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CASE REPORT

INTERMEDIATE

CLINICAL CASE

Pericarditis and Sacroiliitis in a World Traveler

Alessandra Vecchié, MD,[a] Jillian E. Raybould, MD,[b] Kunal Sangal, MD,[a] Aldo Bonaventura, MD, PhD,[a,c] Melissa Gillen, DO,[d] Antonio Abbate, MD, PhD,[a] Sangeeta Sastry, MD,[b] Hem Bhardwaj, MD[a]

ABSTRACT

A 65-year-old immunocompromised woman presented with progressive dyspnea and sacroiliac joint pain. Cardiac magnetic resonance showed abnormal right ventricular filling with septal bounce and abnormal pericardial enhancement, suggestive of constrictive pericarditis. Cultures from pericardium following pericardiectomy grew *Coccidioides immitis*. She was diagnosed with coccidioidomycosis and responded to pericardiectomy and amphotericin. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2021;3:1322–1326) © 2021 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

A physically active 65-year-old Caucasian woman presented to the Virginia Commonwealth University Medical Center in Richmond with 5 months of malaise, fever, night sweats, dry cough, and progressive dyspnea. She also reported left sacroiliac (SI) joint pain for the same duration with significant limitations in mobility.

On admission, she was afebrile and hemodynamically stable. She was found to have bilateral rales, 2+ bilateral lower extremity edema, and jugular vein distension. Musculoskeletal examination revealed restricted active and passive range of motion of the left hip, decreased muscle strength of the left hip flexors, but no tenderness to palpation of the left SI joint or lumbar spine.

LEARNING OBJECTIVES

- To bring awareness to coccidioidal pericarditis, a rare manifestation of disseminated coccidioidomycosis.
- To underline that coccidioidomycosis should remain in the differential diagnosis when clinical suspicion is high, even if initial serological diagnostics are negative.

MEDICAL HISTORY

The patient had a history of hypothyroidism, previously treated latent tuberculosis, and rheumatoid arthritis (on methotrexate and abatacept).

She had an extensive travel history preceding her symptom onset. She visited Kenya 6 months prior to presentation, where she lived in a mud hut, consumed local cuisine including unpasteurized cow milk, spent time in areas with tuberculosis outbreaks, and had contact with animals. Two months after her return from Kenya, she biked and camped along the Pacific coast (Vancouver to Mexico), noting exposure to rodents.

From the [a]VCU Pauley Heart Center, Virginia Commonwealth University, Richmond, Virginia, USA; [b]Department of Internal Medicine, Division of Infectious Diseases, Virginia Commonwealth University Health System, Richmond, Virginia, USA; [c]Department of Internal Medicine, First Clinic of Internal Medicine, University of Genoa, Genoa, Italy; and the [d]Department of Medicine, Duke University Health System, Durham, North Carolina, USA.

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She was initially diagnosed with left SI joint arthritis and received 2 courses of glucocorticoids with some improvement. Chest imaging performed prior to admission revealed patchy airspace disease, right lower lobe consolidation, and pericardial effusion. She received multiple courses of antibiotics for pneumonia and colchicine for pericarditis, without improvement, instead developing shortness of breath, especially during exercise, and orthopnea.

DIFFERENTIAL DIAGNOSIS

Acute systolic heart failure, pericardial effusion, and pneumonia were included in the differential diagnosis.

INVESTIGATIONS

Admission laboratory testing revealed normocytic anemia, mild lymphopenia (0.7×10^9/l) with a normal white blood cell count, and elevated inflammatory markers (C-reactive protein 7.6 mg/dl; normal range: <0.5 mg/dl). Antibodies to human immunodeficiency viruses 1 and 2, syphilis, *Brucella* spp, *Coxiella* spp, and *Coccidioides* spp were negative, as were urinary *Histoplasma* and *Blastomyces* antigens. Bacterial, fungal, and acid-fast bacilli blood cultures were negative. A computed tomographic scan of the chest demonstrated multiple bilateral pulmonary nodules. Subsequent bronchoscopy was unrevealing, with negative bacterial, fungal, acid-fast bacilli, and *Nocardia* cultures. Echocardiography showed mild left ventricular (LV) hypertrophy with a mild reduction of the LV systolic function (ejection fraction 45%). LV diastolic function was normal, and no significant pericardial effusion was observed (Video 1).

