Recurrent Cutaneous *Exophiala* Phaeohyphomycosis in an Immunosuppressed Patient

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PRACTICE **POINTS**

- Phaeohyphomycosis is an infection with dematiaceous fungi that most commonly affects immunosuppressed patients.
- Subcutaneous phaeohyphomycosis may present with nodulocystic lesions that recur over the course of years.
- Tissue fungal culture should be obtained when the diagnosis is suspected, as the risk for dissemination is related to the culprit organism.
- Surgical excision with close follow-up may be an appropriate management strategy for patients on immunosuppressive medications to avoid interactions with azole therapy.

To the Editor:

A 73-year-old man presented with a 2.5-cm, recurrent, fluctuant, multiloculated nodule on the left forearm. The lesion was nontender with occasional chalky, white to yellow discharge from multiple sinus tracts. He was otherwise well appearing without signs of systemic infection. He reported similar lesions in slightly different anatomic locations on the left forearm both 7 and 4 years prior to the current presentation. In both instances, the nodules were excised at an outside hospital without any additional treatment. Histopathology of the excised tissue from both prior occasions demonstrated brown septate hyphae surrounded by suppurative and granulomatous inflammation consistent with dematiaceous fungal infection of the dermis (Figures 1 and 2); the organisms were highlighted with periodic acid–Schiff stain.

The patient's medical history was notable for advanced heart failure with an ejection fraction of 25% and autosomal-dominant polycystic kidney disease. He received an orthotopic kidney transplant 17 years prior to the current presentation. Medications included tacrolimus, mycophenolate mofetil, and prednisone. He denied any trauma or notable exposures to vegetation, and his travel history was unremarkable. A review of systems was negative.

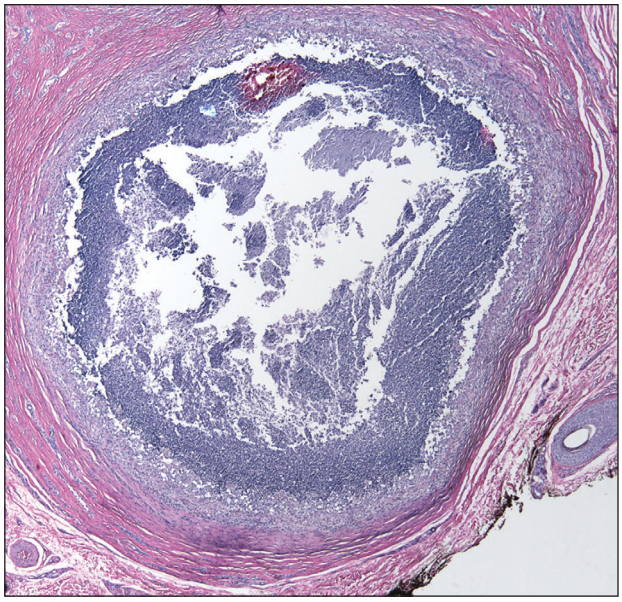

FIGURE 1. A subcutaneous palisaded granulomatous reaction with a central cystic cavity containing a collection of neutrophils and focal pigmented organisms (H&E, original magnification ×40).

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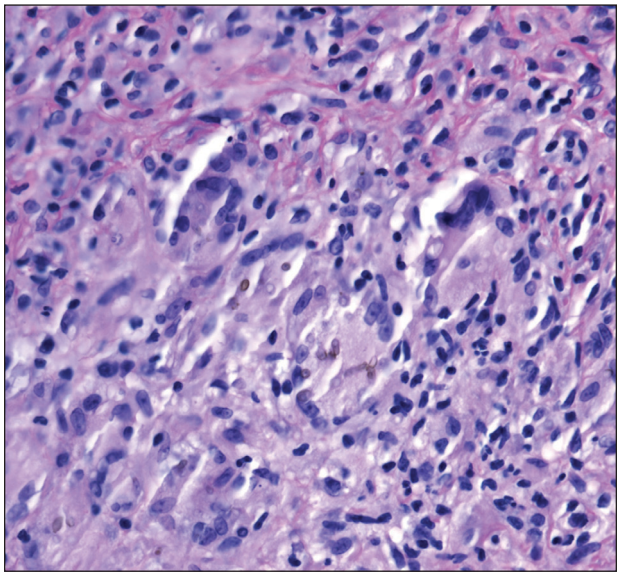

FIGURE 2. Higher magnification revealed brown septate hyphae engulfed by multinucleated giant cells (H&E, original magnification ×400).

At the current presentation, a sterile fungal culture was performed and found positive for *Exophiala* species, while bacterial and mycobacterial cultures were negative. A diagnosis of phaeohyphomycosis was made, and he was scheduled for re-excision. Out of concern for interactions with his immunosuppressive regimen, he chose to forgo any systemic antifungal therapy. He died from hospital-acquired pneumonia and volume overload unresponsive to diuretics or dialysis.

Phaeohyphomycosis is a rare fungal infection caused by several genera of dematiaceous fungi that are characterized by the presence of melaninlike cell wall pigments thought to locally hinder immune clearance by scavenging phagocyte-derived free radicals. These fungi are ubiquitous in soil and vegetation and usually penetrate the skin at sites of minor trauma.[1] Phaeohyphomycosis typically affects immunosuppressed hosts, and its incidence among organ transplant recipients currently is 9%.[2] The incidence in this population has been rising, however, as recent advances in immunosuppressive therapies have increased posttransplant survival.[3]

Subcutaneous phaeohyphomycosis can present with nodules, cysts, tumors, and/or verrucous plaques, and the diagnosis almost always requires clinicopathologic correlation.[3] Rapid diagnosis can be made when septate brown hyphae and/or yeast forms are observed on hematoxylin and eosin stain. Rarely, patients present with disseminated infection, characterized by fungemia; central nervous system involvement; and/or infection of multiple deep structures including the eyes, lungs, bones, and sinuses.[4] The risk for dissemination from the skin likely is related to the culprit organism's genus; *Lomentospora*, *Cladophialophora*, and *Verruconis* often are associated with dissemination, while *Alternaria*, *Exophiala*, and *Fonsecaea* typically remain confined to the skin and subcutis.[5] Due to this difference and its potential to impact management, obtaining a tissue fungal culture is advisable when phaeohyphomycosis is suspected.

There is no standard treatment of phaeohyphomycosis. Regimens typically consist of excision and prolonged courses of azole therapy, though excision alone with close follow-up may be a reasonable alternative.[6] The latter is a particularly important consideration when managing phaeohyphomycosis in organ transplant recipients, as azoles are known cytochrome P450 3A4 inhibitors that can affect serum levels of common immunosuppressive medications including calcineurin inhibitors and mammalian target of rapamycin inhibitors.[3] Local recurrence is common regardless of whether azole therapy is pursued,[7] and dissemination of localized *Exophiala* infections is exceedingly rare.[8] There is a strong argument to be made for our patient's decision to forgo antifungal therapy.

This case underscores the difficulty inherent to eradicating local subcutaneous *Exophiala* phaeohyphomycosis while providing reassurance that with treatment, the risk of life-threatening complications is low. Obtaining tissue for both hematoxylin and eosin stain and sterile culture is crucial to ensuring prompt diagnosis and tailoring the optimal treatment and surveillance strategy to the culprit organism. To avoid delays in diagnosis and treatment, it is important for clinicians to consider phaeohyphomycosis in the differential diagnosis for recurrent nodulocystic lesions in immunosuppressed patients and to recognize that presentations may span many years.

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