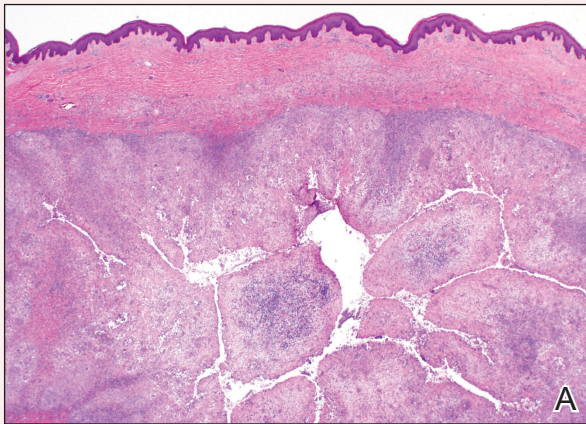


Circumscribed Nodule in a Renal Transplant Patient

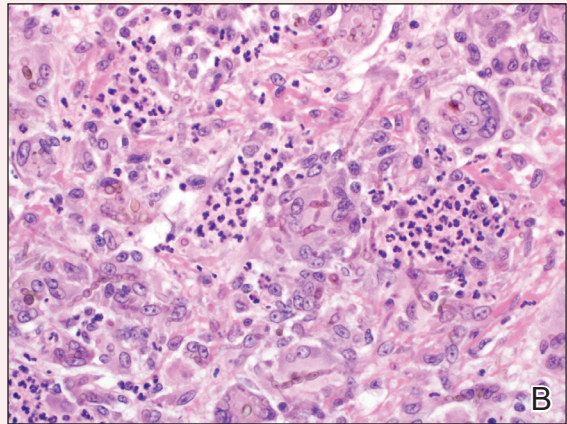
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H&E, original magnification $\times 2$.



H&E, original magnification $\times 40$.

A 63-year-old man on immunosuppressive therapy following renal transplantation 5 years prior presented with a nontender circumscribed nodule above the left knee of 6 months' duration. The patient denied any trauma or injury to the site.

The best diagnosis is:

- chromoblastomycosis
- granulomatous foreign body reaction
- granulomatous tattoo reaction
- subcutaneous hyalohyphomycosis
- subcutaneous phaeohyphomycosis

PLEASE TURN TO PAGE 98 FOR DERMATOPATHOLOGY DIAGNOSIS DISCUSSION

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The authors report no conflict of interest.

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The Diagnosis: Subcutaneous Phaeohyphomycosis

Subcutaneous phaeohyphomycosis (SP), also called mycotic cyst, is characterized by a painless, nodular lesion that develops in response to traumatic implantation of dematiaceous, pigment-forming fungi.¹ Similar to other fungal infections, SP can arise opportunistically in immunocompromised patients.^{2,3} More than 60 genera (and more than 100 species) are known etiologic agents of phaeohyphomycosis; the 2 main causes of infection are *Bipolaris spicifera* and *Exophiala jeanselmei*.^{4,5} Given this variety, phaeohyphomycosis can present superficially as black piedra or tinea nigra, cutaneously as scytalidiosis, subcutaneously as SP, or disseminated as sinusitis or systemic phaeohyphomycosis.

Coined in 1974 by Ajello et al,⁶ the term *phaeohyphomycosis* translates to “condition of dark hyphal fungus,” a term used to designate mycoses caused by fungi with melanized hyphae. Histologically, SP demonstrates a circumscribed chronic cyst or abscess with a dense fibrous wall (quiz image A). At high power, the wall is composed of chronic granulomatous inflammation with foamy macrophages, and the cystic cavity contains necrotic debris admixed with neutrophils. Pigmented filamentous hyphae and yeastlike entities can be seen in the cyst wall, in multinucleated giant cells, in the necrotic debris, or directly attached to the implanted foreign material (quiz image B).⁷ The first-line treatment of SP is wide local excision and oral itraconazole. It often requires adjustments to dosage or change to antifungal due to recurrence and etiologic variation.⁸ Furthermore, if SP is not definitively treated, immunocompromised patients are at an increased risk for developing potentially fatal systemic phaeohyphomycosis.³

