

Case Report: Coral Reef Pathogen *Aspergillus sydowii* Causing Black Grain Mycetoma

Lucio Vera-Cabrera,^{1*} Jesus Alberto Cardenas-de la Garza,² Adrian Cuellar-Barboza,¹ Anabel Gallardo-Rocha,¹ Carmen Amelia Molina-Torres,¹ Wendy Escalante-Fuentes,¹ and Jorge Ocampo-Candiani¹

¹Laboratorio Interdisciplinario de Investigación Dermatológica, Servicio de Dermatología, Hospital Universitario “Dr. José Eleuterio González”, Universidad Autónoma de Nuevo León, Monterrey, México; ²Rheumatology Department, Hospital Universitario “Dr. José Eleuterio González”, Universidad Autónoma de Nuevo León, Monterrey, México

Abstract. Mycetoma is an infrequent subcutaneous infection caused by true fungi (eumycetoma) or aerobic actinomycetes (actinomycetoma). We report the case of a 62-year-old man with eumycetoma involving the left foot and ankle. Skin biopsy revealed black-brown grains, and in culture, a white colony fungus grew at day 8. Molecular sequencing using ITS1-ITS4 primers identified the species as *Aspergillus sydowii*. The patient was treated with itraconazole 200 mg twice daily and terbinafine 250 mg daily for 8 months, with complete response and no recurrence after 2.5 years of follow-up. *Aspergillus sydowii* is a saprotrophic fungus that rarely causes skin or nail disease. No cases of eumycetoma caused by this agent have been previously reported. As its geographic distribution continues to expand, it may increasingly be recognized as a cause of human disease.

INTRODUCTION

Mycetoma is a chronic subcutaneous infection caused by true fungi (eumycetoma) or aerobic actinomycetes (actinomycetoma). It is considered a neglected tropical disease and, although most cases occur in the “mycetoma belt” (area 15° latitude south and 30° latitude north that includes Sudan, Mexico, Senegal, and India), sporadic autochthonous cases are reported worldwide, including the United States and Europe.¹ *Aspergillus sydowii* is a saprotrophic and cosmopolitan fungus that causes devastating aspergillosis in coral reefs, but seldom affects humans.² Herein, we report a case of *A. sydowii* eumycetoma successfully treated with systemic antifungals.

CASE PRESENTATION

A previously healthy 62-year-old man presented to the dermatology outpatient clinic with a 14-year evolution of left foot and ankle swelling. Clinical examination revealed firm, painless swelling with foot deformity, nodules, and fistulae that drained a seropurulent discharge (Figure 1A and B). He had received previous treatment with antibiotics for years without improvement. Direct microscopic examination of the exudate did not reveal microorganisms. Histopathological examination showed granulomatous inflammation surrounding black-brown grains. Culturing of the skin biopsy in Sabouraud agar, added of chloramphenicol and cycloheximide, resulted in the isolation of a white, velvety colony with a greenish center on day 8. Microscopic examination of the colony showed septate hyphae with conidiophores ending in a vesicle with round conidia suggestive of *Aspergillus* spp. (Figure 1C–E). Two subsequent biopsy specimens grew a colony with the same characteristics. Molecular sequencing using ITS1-ITS4 primers identified the species as *A. sydowii* (100% identity; GenBank accession number MT625245).

Eumycetoma caused by *A. sydowii* was diagnosed. Treatment with itraconazole 200 mg twice daily and terbinafine 250 mg daily combination for 8 months achieved complete resolution without recurrence after 2.5 years of follow-up. No liver function tests abnormalities or other adverse events were identified during treatment.

DISCUSSION

Aspergillus spp. eumycetomas are very rare.^{3,4} They have infrequently been reported to cause white-grain or black-grain cases. As many *Aspergillus* species are ubiquitous in the environment, their geographic distribution is more widespread than other mycetoma agents that present distinctive endemicity. *Aspergillus sydowii* is a cosmopolitan and saprotrophic fungus that has been reported to cause disease in humans, animals, and plants. Particularly, it is responsible for aspergillosis in corals, which has caused important deterioration of coral reefs in the Caribbean Sea. *Aspergillus sydowii* is a terrestrial fungus, but it is also capable of surviving and reproducing in water, even with high salinity; it is considered a halophilic fungus capable of thriving in hypersaline environments.⁵ Dust storms may play a role in the worldwide dissemination of *A. sydowii*.² *Aspergillus* spp. are hyalohyphomycetes that habitually produce white-grain eumycetoma.⁶ Exceptionally, some species have been reported to produce black mycetoma grains.³

