
CASE REPORT

SCEDOSPORIUM PROLIFICANS: AN UNCOMMON CAUSE OF SEPTIC ARTHRITIS

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Septic arthritis due to fungal infection is uncommon, but when it does occur it can have a devastating effect. *Scedosporium prolificans* is an emerging fungal pathogen that appears to have a predilection for bone and cartilaginous surfaces. This fungus is resistant to most commonly prescribed antifungal agents. We report the successful treatment of *Scedosporium prolificans* septic arthritis with a combination of surgery and new antifungal agents.

Key words: fungal infection, *Scedosporium prolificans*, septic arthritis.

Abbreviations: CRP, C-reactive protein; ESR, erythrocyte sedimentation rate.

INTRODUCTION

Fungi are rare causes of septic arthritis and cases that do occur usually result from common pathogenic fungi such as *Candida*.¹ *Scedosporium prolificans* is a fungal species that is usually associated with disseminated and local infection in immunocompromised patients.^{2–8} It is also a rare cause of infection in immunocompetent hosts.^{2,3,9} Septic arthritis due to *S. prolificans* infection is usually associated with penetrating trauma and follows a protracted clinical course with a variable outcome that includes arthrodesis, amputation or complete cure.^{2,3,9} The difficulty in treating this infection is in part because of its resistance to commonly given antifungal agents, such as amphotericin B.^{4,6,10,11} Another important factor in the treatment difficulty is the immunocompromised state of most of the hosts.² Recently, *S. prolificans* has been reported to be susceptible to some of the newer antifungal agents *in vitro*, but there is limited *in vivo* experience with these agents.^{11,12} The aim of this paper is to present a case of septic arthritis due to *S. prolificans* infection that was cured with a combination of surgery and new antifungal agents.

CASE REPORT

We report a case of *S. prolificans* septic arthritis in an immunocompetent, previously well 5-year-old boy. The patient was initially presented to hospital with a 3-week history of a painful right ankle. Although there was no history of penetrating trauma, the child had fallen from his bicycle 3 weeks before the onset of symptoms with a resultant minor ankle abrasion.

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On examination, the child was partially able to weight-bear on the lower limb and was afebrile. The ankle was mildly swollen and tender over the medial malleolus, but there was no erythema. There was minimal discomfort on ankle movement and no limitations to range. An initial radiograph showed a small lucent region over the medial malleolus (Fig. 1). Initial blood tests showed a white cell count of $9.5 \times 10^9/L$, an erythrocyte sedimentation rate (ESR) of 40 mm/h and a C-reactive protein (CRP) of 6.9 mg/L. The child was initially monitored and then commenced on flucloxacillin for presumptive osteomyelitis of the distal tibial epiphysis. Over the following week, the child remained afebrile and well, but pain and mild swelling persisted about the distal tibia and ankle. A decision was then made to surgically explore the region. The findings at surgery were a subcutaneous collection of fluid together with an epiphyseal erosion and serous fluid within the ankle joint. Swabs and tissue samples were taken for microscopy and culture. The area was debrided, washed out and closed over a drain. I.v. antibiotics were continued postoperatively. On postoperative day 4, the patient spiked his first temperature to 39°C and his pain was not settling. ESR had risen to 120 mm/h and CRP to 64 mg/L. The initial tissue and swab specimens from the incision and drainage grew a pure culture of fungus that was subsequently identified as *S. prolificans*. Blood cultures remained negative. The patient was returned to the operating theatre for a further washout and debridement. At this time, the distal tibia was drilled to explore for a possible metaphyseal collection, but none was found. Further swabs and tissue specimens were taken for microscopy and culture. The wound was closed over a drain.

Tissue specimens and swabs from the second surgery again grew *S. prolificans* and hence the diagnosis of fungal osteomyelitis and associated septic arthritis was confirmed. As this fungus is usually resistant to amphotericin B, initial antifungal treatment commenced with oral itraconazole 200 mg (10 mg/kg) b.i.d. When further microbiological identification and susceptibility testing results became available, this was replaced with oral terbinafine 250 mg daily and oral voriconazole 200 mg b.i.d.



Fig. 1. Initial radiograph on presentation. Note the small lucent lesion over the medial aspect of the epiphysis.

loading dose for 1 day then 100 mg b.i.d. The patient remained well and afebrile. The pain and discomfort about the distal tibia and ankle decreased and he was discharged home on his oral voriconazole and terbinafine 9 days after the second surgery. Results of antifungal susceptibility testing carried out at the national mycology reference laboratory were obtained at this time, using a broth microdilution method according to National Committee for Clinical Laboratory Standards guidelines.¹³ The isolate was resistant to amphotericin B, 5-fluorocytosine, fluconazole, itraconazole and ketoconazole. The most active antifungal agents were terbinafine (minimal inhibitory concentration (MIC) 8 mg/L) and voriconazole (MIC 8 mg/L). Synergy testing was carried out using a microdilution chequerboard method¹⁴ and this showed marked synergy with fourfold reduction of both terbinafine and voriconazole MIC.¹²

The patient was closely followed up in both the Orthopaedic and Infectious Disease Outpatient departments. The patient remained well. The wound had a slight discharge and the mother reported occasional, raised temperatures of up to 38°C. The ESR and CRP decreased to 90 mm/h and 12 mg/L, respectively, 3 weeks after the second washout and debridement. On review, 4 weeks after the second surgery, there remained a slight malodorous discharge from the wound and an occasional raised temperature in the boy was still reported from the mother. The patient was readmitted to hospital for surgical investigation and wash out, at which there was no operative evidence of infection. The ankle joint was closed and the superficial wound packed open to heal by secondary intention. The patient was discharged home the next day to continue his antifungal medication.

