Case Report

Scedosporium apiospermum fungaemia: the ramification of broad spectrum antimicrobial treatments

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Abstract:

Scedosporium apiospermum is a cosmopolitan mycotic agent with unique characteristics. This is a case of a 65-year-old immunocompetent patient who presented with shortness of breath and fever. Consolidation was observed in both lung fields on chest X-ray. A diagnosis of aspiration pneumonia was made. Extended-spectrum β-lactamase (ESBL)-producing Klebsiella pneumoniae was identified from his tracheal aspirate and imipenem was administered. Initial blood cultures were negative but after 10 days on imipenem, Candida glabrata was isolated. Amphotericin B was added to the treatment regimen, but after a week on this antifungal, Scedosporium apiospermum was cultured from the blood. The patient succumbed to illness before a change in the antifungal regimen. The case highlights the unwelcome consequence of using a broad spectrum antibiotic and later a broad spectrum antifungal agent.

Key words: Amphotericin B; fungaemia; Pseudallescheria boydii; Scedosporium apiospermum; broad spectrum

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Introduction

Scedosporium apiospermum (teleomorph: *Pseudallescheria boydii*) is a ubiquitous saprophytic mold readily isolated from numerous environmental sources such as soil, sewage and decaying vegetation[1]. It is a fungus of increasing clinical importance, especially in patients with underlying medical conditions[2]. Disease states produced by *Scedosporium apiospermum* are broad, ranging from cutaneous and subcutaneous tissue infections to disseminated infections[3]. The mold is a potent agent of severe infections in both immunocompromised and immunocompetent patients[4]. It is almost always resistant to amphotericin B[5], and its emergence may even be favoured by the long-term usage of amphotericin B[6].

Case report

A 65-year-old Chinese gentleman was brought by family members to our medical centre after he developed shortness of breath on the same day. He had been vomiting 3 to 4 times a day for the last two days. His family also noted that he was feverish. The patient was diagnosed with nasopharyngeal carcinoma 20 years ago and has completed radiotherapy treatments. However, he developed multiple (IX to XII) cranial nerve palsies following the radiotherapy, requiring a tracheostomy for bilateral vocal cord palsy and percutaneous endoscopic gastrostomy (PEG) tube feeding for the loss of gag reflex.

On examination, he was fully conscious. He had low grade fever (37.8°C), was tachypnoeic (respiratory

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rate of 40 breaths per minute) and tachycardic (heart rate of 135 beats per minute). The blood pressure was 110/50 mmHg. Pulse oximetry recorded an oxygen saturation of 45% in ambient air. Auscultation of his lungs revealed bilateral basal crepitations with poor air entry. A chest X-ray showed consolidation at the lower zone of both lung fields. His full blood count revealed a total white cell count of 11 x 10^9 cells/L with a predominance of neutrophils (8.7 x 10^9 cells/L). The C-reactive protein level was markedly elevated at 13.2 mg/dL and the procalcitonin level exceeded 100 ng/mL.

A working diagnosis of aspiration pneumonia with type I respiratory failure was made. Assisted ventilation was started via the tracheostomy tube. A tracheal aspirate and blood sample were sent for bacteriological culture and the patient was given empirical antibiotic therapy consisting of IV ceftriaxone 2 g daily and IV azithromycin 500 mg daily. His condition rapidly deteriorated with the development of hypotension, requiring inotropic support and intensive care.

ESBL-producing *Klebsiella pneumonia* was isolated from the tracheal aspirate and his antibiotic regimen was changed to IV imipenem/cilastatin 500 mg/500 mg tds. His blood culture was negative at this time. A repeat peripheral blood culture on day 10 of admission grew *Candida glabrata* and IV amphotericin B deoxycholate at a dose of 1 mg/kg was added. Another peripheral blood specimen taken on day 17 of admission which yielded *Scedosporium apiospermum* (Figures 1 and 2). Before the administration of an alternative antifungal agent, the patient passed away due to severe sepsis and multiorgan failure.

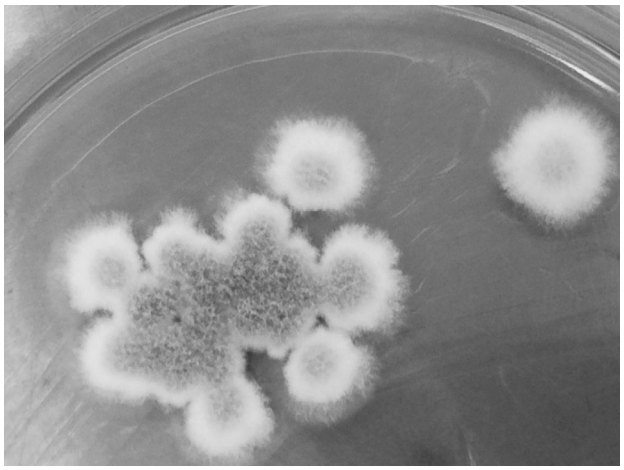

Figure 1: *Scedosporium apiospermum* on Sabouraud dextrose agar showing gray centered colonies with white cottony borders.

