Coccidioidomycosis Acquired in Washington State


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Clinical, laboratory, and epidemiologic evidence suggest that 3 individuals with acute coccidioidomycosis were exposed in Washington State, significantly beyond previously identified endemic areas. Given the patients’ lack of recent travel, coccidioidomycosis was not suspected, leading to delays in diagnosis and appropriate therapy. Clinicians should be aware of this possibility and consider the diagnosis.

Keywords. Coccidioides; coccidioidomycosis; endemic fungi; Washington

Coccidioidomycosis is caused by the soil-dwelling fungi *Coccidioides immitis* and *Coccidioides posadasii* [1]. Pulmonary disease is the most common presentation, with symptoms beginning 1–4 weeks after exposure [2]. Disseminated infections can occur acutely or reactivate months later.

*Coccidioides* species are endemic to the southwestern United States and parts of Central and South America [3, 4] but not the Pacific Northwest. In Washington State, residents with coccidioidomycosis typically have recent exposure in known endemic areas. However, between June 2010 and May 2011, physicians diagnosed 3 unrelated cases of acute coccidioidomycosis in eastern Washington residents without recent travel.

We obtained in-depth exposure and travel histories and reviewed medical records. Initial diagnostic testing was done using DNA probe of fungal cultures [5] and enzyme immunoassay. The University of California, Davis (UCD) Coccidioidomycosis Serology Laboratory and the Centers for Disease Control and Prevention Mycotic Diseases Branch performed confirmatory testing by immunodiffusion to detect early immunoglobulin M (IgM) tube precipitin (IDTP) and complement fixation (CF) immunoglobulin G (IgG) antibodies (IDCF), with quantitative IgG titers. UCD identified 1 isolate as *C. immitis* by polymerase chain reaction amplification and sequencing of the serine proteinase gene [6].

CASE REPORTS

Case 1
A 12-year-old boy developed chest pain on 1 June 2010. Outpatient chest radiography (CXR) 2 days later was clear. Three days later, CXR to evaluate worsening chest pain, fever, and difficulty breathing revealed right lower lobe parenchymal infiltrate and pleural effusion. The patient was admitted, prescribed vancomycin and ceftriaxone for pneumonia and azithromycin for erythema multiforme, then discharged 6 days later on oral amoxicillin/clavulanate.

Worsening symptoms led to a 6-day readmission and treatment with intravenous ceftriaxone. CXR and chest computed tomography confirmed a large, increasing right-sided effusion. Lung decortications and chest tube placement were performed. The patient was discharged on intravenous ceftriaxone, but once *Coccidioides* was isolated from pleural fluid cultures, oral fluconazole produced prompt improvement. Serology at diagnosis detected IDTP and IDCF, with CF titer increasing from 1:2 to 1:16 within a week; 6 months later only IDCF was detected (Table 1).

The patient regularly bicycled, played, and dug in a dirt canyon with native desert vegetation. His only travel outside Washington and an adjacent Oregon county was a 2-day trip to Santa Maria, California, in July 2008. The family flew to Sacramento then drove to Santa Maria, potentially using roadside rest stops. The boy played outside a relative’s home and visited the Hearst Castle and gardens in San Simeon. No acute illness occurred at that time. Shoulder radiography 9 months later included a portion of the right upper lung, which was clear.

Case 2
On 31 July 2010, a 15-year-old adolescent boy sustained contusions and lacerations of the right pretibial area and left...
prepatellar bursa from an all-terrain vehicle crash on a dirt track. Sutures were placed for 10 days, leaving dry scabs upon removal. He swam in the Columbia River the following day, then developed a fever and painful, swollen left knee 3 days later. Clinical progression despite antibiotics prompted a wound culture and vancomycin prescription at an emergency room visit.

