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An immigrant with acquired immunodeficiency syndrome presenting with a rash: A case report

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Abstract

A 58-year-old woman from Zimbabwe, with a history of untreated human immunodeficiency virus, presented with leonine facies and a diffuse rash. The rash occurred in the context of a 1-year history of constitutional symptoms and cognitive decline. Laboratory investigations confirmed that her human immunodeficiency virus had progressed to acquired immunodeficiency syndrome. Through imaging, tissue biopsies, and polymerase chain reaction, a diagnosis of disseminated histoplasmosis was made. Since there was no history of travel and histoplasmosis is not locally endemic, the patient likely contracted this fungal infection more than 7 years ago, while living in Africa. We speculate that the histoplasmosis remained latent until her immune system began to decline. The work-up and management of this rare cutaneous presentation of a systemic disease, which should be added to the list of "great mimickers" in dermatology, are discussed.

Keywords

Histoplasmosis, infectious diseases, dermatology, human immunodeficiency virus

Case report

A 58-year-old woman with a 30-year history of human immunodeficiency virus (HIV) presented to the emergency department in Calgary, AB, with a mildly pruritic rash. Originally from Zimbabwe, the patient immigrated to Calgary 7 years ago, at which point she stopped her antiretroviral therapy for reasons that were not clear. After immigration, there was no further history of travel. Over the previous year, she and her family had noted weight loss, as well as general functional and cognitive decline. More recently, she developed a 3-month history of a widespread rash accompanied by fevers, night sweats, headaches, cough, and dyspnea. The rash started on her face and progressed cephalocaudally. On admission to hospital, her CD4+ cell count was 1 cell/μL and her HIV viral load was 5.28 $\log_{10}$ copies/mL, confirming that her HIV had progressed to full-blown acquired immunodeficiency syndrome (AIDS).

On examination, her face was diffusely infiltrated with scaly, verrucous, hyperpigmented plaques, producing leonine facies (Figure 1). Examination of her torso and extremities revealed non-blanching, violaceous-to-brown papules and plaques of varying sizes. These were haloed by blanchable, erythematous patches (Figure 2). The clinical differential diagnosis for her rash included a systemic fungal infection, mycobacterial infection, viral exanthem, disseminated leishmaniasis, crusted scabies, cutaneous lymphoma, and Kaposi's sarcoma.

A computed tomography scan revealed calcified granulomata in both upper lobes of her lungs. Bulky mesenteric and retroperitoneal lymphadenopathy was also noted. A magnetic resonance imaging scan of her brain identified a small lesion within her right parietal lobe.

A lesional skin biopsy, processed with hematoxylin and eosin staining, revealed a dermal infiltrate of histiocytes containing numerous ovoid, yeast-like organisms (Figure 3). These organisms were more clearly defined using periodic acid-Schiff, Grocott's methenamine silver (Figure 4), and Giemsa stains, supporting a fungal etiology. A second lesional skin biopsy for culture grew *Histoplasma capsulatum*. Biopsies of her bone marrow and retroperitoneal lymph nodes also grew *H. capsulatum*, as did her blood cultures. Polymerase chain reaction (PCR) testing failed to further subspeciate the fungus, but the morphology and size of the organisms seen on staining were most consistent with *H. capsulatum var. capsulatum*. No acid-fast bacilli were detected in any samples. Additional pertinent negative laboratory

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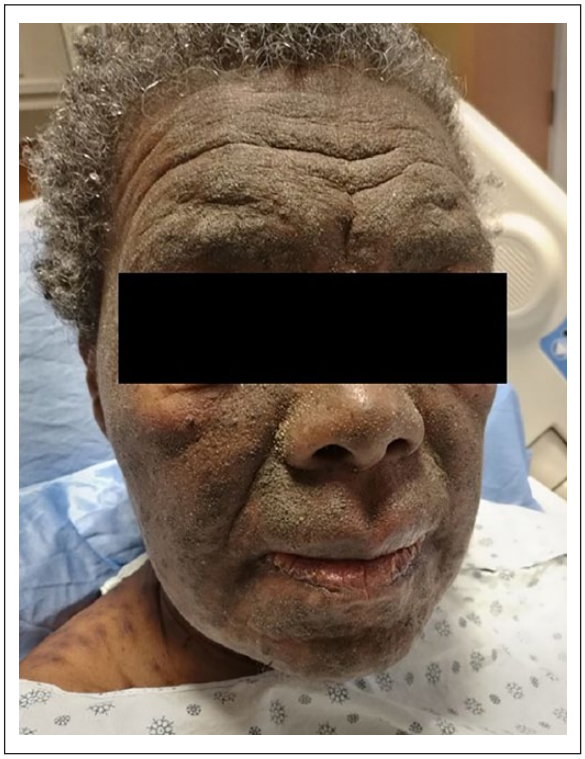

Figure 1. The patient's face was diffusely infiltrated with scaly, verrucous, hyperpigmented thick plaques, producing a leonine facies appearance.