Chromoblastomycosis (CBM), also caused by dematiaceous fungi, is characterized by an initially indolent clinical presentation. Typically found on the legs and lower thighs of agricultural workers, the lesion begins as a slow-growing, nodular papule with subsequent transformation into an edematous verrucous plaque with peripheral erythema.⁹ Lesions can be annular with central clearing, and lymphedema with elephantiasis may be present.¹⁰ Histologically, CBM shows pseudoepitheliomatous hyperplasia and intraepidermal pustules as the host rids the infection via transepithelial elimination. Dematiaceous fungi often are seen in the dermis, either freestanding or attached to foreign plant material. Medlar bodies, also called copper penny spores or sclerotic

bodies, are the most defining histologic finding and are characterized by groups of brown, thick-walled cells found in giant cells or neutrophil abscesses (Figure 1). Hyphae are not typically found in this type of infection.¹¹

Granulomatous foreign body reactions occur in response to the inoculation of nonhuman material and are characterized by dermal or subcutaneous nodules. Tissue macrophages phagocytize material not removed shortly after implantation, which initiates an inflammatory response that attempts to

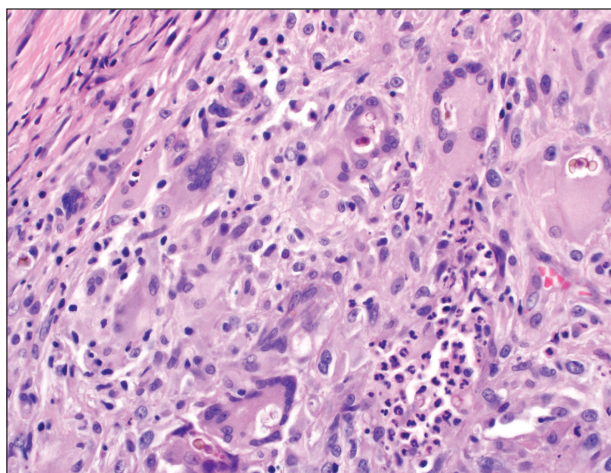


Figure 1. Medlar bodies (copper penny spores) of chromoblastomycosis within several giant cells (H&E, original magnification $\times 40$).

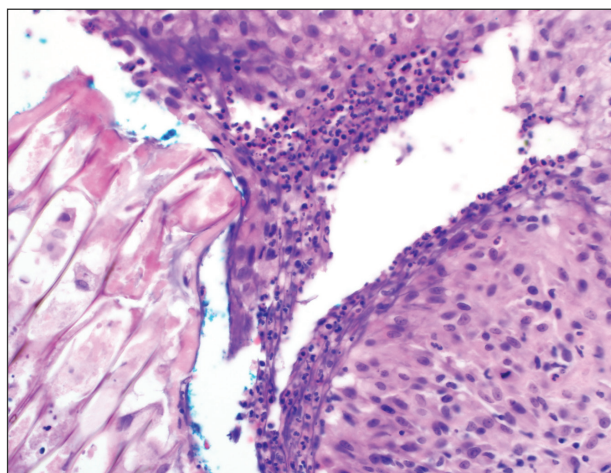


Figure 2. Plant material encased within an abscess. The wall of the abscess contains epithelioid histiocytes with pale-staining eosinophilic cytoplasm admixed with lymphocytes and neutrophils (H&E, original magnification $\times 40$).

