



## Case of the Month

### Unusual Presentation of Pulmonary Coccidioidomycosis in a Traveler

Gauri Radkar, DO and Duane Hospenthal, MD, PhD  
Department of Medicine  
Tripler Army Medical Center

#### Introduction

The convenience of modern air travel has allowed us accessibility to virtually all parts of the world. Individuals may now be exposed to endemic diseases both where they live and where they travel. The modern physician must include in their differential diagnosis diseases not only endemic to their locale, but also of those places where patients have visited or are traveling from. Coccidioidomycosis is a fungal infection endemic in the southwestern United States, northern Mexico and certain areas of Central and South America. Presentation of coccidioidal disease can range from asymptomatic to disseminated and life-threatening. Symptomatic acute disease occurs in about 40% of patients, lasting a few weeks and resolving without specific therapy. Chronic disease is rare and may be limited to the lung, manifested by cavitary lesions or slow, progressive disease. Our patient was a long-term resident of Arizona who presented with coccidioidomycosis while vacationing in Hawaii. We describe this presentation of coccidioidomycosis in a traveler and long-term resident of Arizona. His presentation was one of persistent pulmonary coccidioidomycosis, an uncommon form of this mycosis.

#### Case Report

A previously healthy 76 year old Caucasian male vacationing in Hawaii from Arizona presented to our facility with a six week history of documented fever to 103 degrees Fahrenheit, chills, night sweats, decreased appetite, and a sixteen pound weight loss. He had been on the Island of Oahu for 2 days prior to admission. He was previously treated in Arizona with a ten day course of erythromycin for presumed bacterial bronchitis. His history was also notable for twenty pack years of tobacco use. Physical exam was notable for clear lung fields bilaterally with decreased breath sounds in the right upper lobe and no wheezes. Chest radiograph revealed a patchy right upper lobe infiltrate (Figure 1). Laboratory evaluation revealed a leukocytosis of 17,000 white blood cells (WBC)/FL associated with 74% granulocytes, and eosinophilia of 1400 cells/FL. Computed tomography of the chest revealed extensive airspace consolidation of the right upper lobe with several large bullae and calcified granulomas (Figure 2). Lymph nodes were noted in the

Reprints or correspondence: Dr. Gauri Radkar, Department of Medicine (MCHK-DM), Tripler Army Medical Center, HI 96859-5000

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Figure 1.- Chest Radiograph

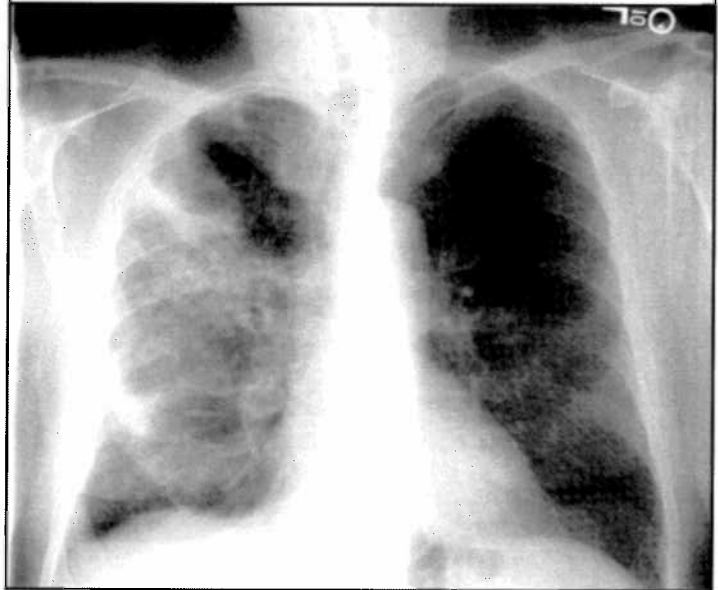
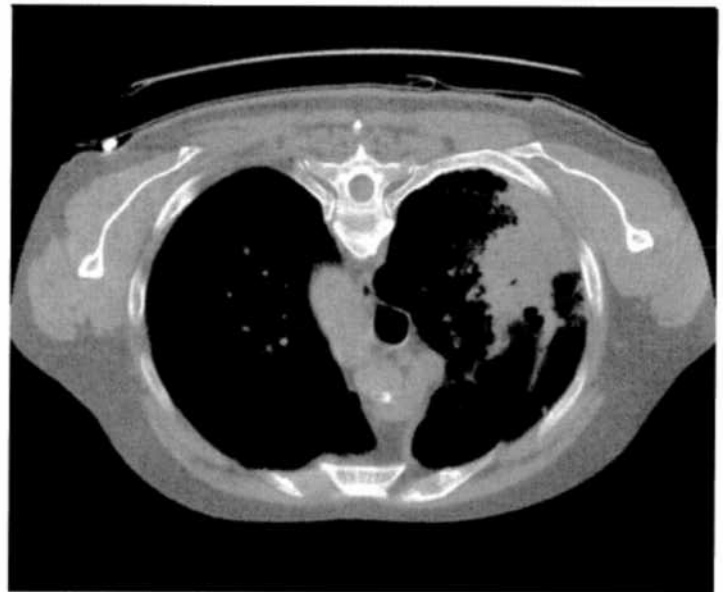


Figure 2.- Chest Computed Tomography



right hilar, peritracheal, and subcarinal regions. Sputum cultures recovered *Coccidioides immitis*. Mycobacterial smear and culture of sputum was negative.

