Posttraumatic Endophthalmitis Caused by *Medicopsis romeroi*

Case Report and Analysis of a Comprehensive Case Series

Francesca Garofalo, Jonathan Wilcock, MD,† and Tim Lahey, MD, MMSc*‡*

Abstract: Fungal exogenous endophthalmitis is rare. Here, we report a case of posttraumatic endophthalmitis caused by *Medicopsis romeroi* in a 64-year old man. After a tree branch punctured his right eye while hiking in Laos, the patient's symptoms included pain, blurry vision, limited vision of light and dark, and sensation of a foreign body. The patient was unsuccessfully treated in Thailand with itraconazole and intraocular amphotericin. Upon return to the United States, the patient underwent extensive ophthalmic surgery and voriconazole was prescribed. Fundoscopic examination showed resolution of inflammation 3 months after the surgery, but despite symptomatic improvement, severe visual deficits remained. We performed a comprehensive case review of reported cases of *M. romeroi* infection, revealing that *M. romeroi* commonly manifests as a subcutaneous infection on the extremities in immunosuppressed patients who usually resolved with antifungal and surgical therapy. Many patients living in temperate climates were reported to have a travel and/or an immigration pattern from a tropical zone. This case and review extend the clinical spectrum of *Medicopsis* to include ocular infections, illustrates the importance of considering rare pathogens in patients with exogenous endophthalmitis, and encourages prompt medical and surgical treatment of *Medicopsis*.

Key Words: endophthalmitis, fungal infection, *M. romeroi*

(*Infect Dis Clin Pract* 2022;30: e1138)

Infection of the aqueous and/or vitreous humor of the eye, or endophthalmitis, is divided into endogenous and exogenous types. Endogenous endophthalmitis results from hematogenous seeding, whereas exogenous endophthalmitis results from introduction of pathogens directly into the eye. Fungal exogenous endophthalmitis is most commonly a result of fungal keratitis and less commonly after intraocular surgery and trauma.[1] Fungal endophthalmitis, a rare disease, most frequently results from *Aspergillus* and *Candida*.[2] Here, we report a rare case of *Medicopsis romeroi* endophthalmitis.

Medicopsis romeroi, formerly *Pyrenochaeta romeroi*, is a melanized coelomycetous fungus generally found in soil and plants in tropical regions.[3] *Medicopsis* species only rarely cause infection in humans. When its spores are introduced into cutaneous and subcutaneous tissue through trauma, they may cause immediate infection or may remain dormant until immunosuppression allows infection to emerge.[4,5] Most *M. romeroi* infections manifest as subcutaneous nodules and cysts on the limbs and extremities. Here, we report a case of a 64-year old man with posttraumatic *M. romeroi* endophthalmitis and summarize the literature on infections caused by this rare pathogen.

From the *Larner College of Medicine at the University of Vermont; and Departments of †Pathology and ‡Medicine, University of Vermont Medical Center, Burlington, VT.

Correspondence to: Francesca Garofalo, Robert M. Larner College of Medicine, Given N-100, 89 Beaumont Ave, Burlington, VT 05405. E-mail: Francesca.Garofalo@med.uvm.edu.

The authors have no funding or conflicts of interest to disclose.

ISSN: 1056-9103

CASE REPORT

A 64-year old male resident of the United States was hiking in Laos in early January 2019 when his right eye was punctured by a small trail-obstructing tree branch on which a friend lost his grip. The patient experienced instantaneous loss of vision and severe pain in the right eye, but he decided to continue hiking. With worsening symptoms, he presented to care in Bangkok, Thailand, 3 weeks later. Corneal scrapings at that time showed hyaline septate hyphae and mold. Topical voriconazole and levofloxacin were started along with oral itraconazole 100 mg. The patient received intravitreal amphotericin B in January and in March 2019 as well.

Four months after the injury, upon his planned return to the United States, the patient presented to care with deteriorating eyesight and continued pain. He admitted to inconsistent adherence to itraconazole, in part because of the challenges of obtaining affordable prescriptions while traveling. He reported limited vision of light and dark, foreign body sensation, and 2/10 pain in his right eye. Visual acuity testing confirmed that the patient could only see hand motion but was unable to count fingers on the examiner's hand. The patient was placed on oral voriconazole 200 mg twice daily, topical voriconazole, acetazolamide 500 mg, and topical prednisolone as ophthalmological workup and treatment continued.

