Clinical, Cosmetic and Investigational Dermatology

Dovepress
Taylor & Francis Group

Open Access Full Text Article

CASE REPORT

Cutaneous Talaromyces marneffei Infection in an Immunocompetent Adolescent: A Case Report

Yue Chen*, Xiaodong Li*, Chao Bi, Yan Yang, Siying Xiong, Xin Tian, Daoqing Zhong, Yichuan Gan, Aili Gao

Department of Dermatology, Guangzhou Dermatology Hospital, Guangzhou, Guangdong, People's Republic of China

*These authors contributed equally to this work

Correspondence: Aili Gao, Department of Dermatology, Guangzhou Dermatology Hospital, Guangzhou, People's Republic of China, Email alicegao197897@163.com

Abstract: *Talaromyces marneffei* (TM) infection is a rare but potentially fatal deep fungal disease that typically affects immunocompromised individuals in endemic regions. However, an increasing number of cases have been reported in HIV-negative, immunocompetent patients without classical risk factors. We report the case of a 15-year-old girl residing in urban southern China who presented with chronic cutaneous plaques and cervical lymphadenopathy, initially misdiagnosed as tuberculous lymphadenitis. Despite one year of anti-tuberculosis therapy, her condition worsened and liver dysfunction developed. Subsequent skin biopsy, fungal culture, and metagenomic next-generation sequencing (mNGS) confirmed localized cutaneous TM infection. The patient responded well to oral itraconazole, and lesions resolved after four months of treatment, with no recurrence during an 18-month follow-up. This case highlights the importance of considering deep fungal infections in the differential diagnosis of chronic granulomatous skin lesions, even in immunocompetent hosts, and emphasizes the diagnostic utility of mNGS in atypical presentations.

Keywords: *Talaromyces marneffei*, cutaneous fungal infection, adolescent, HIV-negative, itraconazole, granulomatous dermatitis, metagenomic next-generation sequencing, mNGS, deep mycosis

Introduction

Talaromycosis marneffei (TSM) is a life-threatening deep fungal infection caused by *Talaromyces marneffei* (TM, formerly *Penicillium marneffei*), predominantly affecting immunocompromised individuals.[1,2] In recent years, however, an increasing number of TSM cases have been reported in HIV-negative populations.[3] Without timely diagnosis and appropriate treatment, the mortality rate has been reported to range from 50.6% to 97%.[4] The clinical manifestations of TSM are often nonspecific, and when patients present with isolated cutaneous lesions such as nodules or abscesses, the condition may be misdiagnosed—particularly during the initial dermatologic evaluation—as other granulomatous disorders, including histoplasmosis, tuberculosis, or sarcoidosis, especially in the absence of systemic symptoms.[5] The application of mNGS in recent years has improved the detection of TM, facilitating earlier diagnosis and targeted antifungal therapy, which may significantly improve patient outcomes.[6] Here, we report the case of an adolescent girl who was initially misdiagnosed with tuberculous lymphadenitis. A definitive diagnosis of localized cutaneous TM infection was subsequently established through skin biopsy, fungal culture, and mNGS, with marked clinical improvement following antifungal therapy.

Case Present

A 15-year-old girl presented with a 2-year history of painless, nonpruritic swelling on the left side of her neck. Two years earlier, she had undergone fine-needle aspiration of a cervical lymph node at a local hospital, where histopathology revealed granulomatous inflammation suggestive of tuberculous lymphadenitis, although *Mycobacterium tuberculosis* was not detected. She received standard anti-tuberculosis therapy with isoniazid, rifampicin, pyrazinamide, and ethambutol for one year; however,

