Disseminated Cryptococcosis Presenting as Pseudofolliculitis in an AIDS Patient

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We report the case of a 42-year-old man with AIDS and an unusual presentation of disseminated cutaneous cryptococcosis. The eruption was characterized by excoriated papules of the upper body and was initially diagnosed as folliculitis. A pseudofollicular eruption is a rare presentation for disseminated cryptococcosis.

Cryptococcosis is an opportunistic systemic infection caused by the encapsulated yeast, *Cryptococcus neoformans*. *C neoformans* is a saporophytic organism that infects the host primarily through pulmonary inoculation. Although the organism has been isolated from soil and fruit, the more common reservoir for *Cryptococcus* is pigeon excreta. Exposure to soil rich in pigeon droppings or to any location where pigeons congregate increases the likelihood of contact with the organism. Pulmonary infection in the immunocompetent individual is either asymptomatic or evidenced by a mild pulmonary disease that spontaneously resolves after the organism is contained by an activated immune system.[1] Cryptococcosis most commonly disseminates to the central nervous system[1,2] and less frequently to the skin. Approximately 6% to 12% of AIDS patients become infected with *C neoformans*,[3,4] and 89% of these cases present as meningitis.[5] It is the leading cause of meningitis in patients with AIDS.[3] Metastasis to the skin occurs in 10% to 20% of AIDS patients[1,3,6] and has a variable appearance. Cutaneous involvement is usually confined to the head and neck[1,7,8] and is typically described as resembling molluscum contagiosum.[9-11] The following describes an unusual case of cutaneous cryptococcosis that presented as excoriated papules resembling folliculitis.

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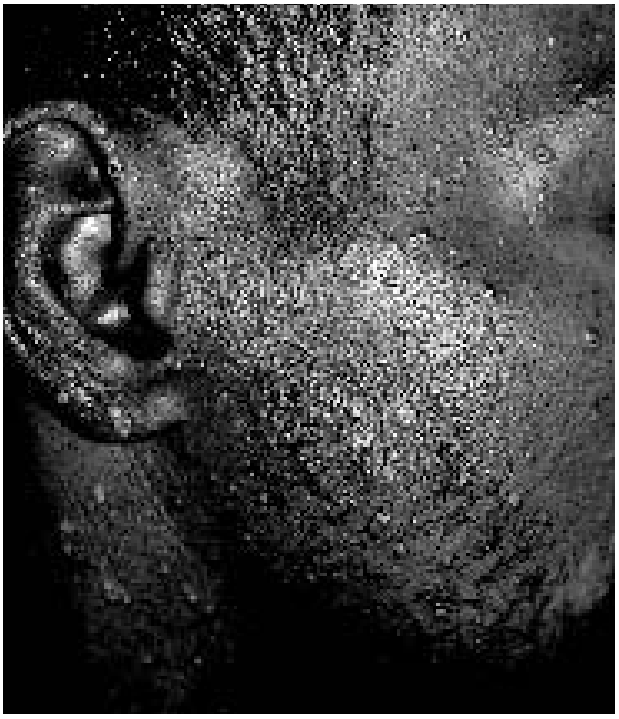

FIGURE 1. Numerous dome-shaped, flesh-colored papules were distributed in a follicular manner across the face.

Case Report

A 42-year-old African American male with AIDS was admitted to internal medicine with diarrhea, and a dermatology consult was obtained for evaluation of a pruritic eruption on his arms, face, and trunk. The same patient had presented to dermatology as an outpatient complaining of pruritis 16 days earlier. At that time the patient exhibited xerosis and areas of excoriation. No other gross skin lesions were apparent and the patient received outpatient therapy for xerosis. At the time of his hospital admission, physical examination revealed a papular eruption involv-

