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CASE REPORT

A Case of Invasive Fungal Infection Due to *Scedosporium apiospermum* in a Patient with Psoriasis

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Abstract: *Scedosporium apiospermum* (*S. apiospermum*) is typically reported to be involved in superficial and subcutaneous fungal infections but overlooked in invasive infections, which is associated with a high mortality rate. It poses a diagnostic challenge due to its confusable characteristics to other hyaline hyphomycetes. Here, we reported a psoriasis patient with an invasive *S. apiospermum* infection. The patient presents an abscess at the intermuscular space of the left hip and an increased C-reactive protein level. Pus culture showed white-greyish, cottonlike colonies with aerial mycelium and terminal oval conidia, suggesting *S. apiospermum*. This rare fungus was rapidly confirmed by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry and RNA sequencing. The patient was successfully treated with voriconazole with no recurrence of the abscesses despite delayed treatment. This is the first such case infection report from China that described an unusual case of intermuscular space abscesses due to *S. apiospermum*. This report highlights the possibility of fungal infections in deeper tissue, as well as the necessity of thorough evaluation and microbiological diagnosis for invasive infections, particularly in immunocompromised patients.

Keywords: fungi, fungal infections, infectious diseases, *Scedosporium*, abscesses, voriconazole

Introduction

Fungal infections are common in humans that range from common, mild superficial infections to life-threatening invasive infections and are increasing at an alarming rate.[1,2] The most frequently encountered pathogens are *Candida* and *Aspergillus* species, but other fungi are increasingly important.[3] Among them, *Scedosporium apiospermum* (*S. apiospermum*) is considered an emerging opportunistic fungus, which may cause either localized or systemic manifestations through inhalation or traumatic inoculation.[4] It was commonly involved in asymptomatic pulmonary colonization or superficial and subcutaneous infections (eg, cutaneous infection, arthritis, osteomyelitis).[5] In certain circumstances, *S. apiospermum* can also cause severe and even fatal invasive and disseminated infections, in which mortality rates may be over 80%.[6] Despite the high mortality rates of invasive infections, they remain understudied and underdiagnosed. Recent reports have also demonstrated a steady increase in the infection rates of this species in both immunocompromised and immunocompetent hosts.[7] However, the timely diagnosis of *S. apiospermum* infection is difficult, because the clinical features and histopathology are similar to those of *Aspergillus spp., Fusarium spp*., or other hyaline hyphomycetes.[8] Meanwhile, the high degree of intrinsic antifungal resistance makes these infections difficult to manage.[9] One typical manifestation of this disease was abscess in infection sites, predominantly reporting in brain[10] and also including thyroid,[11] nasal septum,[12] cornea,[13] and soft tissue abscess.[14] Despite multiple infection types reported, to date, the majority was located in the superficial layer of subcutaneous tissue;[15] on the contrary, most deep infections arise from the extension of local disease, deep puncture wounds or a history of trauma.[16] Thus, the infection risk of *S. apiospermum* in deeper tissue was overlooked due to the limited reports. Here, we present a successfully treated

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S. apiospermum infection in a psoriasis patient, which was rapidly identified by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) and RNA sequencing. The infection occurred in an unusual, deep-seated tissue (intermuscular space), providing the additional evidence for the pathogenic potential of *S. apiospermum* in deep-seated tissue even in the absence of trauma.