The patient's condition continued to improve over the ensuing weeks. The wound slowly healed well by secondary intention. No further instances of raised temperatures in the child were reported. By 4 months after the original presentation, the patient was well and actively running and playing pain free at home. The CRP was <1 mg/L and the ESR 13 mm/h. On review 7 months after the original presentation, the patient was well, fully active with completely pain-free range of motion of his right ankle. A radiograph showed a significant lytic lesion with the distal epiphysis of the right tibia (Fig. 2), but a gallium scan at this time was reported as normal with no evidence of ongoing infection. The antifungal medication was therefore ceased at this time. A long-term follow up was organized to monitor the involved joint and epiphysis and

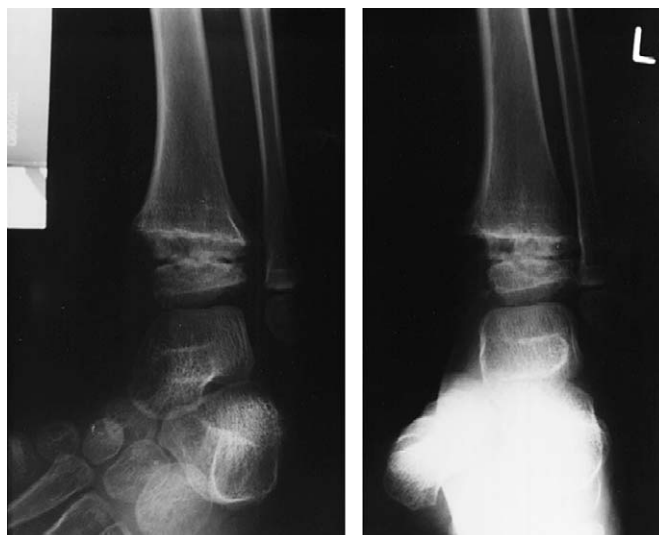


Fig. 2. Follow-up radiograph 7 months following the initial presentation. Note the lytic lesion of the epiphysis and distal metaphysis medially.

currently, 6 months after stopping antifungal therapy, the patient remains well and symptom free.

DISCUSSION

Human fungal infections due to *S. prolificans* were first described in 1984 by Malloch and Salkin.¹⁵ They isolated the fungus from a bone biopsy specimen from an area of osteomyelitis in an immunocompetent 6-year-old boy. Initially the fungus was named *S. inflatum*, but this was subsequently changed to *S. prolificans*.^{16,17} This fungus is widespread in nature as a soil saprophyte.^{3,4,18–20}

Several case reports have appeared in the published works of both localized and disseminated infections due to this fungus. Most reports have occurred in Australia, Spain and North America and the infection may be specific to the climates of these regions.^{2–4,7–9,11,17,18,20} Disseminated infections usually occur in immunocompromised hosts^{2–7} and are believed to result from respiratory seeding.^{6,7,20} In immunocompetent patients, infection is usually localized. *S. prolificans* infection resulting in septic arthritis and osteomyelitis is more common in immunocompetent patients^{2,3,9} but can also occur in the immunocompromised.⁸ To date, it has been reported to result from a penetrating injury in all but one case where haematogenous spread was suspected but not confirmed.^{8,9} The case history presented in this paper was a localized infection in an immunocompetent patient without apparent penetrating injury but with a minor abrasion, presumably the portal of entry of the fungus in this case. Blood cultures were always negative and the patient, although febrile, remained systemically well, making a haematogenous source unlikely.

The treatment of *S. prolificans* is difficult and cure is dependent on both the host status and the presentation of the infection (localized vs disseminated). Disseminated infections are usually unresponsive to antifungal therapy and are often fatal.^{2–7} Treatment of localized infection remains difficult and requires a protracted course of combination therapy with surgery and antifungal therapy.^{2,3,8,9} Previous reports of *S. prolificans* septic arthritis have used older antifungal agents (amphotericin B, ketoconazole,

itraconazole, nystatin, 5 flucytosine and fluconazole)^{2,3,8,9} to which *S. prolificans* is usually intrinsically resistant on *in vitro* testing.^{4,6,10,11} Despite the known *in vitro* resistance of *S. prolificans* to older antifungal agents, there are reports of successful clinical outcomes in some cases. This is probably due to early and aggressive surgical debridement of these infections.

New antifungal agents such as voriconazole have variable susceptibility to *S. prolificans* in the *in vitro* setting.^{10–12} Voriconazole as a single agent has been shown to inhibit many strains of *S. prolificans in vitro*.¹² Combination therapy of voriconazole together with terbinafine or itraconazole has also shown an enhanced synergistic effect *in vitro*, as occurred with our patient's isolate.^{10,12} Extrapolation of *in vitro* results to the *in vivo* clinical setting is difficult and to date the clinical efficacy of voriconazole and terbinafine against *S. prolificans* septic arthritis has not been reported. We believe that this case is the first such report.

Our case has shown that surgery in combination with new antifungal agents such as terbinafine and voriconazole can be successful in treating septic arthritis due to *S. prolificans* infection. Prolonged treatment and careful long-term follow up of these patients is recommended until evidence that infection has been completely eradicated.

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