FUNGAL CORNEOSCLERITIS COMPLICATING BETA-IRRADIATION-INDUCED SCLERAL NECROSIS FOLLOWING PTERYGIUM EXCISION

A. P. MORIARTY[1], G. J. CRAWFORD[1], I. L. McALLISTER[1] and I. J. CONSTABLE[2]
Perth, Australia

SUMMARY

Four cases of fungal corneoscleritis complicating beta-irradiation-induced scleral necrosis after pterygium excision have presented to our institution in recent years. Two cases were due to *Petriellidium boydii* and one each to *Fusarium* and *Scedosporium inflatum*. The condition may remain undiagnosed for weeks to months and becomes chronic with perforation or incipient perforation. The infections may masquerade as a chronic red eye, posterior scleritis or serous retinal detachment. Penetrating or lamellar keratoplasty is required following debridement of necrotic tissue. Prolonged systemic antifungal therapy may still fail to eradicate infection. Visual outcome is usually poor, and one of our patients required enucleation. Removal of calcific plaques from ulcer beds should be accompanied by disinfection, debridement and culture, since these beds and plaques are frequently a nidus of infection. Subsequently these ulcers may be covered with lamellar grafts or conjunctiva. We would caution against the use of radiotherapy to prevent recurrence of pterygia.

The use of beta irradiation as an adjunct to pterygium excision has until recently been common practice. However, the complications of such treatment can be devastating.[1] Although bacterial corneoscleritis may complicate scleral necrosis following such therapy[2] we are unaware of reports of fungi causing such infection.

We present four cases of fungal corneoscleritis from our institution. Clinical features, management and suggestions for avoiding this complication are discussed.

CASE REPORTS

Case 1

A 68-year-old woman who had received 2200 rads of beta irradiation to her left eye following removal of a pterygium presented 13 years later with a 1-month history of a persistent red and watering eye. This was due to a calcific plaque covering the bed of a deep scleral ulcer. The plaque was removed and grew *Petriellidium boydii* on culture. The eye became more irritable over the next few days and a lamellar corneal graft was performed to cover the bare area, since there was no evidence of clinical infection in the ulcer bed at that stage. She settled post-operatively on topical steroids and antibiotics and achieved a visual acuity of 6/36.

However, the eye continued to cause increasing pain and discharge over the next 2 months. The sclera and graft became necrotic, requiring debridement and removal of the necrotic graft. Pus was noted on the ciliary body and was cultured but grew no organisms. Impending perforation necessitated a further large penetrating keratoplasty and following this she was treated with topical natamycin hourly and ketoconazole 200 mg per day on the basis that *Petriellidium boydii* was responsible for persistent infection. Over 2 weeks she developed a serous retinal detachment and simultaneously hepatotoxicity from the ketoconazole, and her treatment was therefore converted to intravenous amphotericin B on an inpatient basis.

The serous retinal detachment resolved over 6 months, but retinal exudates have remained (Fig. 1). After a period of 12 months' management she eventually achieved a final visual acuity of 6/36 with a quiet vascularised graft.

Case 2

A 48-year-old woman who had had three doses of 800 rads radiotherapy with beta irradiation following a left pterygium excision 15 years previously developed a red and painful left eye. She saw an ophthalmologist and was treated with topical antibiotics and steroids. Over 2 months she failed to improve and was referred to our unit.

At presentation her visual acuity was 6/9 in the left eye. She had a 3.5 mm × 4.5 mm scleral ulcer which was virtually full thickness. Our previous experience suggested

From: [1]Department of Ophthalmology, Royal Perth Hospital; [2]Lions Eye Institute, 2 Verdun Street, Nedlands, WA 6009, Australia.
Correspondence to: Mr. A. P. Moriarty, Department of Ophthalmology, Royal Perth Hospital, Wellington Street, Perth, WA 6000, Australia.

