Disseminated Coccidioidomycosis in an Immunocompetent Person Living in New York City

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ABSTRACT *Coccidioidomycosis is a disease caused by Coccidioides immitis, a soil-inhabiting fungus endemic to the desert climate of the southwestern United States and Central and South America. We report a case of disseminated coccidioidomycosis in a previously healthy person living in New York City, who was initially thought to have tuberculosis. The incidence of coccidioidomycosis has been increasing in both endemic and nonendemic areas, but diagnosis is often delayed or missed in nonendemic areas, resulting in extensive and unnecessary medical workup for other diseases or progression to serious disease. Therefore, clinicians should increase their awareness and consideration of this disease in patients with chronic systemic illness.*

KEYWORDS *Coccidioidomycosis, Diagnosis, Disseminated.*

INTRODUCTION

Coccidioidomycosis is a systemic fungal infection caused by *Coccidioides immitis*. The disease was originally described by pathologists Wernicke and Posadas in South America in 1892^{1,2} and was first reported in the United States in 1894.³ There is a wide spectrum of clinical manifestations for primary coccidioidal infection, ranging from totally asymptomatic to a mild influenza-like illness to pneumonia. Although otherwise healthy people are susceptible to infection, the resulting syndrome is usually inconsequential and resolves spontaneously. However, in immunocompromised people, those with intense dust exposure, pregnant women, and certain ethnic groups, infection can progress to chronic pneumonia or disseminated disease.⁴⁻⁷ Most cases of disseminated coccidioidomycosis reported in the literature are described in people with intense dust exposure or immune system compromise.^{8,9} We report a case of disseminated coccidioidomycosis in an immunocompetent person living in New York City with no recollection of significant dust exposure.

CASE REPORT

A 34-year-old previously healthy Indonesian man presented the Emergency Department with a 1-month history of a pruritic rash on his head, neck, and upper extremities. He also reported daily episodic fevers and chills, dyspnea on exertion,

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and a minimally productive cough. He denied history of tuberculosis, hemoptysis, significant weight loss, night sweats, chest pain, arthralgias, or headache, as well as any recent travel. He also denied any risk factors commonly associated with HIV infection. Since emigrating from Indonesia 2 years earlier, he had been living with his uncle and sister, neither of who had a similar rash or illness.

On presentation to the hospital his vital signs were blood pressure, 100/58 mm Hg; pulse, 118 beats per minute; respiratory rate, 21 breaths per minute; temperature, 38.6°C; and pulse oximetry, 98% on room air. Physical examination of his skin revealed several 1–2 cm, nodular, excoriated, mildly tender lesions over the face, neck, shoulder, arm, and scalp (Fig. 1). There was significant left sided supraclavicular and superior cervical lymphadenopathy. His lungs were clear to auscultation bilaterally, with no appreciable wheezes, rales, or rhonchi, and the remainder of the physical examination was unremarkable.

Laboratory studies revealed a white blood cell count of 12.4 thousand cells/mm³ with a differential of 63% neutrophils, 13% lymphocytes, 10% monocytes, 13% eosinophils, and 1% basophils, hematocrit 34.3%, and platelets 403,000/mm³. Standard blood chemistries and liver function tests were all within normal range, except for an alkaline phosphatase of 150 IU/L.

Chest radiographs revealed a small left pleural effusion with hilar adenopathy (Fig. 2). The patient was kept in respiratory isolation and admitted to the medical service with the presumptive diagnosis of disseminated tuberculosis. He underwent a diagnostic thoracentesis, which was negative for malignant cells, acid fast bacilli,

FIGURE 1. Nodular, erythematous, crusted lesions over the face, along with cervical lymphadenopathy.

FIGURE 2. PA and lateral chest radiographs reveal hilar adenopathy and a small left sided pleural effusion.

and other organisms on gram stain. On hospital day 6, a biopsy of the skin lesions showed periodic acid-Schiff (PAS) staining for *C. immitis* (Fig. 3). Upon more rigorous and focused questioning the patient admitted to traveling to Southern California for a brief visit 1 year earlier. He denied any previous history of unusual illnesses and was unable to recall any extensive dust exposure during that visit. The patient was started on antifungal therapy with itraconazole 200 mg twice daily. HIV testing was performed. Lumbar puncture showed no evidence of central nervous system involvement. He began to show clinical signs of improvement of hospital day 8. All sputum for acid fast bacilli, sputum cultures, blood cultures, and HIV antibodies were negative. Isolation was discontinued on hospital day 22.

