

Disseminated Cutaneous Coccidioidomycosis Masquerading as Lupus Pernio

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Coccidioides immitis, a pathogenic fungus endemic to arid regions, is the etiologic agent of cutaneous coccidioidomycosis. Primary cutaneous coccidioidomycosis is rare. The majority of cutaneous coccidioidomycosis infections are caused by dissemination of the fungus from the lungs to the skin. Diagnosing cutaneous coccidioidomycosis often can be difficult because it can mimic a variety of other clinical conditions. We present a case of a 45-year-old man presenting with cutaneous coccidioidomycosis on the tip of his nose. This patient had pulmonary symptoms in addition to his cutaneous findings, leading to a diagnosis of disseminated coccidioidomycosis.

Cutis. 2010;86:25-28.

Case Report

A 45-year-old black man presented to our dermatology service with a slightly tender, nonhealing plaque of 2 months' duration on the tip of his nose. The patient's history included several weeks of systemic and pulmonary symptoms, including anorexia, pleuritic chest pain, dyspnea, and intermittent cough, for which he had previously seen a pulmonologist. A chest radiograph and computed tomography scan revealed pleural effusions as well as hilar and mediastinal lymphadenopathy. Bronchoscopy revealed

granulomatous inflammation suggestive of sarcoidosis in the transbronchial biopsy. Fungal and acid-fast bacillus stains were negative for fungal and mycobacterial organisms, respectively. Additionally, testing for *Coccidioides immitis* antibody was positive. The patient was subsequently referred to our dermatology clinic for further investigation of his skin lesion and to potentially clarify the etiology of his pulmonary symptoms.

Physical examination of the skin revealed a 1×1-cm violaceous plaque with multiple erosions and punctate satellite lesions on the right tip of the nose (Figure 1). Both cutaneous coccidioidomycosis and sarcoidosis (lupus pernio) were considered as possible etiologies. Other differential diagnoses included mycobacterial and other deep fungal infections, squamous cell carcinoma, granuloma faciale, Kaposi sarcoma, and herpes simplex virus. A 3-mm punch biopsy of the plaque demonstrated pseudoepitheliomatous hyperplasia overlying granulomatous inflammation that contained scattered thick-walled spherules with endospores that were morphologically consistent with *C immitis* (Figures 2 and 3). An additional specimen of a representative lesion for tissue culture grew *C immitis*.

The patient was started on fluconazole 400 mg daily for disseminated cutaneous coccidioidomycosis in coordination with his pulmonologist. His 3-month follow-up revealed complete resolution of his skin lesion as well as systemic and pulmonary symptoms (Figure 4).

Comment

Coccidioides immitis is a dimorphic fungus endemic in the soil of the southwestern United States and in parts of Mexico and Latin America.¹⁻⁵ The population growth in endemic areas of the United States as well as increased travel to and from these areas has made coccidioidomycosis a growing concern nationwide.⁵⁻¹⁰

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The opinions or assertions contained in this article are the private views of the authors and are not to be construed as reflecting the views of the US Army, US Air Force, or the US Department of Defense.

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Figure 1. Disseminated coccidioidomycosis of the nose resembling lupus pernio.

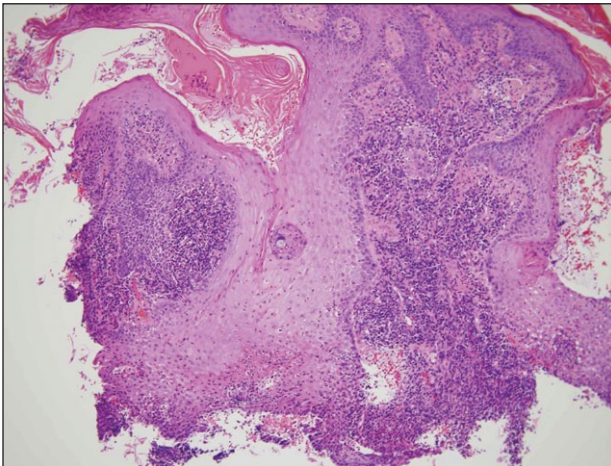


Figure 2. Pseudoepitheliomatous hyperplasia with spherules consistent with *Coccidioides immitis* (H&E, original magnification $\times 10$).