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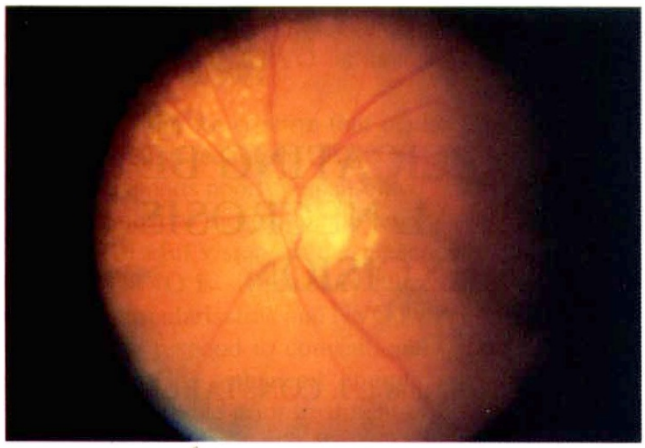

Fig. 1. *Case 1. Retinal exudates remaining following serous retinal detachment.*

that *Pseudomonas* may have been the causative organism. Urgent microscopy of a scrape from the ulcer bed showed no organisms. She was, however, started on intensive topical fortified gentamicin and intravenous gentamicin and cefuroxime. Because of the risk of incipient perforation a 9 mm lamellar corneal graft was performed.

Tissue sent to the laboratory at the time eventually grew *Petriellidium boydii* after 2 weeks of incubation. Meanwhile the scleral abscess surrounding the graft rapidly worsened and the graft became necrotic. The graft was removed and on culture grew no organisms.

Two contiguous large (9 mm) lamellar grafts were performed which successfully eliminated the abscess, and the patient was commenced on hourly natamycin and systemic amphotericin. However, she found that the pain from the eye and the intravenous amphotericin were intolerable and elected for an enucleation.

The enucleated specimen showed no fungal elements in the corneoscleral grafts. However, hyphae were present up to the margins of the grafts (Fig. 2) even though clinically they appeared free of infection, and despite 3 months of topical and systemic antifungal therapy. Her total time of inpatient management was more than 3 months, and of ophthalmic consultation greater than a year.

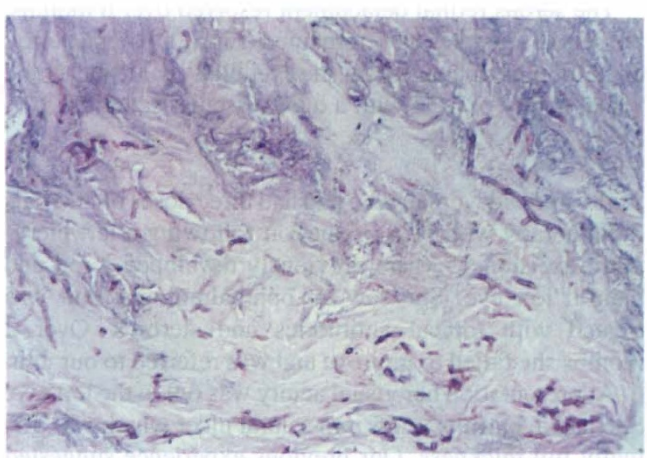

Fig. 2. *Case 2. Fungal elements still present in the enucleated specimen.*

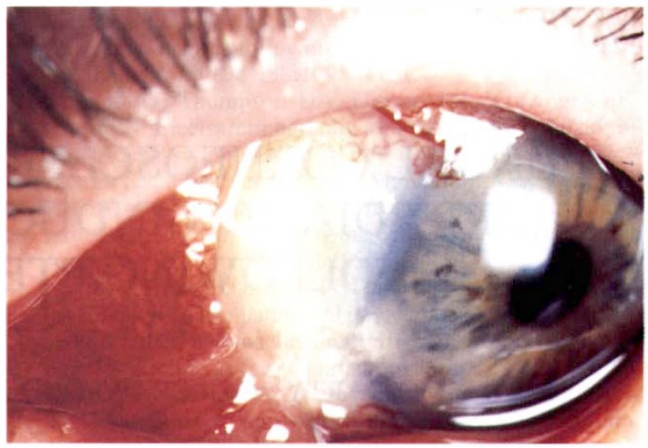

Fig. 3. *Case 3. Necrotic fungal scleral abscess at the site of previous radiotherapy.*