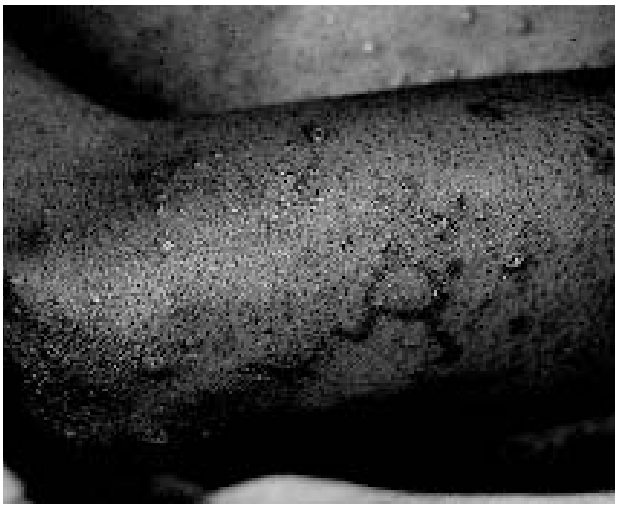

FIGURE 2. Numerous dome-shaped, flesh-colored papules were distributed in a follicular manner across the arms.

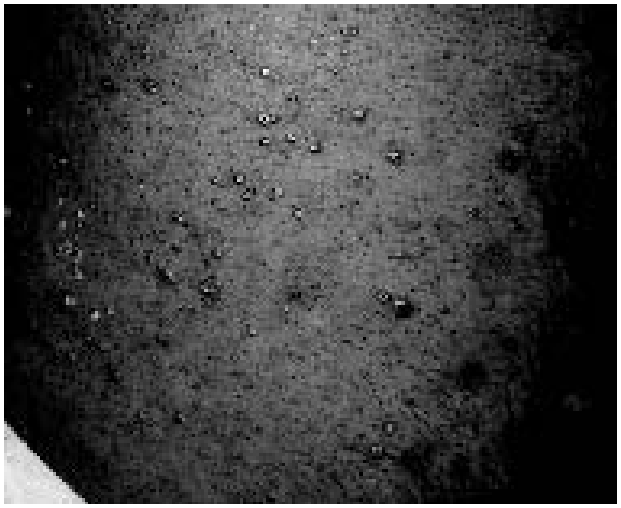

FIGURE 3. Numerous dome-shaped, flesh-colored papules were distributed in a follicular manner across the trunk.

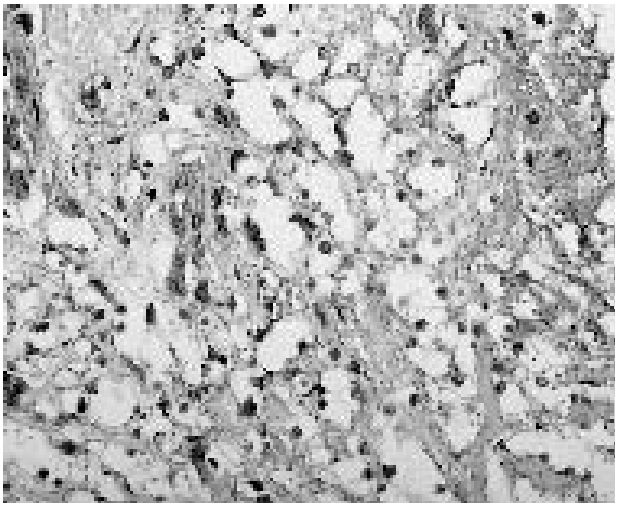

FIGURE 4. In this high-power H&E-stained section, numerous spores with a surrounding clear capsule are present within the dermis. An inflammatory host response is not apparent.