Received: 5 June 2025
Accepted: 17 September 2025
Published: 21 October 2025

her symptoms worsened and hepatotoxicity developed. She was subsequently referred to our institution. The patient had lived her entire life in Guangzhou and denied fever, weight loss, cough, or travel to endemic areas (eg, Guangxi Province in China and high-incidence regions of Southeast Asia such as Thailand and Vietnam). She also reported no history of chronic illness (eg, type 1 diabetes mellitus), recurrent bacterial or viral infections, trauma, or immunosuppressive therapy. Physical examination revealed a thin habitus, with nontender, enlarged lymph nodes in the bilateral cervical and left axillary regions. On the left submandibular area, anterior neck, and upper chest, there were edematous plaques with yellow-brown crusts, central umbilication, desquamation, and serous exudation at the lesion margins. Red nodules without ulceration or crusting were present on the right side of the neck (Figure 1a–c). Laboratory studies, including complete blood count, liver and renal function, HIV, hepatitis B/C serologies, and syphilis testing, were unremarkable. Additional tests for cytomegalovirus, Epstein–Barr virus, measles, rubella, and tuberculosis were negative. Blood glucose levels were within the normal range. The CD4+ T-cell count was 300/μL (reference range: 500–1440/μL); the CD3+ T-cell count was 628/μL (reference range: 770–2860/μL); and the CD4/CD8 ratio was within normal limits. Cervical computed tomography (CT) revealed extensive lymphadenopathy in the bilateral cervical, submandibular, supraclavicular, and superior mediastinal regions. Chest CT showed patchy opacities near the right upper mediastinum, with otherwise clear lung fields and calcified, confluent lymph nodes in the mediastinum and supraclavicular fossae. Skin lesion biopsy from the left cervical region demonstrated chronic granulomatous inflammation with epithelioid histiocytes and multinucleated giant cells; both periodic acid–Schiff and acid-fast stains were negative (Figure 1d and e). A fungal culture from a papule on the left neck yielded TM (Figure 1f and g). Tissue-based mNGS, performed on the same lesion at two time points 18 months apart, confirmed TM DNA with a specific read count of 148 and a relative abundance of 91.69%, without evidence of mycobacterial or viral infection. A diagnosis of cutaneous TM infection was therefore established. The patient was treated with oral itraconazole (200 mg twice daily), compound glycyrrhizin (2 tablets three times daily), and vitamin D (0.25 μg daily). After 4 months, the cutaneous lesions had resolved. Repeat biopsy revealed only fibrotic scarring, and fungal cultures were negative (Figure 2a and b). At the latest follow-up, one year after treatment, no recurrence was observed, and T-cell counts had returned to the normal range.

Discussion

TM infection has traditionally been linked to immunocompromised individuals, particularly patients with HIV/AIDS in endemic regions of Southeast Asia and southern China.[7] However, accumulating epidemiological data indicate a shift toward HIV-negative and immunocompetent populations.[8] In China, sporadic cases have been documented among urban residents without classical risk factors, such as bamboo rat exposure or rural residence.[9] A cohort study from Guangxi Province reported that 59.3% of non-HIV patients with TM infection had no identifiable immune dysfunction.[10] Similar trends have been observed outside mainland China, including in Hong Kong and Thailand, where HIV-negative patients are increasingly being diagnosed with *T. marneffei* infections.[8,11,12] Together with the present adolescent case without discernible immunodeficiency, these findings highlight an underrecognized potential for transmission in urban environments and challenge the conventional "high-risk population" paradigm.

Although no overt immunodeficiency was identified in this patient, subtle immune defects may predispose seemingly healthy hosts to TM infection. Subclinical abnormalities in the interferon-γ pathway, as well as gain-of-function mutations in STAT1 or STAT3, have been shown to impair antifungal immunity.[13] Li et al identified STAT3 mutations in patients with hyper-IgE syndrome and concurrent TM infection.[14] Similarly, defects in the IL-12/IFN-γ axis or CARD9 deficiency have been implicated in susceptibility to deep fungal infections.[15,16] In addition, minor skin trauma, chronic dermatitis, or puberty-associated changes in local cutaneous immunity may facilitate fungal entry. Beyond classical immunogenetics, recent studies suggest that epigenetic mechanisms also contribute. Viral infections such as COVID-19 can induce persistent epigenetic reprogramming of immune pathways, particularly those involving interferon signaling, thereby weakening antifungal defenses in individuals without genetic mutations. Although this adolescent had no history of COVID-19, such mechanisms may offer a plausible explanation for similar cases and merit further investigation.[17] Another noteworthy finding in this case was that the CD3+ and CD4+ T-cell counts were slightly below the normal reference range, despite the absence of HIV infection or overt immunodeficiency. This reduction may be attributable to the infection itself, as severe TM disease could promote recruitment and sequestration of T cells at sites of active inflammation, resulting in relative depletion in the peripheral circulation. Similar infection-driven redistribution