Case 3

A 50-year-old woman received 2200 rads of beta radiotherapy in three divided doses following removal of a left pterygium. She developed a calcific plaque at the site of radiotherapy but this remained asymptomatic. Twenty years after her radiotherapy she presented with a sudden onset of a painful and red left eye. She was started on topical chloramphenicol and then topical steroids by her family practitioner, but failed to improve. Two weeks later she was referred for an ophthalmic opinion but apart from some conjunctival injection there was very little of note. She was treated with topical framycetin and chloramphenicol and showed some improvement over the next week.

Two weeks later she presented with increasing pain and irritation. A marked anterior chamber flare and cellular reaction was present with a definite necrotic scleral ulcer at the site of the previous radiotherapy (Fig. 3). She was referred to our institution and admitted for debridement of the scleral abscess and lamellar corneal graft to the deep ulcer bed. Urgent microscopy of the scleral tissue showed no organisms. She was started on hourly fortified gentamicin and cephalothin topically and intravenous gentamicin. More than 2 weeks later a growth of *Scedosporium inflatum* was obtained from the scleral tis-

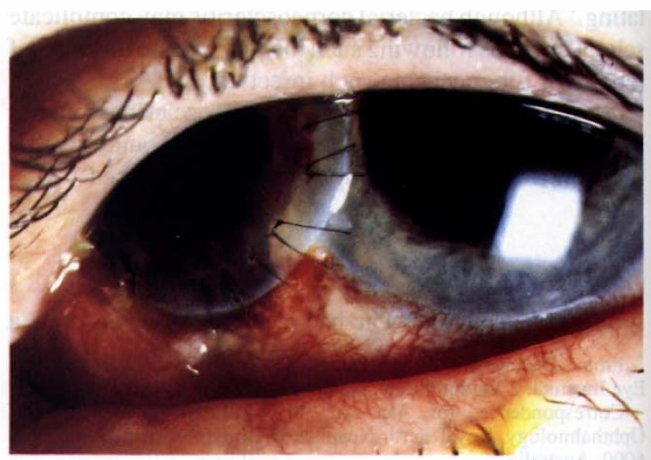

Fig. 4. *Case 4. Successful lamellar keratoplasty to a necrotic scleral abscess and ulcer.*

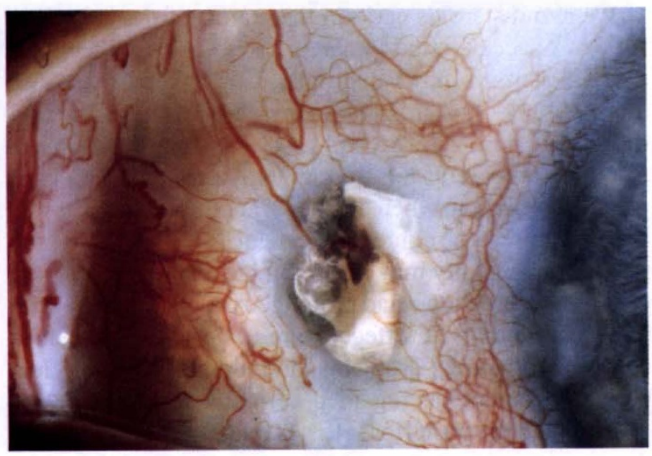

Fig. 5. *Calcific plaque covering a scleral ulcer at the site of radiotherapy.*

sue. Her treatment was thus changed to hourly topical natamycin and systemic fluconazole. Over the next 3 weeks the graft settled reasonably well and the anterior chamber reaction diminished.