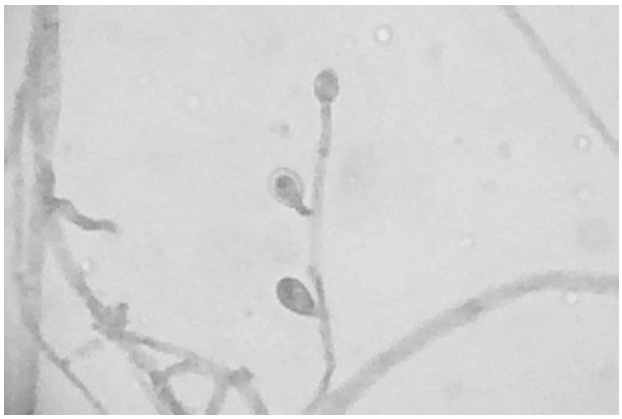

Figure 2: Lactophenol cotton blue stain of *Scedosporium apiospermum* showing hyaline oval truncate conidia borne singly on a conidiophore (magnification x 400).

Discussion

The *Scedosporium* genus has two medically important species of emerging mycotic agents, *Scedosporium apiospermum* and *Scedosporium prolificans*[5]. *Scedosporium apiospermum* has a more uniform worldwide distribution compared to *Scedosporium prolificans*[3]. Speciation is necessary because the latter is often more resistant to antifungal agents and is more invasive than *Scedosporium apiospermum*[2]. Unlike *Scedosporium apiospermum, Scedosporium prolificans* is dematiaceous and does not have a sexual stage (teleomorph). Also, the conidia of *Scedosporium apiospermum* are often produced singly on conidiophores (Figure 2), while those of *Scedosporium prolificans* are usually borne in clusters[3].

Scedosporium apiospermum was recognized as a pathogen in 1911 when it was implicated as an agent of mycetoma[5]. The portal of entry into humans is through the lungs, paranasal sinuses, or via traumatic inoculation[5]. It has been reported that previously damaged airways may be colonized by *Scedosporium apiospermum* and that persistent neutropaenia is a significant risk factor for disseminated disease[3]. Having lost his gag reflex, our patient is at risk of chronic pulmonary aspirations which could have resulted in a damaged tracheobronchial tree. Thus, it is interesting to note that fungaemia occurred in our patient who had no history of trauma, had elevated rather than low neutrophil counts,

and who was not on any immunosuppressive agent.

Using an anti-infective agent against a pathogen which is resistant to the drug can pose as a selection pressure, facilitating colonization by the drug-resistant pathogen. Thus, the broader the antibacterial spectrum of an antibiotic becomes, the higher the risk of "collateral damage" of being colonized by fungal pathogens gets. A prospective study on nosocomial fungaemia found that the majority of patients (87%) had received either vancomycin or imipenem[7]. In our patient, imipenem was administered because an ESBL-producing strain of *Klebsiella pneumoniae* was cultured from his tracheal aspirate and presumed to be the pathogen causing his pneumonia. However, the carbapenem might have predisposed him to *Candida glabrata* colonization and subsequently candidaemia.

The patient was given amphotericin B to treat the *Candida glabrata* fungaemia. While the provision of a polyene in this case is indicated due to the yeast's reduced susceptibility to fluconazole, this measure could have facilitated airway colonization and the subsequent haematogenous dissemination of *Scedosporium apiospermum*. Although fluconazole and ketoconazole do not possess significant activity against *Scedosporium apiospermum*[3], the newer triazole agents (posaconazole, voriconazole and ravuconazole) have been found to be active against it[1]. Voriconazole in particular, has been investigated as a treatment option for scedosporiosis. It was well tolerated and had clinically useful activity in treating both *Scedosporium apiospermum* and *Scedosporium prolificans* infections, with a higher response rate being recorded with the former (54% vs. 40%)[8]. The duration of treatment with voriconazole in patients who respond should also be prolonged, with 28 days being the minimum[8].

Conclusion

Scedosporium apiospermum is an emerging agent of hyalohyphomycosis in patients without significant immunosupression. Although not as frequently implicated in invasive mycosis as *Aspergillus* spp., it is important to identify *Scedosporium apiospermum* due to its resistance to commonly used antifungal agents. Fungal cultures are, therefore, mandatory in all patients with fungaemia with poor response to antifungal therapy, due to the risk of selecting for resistant fungal agents such as *Scedosporium apiospermum.*

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