Ophthalmic examination in the right eye revealed 3+ conjunctival injection, corneal ulcer 2.6 × 3.3 mm, 3+ corneal edema, anterior chamber hypopyon of 1.8 mm, posterior synechiae, glaucoma secondary to inflammation, severe vision loss, and endophthalmitis. Intravitreal injections of voriconazole, vancomycin, and ceftazidime as well as intracameral voriconazole were performed.

The corneal scrapings were planted to potato flake and Mycosel cycloheximide-chloramphenicol agars. Fungal smear with calcofluor white stain was also performed, revealing fungal elements. At 48 hours, the potato flake agar grew a mold with brown pigment on the front and reverse. A scotch tape preparation with lactophenol aniline blue stain confirmed the presence of a dematiaceous mold, which was unable to be identified by morphology alone. The specimen was sent to the Mayo Medical Laboratories for D2 rDNA polymerase chain reaction organism identification.

Ophthalmological examination revealed progressive vitreal inflammation, so the patient underwent penetrating keratoplasty, anterior chamber washout, excision of pupillary membrane, additional intravitreal and intracameral antifungal injections, and lateral tarsorrhaphy of the right eyelid.

Voriconazole and topical medications were continued under close follow-up with infectious diseases and ophthalmology. Ultimately, mold morphology and culture and D2 rDNA polymerase chain reaction confirmed that the organism was *M. romeroi*.

TABLE 1. Clinical Characteristics of the World's Reported Cases of Infection With *M. romeroi*

Reference	Age, Sex	Disease Susceptibility	Location	Travel or Immigration History	Syndrome	Antifungal Therapy	Surgery	Outcome
Abdolrasouli et al[6]	88 M	Sarcoidosis (prednisone)	United Kingdom	Caribbean immigration 20 y prior	Subcutaneous, dorsum hand	Amoxicillin-clavulanate	Excision	No recurrent infection
Armstrong-James et al[7]	NA	Kidney transplant (IS)	United Kingdom	Unknown	Cutaneous, arms & legs	AMB, ITRA	none	No recurrent infection
Babu et al[8]	25 F	None	South Asia—India	NA	Endophthalmitis	VOR, amikacin (failed KET/FLU)	Excision, Vitrectomy, Lensectomy	6/24 visual acuity; no recurrent infection
Badali et al[9]	45 F	None	South Asia—India	NA	Subcutaneous, forearm	None	Excision	No recurrent infection
Cerar et al[10]	56 M	Trauma—barefoot cotton processing	United Kingdom	South Asia—Pakistan	Mycetoma, foot	POSA (failed VOR, ITRA, 5FC)	none	Swelling, extensive bony and soft tissue infection
Chan et al[11]	55 M	Kidney transplant (IS)	Singapore	China	Subcutaneous, thigh	ITRA	Excision	Increased in size until death from MI
Chanyachailert et al[12]	80 M	DM	Southeast Asia—Thailand	NA	Subcutaneous, foot	None	None	No recurrent infection
Destombes et al[13]	NA	Unknown	European Union—France	Somalia	Mycetoma, foot	Unknown	Unknown	Unknown
Detroyer et al[14]	27 F	Kidney transplant (IS)	European Union—Belgium	West Africa—Gambia	Subcutaneous, foot	Terbinafine	None	No recurrent infection
Dinh et al[15]	47 F	DM	European Union—France	West Africa—Benin immigration 4 y prior	Subcutaneous, foot	Amoxicillin-clavulanate	Drainage	No recurrent infection
Current case	64 M	Trauma	Northeast United States	Southeast Asia—Laos	Endophthalmitis, keratitis	VOR; AMB IO (failed ITRA)	PK, washout	20/800 visual acuity; no recurrent infection
Girard et al[16]	45 M	Leprosy (IM dexamethasone)	European Union—France	West Africa—Senegal	Subcutaneous, leg	ITRA	Excision and drainage	No recurrent infection
Guégan et al[17]	47 F	DM	European Union—France	West Africa—unknown country	Subcutaneous, foot	None	Excision	No recurrent infection
Guégan et al[17]	59 F	DM, polymyalgia rheumatica (prednisone)	European Union—France	South Asia—Sri Lanka	Subcutaneous, foot	None	Excision	No recurrent infection
Guégan et al[17]	73 F	Giant cell arteritis (prednisone)	European Union—France	South Asia—India	Subcutaneous, foot, leg	VOR	Excision	No recurrent infection
Guégan et al[17]	65 M	Kidney transplant (IS)	France	West Africa—unknown country	Subcutaneous, knee	POSA	None	No recurrent infection
Guégan et al[17]	53 M	Liver graft (IS)	France	South Asia—Pakistan	Subcutaneous, foot	AMB (failed POSA)	Drainage, excision	No recurrent infection
Hsiao et al[18]	43 M	Asthma (oral steroids)	Taiwan	NA	Cutaneous, forearm, dorsal hand	AMB (failed ITRA)	Excision (failed)	No recurrent infection
Khan et al[4]	47 F	Acute lymphoblastic leukemia (IS)	Kuwait	South Asia—India immigration 4 y prior	Subcutaneous, finger	None	Drainage	No recurrent infection
Kulkarni et al[19]	43 M	Kidney transplant (IS), farmer	South Asia—India	NA	Subcutaneous, lower limb	VOR (failed ITRA, terbinafine)	Debridement	No recurrent infection
Lieberman et al[20]	65, F	Kidney transplant (IS)	WA, United States	Philippines immigration 45 y prior	Subcutaneous, foot	POSA	Excision	No recurrent infection