Over the subsequent month, however, she developed serous retinal detachment with retinal exudates beneath the ulcer bed. The graft began to slough and was removed. The sclera was discovered to be necrotic in the base with vitreous herniation through a perforation site in the ulcer bed. A further lamellar graft was performed (Fig. 4). Histological examination of the necrotic sclera and graft showed that it was infiltrated by fungal hyphae despite 3 months of treatment with natamycin topically and fluconazole systemically. Simultaneously the retinal detachment progressed and the macula detached. The patient was commenced on intravenous amphotericin B as an inpatient, following microbiological advice. Unfortunately her haemoglobin level dropped on this treatment and she required transfusion. She remained for 1 month on further intravenous amphotericin and 5 months following her initial graft the serous retinal detachment began to settle. Retinal exudates began to diminish as did the anterior chamber reaction, but unfortunately she developed irreversible cystoid macular oedema and her best

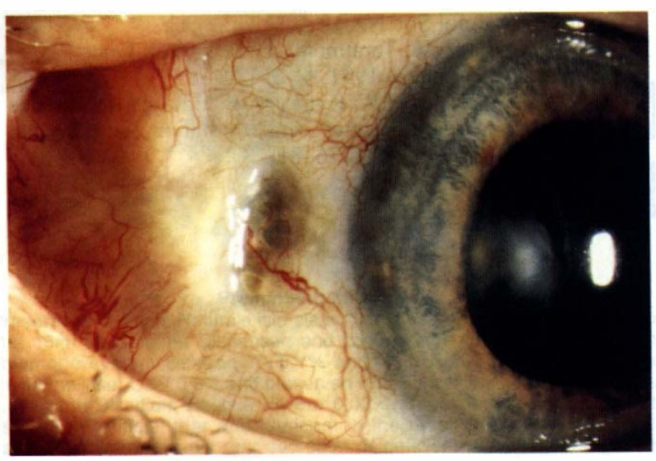

Fig. 6. *Deep scleral ulcer after calcific plaque removal in the area of radionecrosis.*

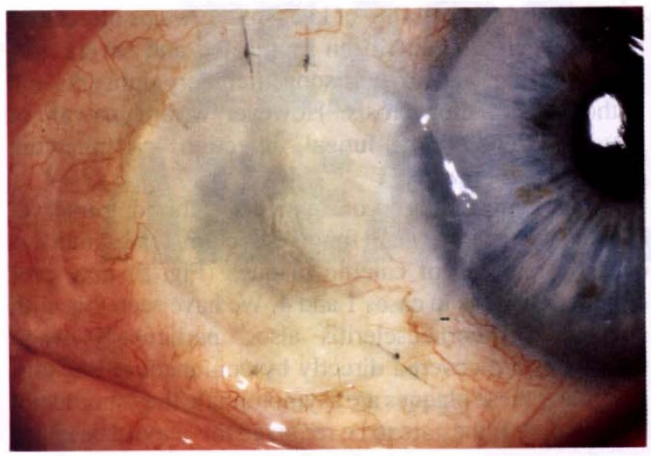

Fig. 7. *Lamellar keratoplasty performed to cover a deep scleral ulcer.*

corrected visual acuity subsequently has been 6/24. This patient's total period of hospitalisation was some 3 months and she had a 4-year history of ophthalmic supervision following this complication.

Case 4

A 71-year-old woman underwent removal of a left pterygium and a course of 2400 rads of radiotherapy in three divided doses. Fifteen years later she presented with a red and painful eye and a calcific plaque covering the base of a scleral ulcer was removed. The bare area was covered with a free conjunctival graft and the patient commenced on topical chloramphenicol and steroids. No debridement of the scleral bed or culture of the calcific plaque was performed.

Two days later she complained of a marked mucopurulent discharge and a swab of this eventually grew *Fusarium.* Her treatment was changed to hourly natamycin and systemic ketoconazole. Despite this the eye became extremely painful and an abscess formed involving approximately 180° of the limbus. This abscess was slow to resolve on this treatment and at 1 month the patient underwent debridement, microbiological specimens from which showed no growth of bacteria or fungi. She remained on topical natamycin and systemic ketoconazole as the original *Fusarium* had been sensitive to this medication, but the scleritis remained active for a further 4 months. The sclera eventually became thinned and a microperforation occurred at the limbus, which was successfully repaired. Further debridement of necrotic sclera was performed and a large ectatic thinned area formed 180° around the limbus.