Cinematic motion imaging of cardiac magnetic resonance (CMR) showed prominent septal bounce, a sign of ventricular interdependence typically observed in constrictive pericarditis. The pericardium appeared circumferentially thickened, and post-contrast images demonstrated abnormal pericardial enhancement (Figure 1A), all consistent with a diagnosis of constrictive pericarditis. The diagnosis was confirmed on simultaneous right heart and left heart catheterization and pressure measurements. Additionally, pelvic magnetic resonance imaging (Figure 1B) confirmed left hip sacroiliitis.

MANAGEMENT

The patient underwent arthrocentesis of her SI joint with growth of *Coccidioides immitis* on joint fluid culture (Figure 2). She underwent pericardiectomy,

ABBREVIATIONS AND ACRONYMS

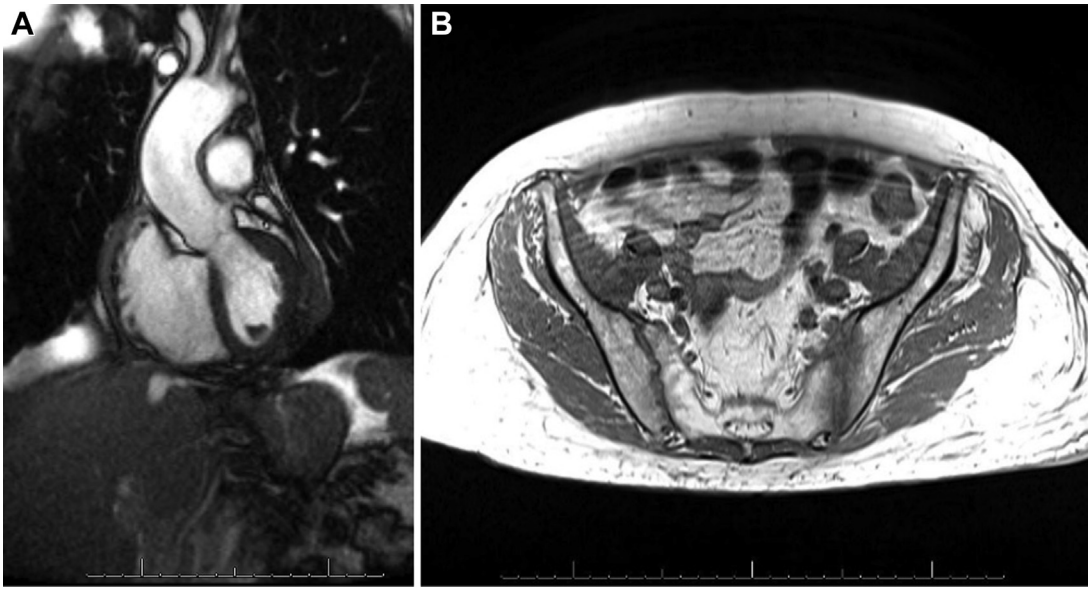
CMR = cardiac magnetic resonance

IV = intravenous

LV = left ventricular

SI = sacroiliac

FIGURE 1 Radiologic Findings of Constrictive Pericarditis and Sacroiliitis



(A) Cardiac magnetic resonance imaging (MRI) showing pericardial enhancement, thickening, and complex fluid along posterior lateral margin of the left ventricle. **(B)** Left sacroiliitis demonstrated on pelvic MRI with and without contrast.

FIGURE 2 ***Coccidioides immitis*** **Growing From Left Sacroiliac Joint Culture**

and culture from pericardial tissue also grew *C immitis*, with histopathologic findings of granulomatous inflammation, foci of necrosis, and spherules (**Figure 3**). Bone marrow biopsy was performed to evaluate for infection localization and also grew *C immitis*. Although serum coccidioidal enzyme-linked immunoassay antibodies to immunoglobulin M and immunoglobulin G and complement fixation antibodies were negative, serum coccidioidal antigen was positive at 0.20 ng.

