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Successful Treatment of *Scedosporium aurantiacum* Osteomyelitis in an Immunocompetent Patient*

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ABSTRACT

***Background*: Bacterial infections are a well-known complication of traumatic amputations. In cases involving contact with soil or water contaminated with manure, one also must be aware of infections with fungi, particularly *Scedosporium* spp. We report on an immunocompetent trauma patient with an infection caused by a recently described *Scedosporium* species, *S. aurantiacum*.**

***Methods*: Case report and literature review.**

***Results*: In a 36-year-old healthy man, entrapment of the right leg resulted in a traumatic amputation just below the knee and contamination of the wound with manure. Six weeks after the initial surgical debridement, he developed a phlegmon. Cultures yielded *Staphylococcus aureus* and *Pseudomonas aeruginosa*, and treatment with ciprofloxacin and clindamycin was started. After several weeks, a fistula developed, and roentgenograms demonstrated osteomyelitis. A pure culture of *Scedosporium* was grown from bone fragments and was identified as *S. aurantiacum* by sequencing of the rDNA internal transcribed spacer 1 region. Following debridement, the wound was drenched in 0.2% polyhexamethylene biguanide for four minutes. A pre-operative culture showed growth of *S. aureus* only. Postoperatively, clindamycin, ciprofloxacin, and voriconazole were started and continued for 12 weeks. At the last follow-up, 15 months after the trauma and nine months after cessation of the antimicrobial agents, the patient had no signs of osteomyelitis.**

***Conclusion*: To our knowledge, this is the first case of osteomyelitis caused by *S. aurantiacum*. The patient was treated successfully by a combination of surgery and voriconazole.**

TRAUMATIC AMPUTATIONS of the lower extremity carry a high risk of postoperative complications. Despite careful debridement and prophylactic antibiotics, wound infections and osteomyelitis may occur in both healthy and immunocompromised patients. These infections most often are caused by *Staphylococcus aureus*, but gram-negative bacilli such as *Enterobacteriaceae* and *Pseudomonas aeruginosa* as well as anaerobes also are found regularly

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[1–3]. In addition to bacterial infections, osteomyelitis caused by fungi such as *Scedosporium* spp. has been described [4–6].

Scedosporium species are of worldwide distribution and are abundant in soil contaminated with manure and in ditchwater, although they also may be found in indoor plant pots and greenhouses [4]. Various species have been described. The species *S. apiospermum* (the asexual form or anamorph of *Pseudallescheria boydii*) and *S. prolificans* are the most commonly associated with human infections [7]. The first-named species is a well-known cause of mycetoma after trauma and may be responsible for lung and cerebral infections in near-drowning patients as well as for systemic infections in immunocompromised patients [4,8]. *Scedosporium prolificans* is found mainly in immunocompromised patients, in whom it causes systemic infections [9]. *Scedosporium aurantiacum* was recently described as a new species by Gilgado et al. [10]. It is difficult to distinguish morphologically from *S. apiospermum*.

In this case report, we describe the treatment of osteomyelitis of the femur caused by *S. aurantiacum* after a traumatic amputation in an immunocompetent patient.

CASE REPORT

A 36-year-old man without significant medical history was admitted to the emergency department following entrapment of his right leg in an agricultural machine, resulting in traumatic amputation just below the knee. The wound was macroscopically contaminated with manure. Given the extensive soft-tissue damage, a patella-preserving guillotine amputation was performed after extensive debridement. Bacterial cultures taken from the wound yielded *Aeromonas hydrophilia*, *Citrobacter freundii*, *Klebsiella pneumoniae*, *Streptococcus milleri*, *Enterococcus* spp., and *Bacteroides fragilis*. Postoperatively, the patient was treated with intravenous amoxicillin/clavulanate (1000/200 mg qid) for one week. On the second postoperative day, another debridement was performed for progressive necrosis of the soft tissue. Thereafter, the wound granulated well and could be closed by a split-thickness skin graft three weeks after the trauma. At day 33, the patient was discharged from the hospital in good ambulatory condition.

Six weeks after the accident, the patient was re-admitted with a phlegmon. Blood examination showed a normal leukocyte count (8.2×10^9/L) and an elevated C-reactive protein (CRP) concentration (44 mg/L). Bacterial cultures were taken, and amoxicillin/clavulanate (500/125 mg orally tid) was started. Bacterial cultures of the wound yielded *Staphylococcus aureus* and *Pseudomonas aeruginosa*, so amoxicillin/clavulanate was replaced by ciprofloxacin (500 mg orally bid) and clindamycin (600 mg orally tid). Within a few days, the acute symptoms of infection such as erythema and edema had disappeared, yet a 6-cm deep fistula appeared anteromedially in the amputation stump. Roentgenograms of the femur demonstrated osteomyelitis of the distal part of the bone (Fig. 1).