The primary mechanism of infectivity is respiration of airborne dust harboring the 3- to 5- μm arthroconidia that are released into the soil by the mold form of *C immitis*. Once these arthroconidia are inhaled into the lungs, they undergo morphologic change into 20- to 100- μm round spherules that internally divide to form hundreds of endospores. These endospores are released upon rupture of the spherule's wall and have the potential to develop into more spherules that repeat the life cycle of *C immitis*.^{6,8-12}

Coccidioidomycosis results in symptomatic infection that is brought to the attention of healthcare

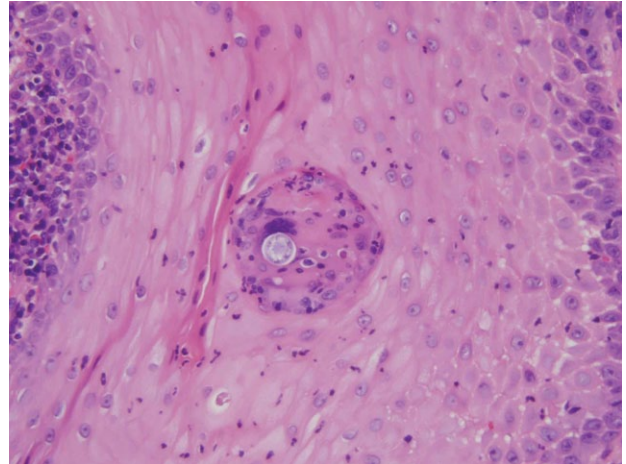


Figure 3. *Coccidioides immitis* spherule within a granuloma (H&E, original magnification $\times 40$).

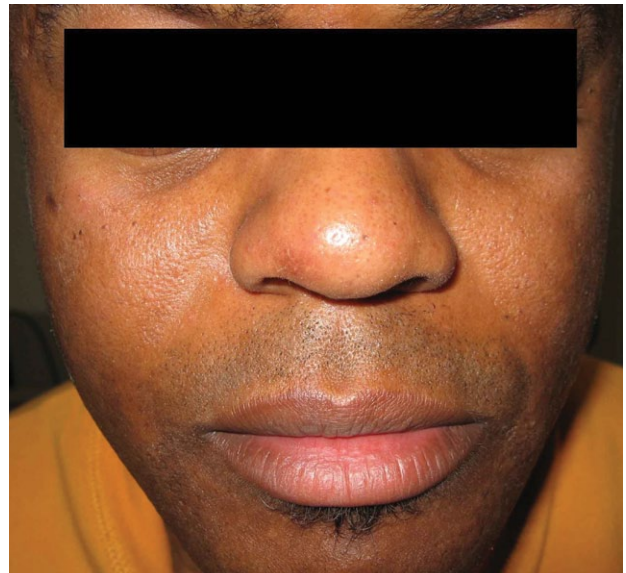


Figure 4. Patient after 3 months of fluconazole therapy.

providers in approximately one-third of cases, with symptoms ranging from mild sore throat, fever, fatigue, and headache, to cough, chest pain, dyspnea, hemoptysis, and arthralgia.^{3,7-9} In most patients with symptomatic primary pulmonary coccidioidomycosis, their infections are self-resolving without therapy within 3 weeks to 3 months with the subsequent development of cell-mediated immunity.^{1,6,8,9} In 0.5% of all infections to 7% of those ill enough to initially warrant serologic studies, the organism disseminates from the lungs to other sites.^{1,5,8,9,13} Although any organ may be involved, the most common extrapulmonary sites are the skin, bones, joints, subcutaneous tissues, lymph nodes, and meninges. Dissemination to only one site is not uncommon.^{1,7,8,13} Risk factors for dissemination

include male gender; certain racial groups, especially black individuals and Filipinos; pregnant women in the third trimester; and immunodeficiency.^{2,3,5-7,10,12}

