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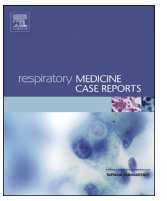

Case Report

# A case of *Scedosporium prolificans* pulmonary infection in a patient with acute myeloid leukemia

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ABSTRACT

An elderly woman with a history of myelodysplastic syndrome complicated by cavitary pneumonia treated with antibiotics and antifungal therapy was admitted with severe sepsis and pulmonary opacities on imaging. Pulmonary infection with *Scedosporium prolificans*, was diagnosed on bronchopulmonary lavage (BAL). This common environmental fungus is known to cause rare but severe infection in immunocompromised hosts. The patient was diagnosed with progression to acute myeloid leukemia during the hospitalization for which chemotherapy was initiated. Despite broadening antifungal therapy, the patient developed multi-organ system failure and died.

## 1. Introduction

First described in 1984, *Scedosporium prolificans* (synonymously known as *Lementospora prolificans* and *Scedosporium inflatum*), is a ubiquitous, filamentous saprophyte found in soil, sewage and decaying vegetation with most cases representing colonization [1,2]. However, over the past three decades, disseminated infections in immunocompromised hosts and difficult to treat pneumonia with this organism have been reported [1]. More specifically, in neutropenic patients, this infection has innate resistance to common antifungals and carries a poor prognosis and high mortality risk [2,3]. We report the isolation of *Scedosporium prolificans* in a critically ill, immunocompromised cancer patient initially resistant to voriconazole and placed instead on posaconazole [4–6] (see Fig. 1)

## 2. Case presentation

A 63 year old woman presents with a prior history of oligodendroma in remission, monoclonal gammopathy of undetermined significance (MGUS), and more recent history of myelodysplastic syndrome (MDS). MDS was diagnosed on bone marrow biopsy approximately seven months prior to admission. Her initial treatment course for her MDS included azacytidine for three cycles beginning five months prior to current hospitalization. Venetoclax was added three months prior to current hospitalization. She was undergoing evaluation for stem cell transplantation, which had been complicated by prolonged leukopenia present for at least two months prior to admission. Additionally, she developed a left lower lobe (LLL) cavitary pneumonia one month prior to admission. BAL results were positive for *Stenotrophomonas maltophilia* for which she remained on levofloxacin, as well as voriconazole for empiric fungal coverage. She was admitted to the hospital from hematology clinic for evaluation and treatment of sepsis after reporting chills and rigors, and was found to be hypotensive with a blood pressure of 61/46 mmHg. Computed tomography (CT) of the chest demonstrated a LLL and

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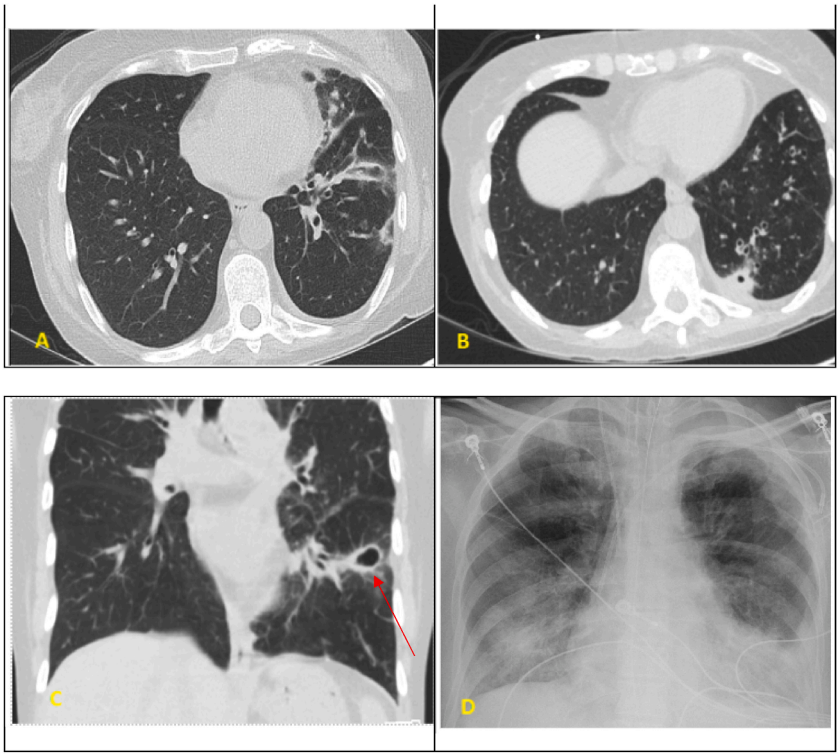


**Fig. 1.** Imaging from *Scedosporium prolificans* infection. Left lower lobe and lingula cavitary lesion seen in radiographic imaging.

lingular multifocal cavitary opacity. Levofloxacin was discontinued and she was initiated on cefepime and azithromycin in the emergency department for community-acquired pneumonia. The infectious diseases team was consulted on hospital day (HD) 0, and changed antimicrobial therapy to cefepime, minocycline, and voriconazole (continued from outpatient).