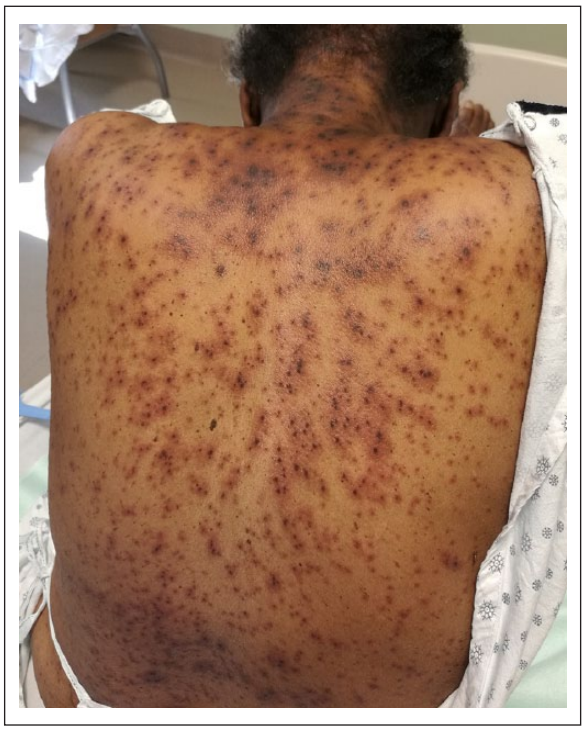

Figure 2. The patient's torso and extremities, showing non-blanching, purpuric, violaceous-brown papules and plaques of varying sizes with blanchable, erythematous haloes.

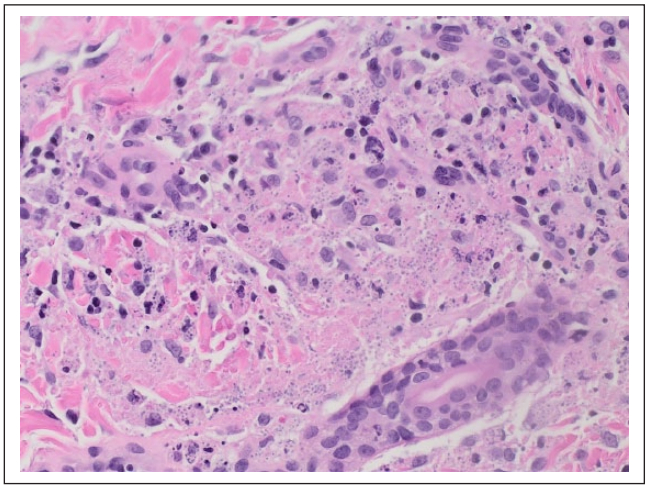

Figure 3. A hematoxylin and eosin–stained section at 40× magnification shows numerous parasitized macrophages containing small, ovoid yeast-like organisms.

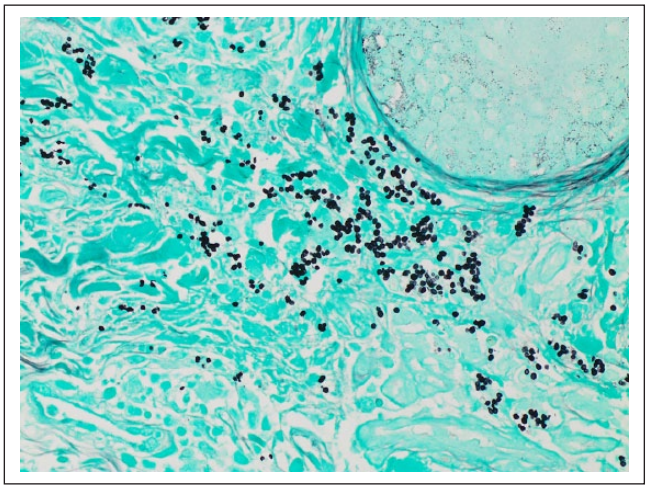

Figure 4. Staining with Grocott's methenamine silver at 40× magnification highlights *Histoplasma capsulatum* within macrophages, allowing differentiation from leishmaniasis which does not stain.

investigations included: *Toxoplasma* IgG, cerebrospinal fluid cryptococcal antigen, hepatitis C antibody, syphilis, *Strongyloides*, and *Schistosoma* serologies. The patient was *Varicella* IgG positive, *Cytomegalovirus* IgG positive, and hepatitis A and B immune. Based on these investigations, a diagnosis of disseminated histoplasmosis was made.