This information led to further evaluation by lumbar puncture. Cerebrospinal fluid (CSF) analysis revealed normal glucose, no WBCs, no organisms on gram stain and fungal smear, and negative *Coccidioides* antibody. Serum *Coccidioides* antibody was positive. The patient was diagnosed with pulmonary coccidioidomycosis with underlying chronic obstructive pulmonary disease (COPD). Therapy with oral fluconazole 400 mg once daily was initiated.

During his six day hospital course, he responded well to this regimen with a defervescence, normalizing leukocytosis and no oxygen requirement. He was discharged home, returning to Arizona several weeks after his hospitalization. He was monitored with serial *Coccidioides* antibody testing. At two months follow up this test became negative. Repeat testing four months later confirmed negative findings and therapy was discontinued. The patient completed six months of treatment and was completely symptom free upon telephonic follow up one month after cessation of therapy.

## Discussion

Coccidioidomycosis is most commonly thought of as a disease of Texas, Arizona, and southern California.<sup>1</sup> Presentation of this mycosis outside its endemic area is not unusual, but frequently remains underdiagnosed. An adequate travel history is essential. Primary coccidioidomycosis presents with minimal or absent symptoms in 60% of patients.<sup>2,3</sup> The remaining 40% most frequently present with a febrile pulmonary illness that resembles influenza. Symptoms include nonproductive cough, fever, fatigue, and pleuritic chest pain, a syndrome referred to as "valley fever". Symptoms of dyspnea, arthralgias, myalgias and cutaneous eruptions (including erythema nodosum and erythema multiforme) have also been noted. Pulmonary infiltrates may be accompanied by hilar adenopathy or pleural effusion. Most cases (95%) of acute infection resolve without therapy. Chronic progressive coccidioidal pneumonia is a less common form of the mycosis that can evolve directly from primary pulmonary coccidioidomycosis or develop years after acquisition of primary infection. Chronic infections tend to be indolent with slow progression of pulmonary destruction but are not likely to disseminate to distant organs. Persistent or recurrent fever in severe primary illness can signal the onset of disseminated diseases. This form may progress rapidly or slowly as bone and joint infection, skin disease, soft tissue abscesses, or meningitis. Meningitis is important to rule out in all infected patients, because untreated, death results in up to 90% of this group of patients.<sup>1</sup>

Our patient's illness does not meet published criteria for acute or chronic infection.<sup>1-4</sup> His presentation is not acute because the duration of symptoms persisted longer than one to three weeks. His disease is not consistent with chronic pulmonary or disseminated infection because typical lung findings or evidence of dissemination were not present. Rather, his presentation is more consistent with persistent pulmonary coccidioidomycosis.<sup>2,4</sup> This syndrome has been reported in small numbers of cases characterized by symptoms of primary infection lasting beyond six weeks. Symptoms include low-grade fever, anorexia, weight loss, cough, and chest pain frequently accompanied by a chest radiograph that fails to show either progression or resolution of abnormalities. This syndrome likely represents a step in the progression of some patients to chronic pulmonary disease. Untreated, this syndrome can be fatal.

Treatment of coccidioidomycosis is seldom indicated in primary pulmonary coccidioidomycosis of mild to moderate severity. Therapy should be considered in patients whose immune status or racial/ethnic background places them at high risk of dissemination. These patient categories include: immunosuppressed patients, diabetics, pregnant women, and black and Filipino males.<sup>5</sup> Treatment is also advised when a primary pulmonary infection is persistent or progressive, as it was in our patient. Effective antifungal agents


include amphotericin B and the azole antifungal agents ketoconazole, itraconazole, and fluconazole.<sup>6</sup> Amphotericin B is recommended in patients with life-threatening disease, usually manifested by respiratory compromise, rapid deterioration, or any meningeal involvement. Oral azole agents are often selected for those with chronic processes. There are no comparative studies demonstrating the superiority of one azole antifungal over another, but ketoconazole is the only orally available agent that is approved for this infection.<sup>1</sup> Clinical trials have indicated that fluconazole and itraconazole are both efficacious in moderate and chronic infection. Because of its good penetration into the CSF, fluconazole is life-saving in the chronic treatment of coccidioidal meningitis.

Our patient is interesting in that he presented with an uncommon form of coccidioidomycosis outside of the endemic area. His syndrome did not clearly fit the classic description of either acute or chronic pulmonary coccidioidomycosis, but rather an intermediate syndrome. Previously undiagnosed COPD likely played a role in his protracted pulmonary infection and placed him at risk for chronic infection. The health care provider must take into consideration the patient's origin and travel in forming a differential diagnosis. As demonstrated in this case, inclusion of origin or travels can assist in the diagnosis of both common and rare forms of endemic infections outside of their areas of endemicity.

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