Endocarditis due to *Coccidioides* spp: The Seventh Case

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*Coccidioides*, a dimorphic fungus endemic within the Americas, primarily causes pulmonary disease but may disseminate. We describe a case of confirmed *Coccidioides* endocarditis, the seventh reported in literature. *Coccidioides* endocarditis often requires tissue diagnosis and combined surgical and medical treatment.

**Keywords.** *Coccidioides*; endocarditis; posaconazole.

CASE PRESENTATION

A 34-year-old Hispanic woman living in Bakersfield, California with a history of disseminated coccidioidomycosis presented in early 2013 with vaginal bleeding due to spontaneous abortion. She underwent dilation and curettage for retained placenta, received blood transfusions and fluid resuscitation for postoperative bleeding, but then developed acute dyspnea. Exam revealed a grade 3 diastolic murmur, chest radiography showed pulmonary edema and pleural effusions, and laboratory results included elevated brain natriuretic peptide and chronically elevated liver function tests attributed to *Coccidioides* granulomatous hepatitis. Transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) revealed severe aortic insufficiency and no vegetation. She improved with diuresis and was discharged on posaconazole with *Coccidioides* complement fixation (CF) titer of 1:4.

Medical history included pulmonary coccidioidomycosis in 2004 when the patient presented during her first pregnancy with fever, cough, and a pulmonary infiltrate. Amphotericin B was initiated but discontinued due to acute shortness of breath during infusion. She received fluconazole for 6 weeks. This pregnancy terminated in a spontaneous abortion. In 2007, the patient presented during her second pregnancy with coccidioidomycosis relapse involving the lungs and liver. She started posaconazole but discontinued it due to cost. She delivered a healthy baby with no evidence of *Coccidioides* transmission. The patient did not follow-up until her third pregnancy in 2010. She restarted posaconazole but had intermittent adherence. This pregnancy resulted in a live healthy birth.

Two months after early 2013 hospitalization, the patient was readmitted with congestive heart failure. Aortic valve replacement was attempted but aborted due to significant mediastinal fibrosis. The patient was transferred to another hospital where 4 sets of routine blood cultures were negative, TEE showed aortic regurgitation and no vegetation, and chest computed tomography revealed a 3.5 by 2.0 cm mediastinal mass with paratracheal and periaortic adenopathy (Figure 1).

Aortic valve replacement was successfully accomplished. Histology showed granulomatous inflammation, multinucleation, and endosporeulating spherules consistent with *Coccidioides* (Figure 2). Culture grew 1 fungal colony identified by DNA probe as *Coccidioides* spp. *Coccidioides* complement fixation titers were 1:8 before surgery and 1:2 after surgery plus 7 months of posaconazole therapy. The patient continues to receive posaconazole, which will be continued indefinitely with monitoring of symptoms, CF titers, and posaconazole levels every 3 months.

DISCUSSION

*Coccidioides* is a dimorphic fungal endemic to the Americas and comprises 2 species, *Coccidioides immitis* and *Coccidioides posadasii*, although they are nearly indistinguishable by laboratory tests [1, 2]. Approximately 40% of cases have self-resolving flu-like symptoms with clinically evident pneumonia, although 5% develop pulmonary nodules or cavities [3]. Dissemination can occur to skin, bone, joints, and meninges [3]. Cardiac involvement is uncommon and can affect the pericardium, but endocarditis is extraordinarily rare even with documented fungemia [1–6]. Our literature review identified 6 case reports and 1
Conference abstract of *Coccidioides* endocarditis that met modified Duke’s criteria for definite or possible endocarditis (Table 1) [7–11]. Other reports lack clinical or histopathological confirmation of endocarditis [5, 8].

Diagnosing *Coccidioides* endocarditis can be difficult: our patient’s routine blood cultures were repeatedly negative, and TTE and TEE showed no vegetation. Among prior cases, 2 had positive blood cultures, 5 had vegetations, 1 had an atrial mass, 1 had a valvular abscess, and CF titers ranged from 1:1 to 1:2048 [7–10]. Reliable diagnostics were culture and histopathology of surgically excised valvular tissue.