Case Presentation

A 49-year-old man who had a 19-year history of psoriasis presented to the department of dermatology in our hospital due to persistently aggravated psoriasis. Before admission, the patient has been intermittently treated with a series of agents (eg, oral Chinese traditional medicine, topical fluocinolone acetonide, budesonide, glucocorticoids, etc.) in a 19-year period due to repeated relapses. After admission, the patient also complained of severe pain located in the inner side of the left thigh with unexplained causes. The admission physical examination showed no obvious abnormality in vital signs, heart, lung, abdomen, and mental state. After admission, he received symptomatic treatments for psoriasis (including polyene phosphatidylcholine, loratadine, fluticasone propionate, and physiotherapeutic). On day 2, severe pain still existed and the patient received a series of examinations. Laboratory tests showed hematuria (1+), a decrease in hemoglobin (122 g/L; reference range, 130–175 g/L), red blood cells (3.86×10^{12}/L; reference range, $4.3–5.8\times10^{12}$/L;), Fe (6.0 μmol/L; reference range, 9–32 μmol/L), and total protein (53.8 g/L; reference range, 60–83 g/L), and the increased level of C-reactive protein (CRP) (69.79 mg/L; reference range, <6 mg/L). Magnetic resonance imaging (MRI) revealed the bilateral avascular necrosis of the femoral head, abscess in the left psoas, gluteus maximus, and iliac muscles, intermuscular encapsulated effusion, as well as enlarged lymph nodes in the left inguinal region (Figure 1A), raising the suspicion of infection. On the 4-day of hospitalization, the Color Doppler ultrasound demonstrated a subcutaneous, honeycomb, hypoechoic area (176mm × 33mm × 136mm; Figure 1B), which confirmed an abscess in the left hip. At the same day (4-day), based on the results of Color Doppler ultrasound, the patient was given empirical antibacterial therapy with cefuroxime-sodium (1.5 g, oral, twice daily [bid]) and levofloxacin (500 mg, intravenous [IV], once daily). After 2 days of antibacterial therapy, the patient underwent puncture and drainage under ultrasound guidance. A large amount of taupe pus with smell was extracted and then collected for both bacterial and fungal culture to confirm the pathogen, considering no obvious abnormality in leukocytes and neutrophils but increased CRP level. Meanwhile, the patient received cefoperazone-sulbactam (3.0 g, IV, three times daily) to replace the cefuroxime-sodium.

After 3 days of incubation, the white-greyish, cotton-like colonies with aerial mycelium grew on the Sabouraud dextrose agar medium (Figure 2A) and Columbia blood agar plate (Figures 2B and C). The lactophenol cotton blue staining showed the thick mycelium, along with the production of terminal oval conidia and a brush of cylindrical conidia (Figure 2D). These morphological characteristics led us to suspect *S. apiospermum* and the patient was given voriconazole (200 mg, oral, bid) instead of cefoperazone-sulbactam. Colonies were further confirmed to be *S. apiospermum* by 16S/18S rRNA sequencing (GenBank accession no. MN540229.1) and MALDI-TOF MS (score, 1.788). Since *S. apiospermum* strain was susceptible to voriconazole according to antibiotic susceptibility testing (Table 1), the patient

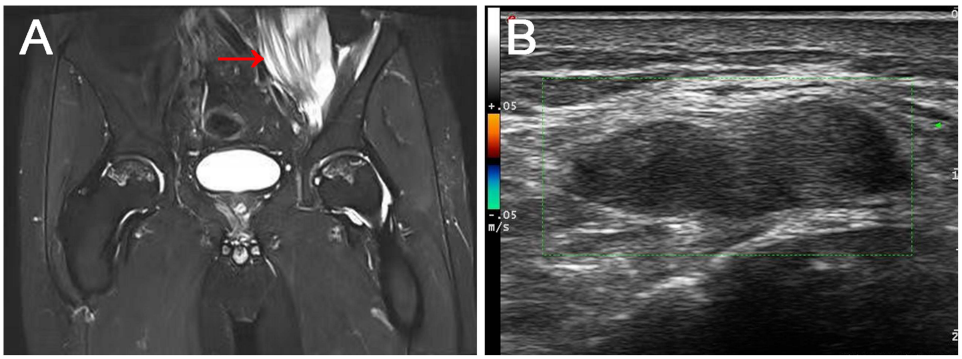

Figure 1 Magnetic resonance imaging results. (**A**) Magnetic resonance imaging revealed the abscess in left psoas, gluteus maximus and iliac muscles (red arrow indicated), intermuscular encapsulated effusion, as well as enlarged lymph nodes in the left inguinal region. (**B**) Color Doppler ultrasound revealed a honeycomb, hypoechoic area in left Hip.

