Coccidioidomycosis with Pericardial Involvement: Case Report and Literature Review

To the Editor:

Coccidioidomycosis, an infection caused by dimorphic fungi *Coccidioides immitis* and *C. posadasii*, is endemic to the southwestern US. It is estimated that there are 150,000 new infections in the US every year. Patients with primary infection are asymptomatic 60% of the time, and 40% have a wide spectrum of clinical manifestations, most commonly a community-acquired pneumonia. Overall, <1% develop extrapulmonary manifestations. Pericardial involvement is rare, with only 23 detailed cases reported in the medical literature. We report the case of our patient and review the relevant published cases of coccidioidal pericarditis.

**CASE REPORT**

A 21-year-old man from Thailand presented to the Student Health Clinic with worsening cough, chest pain, and dyspnea. He had moved to Arizona 2.5 years before his presentation. His illness began with fever and productive cough 2 months before admission. The patient was given a course of levofloxacin for presumed bacterial community-acquired pneumonia. However, his symptoms progressed and included night sweats, decreased appetite, dysphagia, chest pain, and dyspnea. He was seen again at the clinic and subsequently diagnosed with coccidioidomycosis. Labs showed a positive immunoglobulin (Ig)M and IgG enzyme immunoassay with complement fixation titer 1:256

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![Figure](A) Two-dimensional transthoracic echocardiogram in subcostal 4-chamber view showing a large circumferential pericardial effusion (arrow). (B) Subcostal long-axis view showing increased inferior vena cava pressure (<50% collapse during inspiration), which further suggest echocardiographic tamponade. (C) Left supraclavicular mass (arrow). (D) Extensive necrotizing lymphadentitis with involvement of the mediastinum and bilateral hilar causing esophageal impingement (arrow). IVC = inferior vena cava; LA = left atrium; LV = left ventricle; PE = pericardial effusion; RA = right atrium; RV = right ventricle.
<table>
<thead>
<tr>
<th>No</th>
<th>Year</th>
<th>Age/Sex</th>
<th>Race</th>
<th>Pertinent Symptoms</th>
<th>CF Titer</th>
<th>Clinical Manifestation</th>
<th>Diagnosis</th>
<th>Treatment</th>
<th>Outcome</th>
<th>Reference (First Author)</th>
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<tr>
<td>1</td>
<td>1953</td>
<td>49/M</td>
<td>African</td>
<td>CP, SOB, cough</td>
<td>U</td>
<td>Pericardial friction rub, pericarditis</td>
<td>Clinical, +CST</td>
<td>None</td>
<td>R</td>
<td>Larson</td>
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<td>26/M</td>
<td>African</td>
<td>Fever, CP</td>
<td>U</td>
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<td>R</td>
<td>Larson</td>
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<td>60/M</td>
<td>White</td>
<td>Cough, weight loss</td>
<td>U</td>
<td>Chronic adhesive Pericarditis</td>
<td>Autopsy, +CST</td>
<td>None</td>
<td>D</td>
<td>Larson</td>
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<td>4</td>
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<td>44/M</td>
<td>Filipino</td>
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<td>U</td>
<td>Skin lesions, Pericarditis</td>
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<td>None</td>
<td>D</td>
<td>Chapman</td>
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<td>52/M</td>
<td>African</td>
<td>Cough, SOB, orthopnea</td>
<td>U</td>
<td>Subcutaneous nodules, large right supraclavicular mass</td>
<td>Autopsy</td>
<td>None</td>
<td>D</td>
<td>Chapman</td>
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<td>6</td>
<td>1957</td>
<td>48/M</td>
<td>Filipino</td>
<td>Cough, CP, fever, SOB, weight loss</td>
<td>U</td>
<td>Acute and chronic suppurative pericarditis</td>
<td>Autopsy, +CST</td>
<td>None</td>
<td>D</td>
<td>Chapman</td>
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<td>7</td>