Los-Arcos et al[5]	56 F	Kidney transplant (IS)	Spain	South Asia—Pakistan immigration 4 y prior	Subcutaneous, hand	VOR	Debridement	No recurrent infection
Los-Arcos et al[5]	65 M	Liver graft (IS), DM	Spain	South Asia—India	Subcutaneous, foot	POSA	Excision	No recurrent infection
Ocampo et al[21]	66 M	Kidney transplant (IS)	France	Central Africa immigration 40 y prior	Cutaneous, foot	None	Excision	No recurrent infection
Pérez-Blanco et al[22]	18, 42, 54 M	None	Venezuela	NA	Mycetoma, leg, thorax	Unknown	Unknown	Unknown
Sharma et al[23]	61 F	Rheumatoid arthritis (MTX, prednisone)	South Asia—India	NA	Subcutaneous, finger	ITRA	Excision	No recurrent infection
Sharma et al[23]	48 M	DM, leprosy	South Asia—India	NA	Subcutaneous, foot	None	Excision	Unknown
Mathuram Thiyagarajan et al[24]	57 M	Kidney transplant (IS)	United Kingdom	South Asia—Bangladesh immigration, last visit 8 y prior	Mycetoma, knee	VOR	Excision	No recurrent infection
Waldman et al[25]	63 M	Cardiac transplant (IS)	Northeast United States	Unknown, possible immigration*	Subcutaneous, knee	Failed VOR	Excision	Unknown
Yadav et al[26]	50 F	DM	South Asia—India	NA	Subcutaneous, foot	ITRA	Drainage	No recurrent infection
Young et al[27]	42 F	Kidney transplant (IS)	Northeast United States	Caribbean—Jamaica immigration 17 months prior	Subcutaneous, foot	None	Excision	No recurrent infection

5FC indicates 5-fluorouracil; AMB, amphotericin B; DM, diabetes mellitus; F, female; IM, intramuscular; IO, intraocular; IS, immunosuppressive therapy; ITRA, itraconazole; KET/FLU, ketoconazole/fluconazole; M, male; MTX, methotrexate; NA, not available; POSA, posaconazole; PK, penetrating keratoplasty; VOR, voriconazole.

*Personal communication.

Three months after surgery, ophthalmic examination showed resolution of inflammation with substantial residual scarring. The patient ceased systemic voriconazole therapy and returned to Laos in September 2019. At that time, visual acuity in the right eye was rated at 20/800. The patient could count fingers on the examiner's hand but had difficulty recognizing facial expressions with his right eye.

DISCUSSION AND REVIEW OF LITERATURE

We found 30 prior case reports of human infection with *M. romeroi* published from 1973 to 2019 via a comprehensive review of case reports indexed in PubMed by the phrases "*Medicopsis romeroi*" and "*Pyrenochaeta romero*i," or accessible in a complementary hand search of case reviews in the University of Vermont CATQuest database. In Table 1, we summarize case features including age and sex of patient, travel or immigration history, disease susceptibility, infection syndrome, antimicrobial treatment, surgical treatment, and outcome.