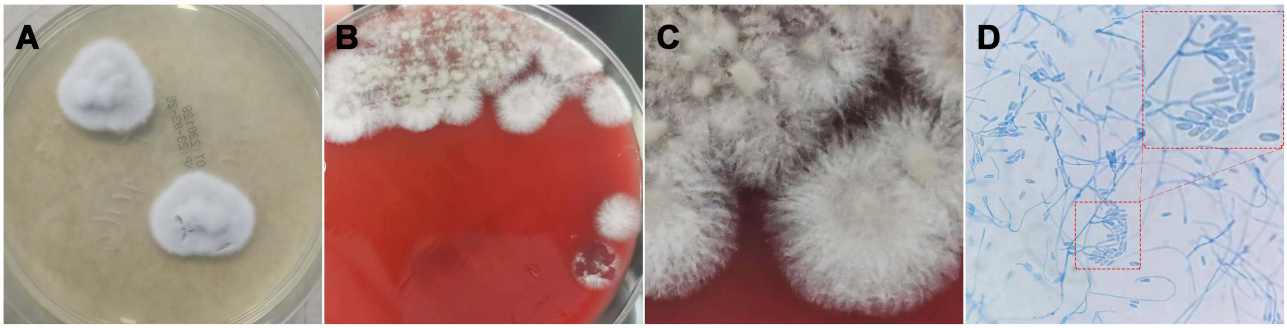

Figure 2 Morphological results of the pus culture. (**A**) Sabouraud dextrose agar medium showed the white-greyish, cottonlike colonies. (**B** and **C**) The thin, septate branching hyphae were observed on Columbia blood agar plate. (**D**) The lacto-phenol cotton blue staining showed the thick mycelium, along with the production of terminal oval conidia and a brush of cylindrical conidia (400× magnification).

was continued with 200 mg voriconazole (oral, bid) for 1 week. After that, the abscess had almost fully resolved, and there was no obvious tenderness in the groin area. The patient was discharged with a favorable outcome on the 16th day of hospitalization. After 2 months, the patient recovered fully with no any symptom and discontinued voriconazole, with no recurrence for 1 year at the recent follow-up by telephone (May, 2023). During the follow-up period, the patient was transferred to a higher-level hospital and received the symptomatic treatment for bilateral osteonecrosis of the femoral heads.

Discussion

Fungi are an important yet frequently overlooked cause of morbidity and mortality in humans.[17] To the best of our knowledge, the presented case is the first published *S. apiospermum* infection with intermuscular space in a patient with psoriasis. Although the infection occurred in deep-seated tissue, patient achieved a full recovery from surgical debridement and systemic voriconazole treatment. This report highlights the possibility of *S. apiospermum* infections in deeper tissue, as well as emphasized the clinical suspicion and awareness of this disease, particularly in immunocompromised patients.

To date, *Scedosporium* infections are still associated with a very high mortality of around 70% in most frequent form of infection.[10,18] Since cases of invasive infections caused by *S. apiospermum* are uncommon, clinicians usually fail to consider this pathogen in the absence of microbiological evidence. Based on the existing evidence, skin, lung, kidney, and brain are frequent involvement sites of invasive *S. apiospermum* infection.[19] Thus, in this case, the initially suspected diagnosis was empirically considered bacterial infection but not *S. apiospermum*

Table 1 Susceptibility Test of *Scedosporium apiospermum* Isolate

Antifungal Agents	MIC (μg/mL)*	Interpretation#
Anidulafungin	4	Sensitive
Caspofungin	2	–
Micafungin	8	–
Amphotericin B	0.5	Sensitive
Itraconazole	0.12	–
Fluconazole	8	–
Voriconazole	0.12	Sensitive
Posaconazole	0.12	Sensitive
Nystatin	16	–
Flucytosine	>64	–

Notes: *Obtained by broth dilution method based on breakpoints available in CLSI guidelines M38-A2. #Susceptibility was interpreted based on breakpoints available in CLSI guidelines M38-A2; for agents without breakpoints in CLSI guidelines M38-A2, only MIC values were reported.
Abbreviation: MIC, minimum inhibitory concentration.

because an abscess was visualized in the intermuscular space of the left hip on MRI and ultrasound scans. In previous reports, abscesses are predominantly observed in brain,[20] as well as the soft tissue,[14] and skin.[21] Unlikely, in our case, the infection occurred in the deeper tissue intermuscular space. It is also because of the deep and uncommon infection site, which lead to lose sight of fungal infection and the delayed initiation of appropriate antifungal therapy. In addition, as previously reported, deep infection is nearly exclusively observed in patients with severe disorders in innate immunity (eg, malignancy, systemic lupus erythematosus), deep puncture wounds, or a history of trauma.[5] Although this patient had no history of trauma, the impaired skin barrier function in psoriasis may provide a portal of entry for this organism. Corticosteroids and/or immunosuppressive therapy, as major risk factors for fungal infection,[22] are also present in our case. Overall, *S. apiospermum* infection should be suspected in immunocompromised patients with abscesses, particularly when no obvious abnormality in leukocytes and neutrophils.

