Subcutaneous Phaeohyphomycosis Caused by *Exophiala jeanselmei* in an Immunocompromised Host

Jenifer Hague, MD; Elizabeth Liotta, MD

Phaeohyphomycosis is an infection caused by dematiaceous fungi, which are ubiquitous throughout the world. We present the case of a 41-year-old immunocompromised man with Cushing syndrome who developed a phaeohyphomycotic infection. The patient presented with painful, progressive nodules that were biopsied and cultured to reveal dematiaceous fungi. Treatment of this condition is particularly difficult as demonstrated by this patient's intolerance to itraconazole and amphotericin B. Because of the increasing number of immunocompromised patients and incidence of phaeohyphomycosis, a heightened level of suspicion is necessary on the part of the clinician for both diagnosis and treatment of this disease.

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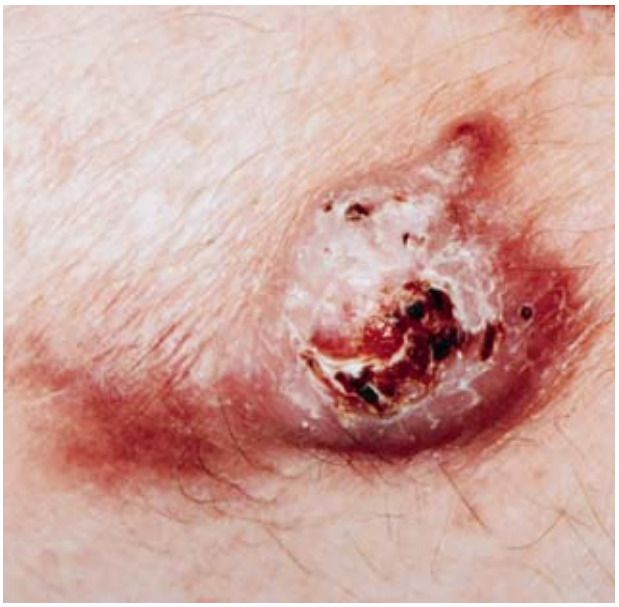

Figure 1. Individual nodular lesion with central ulceration.

Case Report

A 41-year-old white man with steroid-dependent reactive airway disease complicated by iatrogenic Cushing syndrome presented to the dermatology clinic with a 6-month history of progressive skin lesions, occurring at the sites of trauma (Figure 1). The patient was maintained on inhaled steroids and oral prednisone, varying in dose from 20 to 100 mg daily dependent on respiratory symptoms, for his respiratory disease.

The findings from the physical examination revealed a characteristic cushingoid male, with tender hyperkeratotic nodules on the dorsum of both hands and right forearm. The lesions expressed a yellow discharge when manipulated. No erythema or adenopathy was noted. Microscopic evaluation of biopsy specimens revealed pseudoepitheliomatous hyperplasia and dematiaceous fungi. Cultures were positive for *Exophiala jeanselmei* (Figure 2). Slides of the fungi were prepared with Gomori methenamine-silver (Figure 3) and Fontana-Masson stains.

Initial treatment with itraconazole 200 mg orally for 3 weeks was discontinued because of elevated liver function tests. Daily administration of amphotericin B 100 mg intravenously was complicated by hypomagnesemia, interrupting 9 months of continuous treatment. Despite all treatment, the patient developed new nodules identical to those at the original presentation, and treatment was stopped. Currently, the patient is being followed up clinically.

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Dr. Hague is from Dermatology Service and Dr. Liotta is from the Department of Dermatology, Portsmouth Naval Medical Center, Virginia.
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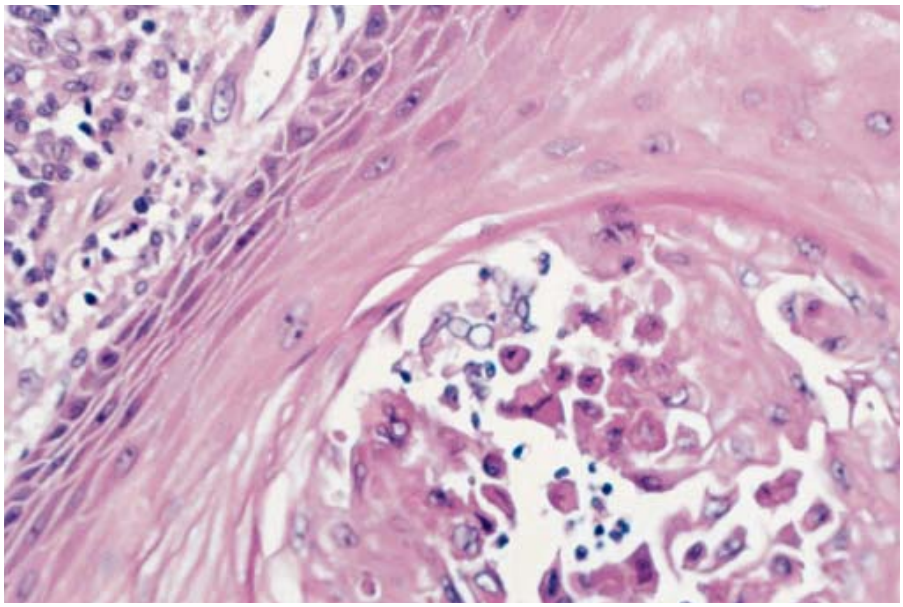

Figure 2. Biopsy section with *Exophiala jeanselmei* (H&E, original magnification ×100).