A diagnosis of disseminated coccidioidomycosis was established with pulmonary, cardiac, bone marrow, and SI joint involvement. The patient responded well to joint washout, pericardiectomy, and intravenous liposomal amphotericin B followed by oral posaconazole.

DISCUSSION

Coccidioides spp, *C immitis*, and *Coccidioides posadasii* are soil-dwelling fungi endemic to the southwestern United States and Central America. Exposure occurs via inhalation of aerosolized spores or, rarely, by cutaneous inoculation. Most patients remain asymptomatic or experience flulike illness. Immunocompromised hosts are more likely to develop "valley fever," which is the most common clinical manifestation and includes fever, cough, chest pain, shortness of breath, and transient rashes (1).

Disseminated disease, via hematogenous spread, may occur in 1% to 5% of cases in the appropriate host or in those with a large inoculation of spores (1). Risk factors include African American race, Filipino ethnicity, and medical conditions that affect T cell function (1). The typical systems involved are musculoskeletal, skin, and central nervous systems.

The diagnosis of disseminated coccidioidomycosis is often delayed months after initial infection, especially if the patient presents outside of endemic areas or with multiorgan involvement. The clinical syndrome can masquerade as other infections, autoimmune processes, and malignancy. Given the duration of symptoms prior to diagnosis, this case highlights the importance of obtaining a thorough exposure history to guide differential diagnosis and work-up.

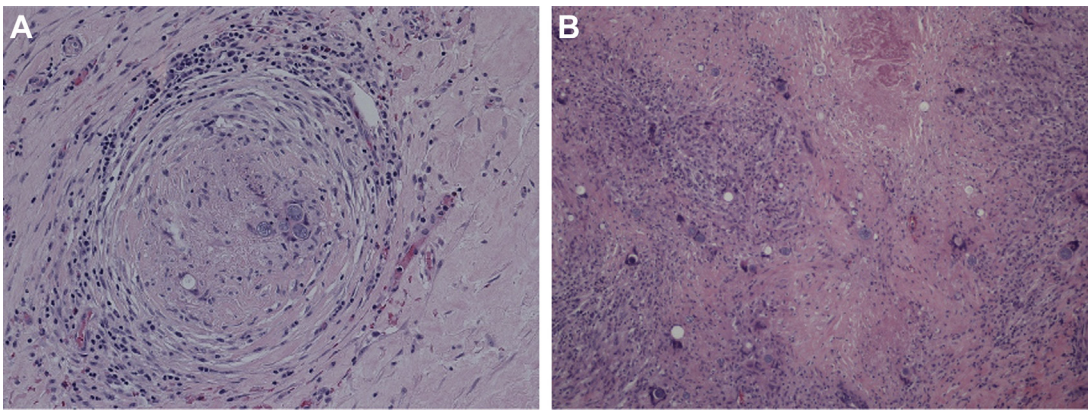
Multiple diagnostic modalities are often needed to confirm the diagnosis of coccidioidomycosis (2–6) (**Table 1**). In our patient, the use of immune-modifying medications likely affected the negative predictive value of coccidioidal serology. This case serves as an example that patients, especially those who are immunocompromised, benefit from undergoing multiple laboratory tests (5).

Musculoskeletal infection is a common extrapulmonary site of infection, occurring in 20% of patients with disseminated disease (3). Vertebral osteomyelitis involving the lumbar spine followed by the thoracic spine is the most frequently reported (7), whereas the knee is the most frequent infected joint (1,2). If diagnosed early, the prognosis of musculoskeletal infection is good, while delayed diagnosis can lead to significant morbidity (2).