The diagnosis of invasive *S. apiospermum* infections based on culture morphology alone is challenging owing to a clinical and morphological similarity with other fungal species (eg, *Aspergillus spp., Fusarium spp*.).[8] Our case showed the suspicion of *S. apiospermum* through the observation of white-greyish, cotton-like colonies, along with the production of terminal oval conidia and a brush of cylindrical conidia. These features are consistent with that reported by Todokoro et al,[23] however, a diagnosis by morphology alone is often unreliable. Similar morphological features may be confused with yeast or *Aspergillus*.[24] Thus, molecular identification is necessary for definitive diagnosis. For definite identification at the species level, the MALDI-TOF MS (a well-established technique in bacteriology laboratories) and rRNA sequencing were used in our case. Although the RNA sequencing here were applied as supporting tool to avoid the low MALDI-TOF MS score, it might not be an ideal choice due to the disadvantages (expensive, time-consuming and prone to environmental contamination). By the MALDI-TOF MS, the isolate was identified to be *S. apiospermum* with a score of 1.788, which is acceptable for the filamentous fungi identification as reported by Motteu et al.[25] Since MALDI-TOF MS offers the advantage of being fast, easy to perform and cost-effective, we recommend that MALDI-TOF MS might be an appropriate option for the rapid identification of this pathogen if conditions permit.

Treatment of *Scedosporium* infection, particularly deep-seated infections, is often challenging due to its intrinsic resistance to traditional antifungals and ability to recur despite demonstrating susceptibility.[24] Although there is no consensus with regard to the therapy of *S. apiospermum* infection, surgical management plus antifungal agents are often recommended as the treatment options.[26] Among antifungals, the broad-spectrum voriconazole showed relatively lower MIC values and superior activity in the *S. apiospermum* infection therapy,[27,28] which has been recommended as the first-line therapy in most cases.[29–31] In addition, susceptibility testing was performed due to the inherent resistance of *S. apiospermum* and identified that this fungus was susceptible to itraconazole, posaconazole, and voriconazole, which is consistent with previous reports.[31] Accordingly, voriconazole was selected as the primary option for our case. Despite the empirical anti-infective therapy using antibiotics leading to the delayed treatment for *S. apiospermum* infection, voriconazole showed the expected and rapid improvement of infection in our case after only 1-week treatment and had no recurrence. Nevertheless, to date, there is no consensus about the treatment duration and efficacy of voriconazole due to a lack of large studies. In clinical, the recommended treatment duration is several months to a few years. Here, our experience might provide additional evidence for the use of voriconazole in the treatment of *S. apiospermum* infection. In recent year, a novel antifungal isavuconazole has been approved for the treatment of invasive aspergillosis based on the pivotal SECURE trial.[32] Due to its non-inferior efficacy, fewer study-drug-related adverse events, and cost-effectiveness over voriconazole,[33] isavuconazole may be a useful alternative for our case but remains further confirmation with large-scale studies. In fact, because of the limited susceptibility of *Scedosporium* species to all current antifungal drugs, lots of attempt have been made to investigate the combinations of antifungal agents in search of new strategies. Based on the potential additive or synergistic effects, several combinations (such as voriconazole plus terbinafine, miconazole plus itraconazole) showed successful outcomes in *S. apiospermum* infection based on case reports.[34,35] Overall, with the expansion of the antifungal armamentarium, the treatment of *S. apiospermum* may be easier with novel antifungal agents or combination strategies.

Conclusion

This report described an invasive fungal infection in an unusual site due to *S. apiospermum*, emphasizing the pathogenic potential of *S. apiospermum* in deep-seated tissue. Surgical debridement combined with systemic voriconazole successfully improved the infection. A greater clinical suspicion and awareness of the rare fungal pathogens in such infections and the relatively easier and economical identification of this pathogen with MALDI-TOF MS are essential for a timely diagnosis and appropriate antifungal therapy, particularly in immunocompromised patients.

Ethics Approval

The studies involving human participants were reviewed and approved by the Ethics Committee of Shengli Oilfield Central Hospital.

