Cutaneous *Curvularia* Infection of the Forearm

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Phaeohyphomycosis *is the general term for infections caused by dematiaceous fungi. Although rare in humans, these infections are being reported at an increasing rate.* Curvularia *is a dematiaceous fungus that is ubiquitous among soil and vegetation in temperate areas and has only recently been revealed to cause human disease. Treatment guidelines have yet to be delineated due to the paucity of reported cases. We report the case of a 73-year-old man with chronic obstructive pulmonary disease, recent pneumonia caused by* Actinomyces*, and a localized plaque on his right lateral forearm extending to his medial arm caused by* Curvularia *species with complete resolution from itraconazole therapy.*

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Case Report

A 73-year-old man with chronic obstructive pulmonary disease presented with a slow-growing, pruritic, burning lesion on his right forearm of 2 months' duration. He denied fever, chills, night sweats, or generalized malaise; he did not recall any trauma to the area. The patient has taken prednisone 10 mg daily for chronic obstructive pulmonary disease for more than 20 years. Of note, he was recently hospitalized with pneumonia caused by *Actinomyces*; he did not recall if the lesion had appeared during his hospital stay. Physical examination demonstrated an irregular, erythematous, and ecchymotic plaque on his right lateral forearm that extended to his medial arm; it measured 30×18 cm at its largest diameter (Figures 1A and 1B). There was no ulceration, focal necrosis, or apparent discharge. Two 4-mm punch biopsies from the center of the lesion were sent for histopathology and culture. Histopathology revealed a normal epidermis with a dermal granulomatous infiltrate and scattered giant cells (Figure 2). Higher magnification revealed yeast forms (Figure 3). Special staining confirmed fungal elements with periodic acid–Schiff stain, specifically multiple yeast forms (Figures 4). Culture grew *Curvularia* species.

The patient was treated with oral itraconazole 200 mg twice daily for 2.5 months, which led to complete resolution of his active lesion and minimal postinflammatory hyperpigmentation (Figure 1C). There was no evidence of recurrence at 18-month follow-up.

Comment

Although an uncommon cause of human disease, dematiaceous fungi have been reported to result in infections ranging from minor to life threatening in both immunocompromised and immunocompetent hosts. These infections are broadly classified as phaeohyphomycosis and are on the rise. Because no simple serologic or antigen test is available for identification, clinical suspicion and detailed culture analyses are crucial for correct and timely diagnosis.[1] More than 100 species and 60 genera of dematiaceous fungi have been discovered to cause human disease, most commonly *Curvularia*, *Bipolaris*, *Exserohilum*, and *Alternaria*.[1,2]

Dematiaceous fungi are deeply pigmented due to melanins within their hyphae and conidia. These melanins not only provide the characteristic black-brown pigmentation of these fungi but also contribute to their pathogenicity.[3,4]

Curvularia species are ubiquitous among soil and vegetation in temperate areas. They are spread via airborne spores and are a common cause of disease in plants.[4] *Curvularia* can be microscopically distinguished from other dematiaceous fungi due to the presence of curved conidia.[5] The first reported human case was in 1959 and involved a corneal infection.[4] Of approximately 40 recognized species, the one most frequently isolated in human infections is

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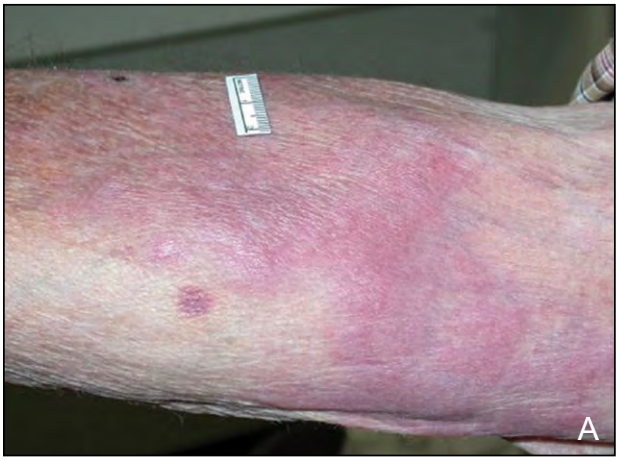

