

REVIEW

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Clinical features and antifungal treatment of invasive *Scedosporium boydii* infection: report of a case and literature overview

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Abstract

Objective This study aims to present a case of persistent mycetoma caused by *Scedosporium boydii* and undertake a systematic literature overview to elucidate the clinical characteristics and antifungal treatment exhibited by such patients.

Methods We report the case of a 24-year-old female who sustained a *Scedosporium boydii* infection in her right foot over a decade ago following a nail puncture. Concurrently, a comprehensive literature overview was conducted on PubMed, focusing on documented cases of *Scedosporium boydii* infections with the intent of extracting relevant clinical data.

Results Our analysis revealed that post-transplantation, trauma, near drowning, corticosteroid administration, and prior surgical history were the main risk factors for *Scedosporium boydii* infection. Prevalent infection sites included skin/bone tissues, the central nervous system, and ocular regions. Among the 49 patients identified, 24 received itraconazole therapy and 25 received voriconazole, with no significant difference in patient outcomes ($P=0.158$). Of these, 12 patients experienced treatment failure. Notably, prolonged antifungal treatment duration was identified as a protective factor against mortality in *Scedosporium boydii* infections [$P=0.022$, OR(95%CI): 0.972(0.949–0.996)]. Conversely, a history of post-transplantation emerged as a potential risk factor for mortality [$P=0.046$, OR(95%CI): 7.017(1.034–47.636)].

Conclusion While uncommon, *Scedosporium boydii* infections carry a significant burden of morbidity and adverse outcomes. Heightened clinical vigilance is warranted in individuals presenting with risk factors for this pathogen. Timely and effective antifungal intervention is crucial, with both voriconazole and itraconazole demonstrating positive treatment outcomes for *Scedosporium boydii* infection. Therefore, prioritizing these antifungal agents should be considered a key therapeutic strategy in the management of this patient population.

Keywords *Scedosporium Boydii*, Fungal infection, Clinical features, Antifungal therapy, Itraconazole, Voriconazole

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Introduction

Fungi belonging to the *Scedosporium/Pseudallescheria boydii* species complex are ubiquitous and saprotrophic organisms, frequently encountered in moist soil, sewage, and decomposing vegetation [1]. Their ability to induce both localized and systemic infections through direct contact, inhalation of airborne spores, and dissemination in immunocompromised individuals (e.g., those with hematological disorders or post-transplant recipients) poses a significant clinical challenge [2]. Notably, *Scedosporium* spp. rank second among filamentous fungi colonizing patients with cystic fibrosis [3, 4]. Invasive infections, characterized by a high mortality rate ranging from 40 to 95%, constitute the most severe clinical manifestation [5, 6]. Among isolated species, *Scedosporium boydii* and *Scedosporium apiospermum* predominate in clinical settings. We present a case of a traumatic mycetoma sustained for 17 years caused by *Scedosporium boydii*.

Case report

A 24-year-old female in a state of good health presented to our institution with right foot swelling and purulent drainage. Notably, in 2006, the patient sustained a penetrating injury to the aforementioned foot due to stepping on a nail. Subsequently, several months later, she developed recurrent episodes of suppurative swelling and severe pain at the affected area, which even led to the patient being unable to stand. During this period, the patient underwent multiple surgical interventions, including wound debridement and drainage, which provided only temporary symptom relief and failed to achieve complete resolution. Additionally, multiple microbiological examinations yielded negative results, and treatment with a combination of antimicrobial agents, including imipenem, vancomycin, and itraconazole (100 mg/d, for 3 month), proved unsuccessful. During the present hospitalization, the patient underwent another surgical intervention, and purulent fluid specimens were obtained for microbial culture. Following a 2-day incubation period, fungal growth was observed. Subsequent morphological and sequencing analyses definitively identified the causative agent as *Scedosporium boydii*. Histopathological examination or direct microscopic examination of biopsy was not performed.

Microbiology

Tissue samples obtained through surgical biopsies and aspirations were cultured on Columbia 5%-sheep-blood agar and China Blue agar plates at 37 °C for a period of two days. Subsequently, the agar plates demonstrated the growth of white, fluffy mycelium. Lactophenol cotton blue staining revealed the presence of solitary, smooth-walled elliptical conidia (Fig. 1). Based on these

morphological characteristics and subsequent rDNA ITS sequencing, the isolate was identified as *Scedosporium boydii*. Antifungal susceptibility testing were determined in vitro using Fungal Antimicrobial Susceptibility Test (Autobio, China), and the minimum inhibitory concentrations (MICs) of the antifungal agents are as follows: anidulafungin (2 mg/L), caspofungin (4 mg/L), micafungin (>8 mg/L), amphotericin B (>32 mg/L), itraconazole (0.5 mg/L), voriconazole (0.25 mg/L), fluconazole (8 mg/L), posaconazole (0.25 mg/L), nystatin (>32 mg/L), and flucytosine (>32 mg/L).