The patient underwent bone marrow biopsy on HD 1 due to concern for possible transformation of the MDS. Cytology demonstrated ~40 % cellular marrow with trilineage dysplasia, relative myeloid hyperplasia, and approximately 40–50 % blasts, consistent with acute myeloid leukemia (AML). These findings were in contrast to bone marrow biopsy two months prior which demonstrated ~10 % cellularity and 5–10 % blasts, consistent with MDS following therapy with azacytidine and venetoclax.

Bronchoscopy with bronchoalveolar lavage of the left lower lobe was performed on HD 3. Acid fast bacteria (AFB), legionella, nocardia, and Pneumocystis jirovecii smears and cultures were negative. Gram stain demonstrated 3+ white blood cells with final culture report positive for normal respiratory flora. Fungal elements were seen on fungal stain, with culture positive for 1+ mold on hospital day 7, identified as 1+ *Scedosporium prolificans* on hospital day 20. Fungal coverage was changed from voriconazole to posaconazole on HD 8 due to concern for voriconazole-resistant organism.

The patient's hospitalization was complicated by liver abscess (biopsied on HD 6 with cefepime-resistant E. coli but no fungal elements), acute kidney injury, and ground-level fall with resultant small subdural hematoma. Chemotherapy for AML was initiated on HD 13. On HD 14, the patient developed acute encephalopathy, acute hypoxemic and hypercapnic respiratory failure requiring endotracheal intubation and mechanical ventilation, and septic shock requiring vasopressor support. Renal function worsened requiring renal replacement therapy the next day. Repeat bronchoscopy was performed on HD 17 due to persistent bilateral pulmonary infiltrates, minimal clinical improvement, and persistent vasopressor requirement. Bronchoalveolar lavage performed in the right lower lobe was positive for vancomycin-resistant *Enterococcus faecium*. Rare hyphal elements were seen on fungal stain, with few colonies of mold on final fungal culture two weeks later without definitive identification despite attempted genetic analysis.

The patient continued to deteriorate clinically, with an increased peripheral percentage of circulating blasts suspected to represent progression of AML. Ongoing discussions with the patient's family resulted in a transition to comfort care, and eventually she expired on HD 21.

## 3. Discussion (clinical discussion)

Scedosporium prolificans is becoming an emerging infectious pathogen as more patients become immunocompromised for longer periods of time. It is found in the soil in Australia, Europe, and the Southern United States and is more common in dry environments [1,2]. It can be contracted through aerosolization of conidia into the lungs or directly into the skin due to trauma/injury. While normally infection remains localized, it can spread directly into the bloodstream [7]. A critical step of pathogenesis is transformation of the conidia into hyphae called germination. Once germination has occurred the hyphae are able to penetrate macrophages, cell walls, and extracellular matrices [8]. They are also harder for the innate immune system to control once forming hyphae. Epidemiologically,

this mold predominantly affects males ages of 50–85 [1,3]. Risk factors include underlying hematologic malignancies, cystic fibrosis, and solid organ transplantation [3,9]. While severe pulmonary infections have been reported most frequently, reports of disseminated infections including central nervous system involvement, keratitis, endophthalmitis, skin, bone and joint infections have also been documented [9]. It normally takes weeks for the fungus to grow on laboratory media; often a patient is postmortem by the time the results are available.

Due to the patient's complicated and prolonged hospital presentation, it is difficult to assess to what extent this pathogen played a role in her decompensation and death. Studies have shown that S. prolificans is associated with high mortality with azole monotherapy [4,5,8,10]. Choosing an appropriate antifungal regimen was complicated by the delay in identification of this organism, which did not occur until HD 20 despite the specimen being collected on HD 3. Numerous sets of blood cultures were drawn during the hospitalization, but none ever returned positive for fungal elements.

## 4. Discussion (imaging discussion)

Imaging showed a cavitary lesion in the LLL with ground glass opacities in the right lower lobe (RLL) as well (Figure 1). The cavitation is characteristic of Scedosporium infections though this finding is more sensitive than specific; other fungal infections (including aspergillus) can present in this way. Antifungal medications tend to have a higher burden of toxicities and side effects, pointing to the importance of bronchoscopic techniques to sample fungi for targeted therapy as imaging findings are not specific. The bronchoscopy showed mucus plugging in smaller airways, worse in the LLL.

## 5. Discussion (Brief review of literature)

A previous review of 12 Scedosporium patient encounters (specifically S. agiospermum and S. prolificans) at a cancer center has demonstrated a particular predilection for S. prolificans infections in patients with hematologic malignancies, and a predisposition of the pathogen to cause pulmonary infections [2]. Likewise, this review found the survival rate of these patients to be poor despite broad-spectrum antifungal coverage [2]. A larger review of similar infections in Australia found similarly poor outcomes with a median time-to-death following diagnosis of invasive fungal disease of nine days [3,9]. This study commented on adjunctive surgery as associated with decreased mortality rates, however this was not controlled for the likely relatively-better health of surgical candidates compared to non-surgical candidates; the patient described in our case would not have been a surgical candidate at the time S. prolificans was diagnosed. Voriconazole has been found in previous studies to be ineffective as prophylaxis and as monotherapy for invasive fungal disease from S. Prolificans, especially when compared to other Scedosporium species [4,10,11]. Data exists to support a treatment regimen of voriconazole and terbinafine, although mortality remains high even with this optimal regimen. Little data is available to support posaconazole therapy in such infections, as used in our patient [4–6].

