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Case Report

Scedosporium apiospermum mediastinitis in an orthotopic heart transplant recipient

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ABSTRACT

Scedosporiosis is an opportunistic mycosis that may cause disseminated disease in transplant recipients. This article reports a case of recurrent *Scedosporium apiospermum* mediastinitis without pneumonia in an orthotopic heart transplant recipient, with durable control achieved by long-term antifungal therapy and serial debridement. This case highlights the importance of an opportunistic scedosporium infection in immunocompromised hosts, given the challenges in microbiological identification and limited treatment options.

Introduction

Scedosporium sp. was first isolated in greenhouse soil in 1974, and was subsequently identified as a human pathogen in select immunocompromised hosts (Malloch and Salkin, 1984). Scedosporiosis largely comprises infections with *Scedosporium apiospermum* complex (*S. apiospermum, S. aurantiacum, S. dehoogii, S. minutisporum and Pseudallescheria minutispora*) (Lackner et al., 2012). *Scedosporium prolificans* has been reclassified as *Lomentospora prolificans* (Chen et al., 2021).

S. apiospermum is known to target the respiratory tract, with secondary central nervous system dissemination and meningitis after near-drowning episodes in both immunocompetent and immunocompromised hosts (Katragkou et al., 2007).

An increasing number of cases of scedosporiosis have been reported in immunocompromised patients as a consequence of corticosteroid, antineoplastic and antirejection medications, and antibiotic exposure. Additionally, the increased use of polyenes and echinocandins may provide selective pressure for the development of scedosporiosis (Lamaris et al., 2006).

S. apiospermum infections in transplant recipients include cutaneous, cardiopulmonary and central nervous system manifestations (Lopez et al., 1998; Castiglioni et al., 2002; Talbot et al., 2002; Clement et al., 2015). The case reported in this article adds to our understanding of scedosporiosis, and is the first described incident of mediastinitis without concomitant pneumonia in a heart transplant recipient.

Case presentation

A 55-year-old male with ischaemic cardiomyopathy underwent an elective orthotopic heart transplant. His postoperative course was complicated by right ventricle dysfunction, requiring delayed mediastinal closure after 2 days. He was discharged 3 weeks later on prednisone, tacrolimus and mycophenolate mofetil. Although limited information was available, the donor had a history of incarceration and intravenous drug use, but no evidence of drowning.

One month after transplant, the patient presented with fever, chills and purulent drainage from the sternotomy wound. Laboratory investigations showed leukocytosis of 25,110 per mm^3 (normal 4400–11,300 per mm^3) with 89% neutrophils, serum (1→3)-β-D-glucan was >500 pg/mL (normal <60 pg/mL), and serum galactomannan assay had an optical density index of 0.05 (normal 0.00–0.49). Blood cultures revealed no growth. Chest computed tomography (CT) demonstrated mediastinal fluid collection (1.7 × 4.2 cm) anterior to the heart, but no pulmonary infiltrates. The patient underwent mediastinal debridement, followed by omental flap closure. Intraoperatively, extensive necrosis and purulence with dense mediastinal adhesions were noted. Mediastinal tissue culture showed cotton white colonies (Figure 1). Gomori's methenamine silver (GMS, Figure 2) stain and periodic acid-Schiff (Figure 3) stain revealed narrow-angle branching, septated hyphae.

Voriconazole and micafungin were initiated empirically, given the initial suspicion of aspergillosis. Operative cultures subsequently identified *S. apiospermum*. No other cases of scedosporiosis were identified at the study institution in the 6 months preceding or following the case patient. No construction work was underway in close proximity to the

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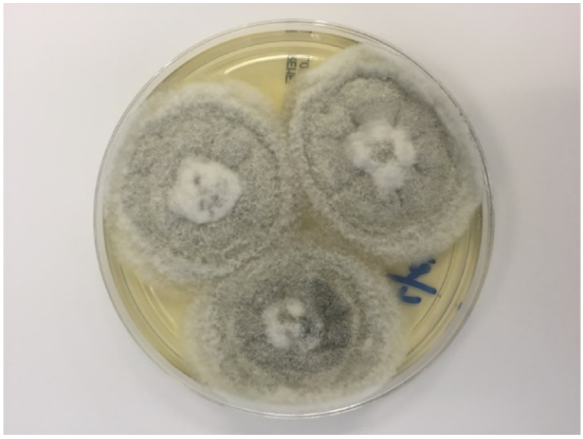

Figure 1. Sabouraud dextrose agar culture showed white-grayish colonies of *Scedosporium apiospermum.*

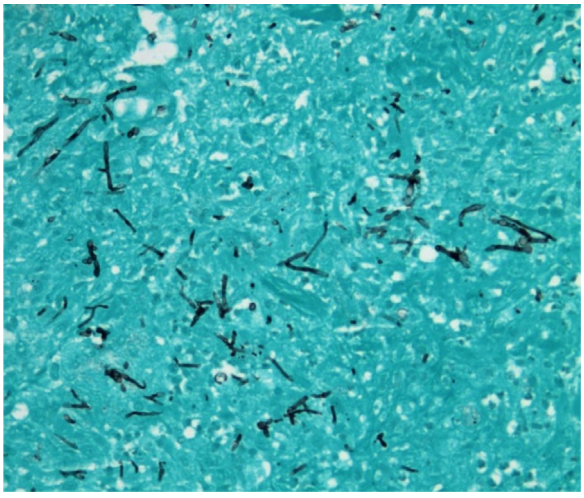

Figure 2. Gomori's methenamine silver stain showed septated acute angle-branching hyphae.