Cardiac infection is a rare manifestation of disseminated coccidioidomycosis. Review articles report about 20 to 35 cases, typically in young men (8). Coccidioidomycosis can involve all layers of the heart but most commonly affects the pericardium through direct extension from nearby structures via rupture of superficial granules or hematogenous spread. Patients who develop pericarditis typically present with constitutional symptoms along with shortness of breath, cough, and chest pain, with or without friction rub (8). Coccidioidal pericarditis may evolve to effusive-constrictive pericarditis or to a chronic form. Recurrent pericarditis has also been described. Echocardiography is usually the first-choice imaging technique to evaluate patients with suspected pericarditis (9). CMR can be now considered as the second-line imaging test, and it is particularly helpful when echocardiographic findings are inconclusive (9). The presence of late gadolinium enhancement on CMR indicates active pericardial inflammation, and it is a predictor of constriction reversibility with anti-inflammatory treatment.

The prognosis of patients with coccidioidal pericarditis has been reported to be poor. In a review of

FIGURE 3 Pathology Findings of the Pericardium



(A) Pericardium with granuloma and *Coccidioides immitis* endospore-filled spherule. **(B)** Closer view of multiple visible spherules.

17 cases, Arsura et al. (10) reported that 9 patients died. Among the 8 patients who recovered, 3 ultimately required pericardiectomy. It has been noted that prompt therapy with active antifungal drugs is fundamental to improve outcomes (8). In our patient, the effusion was identified 2 months after symptom onset, but the delay in diagnosis led to constrictive pericarditis 6 months later. Our patient developed constriction despite the treatment with glucocorticoids and presented symptoms of acute heart failure. Therefore, pericardiectomy was indicated to manage her condition.

Optimal treatment of disseminated coccidioidomycosis should include appropriate antifungal therapy (amphotericin B, fluconazole, itraconazole, or posaconazole) along with timely interventional procedures, particularly for musculoskeletal infections such as vertebral coccidioidomycosis (2,6,7). Pericardiectomy may be necessary in constrictive forms (9). Amphotericin B is recommended for widespread disease, vertebral involvement with concern for cord compromise, or immunocompromised patients, with transition to oral azoles when stable (6). Posaconazole has success in disseminated disease unresponsive to amphotericin B or other azoles (6). Therapy for disseminated disease should be continued for prolonged periods, 6 months to lifelong depending on the extent of disease and immune status of the patient (6).

FOLLOW-UP

The patient had resolution of all symptoms and regained good functional status. *Coccidioides* antigen was negative 5 months after hospital discharge.

CONCLUSIONS

The diagnosis of coccidioidomycosis should be considered in patients with appropriate risk factors,

TABLE 1 Tests Used for the Diagnosis of Coccidioidomycosis

Diagnostic Test	Technique	Strengths	Limitations
Antibody detection IgM: detectable from 1–3 weeks after exposure to 4 months IgG: positive after 3 months, persistent for several months	EIA CF Quantitative test	Excellent specificity Useful to confirm diagnosis and monitor the disease	Low sensitivity in immunocompromised patients (67%) Low sensitivity in immunocompromised patients (67%)
Coccidioidal antigen detection	EIA	Sensitivity of 81% in immunocompromised patients	Reduced sensitivity compared with cultures
Growth of the microorganism in medium culture	Culture from the organ involved	Gold standard	Requires more time

CF = complement fixation; EIA = enzyme-linked immunoassay; IgG = immunoglobulin G; IgM = immunoglobulin M.

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travel histories, and compatible clinical syndromes. Coccidioidomycosis should remain in the differential diagnosis when clinical suspicion is high, even if initial serological diagnostics are negative. Further diagnostics should be pursued, including obtaining appropriate cultures and serum *Coccidioides* spp antigen testing. Prompt diagnosis and early initiation of antifungal agents as well as aggressive surgical debridement, when appropriate, yields improved clinical results.

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ADDRESS FOR CORRESPONDENCE: Dr. Hem Bhardwaj, VCU Pauley Heart Center, Department of Internal Medicine, Division of Cardiology, 1200 E. Marshall Street, Gateway Building, Box 980036, Richmond, Virginia 23298, USA. E-mail: hem.bhardwaj@vcuhealth.org. Twitter: @HemBhardwajMD.

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KEY WORDS ***Coccidioides*, coccidioidomycosis, constrictive pericarditis, sacroiliitis**

APPENDIX For a supplemental video, please see the online version of this paper.