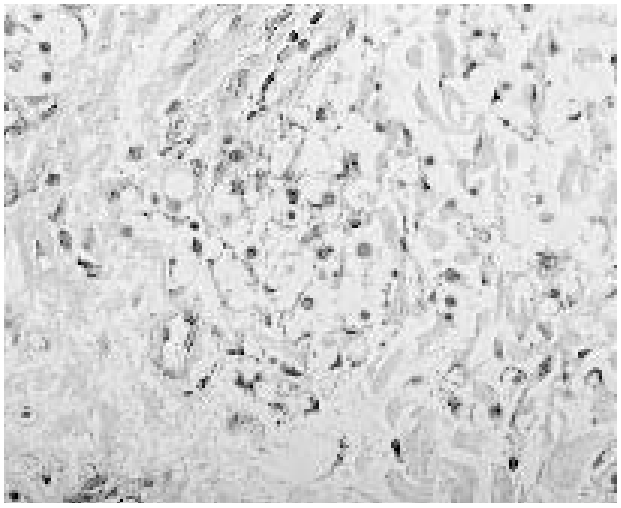

FIGURE 5. In this high-power mucicarmine-stained section, the capsules stained red.

ing his face, neck, arms, and trunk (Figures 1 to 3). There were numerous dome-shaped, flesh-colored papules ranging from 0.5 to 3 mm, many with central crusts or excoriations. The lesions occurred randomly and were most heavily distributed in areas of high follicular density. Additionally, the patient exhibited perifollicular hypopigmentation in these same areas. No pustules, comedones, nodules, or exudates were noted.

Multiple radiologic and laboratory studies were performed. A chest x-ray showed no abnormalities. A sputum culture grew *Mycobacterium avium* complex, and a stool culture was negative for *Salmonella*, *Campylobacter*, and *Yersinia*. Blood cultures grown on acid-fast bacteria medium revealed *Cryptococcus*. The organism was speciated on fungal medium as *C neoformans*. A skin biopsy was taken from a representative lesion[1] on the abdomen and sections were prepared with multiple stains. On hematoxylin- and eosin-stained sections, numerous spores were visible within the dermis, and many of them appeared to be surrounded by a clear capsule. There was no apparent inflammatory host response (Figure 4). On mucicarmine-stained sections, the capsules stained red (Figure 5), and on periodic acid-Schiff–stained sections, the organisms stained red (Figure 6). These findings were consistent with a diagnosis of disseminated cryptococcosis with cutaneous involvement.

Although systemic antifungal therapy was administered, the patient died 3 days after admission.

Comments

The 2 most common fungal infections in HIV patients are candidiasis and cryptococcosis.[12] Although the latter infection is less common, it usually carries a graver prognosis. Cryptococcosis predominantly disseminates to the central nervous system, becoming clinically apparent by symptoms of meningitis. As was the case in our patient, cutaneous dissemination may precede central nervous system symptoms and be the primary expression of the disease.[1] The vast majority of cutaneous cryptococci are a result of hematogenous dissemination. Lesions have the potential to arise anywhere, however, they have been noted to occur most commonly on the head and neck.[1,7,8] Individuals with systemic cryptococcosis may develop genital lesions as a consequence of direct contact with their own infected urine[1,13] and implantation is possible; however, primary cutaneous infections in general are considered extremely rare occurrences.[14,15]

Skin lesions of disseminated cutaneous cryptococcosis have a variable presentation and are frequently confused with a number of different skin diseases. Molluscum contagiosum–like lesions are well documented in disseminated cutaneous cryptococcosis in AIDS patients. They typically appear as flesh-colored or hypopigmented papules with a central umbilication or crust.[9] Lesions may be asymptomatic or painful, solitary or multiple, of variable shape and size, and may exude a liquid or mucinous material.[16,17] Other cutaneous presentations include herpetiform, pustular, cellulitic, purpuric, nodular, acneiform, granulomas, and ulcerative.[18,19] To our knowledge, disseminated cutaneous cryptococcosis presenting as folliculitis has not previously been reported.

The differential diagnosis of folliculitis or a pseudofolliculitis in the immunocompromised patient includes *Staphylococcus aureus* folliculitis (most common), candidiasis, pseudomonal folliculitis ("hot tub" folliculitis), *Pityrosporum orbiculare* folliculitis, HIV-associated eosinophilic folliculitis, molluscum contagiosum, acne vulgaris, other acneiform eruptions, scabies, and demodex folliculitis. Histologic examination of a biopsied skin lesion will often reveal the correct diagnosis.