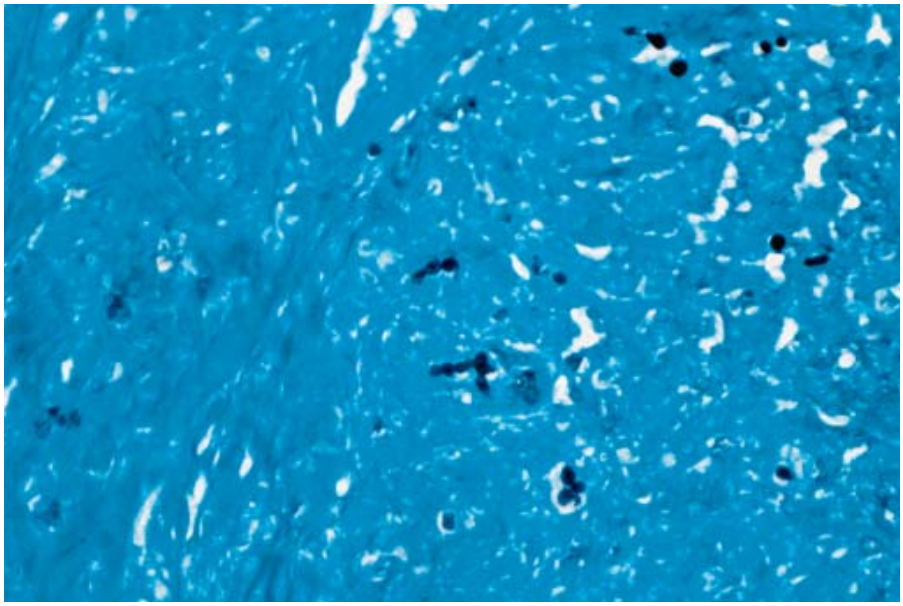

Figure 3. Dark staining *Exophiala jeanselmei* (Gomori methenamine-silver, original magnification ×100).

Comment

Phaeohyphomycosis is a fungal infection caused by dematiaceous (melanin-containing) fungi.[1] More than 50 organisms cause this infection. The most common organisms reported in the literature are *Bipolaris spicifera* and *E jeanselmei*.[2] The differential diagnosis for phaeohyphomycoses includes mycetoma and chromoblastomycosis. These can be ruled out microscopically by the absence of grains and brown-pigmented sclerotic bodies, respectively.[3] Furthermore, mycetoma and chromoblastomycosis are prevalent in tropical and subtropical regions, whereas phaeohyphomycosis has a global distribution.[4]

McGinnis et al[5] described 4 classes of phaeohyphomycoses in 1985: (1) superficial, (2) cutaneous and corneal, (3) subcutaneous, and (4) systemic. Phaeohyphomycotic infections can occur as a primary lesion resulting from inoculation at the site of trauma, as well as a secondary lesion following dissemination. The latter occurs most frequently in immunocompromised hosts. Risk factors for secondary infections are prolonged neutropenia, systemic corticosteroid use, hematologic malignancy, organ transplantation, or prolonged antibiotic therapy.[6] In the case presented here, the patient's

systemic corticosteroid use predisposed him to the development of secondary lesions after the initial inoculation at a site of trauma.

Clinical suspicion is important for making the diagnosis of subcutaneous phaeohyphomycosis. Patients often present with nonspecific-appearing nodules and cannot recall any preceding trauma. The infection typically occurs on an extremity, and the lesion, usually singular, is present for months to years before the patient goes for evaluation.[7] Lesions are generally small, pus-filled granulomatous nodules that enlarge over time. They may develop a pseudocapsule around the pus, leading to the common use of the term *phaeohyphomycotic cyst*, even though there is no true capsule. The epidermis overlying the infection is intact, initially. However, it may become ulcerated or drain spontaneously, changing the appearance of the lesion. Multiple lesions and wood splinters in the nodules have been reported in the literature.[8]

Dematiaceous fungi are identified microscopically as hyphal elements that absorb stains, particularly the Fontana-Masson, which demonstrates melanin. Culture of the fungal elements is necessary to determine the exact organism. *E jeanselmei*, identified in this case, is found in the soil and has been isolated from wood pulp.

Numerous therapeutic modalities have been used for the treatment of subcutaneous phaeohyphomycotic infections. Treatment with antifungal agents amphotericin B, 5-fluorocytosine, ketoconazole, and miconazole has had variable success.[7] Generally, total excision is the treatment of choice for subcutaneous phaeohyphomycotic infections.[9]

In summary, this case represents an infection made possible by a necessary and appropriate medical intervention. The incidence of this type of infection will only increase as medical therapeutic interventions continue to progress. Clinicians' heightened awareness is essential for the diagnosis and treatment of these potentially life-threatening infections, not only because they are increasing in number but also because of the difficulty of diagnosis and treatment of these infections.

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