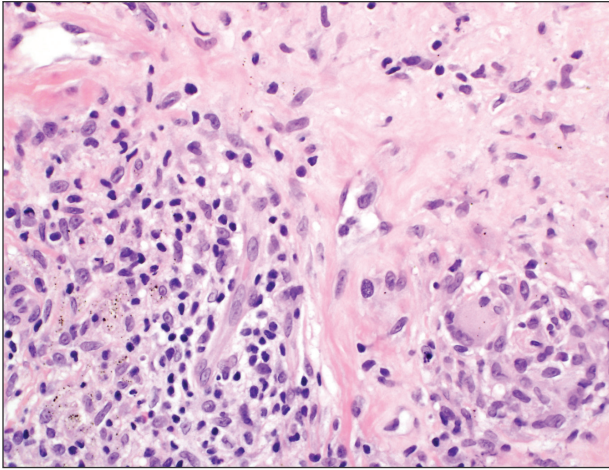


Figure 3. Tattoo reaction with brown or black pigment chiefly localized around vessels, and minimally interspersed between collagen bundles. Lymphohistiocytic infiltrate with plasma cells usually most noticeable periadnexally (H&E, original magnification $\times 40$).

isolate the material from the uninvolved surrounding tissue. Vegetative foreign bodies will cause the most severe inflammatory reactions.¹² Histologically, foreign body granulomas are noncaseating with epithelioid histiocytes surrounding a central foreign body (Figure 2). Occasionally, foreign bodies may be difficult to detect; some are birefringent to polarized light.¹³ Additionally, inoculation injuries can predispose patients to SP, CBM, and other fungal infections.

Tattoos are characterized by exogenous pigment deposition into the dermis.¹⁴ Histologically, tattoos display exogenous pigment deposited throughout the reticular dermis, attached to collagen bundles, within macrophages, or adjacent to adnexal structures (eg, pilosebaceous units or eccrine glands). Although all tattoo pigments can cause adverse reactions, hypersensitivity reactions occur most commonly in response to red pigment, resulting in discrete areas of spongiosis and granulomatous or lichenoid inflammation. Occasionally, hypersensitivity reactions can induce necrobiotic granulomatous reactions characterized by collagen alteration surrounded by palisaded histiocytes and lymphocytes (Figure 3).^{15,16} There also may be focally dense areas of superficial and deep perivascular lymphohistiocytic infiltrate. Clinical context is important, as brown tattoo pigment (Figure 3) can be easily confused with the pigmented hyphae of phaeohyphomycosis, melanin, or hemosiderin.

Subcutaneous hyalohyphomycosis is a nondematiceous (nonpigmented) infection that is caused by hyaline septate hyphal cells.¹⁷ Hyalohyphomycosis

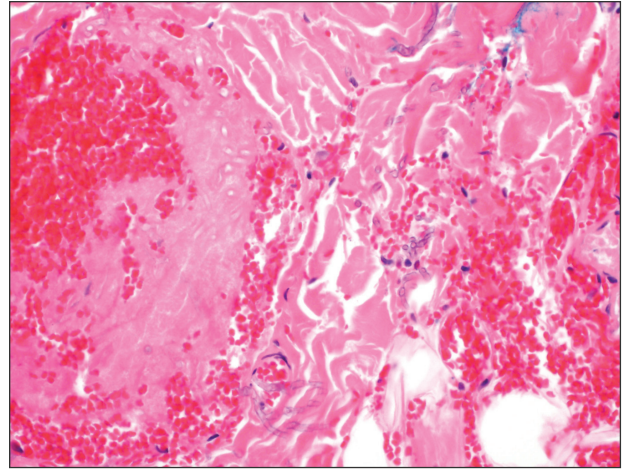


Figure 4. Nonpigmented, branching, septate hyphae (*Aspergillus* species) dispersed throughout the reticular dermis. A fibrinous intravascular clot and angioinvasion are commonplace, leading to epidermal necrosis (H&E, original magnification $\times 40$).

skin lesions can present as painful erythematous nodules that evolve into excoriated pustules.¹⁸ Hyalohyphomycosis most often arises in immunocompromised patients. Causative organisms are ubiquitous soil saprophytes and plant pathogens, most often *Aspergillus* and *Fusarium* species, with a predilection for affecting severely immunocompromised hosts, particularly children.¹⁹ These species tend to be vasculotropic, which can result in tissue necrosis and systemic dissemination. Histologically, fungi are dispersed within tissue. They have a bright, bubbly, mildly basophilic cytoplasm and are nonpigmented, branching, and septate (Figure 4).¹¹

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