Infection with *M. romeroi* commonly manifests as a subcutaneous infection, known as phaeohyphomycosis, on the extremities in patients undergoing immunosuppressive therapy that almost always resolved with antifungal and surgical therapy. Of note, 42% of patients were transplant recipients, and 23% were undergoing corticosteroid therapy for immune-mediated diseases, such as giant cell arteritis and sarcoidosis, 10% had no risk factors. Antifungal treatment varied greatly, with 29% of cases receiving itraconazole, 26% receiving voriconazole, 16% receiving posaconazole, and 26% receiving no antifungal therapy. However, 44% failed itraconazole therapy, compared with 25% and 20% failure rate for voriconazole and posaconazole, respectively. For most cases (77%), surgery was performed to excise the lesion. Infection with *M. romeroi* is relatively benign, as 85% of reported or known outcomes were of no recurrent infection or adverse sequelae.

Infection with *M. romeroi* is often described as occurring in tropical locales, but most patients in our comprehensive review did not reside in tropical areas. This suggests either that the association between *M. romeroi* and tropical areas is false, or that *M. romeroi* is underdiagnosed in tropical countries, or that residency outside of tropical countries enhances susceptibility to *M. romeroi* infection acquired in tropical areas. Notably, many patients living in temperate climates were reported to have a travel and/or immigration pattern from a tropical zone, thus potentially obscuring the location that *M. romeroi* was contracted. Patterns of travel and immigration are represented in Figure 1. An example of this global travel is that all cases reported from France immigrated from West Africa, South Asia, Somalia, or Central Africa up to 40 years prior.

Our novel case report extends the clinical spectrum of *M. romeroi* infection depicted in our comprehensive care review to include rare ocular disease. Regardless of the clinical manifestation, the most common approach to management of *M. romeroi* infection was treatment with azole antifungals along with surgical excision. It is unclear which antifungal is the drug of choice, because most azoles had a relatively high failure rate, whereas the low reported minimum inhibitor concentrations and favorable side effect profile of voriconazole support its use against *M. romeroi*.[28] Itraconazole, which our patient received first, is not expected to have as reliable activity against *Medicopsis*.[5,9,17,28] Surgical excision of infected tissue also seems an important approach to clearing *Medicopsis* infections.

This case report and comprehensive review reinforces the importance of considering rare pathogens in fungal endophthalmitis and, when suspected, the concomitant use of newer

