Verrucous Lesions Caused by Disseminated Coccidioidomycosis

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Abstract
This report describes the case of a young black man in whom disseminated Coccidioidomycosis produced a visually striking facial skin condition. The recognition of the cutaneous signs of diseases that primarily affect the pulmonary system may assist the clinician in diagnosis. Findings on the skin are very helpful in exposing an underlying systemic condition that can be particularly life threatening, and early detection and treatment may impact the course of a patient’s life.

Case Presentation
A 34-year-old African American man presented with one-month history of fatigue, diminished appetite, weight loss of 20 lbs, fevers, and cough with purulent sputum production. Two-weeks prior to presentation to the hospital, he developed non-painful and non-pruritic skin lesions over his forehead and nose. The patient visited California almost 11 months before the appearance of his clinical manifestations. Examination revealed a high-grade fever of 105°F, hypoxemia with oxygen saturation of 87% without supplemental oxygen, and tachycardia of 117 beats per minute. The patient was confused, with slow speech, but neurological examination was non focal. His lung exam revealed diffuse bilateral wheezes. The skin lesions had progressed to verrucous nodular lesions on his face (forehead and nose) (Figure 1). Laboratory testing revealed a white blood cell count of 6500 cells/mm³ (10% eosinophils), LDH levels of 636 IU/L, ALT of 102 IU/L, creatinine of 2.3 mg/dL and BUN of 60 mg/dL. A computerized tomography scan demonstrated innumerable military nodules with associated interstitial thickening with hilar and sub clavian lymphadenopathies (Figure 2). Magnetic resonance of the brain showed advanced cortical atrophy. Bronchoscopy revealed multiple necrotic lesions at the main carina and its bifurcation. Serum Coccidioides, Bastomyces and Histoplasma serologies, urine Histoplasma antigen assay and tuberculous skin tests were negative.

Diagnosis
Spherules of Coccidioides were identified on a skin and transbronchial biopsy samples, and tissue cultures grew Coccidioides immitis after 4 days (Figures 3A and B). The fungus was also isolated from the blood cultures. Disseminated Coccidioidomycosis was diagnosed.

Discussion
Coccidioidomycosis is well known for its ability to masquerade as other infectious and non-infectious disease processes. Disseminated cutaneous coccidioidomycosis should be considered in the differential diagnosis of any chronic nodular or verrucous skin lesions, especially when associated with pulmonary manifestations.

Coccidioides infection is caused by the highly infectious dimorphic fungi of the genus Coccidioides (C. immitis and C. posadasii) [1]. Coccidioides species are endemic to desert regions of the Southwestern United States, northern Mexico, and scattered areas in Central America and South America [2]. However, infections have been reported outside these endemic areas [3]. In fact, travel plays a major role in the diagnosis of different fungal infections and even a short exposure history should not be ignored. The use of potent antiretroviral therapy (ART), which results in immune restoration and increased CD4 cell count, appears to have a marked effect on both the incidence and the severity of symptomatic coccidioidomycosis [4,5]. In one study, almost one half of the cases of coccidioidomycosis in AIDS patients were from non-endemic areas of the United States [6]. Thus, reactivation of latent infection should be suspected in patients diagnosed with coccidioidomycosis who have not recently been in the area of endemcity [6,7,8]. Coccidioides infection is always acquired...
by inhalation of soil or dust containing the fungus. Within the lung, an arthroconidium changes from a barrel-shaped cell to a spherical structure called spherule. Enlarging spherules produce internal septations, and within each of the resulting sub compartments individual cells (endospores) evolve. After several days, mature spherules rupture releasing endospores into the infected tissues; each endospore can produce another spherule [1]. Coccidioidomycosis commonly spreads from the thoracic cavity to other parts of the body and can cause lymphatic, meningeal, mucocutaneous, and musculoskeletal involvement [9]. Cutaneous presentations may be divided into reactive or organism-specific reactions. Patients with primary pulmonary infection may present with reactive erythema nodosum, erythema multiforme, sweet’s syndrome, or a generalized morbilliform rash. Organism-specific cutaneous involvement is generally secondary to hematogenously disseminated disease but can rarely represent primary disease from direct inoculation [10].

Disseminated cutaneous lesions are typically localized to the head and neck. These lesions vary widely in appearance from papules, nodules, plaques, ulcerations, and abscesses to lesions that imitate T-cell lymphoma mycosis fungoides [10]. Primary cutaneous infections are often self-limited and heal within weeks [11]. They present as ulcerated nodules at the site of inoculation with associated lymphadenopathy with further development of nodules along the draining lymphatic tracts. Diagnostic criteria to distinguish primary cutaneous disease include an absence of pulmonary involvement, evidence of traumatic inoculation of skin site, incubation of 1–3 weeks before visible lesion, and low level complement fixation titers [11].

Management

Given the acuity, extent and severity of our patient’s disease, therapy was promptly initiated with systemic amphotericin B deoxycholate and fluconazole. Disseminated coccidioidomycosis may progress to severe disease and a potentially fatal outcome, thus warranting timely recognition and accurate management. The Infectious Disease Society of America published in 2005 detailed guidelines on the treatment of systemic coccidioidomycosis [3]. Symptomatic disseminated disease requires immediate treatment with Amphotericin B or an azole antifungal. After initial treatment of the disseminated infection, maintenance therapy for 1 to 2 years or life-long therapy may be required. Because the critical factor in the control of coccidioidomycosis is cellular immune function, effective ART was instituted concomitantly with initiation of antifungal therapy. Immune response inflammatory syndrome (IRIS) has been observed in HIV-infected patients with a variety of underlying infections as they respond to potent antiretroviral therapy [12].

Fortunately, our patient demonstrated a fast response to medical therapy. Respiratory, cutaneous, and systemic manifestations as well as radiographic abnormalities had markedly improved. Findings on the skin were very helpful in exposing an underlying life threatening systemic condition, leading to early detection and treatment that had positively impacted the course of our patient’s life.

Authorship Statement

All work in this manuscript is original. All authors had access to the data and played a role in writing the manuscript and each accepts responsibility for the content.

References