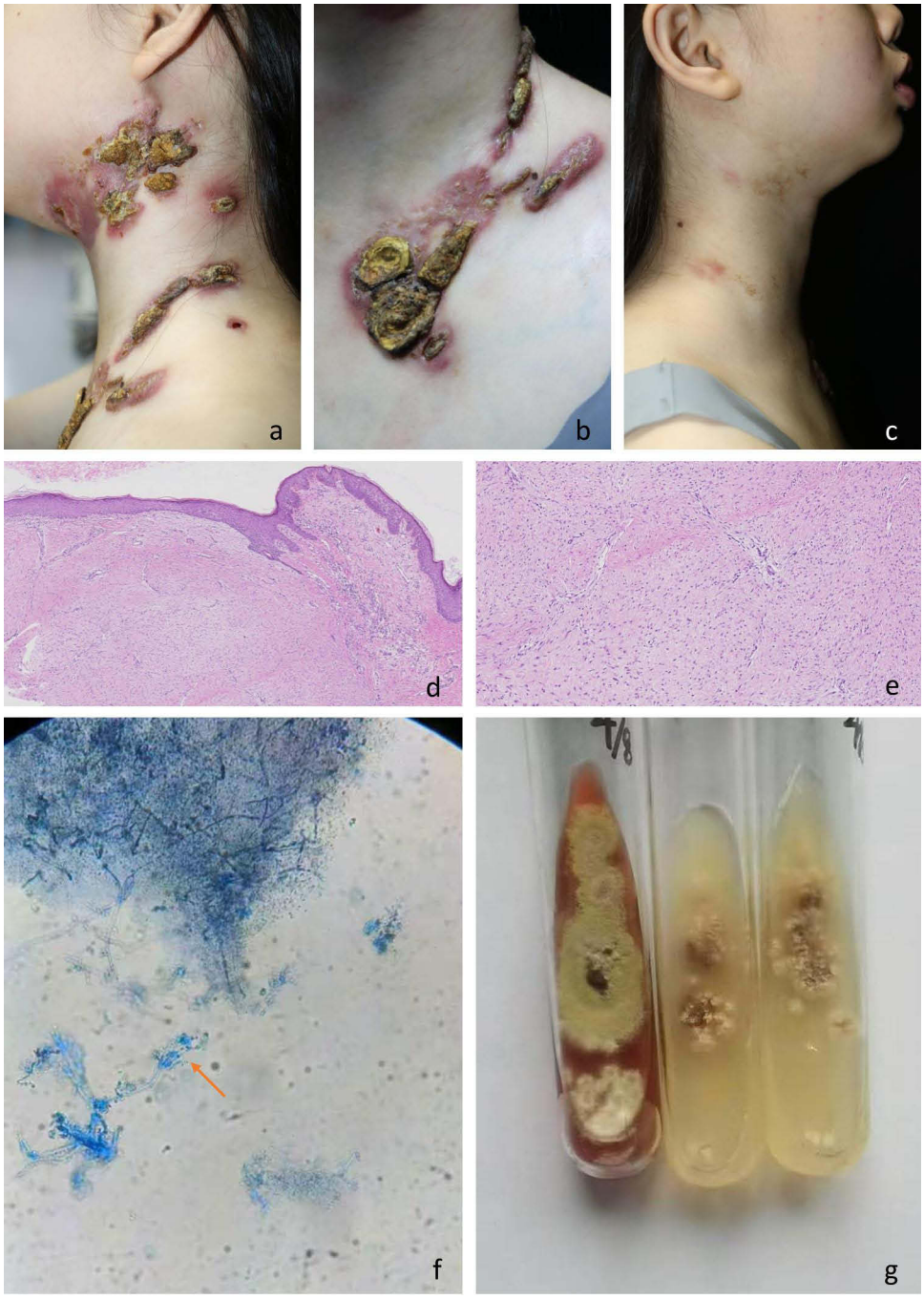

Figure 1 (**a**–**c**) Clinical presentation at initial hospital visit showing edematous plaques with yellow-brown crusts, central umbilication, desquamation, and serous exudation along the margins on the left submandibular, anterior cervical, and upper chest areas; an erythematous plaque is visible on the right side of the neck. (**d** and **e**) Histopathology of the left neck lesion revealing dense inflammatory infiltration composed of neutrophils, monocytes, lymphocytes, epithelioid cells, and multinucleated giant cells, with focal granulomatous nodule formation (H&E staining; original magnification: (**d**) ×4; (**e**) ×10). (**f**) Lactophenol cotton blue staining showing characteristic brush-like conidiophores of *T. marneffei* (Orange arrow). (**g**) Culture on Sabouraud dextrose agar at 25 °C displaying rapid growth of filamentous colonies with suede-like to woolly texture and a characteristic diffusible red pigment.