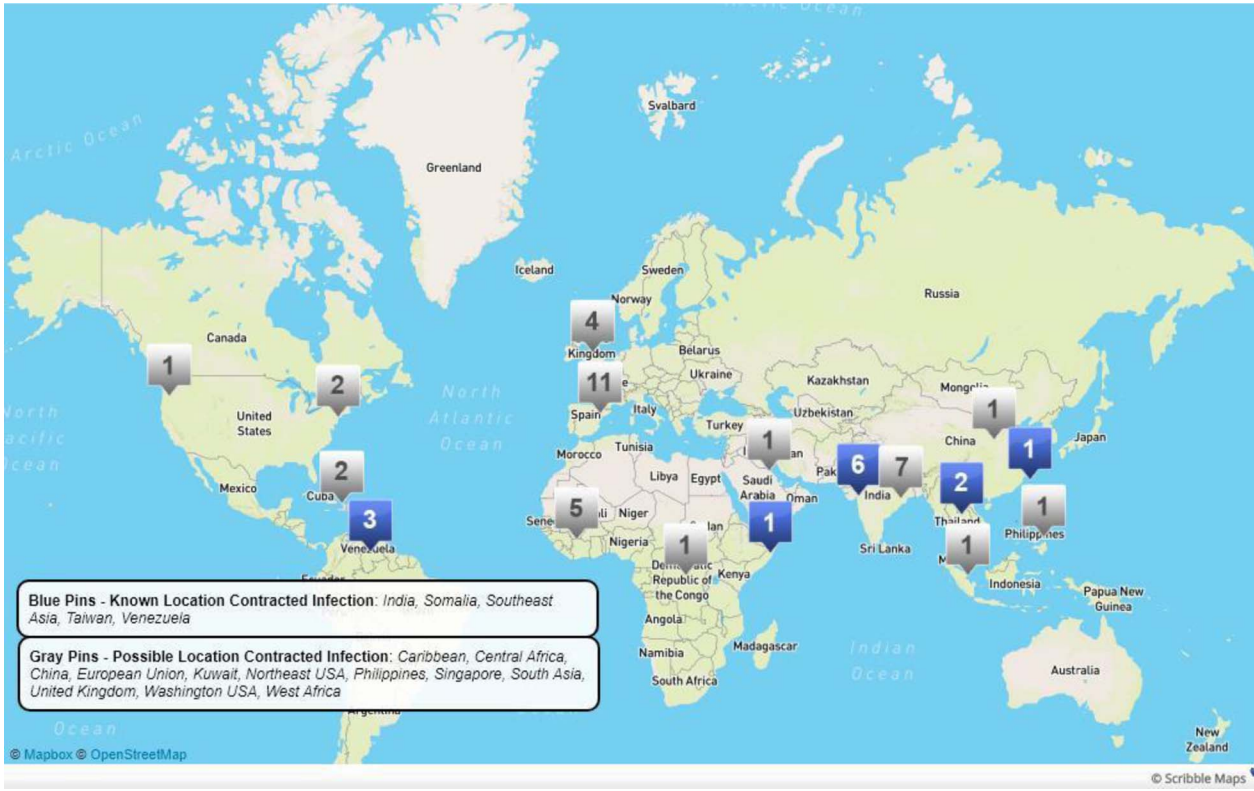

FIGURE 1. Geography of *M. romeroi* infection. Some patients contracted *M. romeroi* in tropical countries, but many more had previously lived or traveled to tropical areas, making the true range of *M. romeroi* unknown. Blue pins indicate a known location that *M. romeroi* was contracted; white/gray pins indicate a possible location due to travel and/or immigration history. The number inside the pin refers to the number of cases. Map created using Scribble Maps (https://scribblemaps.com).

broad-spectrum antifungals, such as voriconazole. The travel and immigration history can signal risk of unusual fungi, such as *M. romeroi*.

PERMISSIONS AND PATIENT PRIVACY PROTECTIONS

The patient whose case we report here gave permission for this case report, and his identity has been hidden via the omission of identifying details.

REFERENCES

1. Wykoff CC, Flynn HW Jr., Miller D, et al. Exogenous fungal endophthalmitis: microbiology and clinical outcomes. *Ophthalmology*. 2008;115(9):1501–1507.e2.
2. Chakrabarti A, Shivaprakash MR, Singh R, et al. Fungal endophthalmitis: fourteen years' experience from a center in India. *Retina*. 2008;28(10):1400–1407.
3. de Hoog G, Guarro J, Gene J, et al. *Atlas of Clinical Fungi*. 2nd ed. Washington, DC: ASM Press; 2000.
4. Khan Z, Ahmad S, Kapila K, et al. *Pyrenochaeta romeroi*: a causative agent of phaeohyphomycotic cyst. *J Med Microbiol*. 2011;60(6):842–846.
5. Los-Arcos I, Royuela M, Martín-Gómez MT, et al. Phaeohyphomycosis caused by *Medicopsis romeroi* in solid organ transplant recipients: report of two cases and comprehensive review of the literature. *Transpl Infect Dis*. 2019;21(3):e13072.
6. Abdolrasouli A, Gonzalo X, Jatan A, et al. Subcutaneous phaeohyphomycosis cyst associated with *Medicopsis romeroi* in an immunocompromised host. *Mycopathologia*. 2016;181:717–721.
7. Armstrong-James D, Teo IA, Shrivastava S, et al. Exogenous interferon-γ immunotherapy for invasive fungal infections in kidney transplant patients. *Am J Transplant*. 2010;10(8):1796–1803.
8. Babu K, Murthy PR, Prakash PY, et al. Chronic endophthalmitis due to *Pyrenocheta romeroi* in an immunocompetent host—a case report from southern India. *Retin Cases Brief Rep*. 2014;8(3):197–199.
9. Badali H, Chander J, Gulati N, et al. Subcutaneous phaeohyphomycotic cyst caused by *Pyrenochaeta romeroi*. *Med Mycol*. 2010;48(5):763–768.
10. Cerar D, Malallah YM, Howard SJ, et al. Isolation, identification and susceptibility of *Pyrenochaeta romeroi* in a case of eumycetoma of the foot in the UK. *Int J Antimicrob Agents*. 2009;34(6):613–614.
11. Chan YY, Tan AL, Tan BH. Subcutaneous abscess due to *Pyrenochaeta romeroi* in a renal transplant recipient. *Singapore Med J*. 2014;55(4):e64–e66.
12. Chanyachailert P, Leeyaphan C, Bunyaratavej S, et al. Subcutaneous phaeohyphomycosis from *Medicopsis romeroi* in a diabetic patient. *Med Mycol Case Rep*. 2019;26:69–72.
13. Destombes P, Mariat F, Rosati L, et al. Mycetoma in Somalia—results of a survey done from 1959 to 1964. *Acta Trop*. 1977;34(4):355–373.
14. Detroyer D, Deraedt K, Schöffski P, et al. Resolution of diffuse skin and systemic Kaposi's sarcoma in a renal transplant recipient after introduction of everolimus: a case report. *Transpl Infect Dis*. 2015;17(2):303–307.
15. Dinh A, Levy B, Bouchand F, et al. Subcutaneous phaeohyphomycosis due to *Pyrenochaeta romeroi* mimicking a synovial cyst. *Front Microbiol*. 2016;7:1405.
16. Girard C, Dereure O, Rispail P, et al. Subcutaneous phaeohyphomycosis due to *Pyrenochaeta romeroi* in a patient with leprosy. *Acta Derm Venereol*. 2004;84(2):154–155.

