowheads) and large (arrow) terminal vesicular swellings, inflammatory cells and necrotic debris are enmeshed in a fibrinous network. Descemet's membrane (DM) is destroyed by this process. (PAS, ×630).*

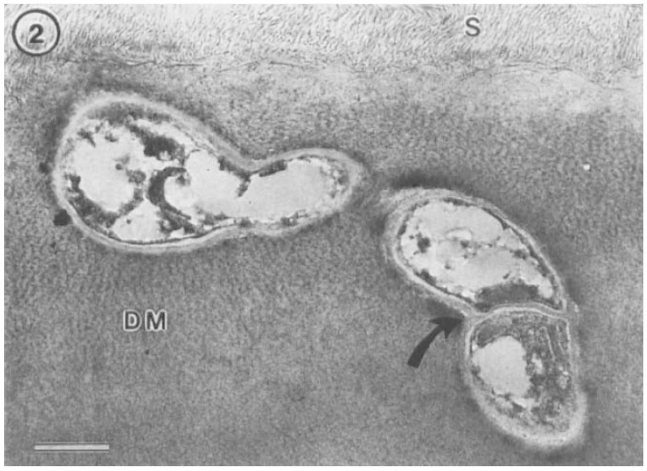

Fig. 2. *Transmission electron microscopy shows a septate (arrow) fungus, 1.5–2 μm in sagittal section, at the level of Descemet's membrane (DM). S, stroma. Scale bar represents 1 μm.*

Many of the hyphae had large terminal vesicular swellings up to 10 μm in diameter (Fig. 1b). Irregular large and small round forms, some with single buds, were also present. Single fungi were also present distant from the main conglomeration, particularly in the posterior stroma. The hyphae were not arranged with the long axis in any particular direction.

Microbiological findings: The corneal scrape did not contain any identifiable organisms, but one colony of *Acremonium* sp. was cultured from the keratoplasty specimen using Sabouraud's agar.

Transmission electron microscopy: Septate fungi were present within the stroma and Descemet's membrane (Fig. 2). The endothelium was absent in the axial, most affected part of the cornea.

Discussion

Histopathological examination revealed deep corneal involvement with many fungi on the endothelial aspect of the cornea, which suggests that endophthalmitis could easily have developed in this patient. There was minor inflammatory infiltrate, vascularisation was absent and fungi were rare in the superficial stroma. There was cellular fragmentation of keratocytes in the tissue. A superficial scrape in this cornea would have been unlikely to yield diagnostic material. The main focus of the inflammatory reaction was the granulomatous infiltrate around Descemet's membrane. In a large histopathological study of mycotic keratitis in the USA Naumann *et al.*[3] showed that hyphae are often found deep in the corneal stroma adjacent to Descemet's membrane and orientated parallel to stromal lamellae. In cases treated with corticosteroids, some fungal forms were oriented perpendicular to the lamellae. That study[3] showed that, as in the present case, Descemet's membrane does not provide an effective barrier to intraocular spread. The histological appearance of the fungus is distinctive, because of the most unusual pleomorphism of the septate filamentous forms and the large variation in size of the round forms. The other septate filamentous fungi include *Aspergillus*, *Alternaria* and *Fusarium* sp. The septate branching appearance of *Aspergillus* is well known. However, on purely histological grounds it is impossible to distinguish *Acremonium* from *Alternaria* and *Fusarium*, since species identification is made by examination of the type and arrangement of fungal spores and fungi do not sporulate in tissue. In our case, only one colony was grown on culture from the scrape, which is not surprising as the cornea had been intensively treated prior to surgery and the majority of the organisms were present in the posterior cornea.

Acremonium is a soil saprophyte and environmental contaminant, but an infrequent human pathogen.[4] Only seven species have been shown to cause infection in man.[4] In the majority of reports, fungus identification has been limited to the genus.[4] Fungal keratitis should be suspected in any case of trauma, especially when vegetable matter, viz. wood, may have been involved in the injury. A severe corneal ulcer due to *Acremonium recifei*[11] was reported in a patient who had suffered a corneal abrasion when a piece of coconut shell he was cracking flew into his eye. He required keratoplasty in addition to local and intravenous miconazole and oral ketaconazole. The insidious clinical course in our case was not unusual. Apparent cure of fungal keratitis due to *Acremonium potronii* without antifungal therapy followed by posterior corneal abscess 8 months later was reported by Forster *et al.*[12] The history in our case is quite similar and highlights the necessity to investigate the cause of an infectious keratitis aggressively if the usual investigations are negative, even when there is an apparent cure. It seems likely in this case that the patient may have had a long-standing fungal infection as a result of the corneal injury which occurred some months before he presented with keratitis, although mycotic superinfection aggravated by corticosteroid therapy cannot be completely ruled out. *Acremonium* may have a predilection to colonise extended-wear contact lenses. Liolet and Warnet[13] studied 113 contact lenses colonised by fungi. *Acremonium* was found in the majority (59.4%). The most recently published case of keratitis caused by *A. kiliense* was also reported in a contact lens wearer and in this case the fungus was also cultured from the lens storage liquid.[14] Yamamoto *et al.*[15] raised the possibility that there may be some enzymatic activity of this fungus predisposing to infection of certain soft lenses. *Acremonium* sp. have also been documented as one of the organisms causing superinfection in herpes simplex keratitis.[16]

Obtaining diagnostic material in keratomycotic infection can be difficult. Multiple scrapes from the base and edge of the ulcer under biomicroscopic observation are advisable.[17] Lund *et al.*[14] found that a tap of the aqueous humour may provide a diagnosis in cases when corneal scrape cultures are negative. This diagnostic procedure can be combined with a therapeutic instillation of an antifungal agent into the anterior chamber.

In conclusion, although *Aspergillus* and *Candida* are the common causes of keratomycosis, unusual organisms such as *Acremonium* may occasionally be seen, particu-

larly after a corneal abrasion by vegetable matter or in the setting of contact lens wear. The organism has a distinctive histopathological appearance, but a deep scrape, superficial keratectomy or an anterior chamber tap is required to obtain diagnostic material.

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Sir,

Acute Kerato-uveitis Associated with Topical Self-administration of the Sap of the Petty Spurge (*Euphorbia peplus*)

Petty Spurge (*Euphorbia peplus*) (Fig. 1) is a common weed found in gardens and waste-ground and is widely distributed throughout Europe and beyond. It is a member of the family Euphorbiaceae, a diverse group of flowering plants rich in terpenoids and alkaloids which deter herbivores by virtue of their irritant properties on gut, skin and the eye.

Medicinal use of the sap of Euphorbiaceae has been described since ancient times, particularly as a purgative (hence the name 'spurge') and as a wart cure.

Most cases of ocular irritation associated with spurges

Fig. 1. *Petty Spurge* (Euphorbia peplus). *(Specimen height 15 cm.)*