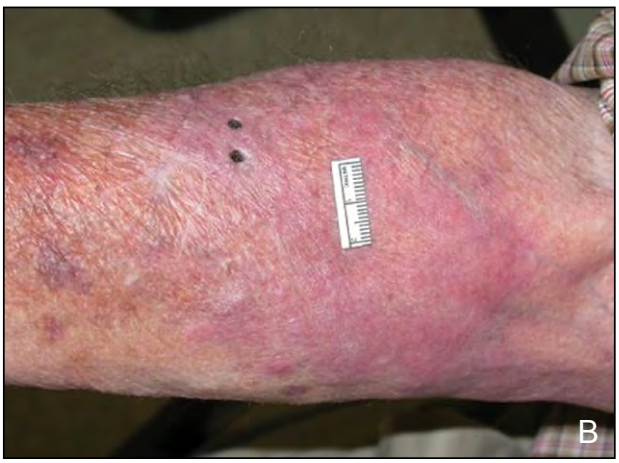

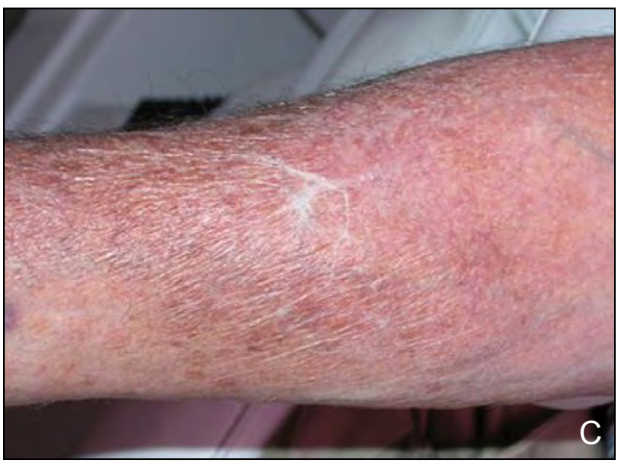

Figure 1. Clinical presentation of an erythematous and ecchymotic plaque located on the patient's right forearm and extending to his medial arm, measuring 30×18 cm at its largest diameter (without flash [A]; with flash [B]). Complete resolution of the active lesion was achieved with minimal postinflammatory hyperpigmentation following a 2.5-month course of oral itraconazole (C).

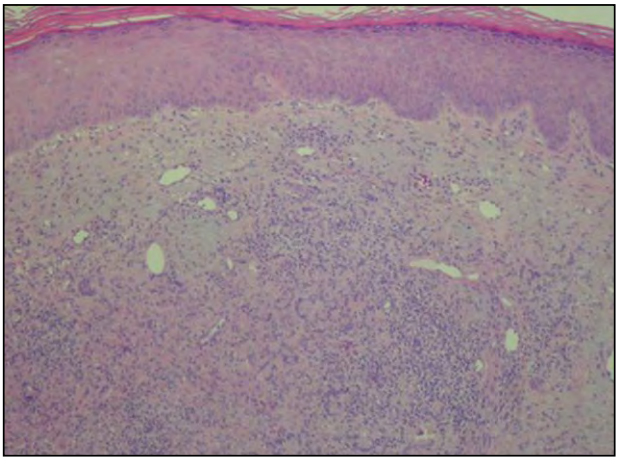

Figure 2. Histopathology revealed a normal epidermis with a dermal granulomatous infiltrate without areas of necrosis (H&E, original magnification ×200).

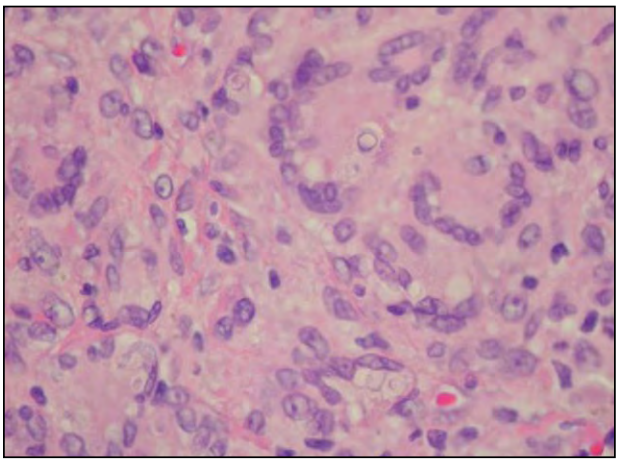

Figure 3. Granulomatous infiltration was seen with giant cells and multiple yeast forms (H&E, original magnification ×400).

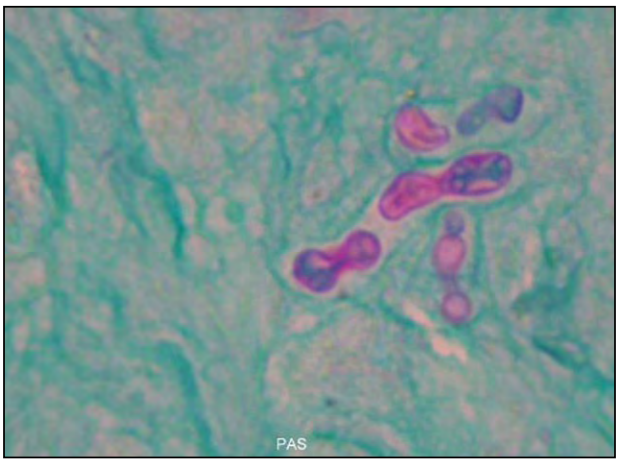

Figure 4. Yeast forms were present with special staining (periodic acid–Schiff, original magnification ×400).