17. Guégan S, Garcia-Hermoso D, Sitbon K, et al. Ten-year experience of cutaneous and/or subcutaneous infections due to coelomycetes in France. *Open Forum Infect Dis*. 2016;3(2):ofw106.
18. Hsiao YW, Chia JH, Lu CF, et al. Molecular diagnosis and therapeutic experience of subcutaneous *Pyrenochaeta romeroi* infection: a case report and review of the literature. *Int J Dermatol*. 2013;52(10):1237–1240.
19. Kulkarni M, Jamale T, Hase N, et al. Subcutaneous phaeohyphomycosis caused by *Pyrenochaeta romeroi* in a kidney transplant recipient: a case report. *Exp Clin Transplant*. 2017;15(2):226–227.
20. Lieberman JA, Fiorito J, Ichikawa D, et al. Long-term carriage of *Medicopsis romeroi*, an agent of black-grain mycetoma, presenting as phaeohyphomycosis in a renal transplant patient. *Mycopathologia*. 2019; 184:671–676.
21. Ocampo MA, Kanitakis J, Bienvenu A-L, et al. Phaeohyphomycosis caused by *Pyrenochaeta romeroi* mimicking a plantar wart in a kidney transplant recipient. *Transpl Infect Dis*. 2012;14(6):E173–E174.
22. Pérez-Blanco M, Hernández-Valles R, Fernández-Zeppenfeldt G, et al. Mycetoma: report of 3 cases in Falcón state, Venezuela. *Invest Clin*. 1996; 37(1):61–73.
23. Sharma S, Capoor MR, Singh M, et al. Subcutaneous phaeohyphomycosis caused by *Pyrenochaeta romeroi* in a rheumatoid arthritis patient: a case report with review of the literature. *Mycopathologia*. 2016;181 (9–10):735–743.
24. Mathuram Thiyagarajan U, Bagul A, Nicholson ML. A nodulo-cystic eumycetoma caused by *Pyrenochaeta romeroi* in a renal transplant recipient: a case report. *J Med Case Reports*. 2011;5(1):460.
25. Waldman A, Ezaldein H, Tomayko M, et al. Nodular plaque in a cardiac transplant patient. *J Am Acad Dermatol*. 2015;72(5):e111–e112.
26. Yadav S, Agarwal R, Singh S, et al. *Pyrenochaeta romeroi* causing subcutaneous phaeohyphomycotic cyst in a diabetic female. *Med Mycol Case Rep*. 2015;8:47–49.
27. Young NA, Kwon-Chung KJ, Freeman J. Subcutaneous abscess caused by *Phoma* sp. resembling *Pyrenochaeta romeroi*: unique fungal infection occurring in immunosuppressed recipient of renal allograft. *Am J Clin Pathol*. 1973;59(6):810–816.
28. Ahmed SA, de Hoog GS, Stevens DA, et al. In vitro antifungal susceptibility of coelomycete agents of black grain eumycetoma to eight antifungals. *Med Mycol*. 2015;53(3):295–301.