Aspergillus sydowii is a very infrequent cause of human disease. We performed a systematic review of human infections of the skin, hair, or nails caused by *A. sydowii*. We searched the PubMed (Medline) database (May 25, 2020) using the keywords “*A. sydowii*” and screened results in English, French, or Spanish that reported human infections by *A. sydowii* confirmed by molecular techniques. We excluded cases that did not involve the skin, hair, or nails; that were in other languages; that only had morphological confirmation; or that did not specify the type of infection.

After screening the 159 results retrieved, 26 were evaluated for inclusion. We excluded 10 because they lacked specification of the type of infection, five because they involved infections in other sites, three because of lack of molecular species confirmation, and three because of language. We included five reports of nine patients (Table 1).^{7–11} The infections

* Address correspondence to Lucio Vera-Cabrera, Laboratorio Interdisciplinario de Investigación Dermatológica, Servicio de Dermatología, Hospital Universitario “Dr. José Eleuterio González”, Universidad Autónoma de Nuevo León, Av. Gonzalitos No. 235 Nte., Col. Mitras Centro, Monterrey 64460, Mexico. E-mail: luvera_99@yahoo.com

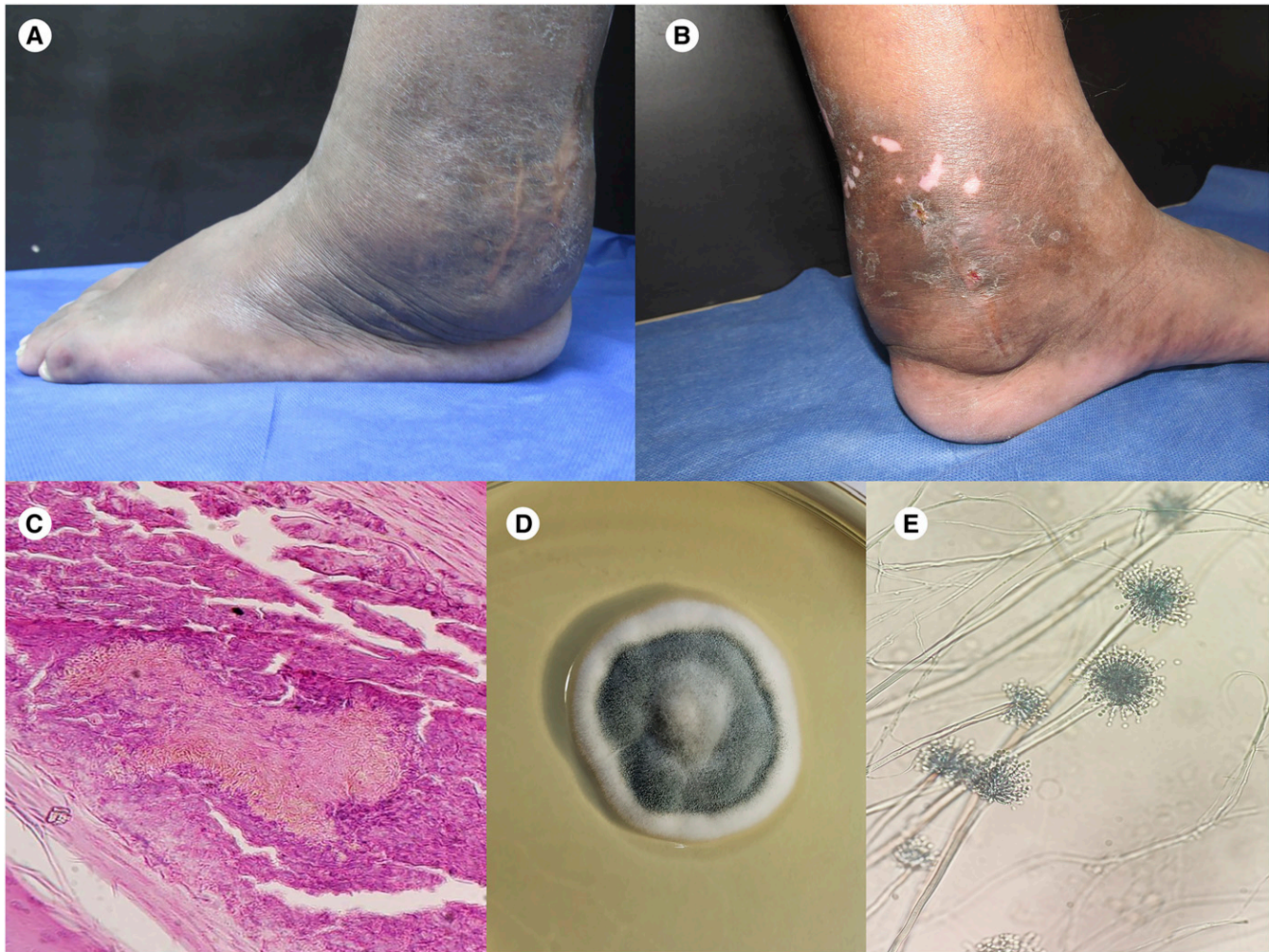


FIGURE 1. Clinical, histopathological, and microbiological characteristics of eumycetoma by *Aspergillus sydowii*. (A and B) Left foot painless swelling with deformity, nodules, and fistulae that drained a seropurulent discharge. (C) Histopathological examination (hematoxylin and eosin; original magnification $\times 100$) revealing a black-brown grain. (D) Fungal culture of the skin biopsy showing a white, velvety colony with a greenish center. (E) Microscopic examination of the colony showed septate hyphae with conidiophores ending in a vesicle with round conidia suggestive of *Aspergillus* spp. This figure appears in color at www.ajtmh.org.

TABLE 1
Aspergillus sydowii infections affecting the skin, nails, or hair