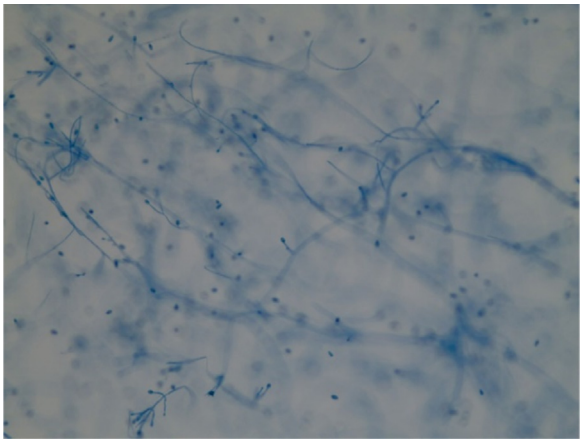

Figure 3. Periodic acid-Schiff stain showed terminal and lateral conidia.

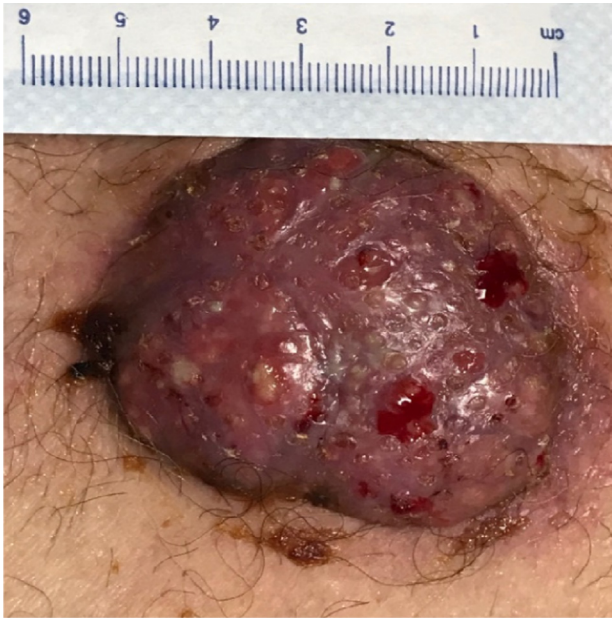

Figure 4. Fungating growth of breakthrough *Scedosporium apiospermum* infection on the chest wall on posaconazole therapy.

operative suites or patient's room at the time of diagnosis. Hospital environmental sampling failed to recover *Scedosporium* spp. The patient reported that he had used power-tool drills for wood carving and had mown the lawn after receiving the heart transplant.

Susceptibility testing showed that the minimum inhibitory concentration (MIC) of posaconazole was 2 μg/mL and the MIC of voriconazole was 1 μg/mL (LabCorp, Dublin, OH, USA). Micafungin was discontinued. The patient developed mild liver dysfunction (aspartate aminotransferase 79 U/L, alanine aminotransferase 46 U/L, alkaline phosphatase 247 U/L, total bilirubin 4.7 mg/dL) which normalized after replacement of voriconazole with delayed-released posaconazole tablets. Immunosuppression was reduced to tacrolimus monotherapy. The patient was subsequently discharged home with a planned 1-year course of posaconazole.

Eight months later, serum (1→3)-β-D-glucan had decreased to 245 pg/mL (normal <60 pg/mL). One year into the antifungal therapy, surveillance high-resolution chest CT showed a sternotomy defect with dehiscence and foci of bone resorption, although the patient remained asymptomatic. Posaconazole therapy was extended.

After 18 months of antifungal therapy, the patient presented with a 3-day history of a rapidly enlarging, tender, circumferential upper sternal lesion at the site of a chronic nodule, previously attributed to benign postsurgical changes. He reported complete adherence to the antifungal therapy, and the posaconazole trough level 1 month prior to presentation was therapeutic (3.1 μg/mL, normal >1.25 μg/mL; performed at LabCorp). Physical examination showed a fleshy, tender nodule over the upper third of the sternum without fluctuance or drainage (Figure 4). Chest CT revealed an infiltrating left parasternal anterior thoracic wall mass measuring 5 × 4.1 cm, and mediastinal adenopathy. CT-guided left chest wall needle biopsy specimen demonstrated septated hyphae with acute angle branching on GMS stain, later confirmed as *S. apiospermum*; subsequent excisional debridement was performed. Susceptibility testing identified the following MICs: amphotericin B 8 μg/mL, micafungin 1 μg/mL, posaconazole 2 μg/mL, voriconazole 0.5 μg/mL, and isavuconazole 4 μg/mL. As these results were identical to the original isolate, posaconazole was continued.