The patient completed a 2-week course of liposomal amphotericin B before transitioning to itraconazole 200 mg PO BID for a planned 12-month course. Serial serum *Histoplasma* antigen titers were used to assess her response to treatment. After initiating antifungal therapy, she was started on highly active antiretroviral therapy and trimethoprim-sulfamethoxazole prophylaxis. At an outpatient follow-up appointment 2 months later, her rash

had significantly improved and she was noted to be afebrile, her headaches had resolved, and she denied any ongoing pulmonary symptoms.

Discussion

Histoplasmosis is the most common respiratory mycosis worldwide.[1] Infections in humans may be caused by *H. capsulatum var. capsulatum*, causing classical histoplasmosis, or *H. capsulatum var. duboisii*, causing African histoplasmosis. Although *H. capsulatum var. capsulatum* is often cited as being endemic in the Mississippi and Ohio River Valleys in the United States, as well as in many countries of Central and South America,[1] it is also endemic to many parts of Africa, including Zimbabwe.[2] In Canada, *H. capsulatum var. capsulatum* (classical histoplasmosis) is endemic in the St. Lawrence Valley, particularly near Montreal. Locally acquired infections have also been documented in Northern Alberta (not Calgary), Southern Manitoba, Southern Ontario, and Nova Scotia.[3–6] Although *H. capsulatum var. capsulatum* (classical histoplasmosis) is endemic in many parts of Africa, *H. capsulatum var. duboisii* (African histoplasmosis) is also endemic in West and Central Africa, as well as Madagascar.[7]

Histoplasmosis is commonly transmitted through the inhalation of fungal microconidia from soil contaminated with infected bird or bat guano.[8] Cutaneous disease can result from hematogenous dissemination, and rarely from implantation directly into the skin.[1] Both classical and African histoplasmosis can reactivate from latent granulomata decades after the primary infection.[9,10] In 95% of cases, acute infections are asymptomatic or mild.[1] Our patient likely contracted mild pulmonary infection with *H. capsulatum* while living in Africa. This was felt to be the most likely source since a detailed history failed to identify any history of travel, or possible sources of infection, since moving to Canada. In addition, exposure to *H. capsulatum* in Calgary, Alberta, an urban setting, would be unlikely. We suspect that this patient had a latent infection for many years, which reactivated, and became disseminated, when her CD4+ count dropped to 1 cell/μL after discontinuing her antiretroviral regimen.

Classical histoplasmosis commonly involves the lungs, lymph nodes, liver, spleen, adrenal glands, central nervous system, and bone marrow,[10] but seldom the skin.[9,10] Cutaneous involvement occurs in only 6% of disseminated cases[7] and 10%–30% of patients infected with HIV.[1,11] Hematogenous spread, and resultant cutaneous manifestations, is thought to be more likely when the CD4+ cell count drops below 200 cells/μL.[1] When either species of *Histoplasma* infects patients with HIV, the mortality rate is over 50%.[11]

Cutaneous histoplasmosis is sometimes referred to as "fungal syphilis" due to its protean presentations, including macules, papules, plaques, nodules, erosions, and ulcers. Further reported morphologies include erythematous, purpuric, hyperpigmented, crusted, keratotic, molluscum like, and acneiform.[9] Presentations mimicking dermatitis, cellulitis, abscesses, panniculitis, and pyoderma gangrenosum have also been reported.[1] Finally, hypersensitivity reactions, in which no organisms can be demonstrated within the cutaneous lesions, have also been reported, including polymorphous erythema, erythema nodosum, and exfoliative erythroderma.[1]

The gold standard for diagnosis consists of demonstrating organisms on histopathology or in culture. Antigen detection by enzyme immunoassay can be highly sensitive, but results must be interpreted carefully due to cross-reactivity with other fungi. Antibodies against *Histoplasma* start to appear 4–8 weeks after infection, but may not be detectable in patients with impaired humoral immunity. Other less common diagnostic techniques include PCR, fluorescence in situ hybridization (FISH),[10] and histoplasmin skin testing.[1]

Although asymptomatic pulmonary histoplasmosis does not require therapy, disseminated histoplasmosis must always be treated. An initial 2-week intravenous course of liposomal amphotericin B should be followed by oral itraconazole for a minimum of 12 months. Indefinite treatment may be necessary in patients who have irreversible immunosuppression. Patients with HIV should be treated with antiretroviral therapy to a target of a CD4+ count greater than 150 cells/μL and a viral load of less than 50 copies/mL.[10]

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Informed consent

Informed consent was obtained to publish the patient's information and photographs.

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