Therapy and outcome

Subsequently, the patient began treatment with voriconazole (200 mg twice daily). Six months later, a significant improvement in the patient's health status was observed, with complete wound healing achieved. During this period, no side effects were observed.

Literature overview

A comprehensive literature search was conducted on PubMed using the keywords "*Pseudallescheria boydii*" (sexual stage of the fungus) or "*Scedosporium boydii*" (asexual stage of the same fungus) to identify published cases of *Scedosporium boydii* infections treated with either itraconazole or voriconazole. Cases where treatment outcomes cannot be tracked or where itraconazole or voriconazole were not used are excluded. 43 relevant publications were retrieved. Demographic information, such as age, gender, and site of infection, along with medical history, antifungal treatment duration, and clinical outcomes, were extracted and compiled [7–49]. Statistical analysis was performed using SPSS software version 26. Categorical variables were analyzed using either the chi-square test or Fisher's exact test, while non-parametric tests were employed for continuous variables. Candidate variables with a univariate analysis P -value ≤ 0.1 were included in a forward stepwise logistic regression model for further exploration. Subsequently, a multivariate logistic regression model was utilized to identify independent risk factors associated with treatment outcomes. Statistical significance was defined as a P -value ≤ 0.05 . Age and duration of therapy were reported using the median and interquartile range.

Results

We identified 43 articles covering a total of 48 cases, with several articles reporting multiple cases. After including this case, a total of 49 cases were included in this study (Table 1). Notably, 16 patients (32.7%) exhibited some form of immunodeficiency, while 16 (32.7%) reported a history of direct exposure to environmental conditions such as sewage, soil, or similar settings. Among all cases, the most prevalent predisposing factor was