Eventually on medical therapy the condition settled without requiring lamellar graft, although the patient rapidly developed a lens opacity. Some 18 months later she underwent a successful extracapsular cataract extraction with intraocular lens and managed to achieve a visual acuity of 6/6 with a comfortable eye.

DISCUSSION

Previous reports of beta-irradiation-induced scleral nec-

rosis stress the possibility of late *Pseudomonas* infection.[1] Streptococci have also been implicated and severe corneoscleritis may occur quite soon after pterygium excision without prior radionecrosis.[2] However, we are unaware of previous reports of fungal infection complicating radionecrosis.

A common finding in our patients is the long interval between radiotherapy and fungal infection. Often interference by removal of calcific plaques (Fig. 5) may precipitate sepsis, as in cases 1 and 4. We have seen this with streptococcal corneoscleritis also,[3] particularly when these beds are covered directly by conjunctiva. We suggest that if these plaques are asymptomatic they should not be removed. If they are to be removed this should be under aseptic conditions with disinfection and culture of the scleral bed. The plaques and ulcer beds (Fig. 6) appear to form reservoirs and a nidus for infection.[3] Only when sterility is certain should these be covered by lamellar grafts (Fig. 7) or free conjunctival autografts.

Most commonly fungal corneoscleritis is chronic and treated as a bacterial infection, often with antibiotics and steroids. Whether this may mask the condition and then accelerate it remains a possibility. A high index of suspicion of fungal infection should be maintained, especially if neither *Pseudomonas* nor *Streptococcus* is identified on gram staining or culture.

Once corneoscleritis is established, early debridement is essential and tissue must be cultured for bacteria and fungi, since the diagnosis may otherwise be missed and the organisms can be rare ocular pathogens. Microbiological advice with respect to culture identification and sensitivities is important early in the condition and close cooperation with microbiologists essential. Systemic antifungal therapy is necessary to improve drug delivery to the sclera; the choice of drug is dependent on microbiological advice. It is important to be aware of the toxic side effects of prolonged administration of these drugs.

The condition may become chronic unless adequate debridement or removal of necrotic tissue is performed. Occasionally an emergency graft may be necessary if there is impending perforation, but excision of as much necrotic tissue as possible is necessary. Grafts performed prior to adequate debridement and antifungal therapy have a high risk of necrosis and sloughing. Even with debridement and prolonged topical and systemic antifungal therapy viable fungi can still be found in tissues many months later (cases 2 and 3).

We avoid steroids early in the course of the infections for fear of accelerating fungal or pseudomonal infections, and feel steroids may be partially responsible for accelerating the infection in some cases. Occasionally the condition may mimic an idiopathic scleral melt or a posterior scleritis and careful ultrasonographic examination of the posterior segment, when the media are turbid, is necessary to exclude serous retinal detachment.

Visual morbidity may be prolonged and severe in these cases. All our patients had prolonged problems, some with severe systemic side effects from toxic drugs as well as severe ophthalmic problems and domestic disruption. Only one patient has regained normal visual acuity.

Although the posterior sclera is relatively radioresistant the anterior sclera is known to be more susceptible[4] to the effects of radiotherapy. In recent years limited radiotherapy has been practised but post-operative radiotherapy of approximately 2000 rads is still commonly applied.[5] The complications described arose with doses in the order of 2200–2400 rads, which may produce a combination of necrotic ulcer beds, ischaemic conjunctiva and poor tear-film. When these complications are compounded by epithelial defects produced by removal of calcific plaques and the use of topical steroids then fungal corneoscleritis may ensue.

In view of the devastating side effects of radiotherapy – a risk of scleral necrosis of 4.5% and a lifelong risk of endophthalmitis[6] – we feel that this treatment should be avoided. We perform in excess of 150 pterygium operations per year and conjunctival autografting is now our treatment of choice to reduce recurrences.

Key words: Corneoscleritis, Fungal infections, Pterygium, Radionecrosis.

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