

Coccidioidomycosis Involving Lungs and Skin: A Mimicker of Metastatic Disease

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Abstract: Coccidioidomycosis is the major systemic mycoses, considered to be 1 of the most infectious fungal diseases. In symptomatic patients, the most common manifestation is pulmonary disease, but many other organs can be affected. Disseminated disease occurs in 1%–5% of all patients affected by coccidioidomycosis and can affect any organ, with the skin, central nervous system, and musculoskeletal system being reported as the most prevalent. Here, we report a 42-year-old male farmer from the west Texas who presented with an approximately 2-month history of progressive shortness of breath and dyspnea on exertion, weight loss, and night sweats. He was treated with various antibiotics for possible upper respiratory tract infection without symptomatic improvement. Computed tomography of the chest revealed numerous subcentimeter noncalcified pulmonary nodules scattered throughout both lungs with extensive mediastinal and bilateral hilar lymphadenopathy. The patient was referred to our hospital for further evaluation of suspected metastatic lung disease. Physical examination revealed an erythematous 1.2 cm nodule on his left medial eyebrow. Skin biopsy of the lesion revealed prominent squamous epithelial hyperplasia with basal keratinocytic atypia and associated mixed inflammatory infiltrate and scattered large thick-walled spherules containing variable-sized endospores, predominantly within the multinucleated giant cells. Special stain Periodic acid–Schiff tissue culture studies confirmed these to be *Coccidioides immitis*. After appropriate treatment with antifungal therapy for 5.5 months, his symptoms have improved with complete disappearance of lung nodules and a partially cavitated (1.1 × 1.1 cm) lesion in the left upper lung confirmed by follow-up chest computed tomography. With this report, the authors highlight disseminated coccidioidomycosis, a great mimicker of metastatic lung disease, which was diagnosed by skin biopsy, to ensure its prompt recognition and appropriate antifungal therapy.

Key Words: coccidioidomycosis, metastatic neoplasm

(*Am J Dermatopathol* 2017;0:1–3)

INTRODUCTION

Coccidioidomycosis is a disease caused by the spores of the fungus *Coccidioides*. The most common subtype of this

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The authors declare no conflicts of interest.

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family of fungus is the *Coccidioides immitis*, which is often found in desert regions.^{1,2} It is also known as coccidiosis, desert rheumatism, San Joaquin valley fever, or valley fever. *Coccidioides* sp. are found in the soil and dirt of places with minimal rain or high temperatures during the summer, such as Mexico, Central and South America, and South of the United States.^{3,4}

This infection is caused by 2 virtually identical species of *C. immitis* or *C. posadasii*. *C. immitis* is a dimorphic, saprophytic fungus that grows as a mycelium in the soil and produces a spherule form in the host organism. The mode of transmission occurs when airborne arthroconidia from polluted soil are inhaled in endemic areas, usually because of occupational and recreational activities.⁵

The people who are most vulnerable, as in other fungal infections, are immunocompromised individuals including pregnant women, HIV/AIDS patients, and patients with a history of diabetes and transplant, to mention a few.⁶ In a competent population that is affected, they are less likely to present with any symptoms, and are only identified if a coccidioidin skin test is performed; however, when the person affected is immunocompromised, the disease can present as an acute, chronic or disseminated episode. It is important to take into account that the incubation period is usually 7–21 days after exposure.^{7–10}

CASE REPORT

A 42-year-old male patient with type 2 diabetes mellitus and hyperlipidemia, a farmer from West Texas, presented to our Cancer Center with an approximately 2-month history of progressive shortness of breath and dyspnea on exertion, weight loss, and night sweats. He reported that he had used his son’s nebulizer machine and received antibiotic therapy with azithromycin from his primary care physician for an upper respiratory tract infection without any improvement. During this time period, he had traveled to Colorado and Mexico, where his symptoms worsened, and his primary care physician treated him with Bactrim and ciprofloxacin, although the patient stated that the symptoms were already present before both of those trips.

A chest computed tomography (CT) was performed, which showed an infiltrate with consolidation or pneumonia in the lingula. Also, there were innumerable, small subcentimeter, noncalcified bilateral pulmonary nodules with extensive mediastinal and bilateral hilar lymphadenopathy (Fig. 1A). The differential diagnosis included metastatic pulmonary disease and he was transferred to our institute for further evaluation. At initial evaluation, the dermatology team identified a macular lesion on his left eye brow and biopsied it with the clinical impression of squamous cell carcinoma.