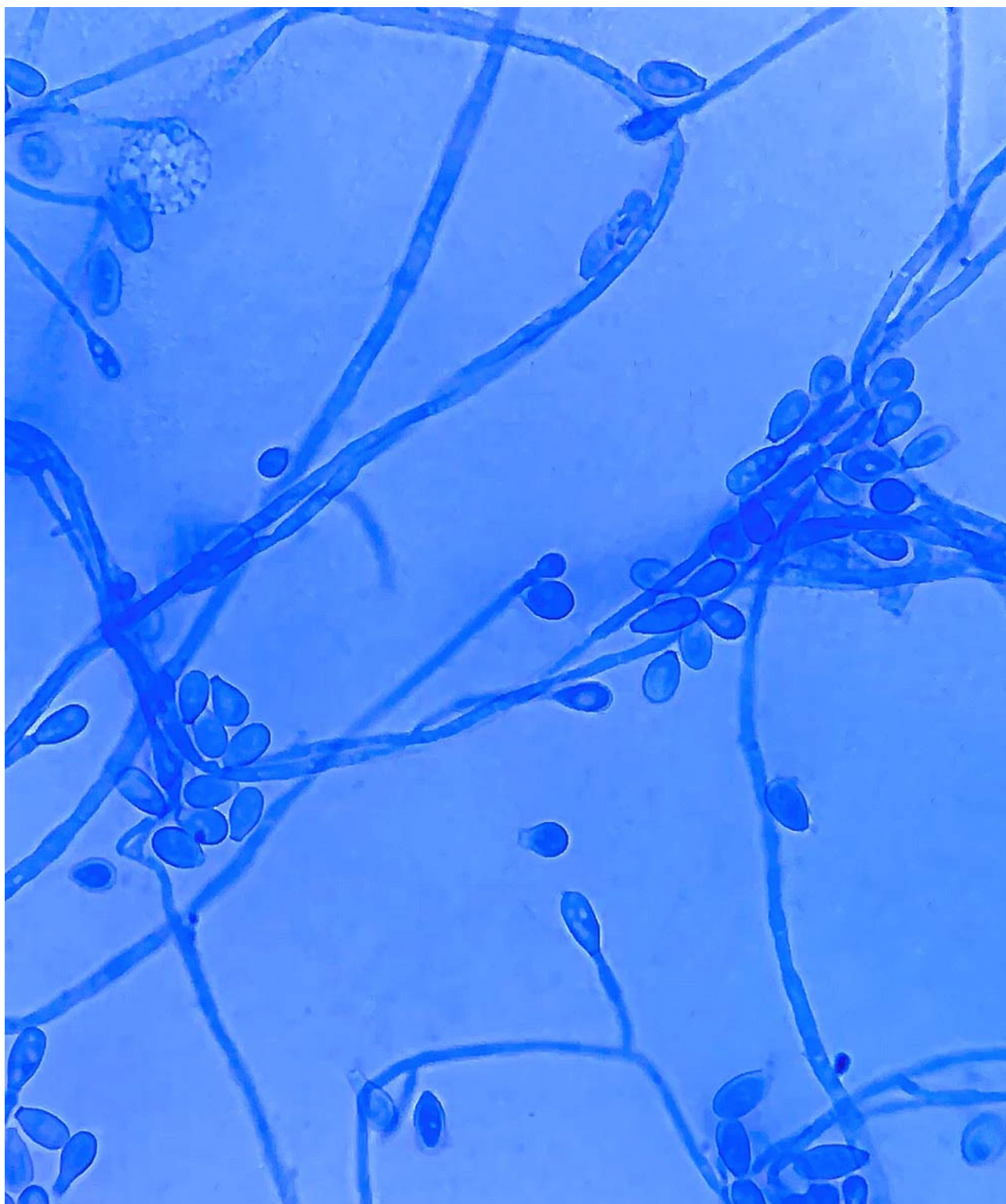


Fig. 1 Lactophenol cotton blue stain of *Scedosporium boydii* showing hyphae and conidia

Table 1 Clinical characteristics of 52 cases of *Scedosporium boydii* infection

Characteristics	All patient (N=49)	Cured (N=37)	Treatment failure (N=12)	univariate analysis	multivariate analysis	
				P value	P value	OR(95%CI)
Male	33	27	6	0.169	-	-
Age, years, median (Interquartile range)	48(32–60)	45(26–59)	48(39–59)	0.633	-	-
Predominant underlying condition					-	-
Trauma	11	11	0	0.045	0.243	-
Near drowning	5	3	2	0.584	-	-
Surgical operation	7	6	1	0.665	-	-
Intravenous history	1	1	0	0.999	-	-
Post-transplantation	13	7	6	0.034	0.046	7.017(1.034–47.636)
Idiopathic autoimmune disease	4	4	0	0.560	-	-
HIV/AIDS	2	1	1	0.434	-	-
Corticosteroid pharmacotherapy	6	5	1	1.000	-	-
Infection site					-	-
Skin/bone	24	20	4	0.212	-	-
Brain	12	7	5	0.136	-	-
Eye	7	5	2	1.000	-	-
Others	6	5	1	1.000	-	-
antifungal treatment duration, days, median (Interquartile range)	90(33–182)	110(60–303)	23(13–68)	0.004	0.022	0.972(0.949–0.996)
Antifungal therapy						
voriconazole	25	21	4	0.158	-	-
itraconazole	24	16	8			

post-transplantation ($n=13/49$, 26.5%), followed by a history of trauma ($n=11/49$, 22.4%), surgical procedures ($n=7/49$, 14.3%), corticosteroid use ($n=6/49$, 12.2%), near drowning accidents ($n=5/49$, 10.2%), and idiopathic autoimmune diseases ($n=4/49$, 8.2%).

Scedosporium boydii most frequently induced localized infections of the skin and bone (24/49, 49.0%), followed by the central nervous system (12/49, 24.5%) and ocular regions (7/49, 14.3%). Within the cohort of patients with skin/bone infections, a significant proportion displayed immune dysfunction ($n=12/24$, 50%), and reported a history of trauma ($n=8/24$, 33.3%). Notably, among those with neurological system infections, 4 underwent transplant surgery, 4 contracted infections after near drowning incidents, and 2 underwent surgical procedures. In addition, Among the 7 patients with eye infections, 6 individuals reported a history of either surgical interventions or exposure to contaminated objects. Interestingly, multivariate regression analysis identified antifungal treatment duration [$P=0.022$, OR(95%CI): 0.972(0.949–0.996)] as a protective factor against mortality in *Scedosporium boydii* infections. Conversely, post-transplantation status emerged as a significant risk factor for mortality [$P=0.046$, OR(95%CI): 7.017(1.034–47.636)] (Table 1).