<td>1958</td>
<td>21/M</td>
<td>African</td>
<td>Fever, SOB</td>
<td>U</td>
<td>Subcutaneous abscesses, pericarditis</td>
<td>Autopsy</td>
<td>None</td>
<td>D</td>
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<tr>
<td>8</td>
<td>1976</td>
<td>64/M</td>
<td>Latino/Hispanic</td>
<td>SOB, CP, orthopnea</td>
<td>1:128</td>
<td>Tamponade</td>
<td>Pericardiocentesis with +P, +C</td>
<td>Amphotericin B</td>
<td>D</td>
<td>Bayer</td>
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<td>9</td>
<td>1976</td>
<td>21/M</td>
<td>White</td>
<td>Fever, CP, SOB</td>
<td>1:32</td>
<td>Pulsus paradoxus, tamponade</td>
<td>Pericardiocentesis with −P, −C, +CST</td>
<td>Amphotericin B, 3 months</td>
<td>R</td>
<td>Bayer</td>
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<tr>
<td>10</td>
<td>1976</td>
<td>26/M</td>
<td>White</td>
<td>Fever, CP, fatigue</td>
<td>1:128</td>
<td>Pulsus paradoxus, tamponade, constructive pericarditis</td>
<td>Pericardiocentesis, pericardiectomy with +P</td>
<td>Amphotericin B</td>
<td>R</td>
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<td>White</td>
<td>Fever, cough</td>
<td>1:512</td>
<td>Skin lesions, Pericarditis</td>
<td>Pericardiocentesis with −C</td>
<td>Amphotericin B, hydrocortisone</td>
<td>R</td>
<td>Chowdhury</td>
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<td>12</td>
<td>1993</td>
<td>30/M</td>
<td>U</td>
<td>Cough, SOB, CP, fever</td>
<td>1:128</td>
<td>Pericarditis</td>
<td>Pericardial effusion, endobronchial mass biopsy, +P</td>
<td>Fluconazole 400 mg daily</td>
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<td>13</td>
<td>1995</td>
<td>24/M</td>
<td>Pacific Islander</td>
<td>Fever, SOB, cough</td>
<td>U</td>
<td>Constrictive pericarditis</td>
<td>Pericardiocentesis, pericardiectomy, autopsyp +P</td>
<td>None</td>
<td>D</td>
<td>Oudiz</td>
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<td>14</td>
<td>1999</td>
<td>20/M</td>
<td>U</td>
<td>SOB, CP, weight loss</td>
<td>1:8</td>
<td>Kussmaul's sign, constrictive pericarditis</td>
<td>Pericardiocentesis with +P</td>
<td>Amphotericin B 0.7 mg/kg daily for 6 wks, then fluconazole × 3 months</td>
<td>R</td>
<td>Faul</td>
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<td>15</td>
<td>2003</td>
<td>73/M</td>
<td>U</td>
<td>weight loss</td>
<td>1:2</td>
<td>Constrictive pericarditis</td>
<td>Pericardiocentesis with +P</td>
<td>Amphotericin B 2g over 7 weeks, then fluconazole</td>
<td>R</td>
<td>Visbal</td>
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<tr>
<td>16</td>
<td>2003</td>
<td>78/M</td>
<td>U</td>
<td>SOB, CP, presyncope</td>
<td>1:16</td>
<td>Constrictive pericarditis</td>
<td>Pericardiocentesis with −P; autopsyp +P</td>
<td>None</td>
<td>D</td>
<td>Visbal</td>
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<tr>
<td>17</td>
<td>2004</td>
<td>40/F</td>
<td>African</td>
<td>SOB, CP</td>
<td>1:32</td>
<td>Pericarditis</td>
<td>Pericardiocentesis, paratracheal lymph node and +sputum culture</td>
<td>Amphotericin B for 12 months, then fluconazole for 4 years</td>
<td>R</td>
<td>Crum</td>
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<tr>
<td>18</td>
<td>2004</td>
<td>36/F</td>
<td>African</td>
<td>SOB, CP</td>
<td>1:512</td>
<td>Osteomyelitis, pericarditis</td>
<td>Pericardiocentesis with +C</td>
<td>Amphotericin B, then fluconazole 800 mg daily</td>
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<td>19</td>
<td>2005</td>
<td>34/M</td>
<td>Latino/Hispanic</td>
<td>Fever, cough, weight loss</td>
<td>1:256</td>
<td>Pericarditis</td>
<td>Pericardiocentesis with +C</td>
<td>Fluconazole 1000 mg daily</td>
<td>D</td>
<td>Arsura</td>
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</table>
Coccidioidomycosis serum antigen was positive. Human immunodeficiency virus, QuantiFERON gold (Qiagen, Valencia, CA) tuberculosis, and (1-3)-Beta-D-Glucan tests were negative. The patient was started on oral fluconazole 400 mg daily without improvement.

