

CLINICAL VIGNETTE

Acute Pulmonary Coccidioidomycosis

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Case Presentation

A previously healthy 53-year-old female presented with upper respiratory tract symptoms. She reported a two-week history of nasal congestion, rhinorrhea, postnasal drip and intermittently productive cough. She denied hemoptysis, facial pain, sore throat or sick contacts. Her maximum temperature at home was 99.0 F. She initially had muscle aches which had resolved at the time of clinic presentation. Her travel history included a recent conference in Palm Springs followed by a trip to Arizona. Prior to arrival to Arizona, she had begun to have these symptoms noted were dyspnea during a hike. Additional travel history included camping in Death Valley several months ago, as well as hiking in Simi Valley. She denied any insect/tick bites. She also denied any alcohol, tobacco and drug use, as well as prior TB and STD exposure. She denied any allergies and only medication used was a vitamin D supplement.

On physical exam, she was a well-nourished female in no acute distress. BP 138/88, HR 130—decreased to 102 with re-evaluation. T 98.3 and RR 16 and 98% on RA. Positive findings included cervical lymphadenopathy, nasal congestion, and clear lungs.

Based on history and exam, she was thought to have a viral syndrome and was treated with nasal fluticasone and Guaifenesin along with symptomatic therapy including fluids, rest, gargling, vaporizer/mist. She declined chest x-ray for further evaluation.

She returned two days later with a painful erythematous rash on her lower extremities, which she believed to be an allergic reaction to her new medication. She also reported no improvement in her symptoms. Because of clinical suspicion for Erythema nodosum the patient agreed to get Chest x-ray along with labs. Imaging was significant for ill-defined and nodular airspace opacity within the superior segment of the left lower lobe suspicious for pneumonia.

While Cocci serology, complement fixation, ASO, hepatitis panel, and CBC were collected. The patient was empirically started on Azithromycin, while awaiting labs including serologies.

Labs

Cocci Antibody CF (Complement fixation) Positive 1:16
Cocci IgG EIA 0.666

Cocci IgM EIA 0.982
ASO and hepatitis panel negative

The positive serologies established the diagnosis of acute pulmonary cocci. Infectious Disease was consulted. At the time of ID visit, she reported night sweats and persistent cough. Treatment with Fluconazole was initiated and she was monitored for resolution of symptoms and chest x-ray findings.

Discussion

Coccidioidomycosis, also known as San Joaquin Valley fever refers to the spectrum of disease caused by the dimorphic fungi *Coccidioides* species. *Coccidioides immitis* is the causal agent of coccidioidomycosis in California, Baja California and Washington State, whereas *Coccidioides posadasii* is the causal agent in Arizona, and other parts of the southwest US and South America.¹

Clinical manifestations vary depending upon both the extent of infection and the immune status of the host. Of individuals infected with coccidioides, 60% never develop symptoms and 40% experience mild to severe symptoms.² Coccidioidomycosis has been reported to involve almost all organ systems; however, pulmonary disease is the most common clinical manifestation. The incidence of coccidioidomycosis continues to rise, and primary coccidioidal pneumonia accounts for 17 to 29% of all cases of community-acquired pneumonia in endemic regions.³

Symptomatic pulmonary cocci can present physicians with diagnostic challenges as signs and symptoms overlap with other entities as well as treatment challenges due to the lack of a standard treatment approach for all patients with infection.

Diagnosis

Multiple tests are available for detecting coccidioides which can cause confusion, and confirmatory tests are nearly always needed to establish a diagnosis. Determining which test to use depends on the patient's signs and symptoms.

In the outpatient setting, serologic testing is recommended. Initially, ordering an Enzyme linked immunoassay (EIA) for IgM and IgG is standard practice. Within 7 to 21 days after

exposure to Cocci, antibodies develop. These antibody levels decrease over time and eventually become undetectable in patients who resolve their infection. Therefore, positive EIA with measurable anticoccidial antibodies, suggests recent illness. The serological EIA are the most sensitive tests for early infection.⁴

However, IgM EIA testing can lead to false positive results, and Immunodiffusion tests (ID) are recommended to confirm the diagnosis when an initial EIA is positive. These tests are less sensitive than EIAs but are more specific.⁴ If the Immunodiffusion test is qualitatively positive a titer can also be obtained. In this clinical vignette, immunodiffusion was not initially performed. Instead, a complement fixation assay was ordered to help confirm the diagnosis. This is one of the original methods for detecting coccidial antibodies, particularly IgG. Currently immunodiffusion kits offer the same results and are more commonly used than the complement fixation. The Complement Fixation (CF) test plays an important role in detecting coccidial meningitis because other serological tests performed on the CSF are less useful than the CF titer.⁴

Further Cocci antigen assays are available to detect extrapulmonary disease in the CSF and urine. Extrapulmonary sites of disease include the skin, the skeleton and, rarely, the nervous system. *Coccidioides* spp. do not require special media and can be recovered from sputum and skin lesions, and, in rare cases, may be found on blood cultures.⁵

Treatment

Current guidelines for the treatment of coccidioidomycosis have been published by the Infectious Diseases Society of America (IDSA) and the American Thoracic Society (ATS). These guidelines base their recommendations on the best published evidence available, which is often limited to small populations since coccidioidomycosis is geographically limited. As a result, some of the recommendations lack support from randomized controlled trials. Case series of uncomplicated pulmonary cocci have shown that the majority of patients recovered completely even without treatment. A survey of 354 patients with acute valley fever in central California showed 92% recovered in the absence of treatment.⁵ Without available clinical trial evidence, and the availability of well tolerated triazoles such as fluconazole, some routinely treat all uncomplicated infections. However, the decision to treat should be highly individualized.⁵ Patients most likely to benefit from treatment are those with severe acute disease and those with risk factors for chronic complicated or disseminated coccidioidomycosis.⁶ Although, experts agree that patients with moderate or severe acute pulmonary cocci may benefit, there is no consensus definition. Some experts suggest that the following should prompt antifungal treatment: weight loss of more than 10%, elevated complement fixation titer of more than 1:16, patient age greater than 55, symptoms for at least 2 months, persistent night sweats for more than 3 weeks, and widespread bilateral lung infiltrates.⁷

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