The patient was operated on again 11 weeks after the trauma, and the infected part of the femur was removed. A subcutaneous pocket as well as the bone marrow were filled with gentamicin beads. A Gram stain of the resected femoral fragment revealed no micro-organisms, but all three plates inoculated yielded pure cultures of a *Scedosporium* spp., which became known after the patient had been discharged. By use of DNA sequencing of the internal transcribed spacer 1 (ITS 1) region of the nuclear rDNA, the fungus was identified as *S. aurantiacum* (CBS Culture Collection deposition number 118934), a recently identified species [10,11]. The minimal inhibitory concentrations (MICs) were determined by a broth microdilution method [12] and were: Amphotericin B 16 mg/L, itraconazole 16 mg/L, voriconazole 1 mg/L, posaconazole 1 mg/L, and caspofungin 4 mg/L. Two weeks after the operation, the leukocyte count was normal (7.9×10^9/L), and the CRP concentration was low (7 mg/L), but the erythrocyte sedimentation rate (ESR) was elevated (40 mm/h).

Fifteen weeks after the trauma, the patient was operated on because of the continued presence of a fistula. An abscess was found around the femoral stump, which was treated with extensive debridement of the soft tissue. The wound was drenched with 0.2% polyhexam-

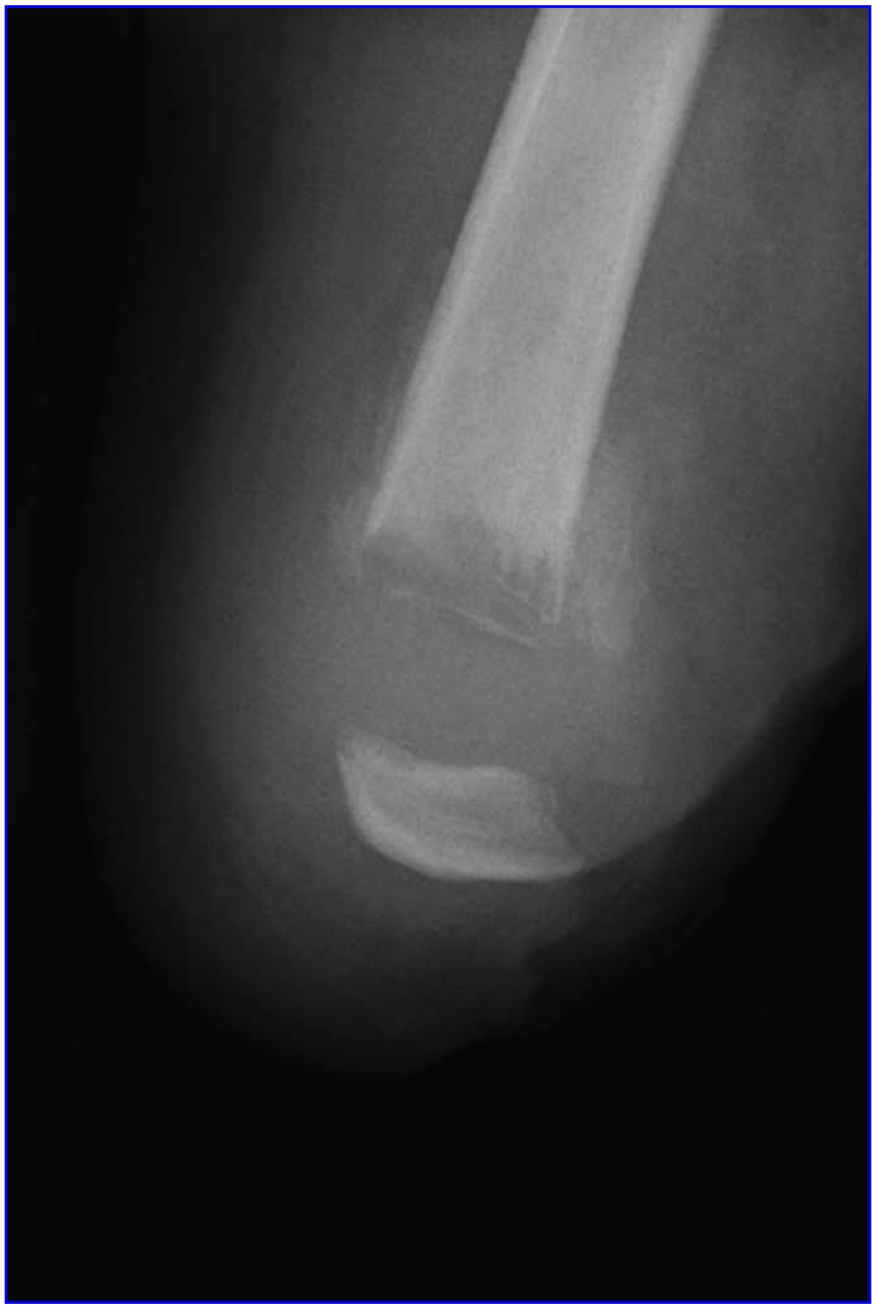

FIG. 1. Osteomyelitis of distal femoral stump. Roentgenogram reveals osteolytic lesion.