On admission, the patient was afebrile and tachycardic with a heart rate of 121 beats per minute. His blood pressure was 108/60 mm Hg. A firm, nontender left supraclavicular mass of 3 cm × 4 cm was present. Complete blood count showed an elevated white blood count of 12,900/μL with 84.3% neutrophils, 8.2% lymphocytes, and 1% eosinophils, normocytic anemia with hemoglobin 9.5 g/dL, and elevated platelet count of 525,000/μL. Transthoracic echocardiogram revealed a large circumferential pericardial effusion with evidence of tamponade (Figure A and B). Computed tomography of the chest showed extensive necrotizing lymphadenitis (Figure C) with involvement of the mediastinum and bilateral hilar adenopathy causing esophageal impingement (Figure D).

Pericardiocentesis was performed with 680 mL of bloody fluid aspirated from the pericardial space. Pericardial fluid showed red blood cell of 2,848,000, white blood count of 5778 with neutrophils 51%, lymphocytes 44%, eosinophils 2%, glucose 70 mg/dL, and lactic dehydrogenase 447 IU/L (serum lactate dehydrogenase 279 IU/L). Gram stain did not show any organisms, and both stains and culture for fungal and acid-fast bacilli were negative. Tuberculosis polymerase chain reaction and adenosine deaminase from the fluid were negative. Cytology was negative for metastatic malignancy. The patient was started on liposomal formulation of amphotericin B at 5 mg/kg, intravenous fluconazole 400 mg twice a day, and prednisone 20 mg daily. The supraclavicular mass was excised, and pathology showed necrotizing granulomatous lymphadenitis with Coccidioides spherules, a positive C. immitis by deoxyribonucleic acid probe, and without evidence of lymphoma. After 10 days of therapy, the patient was discharged from hospital after an oral fluconazole 400 mg daily and a prednisone taper. The patient responded very well to treatment and continued to do well 8 weeks after discharge.

### DISCUSSION

While disseminated coccidioidomycosis occurs <1% of the time, it can be fatal, and patients require prompt antifungal treatment. Male sex and certain ethnicities such as African Americans and Filipinos are more likely to develop disseminated disease. Any organ can be involved, with skin, lymph nodes, bones, and central nervous system being the most common extrapulmonary sites. According to autopsies reported by the Army Institute of Pathology, the pericardium was listed as the 16th structure in frequency of involvement.

Coccidioidomycosis with pericardial involvement is a rare entity, with only 23 cases detailed in the literature (Table). Reports have indicated that over 90%...
(22/24) of these cases occurred in males. While the elderly are at a higher risk of coccidioidomycosis, it appears coccidioidal pericarditis occurred more often in younger individuals (median age = 32.5 years). Most common complaints include cough, chest pain, and dyspnea. Complement fixation titer ranges from 1:2 to >1:32 in disseminated disease. About 37% (9/24) of the patients did not receive any antifungal treatment, and only 20% (2/9) recovered. The remaining 63% (15/24) received antifungal therapy, most commonly amphotericin B and fluconazole, with a significantly higher survival rate of 87% (13/15).

Timely interventional procedures such as pericardiocentesis may also contribute to improved outcomes. Unlike other cases in our review, our patient was treated with low doses of prednisone tapered over 1 month to decrease bulky adenopathy impinging the esophagus and to treat pericarditis and prevent possible progression to constrictive pericardial disease.

Several cases, along with the present case, were initially misdiagnosed. For example, in the case reported by Brilhante et al., the patient was thought to have myopericarditis, then nonspecific pericarditis, and eventually the correct diagnosis of coccidioidal pericarditis was secured. Of note, our patient did not grow Coccidioides from the pericardial fluid. It is possible that a biopsy would have confirmed the diagnosis. However, it is likely that the pericardial effusion was inflammatory in nature, as it has been described in patients with histoplasmosis. Therefore, adjunctive steroid therapy was used in this patient.

CONCLUSION
Coccidioidomycosis with pericardial involvement is rare. Presenting symptoms are frequently nonspecific and overlap with common conditions such as upper respiratory illness, pneumonia, and viral pericarditis. When symptoms occur, imaging is required and diagnostic vigilance is needed when patients travel to areas of fungal endemicity.

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References