and consumption of lymphocytes have been documented in other systemic infections and granulomatous diseases.[18,19] Importantly, T-cell counts returned to normal during follow-up, supporting the interpretation that this reduction was transient and infection-related rather than reflective of an underlying primary immunodeficiency.

In this case, localized cutaneous plaques and superficial lymphadenopathy were the sole clinical manifestations. Histopathology revealed granulomatous inflammation with minimal fungal burden, underscoring the diagnostic

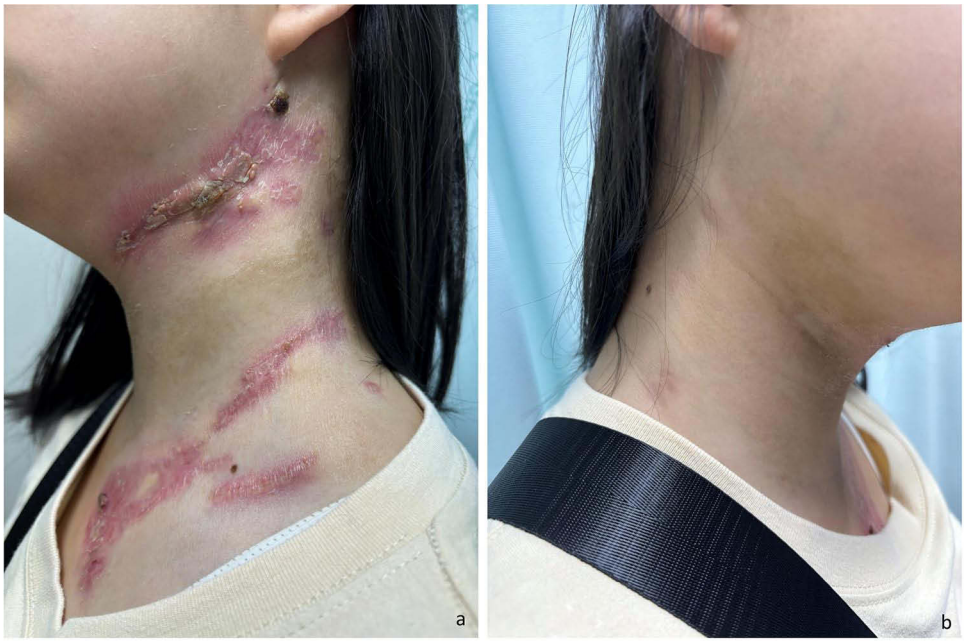

Figure 2 (**a** and **b**) Clinical images taken after 4 months of antifungal treatment showing marked resolution of cutaneous lesions. Residual erythema and localized skin atrophy are visible on the left side of the neck.

challenges. Traditional staining methods were non-revealing, but mNGS confirmed high levels of TM DNA, demonstrating its superior sensitivity. Studies have reported that mNGS achieves a 90% detection rate in culture-negative fungal infections. Integrating mNGS into the diagnostic workflow for refractory cutaneous lesions may therefore expedite diagnosis, reduce misdiagnosis, and guide appropriate antifungal therapy.

At present, no standardized treatment guidelines exist for TM infection in HIV-negative patients. Amphotericin B remains first-line therapy, but its nephrotoxicity and hepatotoxicity often limit use. Triazoles, including itraconazole, voriconazole, and posaconazole, are increasingly applied, particularly in localized disease.[20] In this adolescent, oral itraconazole (200 mg twice daily) was selected due to prior liver injury following prolonged anti-tuberculosis therapy and the potential toxicities of amphotericin B.[21–23] A favorable clinical response was achieved, with cutaneous lesions resolving within 4 months. During an 18-month follow-up period, no recurrence was observed, further supporting itraconazole as a safe and effective treatment option for localized TM infection.