## 6. Conclusion

In this clinical scenario, a profoundly immunocompromised patient with myelodysplastic syndrome transformed to acute myeloid leukemia, on active cancer-directed therapy, was admitted to the hospital for sepsis, hypotension and pneumonia. BAL ultimately demonstrated Scedosporium prolificans. Imaging revealed a cavitary lung lesion in the region from which the BAL was obtained. The literature reviewed in this case study illustrates that a switch from voriconazole to posaconazole may not have been as effective as the addition of terbinafine. It is imperative that oncologic/transplant intensivists and nurse practitioners maintain a high degree of suspicion and actively consider invasive fungal mold infections such as *Scedosporium*, especially as delayed identification of the organism may occur such as in the presented case. When presented with immunocompromised patients with difficult-to-treat pneumonia, or prolonged course of antimicrobial treatments, or atypical pneumonias, we need to involve our infectious disease, hemato-oncology and transplant colleagues early in the therapeutic decision making process. This may hasten the identification, specific treatment and ultimately the timely management of our patients.

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None over the course of the case report. .

## CRediT authorship contribution statement

**Abdullah Arjomand:** Writing – review & editing, Writing – original draft, Conceptualization. **Andrew Myers:** Writing – review & editing, Writing – original draft, Conceptualization. **Padmastuti Akella:** Writing – review & editing, Writing – original draft, Conceptualization.

## Declaration of competing interest

None.

## References

[1] I.B. Gosbell, M.L. Morris, J.H. Gallo, et al., Clinical, pathologic and epidemiologic features of infection with Scedosporium prolificans: four cases and review, Clin. Microbiol. Infection 5 (11) (1999) 672–686.
[2] N.E. Rolfe, R.L. Sandin, J.N. Greene, Scedosporium infections at a cancer center over a 10-year period (2001–2010), Infect. Dis. Clin. Pract. 22 (2) (2014) 71–74.

[3] C.F. Neoh, S.C.A. Chen, A. Crowe, et al., Invasive scedosporium and lomentospora prolificans infections in Australia: a multicenter retrospective cohort study, Open Forum Infect. Dis. 10 (2) (2023) ofad059.
[4] J.D. Jenks, D. Seidel, O.A. Cornely, et al., Voriconazole plus terbinafine combination antifungal therapy for invasive Lomentospora prolificans infections: analysis of 41 patients from the FungiScope® registry 2008-2019, Clin. Microbiol. Infect. 26 (6) (2020) 784.e781–784.e785.
[5] J. Meletiadis, J.W. Mouton, J.F. Meis, P.E. Verweij, Combination chemotherapy for the treatment of invasive infections by Scedosporium prolificans, Clin. Microbiol. Infect. 6 (6) (2000) 336–337.
[6] J. Meletiadis, J.W. Mouton, J.L. Rodriguez-Tudela, J.F. Meis, P.E. Verweij, In vitro interaction of terbinafine with itraconazole against clinical isolates of Scedosporium prolificans, Antimicrob. Agents Chemother. 44 (2) (2000) 470–472.
[7] A. Konsoula, C. Tsioutis, I. Markaki, M. Papadakis, A.P. Agouridis, N. Spernovasilis, Lomentospora prolificans: an emerging opportunistic fungal pathogen, Microorganisms 10 (7) (2022).
[8] T.P. Mello, A.C. Aor, S.S. Oliveira, M.H. Branquinha, A.L. Santos, Conidial germination in Scedosporium apiospermum, S. aurantiacum, S. minutisporum and Lomentospora prolificans: influence of growth conditions and antifungal susceptibility profiles, Mem. Inst. Oswaldo Cruz 111 (7) (2016 Jun 27) 484–494.
[9] J.L. Rodriguez-Tudela, J. Berenguer, J. Guarro, et al., Epidemiology and outcome of Scedosporium prolificans infection, a review of 162 cases, Med. Mycol. 47 (4) (2009) 359–370.
[10] S.Y. Tong, A.Y. Peleg, J. Yoong, R. Handke, J. Szer, M. Slavin, Breakthrough Scedosporium prolificans infection while receiving voriconazole prophylaxis in an allogeneic stem cell transplant recipient, Transpl. Infect. Dis. 9 (3) (2007) 241–243.
[11] P. Troke, K. Aguirrebengoa, C. Arteaga, et al., Treatment of scedosporiosis with voriconazole: clinical experience with 107 patients, Antimicrob. Agents Chemother. 52 (5) (2008) 1743–1750.