Author, country	N	Gender	Age (years)	Comorbidities	Type of infection	Site of infection	Treatment	Outcome	Follow-up (months)
Borghain et al., ⁷ India	1	Male	33	HIV infection	Onychomycosis and superficial skin infection	Right-hand thumb and widespread skin involvement	NA	NA	NA
Zhu et al., ⁸ China	1	Male	58	Onychomycosis and tinea pedis	Hyperkeratosis-like lesions	Right foot	NA	NA	NA
Tsang et al., ⁹ Hong Kong	4	3 females, one male	28, 38, 49, and 56	1: gouty arthritis, 1: diabetic nephropathy, hypertension, gout, hepatitis B infection	Onychomycosis	Toenails	NA	NA	NA
Nouripour-Sisakht et al., ¹⁰ Iran	2	NA	NA	NA	Onychomycosis	NA	NA	NA	NA
Takahata et al., ¹¹ Japan	1	Female	33	None	Onychomycosis	Right first toenail	Surgical removal of the nail	Cure	6
Vera-Cabrera et al. (current report), Mexico	1	Male	62	None	Eumycetoma	Left foot and ankle	Terbinafine and itraconazole	Cure	30

NA = not available.

predominantly involved the nails.^{7–11} No mycetoma cases were recorded. Only one case detailed the treatment and outcome of the infection.¹¹

In conclusion, we present a case of *A. sydowii* mycetoma successfully treated with systemic antifungal treatment. *Aspergillus sydowii* is an infrequent cause of human infection but, as its geographic distribution continue to expand, more cases may be detected in coming years.

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Authors' addresses: Lucio Vera-Cabrera, Adrian Cuellar-Barboza, Anabel Gallardo-Rocha, Carmen Amelia Molina-Torres, Wendy Escalante-Fuentes, and Jorge Ocampo-Candiani, Department of Dermatology, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Mexico, E-mails: luvera_99@yahoo.com, abcuelar89@gmail.com, anabelgrocha@yahoo.com, carmelia7@hotmail.com, wendyescalante64@hotmail.com, and jocampo2000@yahoo.com.mx. Jesus Alberto Cardenas-de la Garza, Department of Rheumatology, Hospital Universitario Dr. José Eleuterio González, Monterrey, Mexico, E-mail: cardenasdelagarza@gmail.com.

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