Consent for Publication

Written informed consent was provided by the patient for the publication of the case details.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Kainz K, Bauer MA, Madeo F, Carmona-Gutierrez D. Fungal infections in humans: the silent crisis. *Microbial Cell*. 2020;7(6):143–145. doi:10.15698/mic2020.06.718
2. Pathakumari B, Liang G, Liu W. Immune defence to invasive fungal infections: a comprehensive review. *Biomed Pharmacother*. 2020;130:110550.
3. Garber G. An overview of fungal infections. *Drugs*. 2001;61(Supplement 1):1–12. doi:10.2165/00003495-200161001-00001
4. Pieta A, Venetsanopoulou AI, Kittas C, Christaki E, Voulgari PV. Recurrent Scedosporium apiospermum cutaneous infection in a patient with rheumatoid arthritis: the potent role of IL-6 signaling pathway blockade: a case-based review. *J Fungi*. 2023;9(6):683. doi:10.3390/jof9060683
5. Guarro J, Kantarcioglu AS, Horré R, et al. Scedosporium apiospermum: changing clinical spectrum of a therapy-refractory opportunist*. *Med Mycol*. 2006;44(4):295–327. doi:10.1080/13693780600752507
6. Bouchara J-P, Papon N. Scedosporium apiospermum. *Trends Microbiol*. 2019;27(12):1045–1046. doi:10.1016/j.tim.2019.07.003
7. Ramirez-Garcia A, Pellon A, Rementeria A, et al. Scedosporium and Lomentospora: an updated overview of underrated opportunists. *Med Mycol*. 2018;56:S102–S125.
8. Lopez FA, Crowley RS, Wastila L, Valantine HA, Remington JS. Scedosporium apiospermum (Pseudallescheria boydii) infection in a heart transplant recipient: a case of mistaken identity. *J Heart Lung Transplant*. 1998;17(3):321–324.
9. Seidel D, Meißner A, Lackner M, et al. Prognostic factors in 264 adults with invasive Scedosporium spp. and Lomentospora prolificans infection reported in the literature and FungiScope®. *Crit Rev Microbiol*. 2019;45(1):1–21. doi:10.1080/1040841X.2018.1514366
10. Wilson HL, Kennedy KJ. Scedosporium apiospermum brain abscesses in an immunocompetent man with silicosis. *Med Mycol Case Rep*. 2013;2:75–78. doi:10.1016/j.mmcr.2013.02.006
11. Sireesha P, Kumar CM, Setty C. Thyroid abscess due to Scedosporium apiospermum. *Indian J Med Microbiol*. 2010;28(4):409. doi:10.4103/0255-0857.71859
12. Kishimoto I, Shinohara S, Ueda T, Tani S, Yoshimura H, Imai Y. Orbital apex syndrome secondary to a fungal nasal septal abscess caused by Scedosporium apiospermum in a patient with uncontrolled diabetes: a case report. *BMC Infect Dis*. 2017;17(1):649. doi:10.1186/s12879-017-2753-6
13. Díaz-Valle D, Del Castillo JMB, Amor E, Toledano N, Carretero MM, Díaz-Valle T. Severe keratomycosis secondary to scedosporium apiospermum. *Cornea*. 2002;21:516–518.
14. Schaenman JM, DiGiulio DB, Mirels LF, et al. Scedosporium apiospermum soft tissue infection successfully treated with voriconazole: potential pitfalls in the transition from intravenous to oral therapy. *J Clin Microbiol*. 2005;43(2):973–977. doi:10.1128/JCM.43.2.973-977.2005
15. Kondo M, Goto H, Yamanaka K. Case of Scedosporium aurantiacum infection detected in a subcutaneous abscess. *Med Mycol Case Rep*. 2018;20:26–27. doi:10.1016/j.mmcr.2018.01.003
16. Cortez KJ, Roilides E, Quiroz-Telles F, et al. Infections caused by *Scedosporium* spp. *Clin Microbiol Rev*. 2008;21(1):157–197. doi:10.1128/CMR.00039-07
17. Luis Enrique Jerez P. Fungal infections in immunosuppressed patients. In: Krassimir M, editor. *Immunodeficiency*. Rijeka: IntechOpen; 2012:6.
18. Torres-Sánchez MJ, Hernández-García E, Gómez-Sánchez J, et al. Severe scedosporium apiospermum infection in a recent renal transplant recipient: case report. *Transplant Proc*. 2018;50(2):683–684. doi:10.1016/j.transproceed.2017.09.051
19. Paajanen J, Halme M, Palomäki M, Anttila V-J. Disseminated Scedosporium apiospermum central nervous system infection after lung transplantation: a case report with successful recovery. *Med Mycol Case Rep*. 2019;24:37–40. doi:10.1016/j.mmcr.2019.03.003
20. Sharma A, D S. Scedosporium apiospermum causing brain abscess in a renal allograft recipient. *Saudi J Kidney Dis Transplant*. 2015;26(6):1253–1256. doi:10.4103/1319-2442.168664
21. Lee H-J, Shin S-B, Ha S-J, et al. A case of cutaneous abscess due to Scedosporium apiospermum. *Korean J Dermatol*. 2001;2001:812–815.
22. Cobo F, Lara-Oya A, Rodríguez-Granger J, Sampedro A, Aliaga-Martínez L, Navarro-Marí JM. Infections caused by Scedosporium/Lomentospora species: clinical and microbiological findings in 21 cases. *Med Mycol*. 2017;56:917–925.