Prognosis depends on combined surgical and medical treatment. Our patient and 2 prior cases survived with surgery and antifungals [7–9]. Our patient is the only adult female among these cases and had pregnancies during infection and treatment. *Coccidioides* can cause aggressive disease during pregnancy with resultant maternal and fetal mortality [1]. Recommendations are to initiate azoles unless with rapidly progressive infection or pregnancy, in which case amphotericin B is recommended [2]. Fluconazole and, less often, itraconazole are often first-line antifungals in coccidioidomycosis, but studies show that posaconazole has over 70% success treating severe infections that are refractory to other antifungals [12, 13]. Our patient did not tolerate amphotericin and relapsed after fluconazole administration.

Evidence on azole safety in pregnancy is conflicting. Studies show that single, low-dose fluconazole is safe, but higher doses are linked with teratogenicity in animals and possibly with tetralogy of Fallot in humans [14, 15]. A systematic review concluded the following: low-dose fluconazole is safe after first trimester, itraconazole and voriconazole should be avoided, and isavuconazole and posaconazole lack conclusive human data [15]. Posaconazole is US Food and Drug Administration-labeled category C [15]. It is difficult to speculate about effects of posaconazole versus *Coccidioides* itself on our patient’s pregnancies [1].

![Figure 1](https://example.com/figure1.png)  
**Figure 1.** (A) Echocardiography demonstrating severe aortic regurgitation. (B) Chest computed tomography demonstrating anterior mediastinal mass (arrow) and right pleural effusion. Abbreviations: AV, aortic valve; LA, left atrium; LV, left ventricle; MV, mitral valve.

![Figure 2](https://example.com/figure2.png)  
**Figure 2.** Pathology of periaortic and valvular tissue: (A) granulomatous inflammation by hematoxylin and eosin (H&E) stain, (B) multinucleation and *Coccidioides* spherule by H&E stain, and (C) endosporulating *Coccidioides* by Periodic acid-Schiff stain.
CONCLUSIONS

In conclusion, *Coccidioides* rarely causes endocarditis, vegetations may not be detected by echocardiography, and a successful outcome can be achieved with combined surgical and medical management.

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Table 1. Seven Cases of *Coccidioides* Endocarditis

| Age  | Sex | Ethnicity | Cardiac Pathology | Echo Blood Cultures | CF Titers | Treatment | Outcome | Ref. |
|------|-----|----------|------------------|---------------------|-----------|-----------|---------|-----|
| 34 yr | F   | Hispanic | Mediastinal mass; aortic valve | No veg Neg | 1:8 | Surgery + Posaconazole | Survived | Current |
| 10 yr | M   | Hispanic | Right atrial mass; tricuspid valve veg +mass | n/a | 1:2048 | Surgery + Amphotericin + Fluconazole | Survived | [7] |
| 3 wk  | F   | White    | Mitral and tricuspid valve veg +veg | Neg | 1:1 | No antifungals | Died | [8] |
| 21 yr | M   | Black    | Mitral valve abscess; myocarditis n/a positive | n/a | No antifungals | Died | [9] |
| 37 yr | M   | White    | Mitral valve veg +veg | Neg | 1:256 | Amphotericin | Died | [8] |
| 53 yr | M   | Hispanic | Prosthetic aortic valve veg +veg | Neg | 1:32 | Surgery + Amphotericin + Fluconazole | Survived | [8] |
| 40 yr | M   | White    | Mitral, aortic, tricuspid, and pulmonic valve veg +veg | Neg | 1:2 | Amphotericin + Fluconazole | Died | [8] |

Abbreviations: CF, serum Coccidioides complement fixation; F, female; M, male; n/a, not available; veg, vegetation(s).