Several limitations should be noted. First, genetic testing for underlying immune defects was not performed, leaving the possibility of subtle or subclinical immunodeficiency unresolved. Second, as a single case report, the observations may not be generalizable, and larger case series are needed to validate treatment outcomes. Third, while follow-up was extended to 18 months, longer surveillance is necessary to fully exclude late relapse.

In conclusion, dermatologists should maintain a high index of suspicion for TM infection in children and adolescents presenting with chronic granulomatous skin lesions, even in urban areas without traditional risk factors. Early biopsy, adjunctive histopathology, and molecular diagnostics such as mNGS are essential to avoid misdiagnosis and enable timely antifungal therapy. This case underscores the evolving clinical spectrum of TM infection and highlights the importance of heightened dermatologic vigilance in populations not traditionally considered at risk.

Conclusion

This case highlights the emerging clinical challenge of TM infection in HIV-negative, immunocompetent individuals living in urban areas without known environmental exposure. Dermatologists should maintain a high index of suspicion for deep fungal infections in patients presenting with chronic granulomatous skin lesions, even in the absence of systemic symptoms or traditional risk factors. Early skin biopsy, comprehensive histopathologic evaluation, and molecular diagnostics such as mNGS are essential tools for accurate diagnosis. In localized cutaneous cases, oral itraconazole

may be a safe and effective alternative to amphotericin B, offering favorable outcomes with fewer adverse effects. Broader recognition of atypical host presentations and integration of advanced diagnostic strategies are critical to reducing diagnostic delays and improving prognosis in non-HIV-associated TSM.

Data Sharing Statement

All data used in this work are publicly available.

Ethical Approval and Consent Statement

The reporting of this study conforms to the CARE guidelines. Ethical review and approval were not required to publish the case details in accordance with the local legislation and institutional requirements. Written informed consent was obtained from the patient for publication of this case report and any accompanying images as per our standard institutional rules.

Acknowledgments

The authors acknowledge the use of ChatGPT (OpenAI, GPT-4, May 2024 version) for language improvement during the preparation of this manuscript. The tool was employed exclusively for grammar correction and stylistic refinement. All content was critically reviewed and revised by the authors, who assume full responsibility for the accuracy, integrity, and originality of the final work.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This study was supported by the Science and Technology Program of Guangzhou (Grant No. 2023A03J0475, Grant No. 2024A03J0650 and Grant No. 2024A03J0480).

Disclosure

The authors declare no conflicts of interest in this work.

References

1. Si Z, Qiao J. Talaromyces marneffei infection. *New Engl J Med*. 2017;377(26):2580. doi:10.1056/NEJMicm1704164
2. Norasethasopon T, Boonyagars L. Talaromycosis. *New Engl J Med*. 2021;384(13):1261. doi:10.1056/NEJMicm2032478
3. He L, Mei X, Lu S, et al. Talaromyces marneffei infection in non-HIV-infected patients in mainland China. *Mycoses*. 2021;64(10):1170–1176. doi:10.1111/myc.13295
4. Lang Q, Pasheed CA, Kong WF, Yan HY. Case report: successful treatment of pulmonary talaromyces marneffei infection with posaconazole in a renal transplant recipient. *Am J Trop Med Hyg*. 2020;104(2):744–747. doi:10.4269/ajtmh.20-0909
5. Aryanian Z, Afshar ZM, Khasti T, Azhari V, Heidari S, Ghandi N. Generalized cutaneous talaromycosis (Penicilliosis) in an immunocompetent individual. *Jaad Case Rep*. 2024;50:97–101. doi:10.1016/j.jdcr.2024.05.029
6. Zhao J, Su HT, Zhang D, et al. The role of mNGS in the diagnosis of talaromycosis and case series. *Bmc Infect Dis*. 2025;25(1):191. doi:10.1186/s12879-025-10529-x
7. He H, Cai L, Xue X, et al. Disseminated talaromycosis in HIV-negative patients with lung cancer: a rare case report and literature review. *Bmc Infect Dis*. 2025;25(1):601. doi:10.1186/s12879-025-10985-5
8. Chan JF, Lau SK, Yuen KY, Woo PC. Talaromyces (Penicillium) marneffei infection in non-HIV-infected patients. *Emerg Microbes Infec*. 2016;5(3):e19. doi:10.1038/emi.2016.18
9. Cao L, Sun Y, Zhou Z, Pan X. Talaromyces marneffei infections in five human immunodeficiency virus-negative patients with the history of predation on wild bamboo rats (Rhizomys spp) - a case series. *Bmc Infect Dis*. 2025;25(1):340. doi:10.1186/s12879-025-10713-z
10. Yu Q, Wei M, Xiao R, et al. Clinical characteristics, course, and long-term outcomes in patients with Talaromyces marneffei infection: a 10-year retrospective cohort study. *Infect Dis Ther*. 2023;12(5):1283–1297. doi:10.1007/s40121-023-00801-5
11. Wong SS, Wong KH, Hui WT, et al. Differences in clinical and laboratory diagnostic characteristics of penicilliosis marneffei in human immunodeficiency virus (HIV)- and non-HIV-infected patients. *J Clin Microbiol*. 2001;39(12):4535–4540. doi:10.1128/JCM.39.12.4535-4540.2001