23. Todokoro D, Hoshino J, Yo A, Makimura K, Hirato J, Akiyama H. Scedosporium apiospermum infectious scleritis following posterior subtenon triamcinolone acetonide injection: a case report and literature review. *BMC Ophthalmol*. 2018;18(1):40. doi:10.1186/s12886-018-0707-4
24. Goldman C, Akiyama MJ, Torres J, Louie E, Meehan SA. Scedosporium apiospermum infections and the role of combination antifungal therapy and GM-CSF: a case report and review of the literature. *Med Mycol Case Rep*. 2016;11:40–43. doi:10.1016/j.mmcr.2016.04.005
25. Motteu N, Goemaere B, Bladt S, Packeu A. Implementation of MALDI-TOF mass spectrometry to identify fungi from the indoor environment as an added value to the classical morphology-based identification tool. *Front Allergy*. 2022;3. doi:10.3389/falgy.2022.826148
26. Tirado-Miranda R, Solera-Santos J, Brasero JC, Haro-Estarriol M, Cascales-Sánchez P, Igualada JB. Septic arthritis due to Scedosporium apiospermum: case report and review. *J Infect*. 2001;43(3):210–212. doi:10.1053/jinf.2001.0866
27. Meletiadis J, Meis JF, Mouton JW, Rodriquez-Tudela JL, Donnelly JP, Verweij PE. In vitro activities of new and conventional antifungal agents against clinical Scedosporium isolates. *Antimicrob Agents Chemother*. 2002;46(1):62–68. doi:10.1128/AAC.46.1.62-68.2002
28. McCarthy MW, Katragkou A, Iosifidis E, Roilides E, Walsh TJ. Recent advances in the treatment of scedosporiosis and fusariosis. *J Fungi*. 2018;4 (2). doi:10.3390/jof4020073
29. K S, B P, M P, M A, V L. A case of bilateral injection abscesses caused by Graphium type of Scedosporium apiospermum. *Med Mycol Case Rep*. 2022;37:8–12. doi:10.1016/j.mmcr.2022.05.001
30. Boyd ME, Dao H, Estep JD, Huttenbach YT, Hemmige V. Utilization of voriconazole drug monitoring in the treatment of cutaneous Scedosporium apiospermum infection. *Med Mycol Case Rep*. 2018;22:52–54. doi:10.1016/j.mmcr.2018.09.002
31. Girmenia C, Luzi G, Monaco M, Martino P. Use of voriconazole in treatment of Scedosporium apiospermum infection: case report. *J Clin Microbiol*. 1998;36(5):1436–1438. doi:10.1128/JCM.36.5.1436-1438.1998
32. Maertens JA, Raad II, Marr KA, et al. Isavuconazole versus voriconazole for primary treatment of invasive mould disease caused by Aspergillus and other filamentous fungi (SECURE): a Phase 3, randomised-controlled, non-inferiority trial. *Lancet*. 2016;387(10020):760–769. doi:10.1016/S0140-6736(15)01159-9
33. Lewis JS, Wiederhold NP, Hakki M, Thompson GR. New perspectives on antimicrobial agents: isavuconazole. *Antimicrob Agents Chemother*. 2022;66(9):e00177–22. doi:10.1128/aac.00177-22
34. Seibert FJ, Grisold A, Ginter G, et al. Scedosporium apiospermum–Associated Gonarthritis. *Arthroscopy*. 2000;16(1):1–6. doi:10.1016/S0749-8063(00)70008-9
35. Jabr R, Hammoud K. Scedosporium apiospermum fungemia successfully treated with voriconazole and terbinafine. *IDCases*. 2020;22:e00928. doi:10.1016/j.idcr.2020.e00928