He was admitted on 21 August with fever and worsening cellulitis. He denied respiratory symptoms. Breath sounds were clear and equal; CXR showed clear lungs bilaterally. Left inguinal lymphangitis, lymphadenopathy, and erythema were observed. Cultures were obtained during knee incision and drainage. Initial piperacillin/tazobactam treatment was changed to vancomycin and voriconazole when fungal cultures returned positive. After 5 days he was discharged on oral voriconazole and clindamycin with intravenous meropenem by peripherally inserted central catheter. Voriconazole was changed to fluconazole when *Coccidioides* was identified 10 days later. Lymphadenopathy of the left groin worsened until the inguinal lymph node ruptured on 27 November; an aspiration culture grew *C. immitis*. Serology at diagnosis detected IDTP only and by January 2011 detected IDCF only (Table 1).

Oral fluconazole was continued through March 2011; lymphadenopathy and knee infection resolved.

The patient’s only travel outside eastern Washington was a weekend trip to Disneyland in March 2008. He flew to Santa Ana, California, using hotel shuttles for land travel. No illness occurred at the time. The patient had no prior CXR.

### Case 3

A 58-year-old man with advanced liver disease presented on 25 May 2011 with 2 weeks of dyspnea and left-sided chest pain despite oral antibiotics. Admission CXR showed bilateral infiltrates and left pleural effusion. He was treated for suspected community-acquired pneumonia with ampicillin/sulbactam and levofloxacin, then transferred owing to respiratory failure that required intubation. Diagnostic thoracentesis identified *Coccidioides*, but was reported after transfer, repeat thoracentesis, bronchoscopy, and bronchoalveolar lavage (BAL). The BAL culture, but not the second pleural fluid culture, grew *Coccidioides*. Initial liposomal amphotericin B treatment was changed to voriconazole, then high-dose fluconazole. His 2-month hospital course was complicated by renal failure.

### Table 1. Laboratory Findings by Case

<table>
<thead>
<tr>
<th>Case</th>
<th>Specimen Source</th>
<th>Days From Onset</th>
<th>Culture Results</th>
<th>Serology Results</th>
<th>EIA</th>
<th>IDTP (IgM)</th>
<th>IDCF (IgG)</th>
<th>CF Titer</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pleural fluid</td>
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<td><em>Coccidioides</em> spp</td>
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<td></td>
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<tr>
<td></td>
<td>Serum</td>
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<td></td>
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<td></td>
<td>Positive</td>
<td></td>
<td>1:2</td>
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<tr>
<td></td>
<td>Serum</td>
<td>48</td>
<td></td>
<td>Positive</td>
<td></td>
<td>Negative</td>
<td></td>
<td>1:16</td>
</tr>
<tr>
<td></td>
<td>Serum</td>
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<td></td>
<td>Negative</td>
<td></td>
<td>Positive</td>
<td></td>
<td>ND</td>
</tr>
<tr>
<td>2</td>
<td>Wound</td>
<td>3</td>
<td><em>Coccidioides</em> spp</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td></td>
<td>Wound</td>
<td>5</td>
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<td>Serum</td>
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<td></td>
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<td></td>
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<tr>
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<td>Serum</td>
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<td></td>
<td>Negative</td>
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<td></td>
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<td>1:16</td>
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<td>Negative</td>
<td></td>
<td>Positive</td>
<td></td>
<td>1:16</td>
</tr>
</tbody>
</table>

Abbreviations: BAL, bronchoalveolar lavage; CF, complement fixation; EIA, enzyme immunoassay; IDCF, immunodiffusion for complement fixation (IgG) antibodies; IDTP, immunodiffusion for tube precipitin (IgM) antibodies; IgG, immunoglobulin G; IgM, immunoglobulin M; ND, not detected (titer <1:2).
pericardial effusion, atrial fibrillation, and pleural effusion. He was discharged on oral fluconazole.

Serology on 13 June detected IDTP only, with IDCF developing later and CF titers increasing to 1:512 (Table 1). His titers declined on long-term fluconazole but he was readmitted March 2012 with coccidioidal meningitis following interrupted therapy; CF titer was 1:16.

The patient worked as a construction excavator in eastern Washington. He did not recall visiting an endemic area other than a plane change in Arizona approximately 3–5 years prior. No prior CXRs were available.