Analysis of treatment data revealed that 24 individuals(49.0%) with a median age of 40 years received itraconazole for a median duration of 60 days, of whom

8(33.3%) experienced treatment failure. In contrast, 25 individuals(51.0%) with a median age of 53 years received voriconazole for a median of 90 days, with 4(16.0%) experiencing treatment failure(Table 2). Statistical analysis indicated no significant differences between the two groups regarding age, gender, underlying health conditions, or overall treatment outcomes. Further examination of 37(75.5%) successfully treated cases revealed the specific durations of itraconazole and voriconazole treatment effective for various infection sites. Among patients diagnosed with neurological *Scedosporium* infections, voriconazole demonstrated longer treatment durations compared to itraconazole. The median treatment duration for voriconazole was 365 days, while only one patient achieved a cure with itraconazole, requiring 300 days of antifungal therapy. For skin/bone infections, the median treatment duration for voriconazole was 132 days compared to 120 days for itraconazole. In patients with eye infections, voriconazole again exhibited a longer median treatment duration of 90 days, with only one patient achieving a favorable outcome with itraconazole at 60 days.

Discussion

While *Scedosporium boydii* is a recognized causative agent of mycetoma, this case of over a decade in an immunocompetent individual underscores the organism's remarkable persistence within the human host. This

Table 2 Clinical characteristics of treatment with itraconazole vs. voriconazole

	Treated with voriconazole(N= 25)	Treated with itraconazole(N= 24)	P value
Male	18	15	0.478
Age, years, median (Interquartile range)	53(37–63)	40(23–53)	0.071
Predominant underlying condition			
Trauma	5	6	0.675
Near drowning	4	1	0.187
Surgical operation	3	4	0.476
Intravenous history	1	0	
Post-transplantation	6	7	0.682
Autoimmune disease	3	1	0.320
HIV/AIDS	1	1	0.745
Corticosteroid pharmacotherapy	3	3	0.646
Infection site			
Skin/bone	10	14	0.178
Brain	9	3	0.056
Eye	3	4	0.476
Others	3	3	0.646
treatment duration, days, median(Interquartile range)	90(49–270)	60(28–181)	0.682
Therapeutic inefficacy	4	8	0.158

persistence highlights the significant challenge of achieving complete eradication and the difficulties associated with its timely detection. Currently, definitive diagnosis of *Scedosporium boydii* infections relies on culture confirmation or histological examination, a method hampered by its relatively low sensitivity. Consequently, patients are often diagnosed at advanced stages, leading to heightened mortality risks and increased healthcare utilization.

According to our research, predisposing factors for *Scedosporium boydii* infections include post-transplantation, trauma, post-surgical procedures, corticosteroid use history, near drowning, and idiopathic autoimmune diseases. Patients infected with *Scedosporium boydii* were predominantly male, and most of these male patients had a history of trauma or transplantation. It is hypothesized that males are more likely to engage in higher-risk and physically demanding activities, leading to an increased risk of trauma. Additionally, studies have indicated that the proportion of males undergoing transplantation is significantly higher than that of females [50, 51], which consequently results in a greater number of post-transplant infections among male patients. Cutaneous/bone tissue is the most common site of infection, followed closely by neurological system and ocular infections. Immunodeficiency and trauma remain the primary causative factors for cutaneous/bone tissue infections. Notably, direct exposure to contaminated materials can be a potential precipitating factor for *Scedosporium boydii* infection in the eye, even without overt trauma. Post-transplantation, near drowning, and post-surgical procedures are the most common causes of neurological system infections. These infections often manifest as

solitary or multiple brain abscesses and frequently culminate in a fatal outcome. Our statistical analysis reveals a high mortality rate (38.5%) for neurological system infections. Short-term antifungal therapy is identified as a risk factor for mortality in *Scedosporium boydii* infections. The median duration of antifungal therapy for successfully treated patients is 110 days, compared to 23 days for those who experience treatment failure. This significantly lower median duration in failed cases highlights the importance of timely initiation and extended duration of antifungal therapy for achieving a favorable outcome. Post-transplantation is also a risk factor for mortality due to the compromised immune status of transplant recipients, making them susceptible to opportunistic fungal infections, including disseminated infections that often lead to death. Notably, *Scedosporium boydii* exhibits resistance to common antifungal drugs like fluconazole and amphotericin B, leading to failed prophylactic or empiric treatment and contributing to the unfavorable prognosis of these infections. Most transplant recipients with *Scedosporium boydii* infections develop them within the first six months post-transplantation. This suggests that when a fungal infection is suspected in this period without definitive microbiological evidence, empirical therapy should consider the potential involvement of *Scedosporium boydii*.