DISCUSSION

Coccidioides immitis is a dimorphic, soil-inhabiting fungus that is endemic to certain regions of North, Central, and South America. Endemic regions in North America include the San Joaquin Valley and south central California, Arizona, New Mexico, western Texas, southern Nevada, the south western corner of Utah, and northern Mexico.¹⁰ Infection with *C. immitis* is acquired by inhalation of airborne arthroconidia released from the soil when mycelia are disrupted by wind or soil excavation. There is an incubation period of 7–21 days. Once in the lung, arthrospores develop and enlarge into spherule endospores. Initially, humoral immune responses occur, but cell-mediated immunity, particularly T-cell function,

FIGURE 3. Skin biopsy specimen showing granulomatous inflammation surrounding a typical spherule of coccidioides (periodic acid-Schiff [PAS] stain, original magnification $\times 400$; courtesy of Hongfa Zhu, MD, PhD, Department of Pathology, NYU Medical Center).

determines a person's response and recovery from infection. There is a wide range of clinical manifestations in people with primary coccidioidal infection. Most people are asymptomatic, approximately 40% develop a mild, self-limited influenza-like illness or pneumonia, and less than 5% develop extra-pulmonary manifestations and severe disease.¹⁰ Although those who are immunosuppressed, pregnant, or of Asian (especially Filipino), Hispanic, African American, and Native American ancestries have an increased risk of developing more severe or disseminated disease, otherwise healthy people may occasionally suffer significant morbidity from coccidioidomycosis.

Symptomatic patients may complain of nonspecific symptoms such as fever, chills, fatigue, night sweats, weight loss, myalgias, cough, chest pain, shortness of breath, arthralgias, or rash. "Valley fever" describes the constellation of fever, arthralgia, and rash seen in those with primary infection.¹¹ Skin lesions in primary infection are thought to be immune-mediated and commonly include erythema nodosum, erythema multiforme, or a nonspecific maculopapular eruption and mild erythroderma. Because the primary focus of infection is usually pulmonary, chest radiographs of infected patients are often abnormal and may reveal pulmonary nodules, cavitations, infiltrates, hilar or mediastinal adenopathy, or pleural effusion. With dissemination of the disease, patients may develop symptoms related to the specific site of spread, such as headache, bony pain, or skin lesion. The skin is a frequent site of dissemination^{11,12}. Dermatologic involvement in dissemination often manifests as pustules, ulcerating nodules, verrucous or granulomatous plaques, papules, or abscesses.^{12,13}

Not surprisingly, this "great imitator" of other diseases is almost never diagnosed promptly or accurately, resulting in an extensive evaluation for malignancy, tuberculosis, and other granulomatous diseases, often combined with empiric treatment with antimicrobial agents.¹⁴ Diagnostic delay may also allow the primary coccidioidal infection to progress to severe or disseminated infection, resulting in significantly greater morbidity and mortality, as well as increased financial costs. For example, hospitalizations and outpatient treatment for coccidioidomycosis amounted to approximately \$66 million in Kern County, California, in the early 1990s, most of which resulted from serious or disseminated cases of infection.^{4,10}

Despite the availability and efficacy of antifungal agents for treating complicated cases of coccidioidomycosis,^{15,16} the incidence of the disease has been increasing not only in endemic areas, but also in nonendemic areas. The Arizona Department of Health Services reported a 186% increase in coccidioidomycosis from 1995 to 2001.¹⁷ Within endemic areas, factors contributing to this trend include environmental conditions, particularly dust storms, weather patterns, earthquakes, as well as human activities, such as excavation and construction.¹⁴ Coccidioidomycosis has also been reported in nonendemic regions with increasing frequency because of the growing number of people with AIDS and those taking chronic immunosuppressive medications, the recent migration of people to endemic regions (the 'Sunbelt' states), and the expansion of the travel industry.¹⁸ Also, some authors have suggested that *C. immitis* may have mutated into a more virulent strain since the introduction of antifungal therapy to treat coccidioidomycosis.¹¹

In the case described above, our patient's race may have predisposed him to developing severe progression of primary infection. Given the time course of his illness and his remote and brief travel history, it is also possible that his presentation could have been a reactivation of a previously acquired infection, although he was

not immunosuppressed. To our knowledge, reactivation of latent infection has only been postulated in patients who are immunosuppressed.^{8,14}

CONCLUSION

Coccidioidomycosis is an emerging infectious disease.¹⁰ Although most cases of coccidioidomycosis are self-limiting and inconsequential, progression or dissemination of disease produces substantial morbidity for the immunosuppressed and occasionally, the immunocompetent. Prompt recognition of infection prevents unnecessary and costly medical treatment and evaluation, helps to allay the patient's anxiety regarding his/her condition or prognosis, and enables appropriate treatment for more serious infections. Health care providers practicing outside endemic areas are likely to encounter patients with both primary and disseminated coccidioidomycosis more frequently, as people passing through endemic areas travel to other regions and advances in medical therapy and technology enable people with HIV, cancer patients, or organ transplant recipients on immunosuppressive agents to live longer. In these nonendemic regions, health care providers who may be unfamiliar and inexperienced with diagnosis and management of the disease may not consider coccidioidomycosis in their differential diagnosis, causing delay in recognition and treatment. When evaluating patients with chronic systemic illnesses or nonspecific systemic and pulmonary symptoms, health care providers should pursue a detailed, meticulous travel history and consider coccidioidomycosis in the differential diagnosis. Hopefully, heightened vigilance from health care providers and the development of effective vaccines will result in earlier diagnosis and treatment, as well as prevention of the disease.

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