Curvularia lunata.[4,6] These fungi have relatively low virulence potential, with disease manifestations and severity depending primarily on host factors.[7] The clinical spectrum of *Curvularia* diseases commonly includes wound infections and mycetomas as well as ocular and allergic pathology. Less commonly, *Curvularia* species have been reported to cause central nervous system infections, postsurgical endocarditis, dialysis-related peritonitis, and atypical skin lesions.[1,4,7] Excluding ocular cases, few *Curvularia* infections are reported in the literature. Of the reported cases, presentations and treatments vary from case to case. Cutaneous infections occur in all age ranges and tend to be more common and more severe in immunocompromised patients; there is a predilection for the extremities, often following traumatic inoculation.[5,7] Bonduel et al[2] reported a *Curvularia* infection on the upper extremity of a 9-year-old boy who presented 8 days after bone marrow biopsy. He was successfully treated with liposomal amphotericin B. Hiromoto et al[8] reported a posttraumatic ulcerated lesion on the upper extremity of a 67-year-old immunocompetent man, which was found to be *Curvularia*. He was treated with terbinafine 250 mg daily with complete resolution of his primary lesion in 1 month, but he had to undergo wide local excision with a subsequent 4-month course of itraconazole due to local recurrence.[8] Fan et al[6] reported a macerated, swollen, suppurative lesion on the foot of a 64-year-old male farmer. *Curvularia clavata* was isolated and the patient was successfully treated with oral fluconazole 100 mg daily in addition to ethacridine lactate solution 0.1% for 12 weeks.[6] Tessari et al[9] reported a disseminated *Curvularia* infection following minor trauma in a 69-year-old immunocompromised man who had received a heart transplant. This case initially began as posttraumatic cutaneous lesions of his upper extremity but then progressed to involve multiple internal organs, which ultimately resulted in death.[9]

High clinical suspicion for *Curvularia* infection is necessary for a proper diagnosis. Multiple diagnostic tests exist and include the following: Gram and/or calcofluor-white stains for hyphal elements, Gomori methenamine-silver stain for fungal biomass, Fontana-Masson silver stain for melanin, and pan-fungal polymerase chain reaction assay for rapid diagnosis.[1,4] Definitive identification of *Curvularia* species requires direct observation of specific morphologic features produced in culture.[6] *Curvularia* species mature rapidly on semisynthetic media at an optimal temperature of 28.5°C, taking approximately 2 days on blood and chocolate agar and 4 days on Sabouraud agar or brain-heart infusion agar.[4] Colonies consist of deeply pigmented (dark green to black) septate hyphae with multicellular conidia that are characteristically curved and measure 18 to 40 μm in length.[4]

To date, there is no standard therapeutic recommendation regarding the best agent or duration of treatment due to the limited number of reported cases.[4,7,8] However, multiple drugs have yielded complete resolution of active lesions.[2-8] Current options for the treatment of dematiaceous fungi infections include azoles (eg, voriconazole, itraconazole), amphotericin B, terbinafine, and echinocandins (eg, caspofungin, micafungin, anidulafungin). Of these agents, voriconazole and itraconazole have had the highest consistent in vitro success, with a minimum inhibitory concentration of 0.125 μg/mL or less. Dosing can range from 200 to 600 mg daily. Fluconazole was found to have negligible anti–dematiaceous fungi activity.[1,7] If dissemination is suspected, prompt hospitalization and initiation of intravenous itraconazole and/or amphotericin B is recommended. Surgical excision is another option, especially if a drug trial alone does not yield resolution or if there is any sign of local recurrence.[7-9] Meticulous follow-up is necessary due to the possibility for recurrence and dissemination, especially in immunocompromised individuals.

Conclusion

Curvularia is a dematiacious fungus that occasionally causes disease in humans. Infections can range in scope from mild to fatal. *Curvularia* species are widely distributed throughout soil and vegetation and therefore have the potential to infect humans due to the high probability of exposure. Cutaneous infections have been increasingly reported in the medical community and should be considered in the differential diagnosis of skin lesions in both immunocompromised and immunocompetent hosts. Treatment options are abundant, with voriconazole and itraconozole having the most reported successes as single-agent therapy if given for at least 2 months' duration.

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