Despite a therapeutic serum posaconazole trough concentration at 1.6 μg/mL (normal >1.25 μg/mL) and reduction in immunosuppression, a follow-up chest CT 4 months later showed an increase in the size of the anterior chest wall parasternal mass. Posaconazole was thus discontinued and voriconazole resumed with close monitoring of liver function tests. The patient was later readmitted for methicillin-resistant *Staphylococcus aureus* (MRSA) bacteraemia from an arteriovenous fistula abscess on the left arm. The surgical team was hesitant to perform additional chest wall debridement because of concurrent active MRSA bac-

Figure 5. Healed chest wall wound after 2 years of voriconazole treatment.

teraemia, and concern regarding the high risk of intra-operative and immediate postsurgical complications, such as wound healing and wound closure from poor nutritional status. As such, no further debridement was performed. Surveillance chest CT performed 1 year after voriconazole resumption revealed complete resolution of the anterior chest wall mass. The patient continued to improve with no further recurrence during follow-up after receiving 2 years of voriconazole, at which time involution of overlying pigmented intact skin was noted (Figure 5).

Discussion

Scedosporium spp. are ubiquitous throughout the environment, found in plants, soil and polluted water. Disseminated scedosporium cases are relatively rare but have been reported in transplant hosts, and require aggressive surgical and antifungal management (Lopez et al., 1998; Castiglioni et al., 2002; Talbot et al., 2002; Husain et al., 2005; Clement et al., 2015). Specifically, *S. apiospermum* infections have presented as cutaneous nodules, ulcers, brain abscesses, pneumonia and endocarditis in heart transplant recipients (Alsip and Cobbs, 1986; Kusne et al., 2000; Perlroth and Miller, 2004; Clement et al., 2015). To the authors' knowledge, only two previous cases of mediastinitis have been described in this patient population (Johnson et al., 2014; Clement et al., 2015).

Microbiological identification of *S. apiospermum* can be difficult as it shares similar characteristics with *Aspergillus* spp. and *Fusarium* spp. (Lopez et al., 1998; Talbot et al., 2002). Early identification is crucial as misdiagnosis can lead to the use of ineffective antifungal agents (Shinohara and George, 2009). *Scedosporium* spp. grow as white-gray colonies on Sabouraud dextrose agar culture medium. Microscopic examination usually shows septate hyphae with conidiophores along with conidia, which are characteristically oval with large apical ends and truncated (Talbot et al., 2002).

Serum (1→3)-β-D-glucan test is a non-specific marker but may be used as a diagnostic adjunct as it has been shown to have good sensitivity in reported cases of invasive scedosporium brain abscess and lometospora fungaemia. Importantly, serial serum (1→3)-β-D-glucan has been used as a prognostic biomarker, as reported in cases of invasive candidiasis. Serum aspergillus galactomannan antigen assay may be positive due to cross-reactivity. No scedosporium-specific commercial assay is available at present (Jaijakul et al., 2012; Chen et al., 2021).

As seen with the case patient, treatment of scedosporiosis often requires a combination of surgery and antifungal therapy to maximize the chance of durable infection control or cure. Although *Lomentospora prolificans* (previously *S. prolificans*) is intrinsically resistant to most antifungal drugs, including amphotericin B and azoles (Lackner et al., 2012), voriconazole remains the drug of choice for *S. apiospermum* infections. One study reported that 66% of 70 patients with *S. apiospermum* infection responded well to voriconazole (Troke et al., 2008). Posaconazole has also demonstrated moderate activity *in vitro*, as well as in isolated case reports, and remains an alternative antifungal therapy for scedosporiosis infection (Lackner et al., 2012).

The case patient had recurrence of infection while on posaconazole, requiring a switch to voriconazole. Voriconazole ultimately proved to be the most effective therapy in this patient, as has been reported previously in other cases. Along with antifungal therapy, surgical source control is crucial. Surgical debridement was an independent predictor of survival in a review of 80 cases of scedosporium infections (Husain et al., 2005).

Disruption of anatomical barriers by trauma or surgery can lead to scedosporium wound infection and contiguous osteomyelitis, which may explain why the case patient had sternal wound infection and mediastinitis without respiratory tract involvement. As additional *S. apiospermum* infections were not identified at the study institution in the 6 months preceding or following this case, and there had not been any hospital construction or renovation in close proximity to the patient, hospital-associated fungal infection appeared unlikely. One possible explanation for the source of infection in the case patient may be his wood carving practice using power tools and lawn mowing, which may have caused a deposit of shavings or grass on his chest wound during the immediate post-transplant period.

To the authors' knowledge, this is the first known case of cure from invasive recurrent *S. apiospermum* mediastinitis without pulmonary involvement following orthotopic heart transplantation. This case highlights the importance of aggressive scedosporiosis treatment with a combination of surgery, antifungal therapy and long-term surveillance.

Conflict of interest statement

None declared.

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Ethical approval

Not required. The authors obtained written and signed consent to publish this case report from the patient.

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