**DISCUSSION**

We propose that these coccidioidomycosis cases represent acute infections acquired in eastern Washington. *Coccidioides* was isolated from each patient, with serologies demonstrating acute infections. Tube precipitin (IgM) antibodies develop within the first 3 weeks of illness, and are generally undetectable after 7 months [7]. Serologic progression from IgM to IgG with increasing IgG titers occurred during acute illnesses in the absence of preexisting pulmonary disease or nodules, consistent with primary disease rather than reactivation of remote infection. In case 3, the patient developed disseminated meningeal disease 10 months after the primary pneumonia. In case 2, the patient had infection localized to the left leg and lymph nodes, which we suspect was primary cutaneous coccidioidomycosis following direct fungal inoculation during trauma, a rare presentation [8, 9].

All 3 patients reside in eastern Washington, which has a semiarid climate produced by the Cascade Mountain range rainshadow. Their homes are within 60 miles of each other, near the intersection of Benton, Franklin, and Walla Walla counties. The low elevation (115–240 m), average temperature (–3°C to 31°C), and annual rainfall (18–20 cm/year) here are within favorable *Coccidioides* growth conditions; monthly climate conditions have been relatively stable for 50 years [10, 11]. Established *Coccidioides*-endemic areas generally have 5–50 cm annual precipitation, hot summers, few winter freezes, and mean annual air temperatures between 0.5°C and 24.4°C, and tend to be at lower elevations with sandy soil [3, 12, 13]. The local environmental conditions and close geographic proximity of cases support local exposure. We suspect that exposures occurred during soil disruption in focal locations within this south-central part of eastern Washington.

Although the possibility that these cases represented reactivations of earlier infections cannot be definitively excluded, other reactivation cases lacking recent travel would be expected in Washington, particularly heavily populated western counties. The Washington State Department of Health has received only 2 other coccidioidomycosis reports among residents without preceding travel (unpublished data). Both resided in south-central Washington but were less compelling as locally acquired owing to absence of culture confirmation and limited serology. During 1997–2012 the Washington Animal Disease Diagnostic Laboratory diagnosed culture-confirmed coccidioidomycosis in 2 dogs living only in the area and a local horse that only traveled within the Pacific Northwest (T. E. Besser and M. A. Davis, personal communication, March 2012), further supporting our hypothesis.

The endemic ranges of mycotic pathogens may be influenced by animal host movement, human-mediated dispersal, and climate changes conducive to colonization, allowing expansion into new regions. We have seen *Cryptococcus gattii*, a fungus previously thought to be limited to tropical and subtropical climates, emerge in the temperate Pacific Northwest [14]. *Coccidioides*-endemic areas were defined in the 1950s [15]; subsequently this pathogen has been found elsewhere. Notably, an outbreak occurred at a Utah archeological site [16], and 2 fossilized bison in Nebraska showed evidence of *Coccidioides* infection [17]. Historical presence in these northern latitudes dating back centuries, possibly from animal or human migration, has been hypothesized. We surmise that *Coccidioides* either has established or is establishing a new niche in eastern Washington.

Definitive evidence of *Coccidioides* in eastern Washington requires further studies, but these cases suggest that the organism occurs much further north than previously recognized. We recognize the limitations, including the small number of cases and their remote travel. However, clinical and laboratory evidence are compatible with recently acquired infections, and the cases are epidemiologically clustered with extensive soil exposures in a habitable climate for *Coccidioides*. Coccidioidomycosis was not initially suspected because these patients lacked recent travel, causing delays in appropriate antifungal therapy and substantial clinical complications. Healthcare providers should be aware of the possibility that *Coccidioides* may occur in localized foci within eastern Washington, particularly in Benton, Franklin, and Walla Walla counties. These counties revised notifiable conditions reporting requirements for healthcare providers to explicitly list coccidioidomycosis rather than rely on the statewide “rare diseases” reporting category. Clinicians should consider the diagnosis for clinically compatible illnesses even without travel to known endemic areas.

**Notes**

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