Skin lesions are common manifestations of disseminated coccidioidomycosis.^{4,10,14-17} In a study conducted by Quimby et al,¹³ patients demonstrated skin lesions anywhere from 1 month to 6 years after initial coccidioidomycosis infection; however, skin infection after 1 year is uncommon with the exception of an immunocompromised host.⁵ Erythema nodosum is the most characteristic reactive cutaneous manifestation of coccidioidomycosis and usually is associated with a favorable prognosis. Other reactive skin manifestations include erythema multiforme, Sweet syndrome, and interstitial granulomatous dermatitis.^{7,8,10,12,18,19} The most common clinical manifestation of disseminated cutaneous coccidioidomycosis is a papule, nodule, or plaque that appears and then enlarges on the central face, most commonly the nasolabial fold.^{7,13,20} Nevertheless, the variable morphology of coccidioidomycosis skin lesions has earned *C immitis* recognition as one of the "great imitators."^{7,10,13,21} Pustules, sinuses, ulcers, nodules, and abscesses are other manifestations that have been described.^{6,7,13,15,20,22,23} Differential diagnoses include sarcoidosis, leprosy, mycosis fungoides, actinic keratosis, squamous cell carcinoma, furuncles, verruca vulgaris, pyoderma plaques, tuberculosis, and keratoacanthoma.^{7,13,15,20,22}

Biopsy and tissue cultures of skin lesions often are necessary to make a correct diagnosis of disseminated cutaneous coccidioidomycosis.^{4,7,13} Biopsy with hematoxylin and eosin stain of suspicious lesions often demonstrates the spherules in a background of pseudoepitheliomatous hyperplasia and granulomatous inflammation with multinucleated giant cells.^{4,7,9,15,20,24} Periodic acid-Schiff or Gomori methenamine-silver stains are occasionally helpful to identify the organism.^{7,11} Tissue cultures are the gold standard for organism identification and often are obtained to definitively establish the diagnosis. The fungus rapidly grows and appears white on standard culture media.^{1,2,9} Other diagnostic adjuncts include chest radiograph and cytologic examination of bronchial washings to identify pulmonary involvement, serologic testing for *Coccidioides* antibodies and antibody titers, and skin testing to assess for coccidioidin sensitivity. In disseminated disease, IgG coccidioidal antibody concentration and complement fixation test antibody titers typically will be high.^{7,9,14,24,25} These antibodies can be serially followed to assess a patient's response to treatment, whereby a downward trend in titers would indicate an appropriate response.^{1,7,24}

Disseminated cutaneous coccidioidomycosis warrants treatment with systemic antifungal agents. Amphotericin B was the treatment of choice for many years prior to the development of less toxic and easier to use oral azoles.^{1,8,11-13,20,24,26} Fluconazole at a dosage of 400 mg daily or more is perhaps the most commonly used azole due to its favorable pharmacokinetics. Response rates of azoles, including ketoconazole, itraconazole, and fluconazole, are 60% to 70%. Treatment typically is extended for 6 months to a year or more.^{1,8,11,12} Relapse rates of disseminated coccidioidomycosis following discontinuation of therapy are notable,²⁷ with recurrence rates as high as 30% reported after itraconazole therapy.¹¹ Relapse is attributed to the fungistatic rather than fungicidal properties of these drugs and is more common in immunocompromised individuals.^{1,8,11,12} Patients with immunodeficiencies have been placed on azoles indefinitely.^{8,12}

Conclusion

We report a case of disseminated coccidioidomycosis presenting with a single cutaneous lesion on the tip of the nose that developed in coordination with pulmonary symptoms. Disseminated cutaneous coccidioidomycosis should be considered in the differential diagnosis of any chronic nodular or verrucous skin lesion associated with pulmonary symptoms so that appropriate diagnostic testing and treatment may be initiated.

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