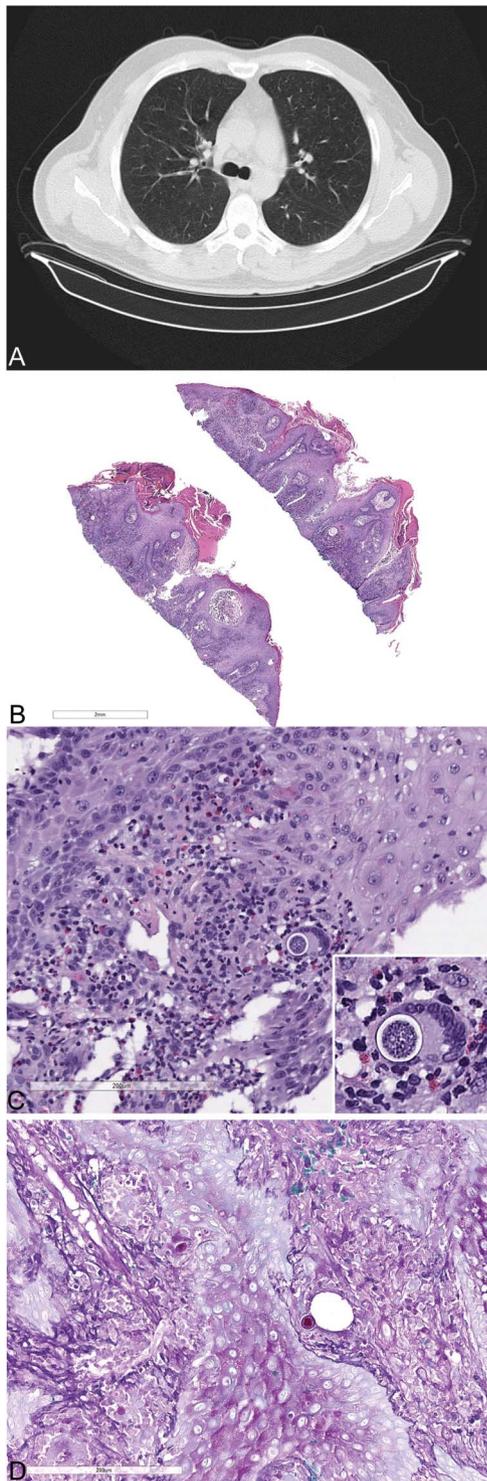


FIGURE 1. A, Computed tomography of the patient’s chest that revealed multiple bilateral nodules and hilar lymphadenopathy. B–C, Histopathology of coccidioidomycosis. B, Skin with abundant acute inflammatory infiltrate and epidermal hyperkeratosis [hematoxylin-eosin (H&E), ×20] and C, *Coccidioides* spherules (H&E, ×200) with endospores, one of them is inside a multinucleated giant cell (high power view, ×400-inset). D, *Coccidioides* organisms highlighted by Periodic acid–Schiff stain (×200).

The histopathology sections from the left eye brow showed skin with squamous epithelium revealing predominantly basal layer cytologic atypia and underlying dense acute and chronic inflammatory infiltrate including multinucleated giant cells (Figs. 1B, C). There were scattered, large thick-walled spherules containing variable-sized daughter cysts/endospores predominantly within the multinucleated giant cells (Fig. 1C; highlighted with Periodic acid–Schiff, Fig. 1D). The histopathologic features were consistent with coccidioidomycosis.

Because of the findings in the bilateral lungs by chest computed tomography, the patient was initially evaluated for metastatic pulmonary lung disease and a bronchoscopic alveolar lavage was performed. During the physical examination, an erythematous nodule of 1.2 cm was identified on the left medial eyebrow area (Fig. 2). The bronchoscopy with the bronchoscopic alveolar lavage did not grow any fungus. Fluconazole was prescribed with a good response.

A tissue culture study taken from the patient’s eye brow lesion isolated a fungal mold, which was confirmed to be *Coccidioides* species; there was no growth of acid fast bacteria. A polymerase chain reaction study was negative with a panel for different viruses. Antibody test for IgG and IgM of *Coccidioides* sp. was sent out and both came back positive. A polymerase chain reaction study for *Mycobacterium tuberculosis* complex was negative. Antibody analysis against *Histoplasma* and *Cryptococcus* was also negative.

DISCUSSION

The patient was initially suspected to have a metastatic neoplasm and referred to our Cancer Center because of significant weight loss, night sweats, and cough for a 2 month-period. After further evaluation in our cancer center, the correct diagnosis of a disseminated coccidioidomycosis was established and he was treated properly.

The antibodies for IgG and IgM against *Coccidioides* were positive in our patient, supporting the above diagnosis. IgM may be detectable within 2 weeks after the onset of symptoms and may stay positive for more than 6 months. However, the presence of IgG antibody may suggest an active or a recent asymptomatic infection with *C. immitis*; however, antibodies may persist after the infection has resolved.^{11,12}

This case highlights the potential pitfall of a metastatic disease, which can lead to misdiagnosis and treatment with an expensive and aggressive surgical/chemo/radiation therapy as well as psychological trauma to the patient.^{13–15}



FIGURE 2. Representative picture of erythematous lesion on his left eyebrow.

In our case, coccidioidomycosis debuted as a disseminated entity, affecting lungs, skin, and lymph nodes. Although radiographic studies are helpful because the results may still overlap or coexist within neoplasms and infectious diseases, correlation with clinical, histopathological, and tissue culture study is essential to establish the correct diagnosis.^{16–18}

In conclusion, we describe an unusual case presentation of a disseminated coccidioidomycosis in lungs and skin that was initially suspected to be a metastatic neoplasm. Biopsy of a skin lesion led to the correct diagnosis. Awareness of this disseminated infectious disease, similar to our case, is very important for treating clinicians and pathologists to avoid unnecessary treatments, especially in the current era of medicine and health care.

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