12. Narayanasamy S, Dat VQ, Thanh NT, et al. A global call for talaromycosis to be recognised as a neglected tropical disease. *Lancet Glob Health*. 2021;9(11):e1618–e1622. doi:10.1016/S2214-109X(21)00350-8
13. Guo J, Ning XQ, Ding JY, et al. Anti-IFN-γ autoantibodies underlie disseminated Talaromyces marneffei infections. *J Exp Med*. 2020;217(12): e20190502. doi:10.1084/jem.20190502
14. Li Z, Yang J, Qiu Y, et al. Disseminated Talaromyces marneffei infection with STAT3-Hyper-IgE syndrome: a case series and literature review. *Open Forum Infect Dis*. 2023;10(4):ofac614. doi:10.1093/ofid/ofac614
15. Li B, Li T, Huang Q, et al. Case Report: anti-interferon-γ autoantibodies in an adolescent with disseminated Talaromyces marneffei and mycobacterial co-infections. *Front Pediatr*. 2025;13:1552469. doi:10.3389/fped.2025.1552469
16. Ba H, Peng H, Cheng L, et al. Case report: talaromyces marneffei infection in a Chinese child with a complex heterozygous CARD9 mutation. *Front Immunol*. 2021;12:685546. doi:10.3389/fimmu.2021.685546
17. Sharquie IK, Sharquie KE. The role of epigenetics in immunosuppression in patients with infectious diseases as a fascinating applied observation. *J Pak Assoc Dermatol*. 2023;33(1):275–282.
18. Xing S, Zhang Z, Liu C, et al. Characteristics of endemic mycoses talaromyces marneffei infection associated with inborn errors of immunity. *J Clin Immunol*. 2024;45(1):17. doi:10.1007/s10875-024-01798-3
19. Kamphuis E, Junt T, Waibler Z, Forster R, Kalinke U. Type I interferons directly regulate lymphocyte recirculation and cause transient blood lymphopenia. *Blood*. 2006;108(10):3253–3261. doi:10.1182/blood-2006-06-027599
20. Vanittanakom N, Cooper CJ, Fisher MC, Sirisanthana T. Penicillium marneffei infection and recent advances in the epidemiology and molecular biology aspects. *Clin Microbiol Rev*. 2006;19(1):95–110. doi:10.1128/CMR.19.1.95-110.2006
21. Patel GP, Crank CW, Leikin JB. An evaluation of hepatotoxicity and nephrotoxicity of liposomal amphotericin B (L-AMB). *J Med Toxicol*. 2011;7 (1):12–15. doi:10.1007/s13181-010-0120-8
22. Winston DJ, Maziarz RT, Chandrasekar PH, et al. Intravenous and oral itraconazole versus intravenous and oral fluconazole for long-term antifungal prophylaxis in allogeneic hematopoietic stem-cell transplant recipients. A multicenter, randomized trial. *Ann Intern Med*. 2003;138 (9):705–713. doi:10.7326/0003-4819-138-9-200305060-00006
23. Pudjiati SR, Radiono S, Soebono H, Siswati AS, Wirohadidjojo YW, Kurniawati C. Successful treatment of AIDS-associated talaromycosis with low-dose itraconazole. *Jaad Case Rep*. 2020;6(12):1278–1280. doi:10.1016/j.jdcr.2020.09.015