ethylene biguanide (Avecia Biocides, Wilmington, DE) in 0.9% NaCl for four minutes. Gentamicin beads were placed and were removed two weeks later, followed by coverage of the defect with a vacuum-assisted closure system (V.A.C.®; KCI Medical Products, Dorset, UK). A gram stain of the abscess showed gram-positive cocci in clusters, and only *S. aureus* grew. Post-operatively, voriconazole (200 mg orally bid), ciprofloxacin (500 mg orally bid) and clindamycin (600 mg orally tid) were started and continued for 12 weeks. The treatment was complicated by a mild skin rash secondary to photosensitivity, which may have been caused by voriconazole or by the antibacterial drugs, particularly ciprofloxacin.

The infection was monitored by serum assays for CRP and ESR, leukocyte count, and frequent roentgenograms of the femur. Eight weeks after cessation of the antimicrobial

agents, all values were normal (CRP 5 mg/L, ESR 6 mm/h, and leukocyte count 5.0×10^9/L), and there were no signs of infection on the roentgenograms. The wound was healed completely, and the patient was being rehabilitated with a prosthesis.

The patient was re-operated on nine months after cessation of the antimicrobial agents because of pain secondary to movement of the patella under the femoral stump. The patella was removed, and the femoral stump was optimized. Roentgenograms and the findings at operation did not indicate infection, and cultures of the resected fragments of the femur showed no growth.

DISCUSSION

To our knowledge, this is the first case report of a bone infection caused by *S. aurantiacum*, which was first described in 2005 by Gilgado et al. [10]. The identity of the fungus was established by sequencing the rDNA ITS.

Scedosporium species are distributed worldwide, being found in soil, manure, polluted water, industrial environments polluted by oils and benzenes, indoor plant pots, and greenhouses [4]. They are opportunistic pathogens, causing systemic or disseminated infections in immunocompromised patients [7,9,13–18]. Infections with *S. prolificans* and, particularly, with *S. apiospermum* also have been described in immunocompetent persons, but these infections followed trauma or near-drowning episodes [5,6,8,15,18–22]. Pulmonary colonization is observed in patients with cystic fibrosis [23]. For a recent review on *S. apiospermum* and the various presentations of *Scedopsporium* infections, see Guarro et al. [4]. The host's immune status is the chief determinant of the severity and prognosis of the infection. In immunocompromised patients, the mortality rate is high [4,7,9].

Treatment of *Scedosporium* infections consists of extensive surgical debridement combined with antimycotic agents [4]. *Scedosporium* spp. generally are resistant to amphotericin B, as well as to many other antifungal drugs [4,24], and *S. prolificans* appears to be resistant to all available antimycotic drugs [24]. In vitro, synergy between triazoles and terbinafine has been demonstrated, and a combination of voriconazole and terbinafine has been successful in an immunocompromised patient with a disseminated *S. prolificans* infection [25]. Voriconazole seems to be the agent most active against *S. apiospermum* [4,24]. In recent literature, voriconazole was reported to be successful in the treatment of *S. apiospermum* infections [5,6,8,9,13,15,19]. The *S. aurantiacum* strain isolated from our patient had an MIC for voriconazole of 1 mg/L, which probably is in the therapeutic range (the breakpoints for voriconazole are not defined).

Voriconazole is derived from fluconazole and is a broad-spectrum antifungal agent that can be given orally or intravenously. It has activity against most *Candida* spp. and several filamentous fungi and has a widespread tissue distribution, including cerebral penetration [26]. Adverse reactions include visual abnormalities, skin reactions such as photosensitivity, elevations in hepatic enzymes, and a high potential for drug interactions. Dose adjustment is recommended in patients with hepatic dysfunction or in those who are receiving possibly interacting drugs [26].

Polyhexamethylene biguanide is a disinfectant with broad antimicrobial activity, including fungi [27]. For example, it has been helpful for the treatment of fungal infections of the ear and parasitic infections of the eye [28,29].

Steinbach et al. reported successful treatment of osteomyelitis in an immunocompetent child caused by *S. prolificans* with six weeks of voriconazole and caspofungin combined with locally applied polyhexamethylene biguanide solution [5]. We decided to follow their strategy, except for the use of caspofungin, in the treatment of our patient, who had osteomyelitis caused by the newly described *S. aurantiacum*. It may be that surgery alone would have been sufficient, as a culture obtained one month after the operation for osteomyelitis was negative. However, we were not sure if a negative culture of pus from the abscess would be sufficient to prove complete elimination of the fungus from the bone. At the time of the second operation, it became known that the isolated fungus had an MIC for voriconazole in the apparent therapeutic range. Because con-

tinued infection after surgery and even dissemination has been described in immunocompetent patients with osteomyelitis caused by *Scedosporium* spp. [5,30], we choose to treat our patient with voriconazole, with apparent clinical success.

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