Currently, the recommended management of *Scedosporium boydii* infections involves a multi-pronged approach combining surgical intervention with adjunctive antifungal therapy. However, the therapeutic landscape is complicated by *Scedosporium*'s high resistance to numerous antifungal agents, including 5-fluorocytosine, amphotericin B, and fluconazole. Additionally, a concerning trend

of decreased sensitivity towards echinocandins, particularly caspofungin and anidulafungin, further restricts the available options [52–54]. This highlights the significant limitations in the effective antifungal spectrum against *Scedosporium*. In response, the European Confederation of Medical Mycology advocates for voriconazole as the first-line treatment and itraconazole as a second-line option [55]. Despite this guidance, the mortality rate for severe infections, such as those involving the central nervous system or disseminated throughout the body, remains alarmingly high. Notably, in vitro susceptibility testing of voriconazole, with a minimum inhibitory concentration below 2 µg/ml, offers a predictive marker for a potentially positive outcome in *Scedosporium* infections [56].

Triazole antifungal drugs possess distinct advantages, including minimal side effects and potent efficacy, rendering them a mainstay in the current armamentarium against fungal infections. Our data reveal the broad applicability of voriconazole and itraconazole in managing skin/bone tissue and corneal infections. In this reported case, the patient used itraconazole but the results were still unsatisfactory, which may be related to the dosage and duration of treatment. Notably, favorable outcomes were observed in two pulmonary infection cases treated with voriconazole (for 1 year, dose unavailable) and itraconazole (400 mg/day for 36 months), respectively. Furthermore, a single case of disseminated infection responded successfully to voriconazole. Interestingly, in patients with neurological system infections, voriconazole demonstrates a significantly higher utilization rate compared to itraconazole. This disparity can be attributed, in part, to the limited cerebral and cerebrospinal fluid distribution of itraconazole, as supported by existing literature [52, 57, 58]. While in vitro antifungal sensitivity tests indicate *Scedosporium* species generally exhibit higher resistance towards itraconazole than voriconazole, our data analysis did not reveal a significant difference in their efficacy against *Scedosporium boydii* infections. Research data revealed that among the 4 patients who experienced treatment failure with voriconazole, 3 had neurological system infections. This may be an important reason why there is no significant difference in prognosis between voriconazole and itraconazole treatments. Due to the limitations of itraconazole distribution in cerebrospinal fluid and brain tissue, voriconazole is more commonly used clinically. However, even with effective surgical intervention or antifungal treatment, neurological system infections caused by *Scedosporium boydii* are still associated with a high mortality rate.

Our analysis of successfully treated patients revealed significant heterogeneity in median treatment duration based on the infection site. Neurological infections, demanding the most protracted intervention,

necessitated a median treatment period of nearly one year. Skin/bone infections followed with a median duration of 120 days, while ocular infections required a median of 90 days. Notably, no statistically significant difference was observed in treatment duration between itraconazole and voriconazole regimens. Adjusting the duration of antifungal therapy based on the specific site of infection may be a critical factor in optimizing the efficacy of antifungal treatment.

Conclusions

Infections attributed to *Scedosporium boydii* exhibit a propensity for insidious progression, often culminating in severe or disseminated disease. The limited therapeutic options available underscore the critical need for heightened clinical vigilance. The implementation of advanced diagnostic tools for early detection and prompt intervention represents a key strategy in improving patient outcomes. Our study found that post-transplantation, trauma, near drowning, a history of corticosteroid use, and surgical history were common risk factors for *Scedosporium boydii* infection. Prolonged antifungal treatment duration was identified as a protective factor against mortality in *Scedosporium boydii* infections. Conversely, a history of post-transplantation emerged as a potential risk factor for mortality. Both itraconazole and voriconazole are effective antifungal agents that can be used for the treatment of *Scedosporium boydii* infection.

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Author contributions

XYP and LXL performed the articles search. XYP wrote the paper. XYP, LXL, HLH, XYH and CXW participated in data cleaning, sorting and analysis. ZQS reviewed the manuscript. All authors read and approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

This study was approved by the Second Affiliated Hospital of Nanchang University Medical Research Ethics Committee.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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