The hallmark of cutaneous cryptococcosis is the presence of encapsulated yeast, which range in size from 3 to 20 μm[17] and are accompanied by a slight, or absent, inflammatory response on histologic examination. In some lesions, a granulomatous response with necrosis is present. This pattern is characterized by rare yeast with an inconspicuous, or absent, capsule. Special stains are often useful. The capsule is made up of mucopolysaccharides, and mucicarmine stains the capsule red while the background becomes a lime-yellow color. This method is helpful when using tissue sections and usually shows the double contour of the capsule. Mucicarmine is also valuable in making this diagnosis, as it does not stain many other types of fungi.[20] Spores will stain red with the periodic acid-Schiff reaction (while the capsule will not) and will stain black with the methenamine silver stain.[21] In cases in which the capsule is not prominent, cryptococcosis may be confused with blastomycosis because there can be some overlap in size. Blastomycosis is noted for its broad-based budding. Of further help in the differentiation, blastomycosis does not stain with mucicarmine. Isolation and identification of the organism make the definitive diagnosis. Cultures can be grown from blood, sputum, cerebrospinal fluid, pus, or skin lesions. The presence of budding yeast cells and identification of the capsule help to establish the diagnosis. In liquid preparations this is facilitated by India ink, which produces a halo effect around the fungal cells because the capsules resist staining.

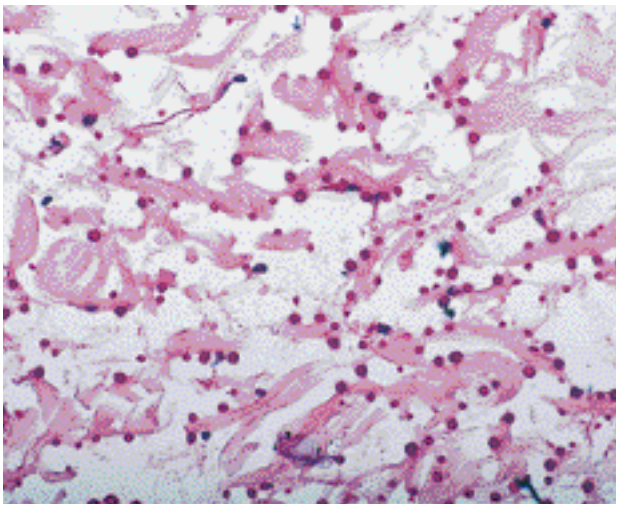

FIGURE 6. In this high-power periodic acid-Schiff–stained section, the organisms stained red.

Once the diagnosis of disseminated cryptococcosis is made, therapy must be instituted quickly. Dromer et al[22] found that disseminated infection at the time of diagnosis was one of several independent predictors of death. Amphotericin B remains the treatment of choice and is administered with or without 5-flucytosine.[23] Other therapeutic options include fluconazole with or without flucytosine,[23] and itraconazole.[24] Additional studies comparing these latter agents with amphotericin B are still needed.

Cryptococcosis is one of many opportunistic infections that may afflict an individual with a com-

promised immune system. The patient population at risk for disseminated cryptococcosis includes those with AIDS, lymphoma, organ transplants,[25] leukemia, sarcoid, and carcinoma,[26] and recipients of prednisone and other immunosuppressants.[16,27] Of this at-risk population, patients with AIDS have probably most increased our awareness that cutaneous manifestations can signal the presence of underlying, often occult diseases. Disseminated cryptococcosis is an important example of a disease with such cutaneous findings, but it may masquerade as multiple unrelated skin disorders. If timely therapy is to be initiated, clinicians must have a high index of suspicion for disseminated cutaneous cryptococcosis in the immunocompromised patient who presents with cutaneous pathology.

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