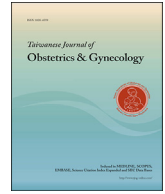




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## Case Report

# Recurrent disseminated coccidioidal meningitis in two subsequent pregnancies

Jonathan E. Blohm<sup>a</sup>, Lee R. McMahon<sup>a</sup>, Chaur-Dong Hsu<sup>a, b, \*</sup><sup>a</sup> University of Arizona College of Medicine-Tucson, University of Arizona, Banner-University Medical Center, Tucson, AZ, United States<sup>b</sup> Department of Obstetrics and Gynecology, University of Arizona, Banner-University Medical Center, Tucson, AZ, United States

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## ABSTRACT

**Objective:** Recurrent disseminated coccidioidal meningitis in two subsequent pregnancies is rare and can pose a challenge in ensuring the health of both mother and baby. In this unique case we highlight this rare occurrence and subsequent treatment.

**Case report:** A 29-year-old G4P1021 with a history of disseminated coccidioidomycosis in a previous pregnancy presented at 8 weeks gestation with nausea, headache, and neck pain. Cerebrospinal fluid analysis was positive for recurrent coccidioidal infection. She was started on Amphotericin and discharged. She re-presented at 30 week's gestation with phonophobia and photophobia, emesis, neck pain and swelling. MRI showed evidence of ventriculomegaly with communicating hydrocephalus. She was treated with therapeutic lumbar punctures throughout her pregnancy and a ventriculoperitoneal shunt following delivery. She had a spontaneous vaginal delivery at 38 weeks and 3 days with no complications.

**Conclusion:** This unique case highlights the susceptibility of recurrent disseminated coccidioidomycosis in subsequent pregnancies and treatment thereof.

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## Introduction

Coccidiomycosis, known to many as “valley fever,” is a fungal infection caused by *Coccidioides immitis* endemic to the Southwest United States and Mexico [1]. Infection is acquired through inhalation of spores and exposure to dust containing the dimorphic fungus in the soil of desert areas. It commonly results in pulmonary disease. However, extrapulmonary dissemination occurs in roughly 1 % of patients with risk factors such as immunosuppression and pregnancy [2]. Previous studies have elucidated the risk of disseminated disease in pregnant women infected with coccidioidomycosis as high as 40 to 100 times that of the general population [3]. Dissemination of coccidioidomycosis in pregnancy has been shown to involve extrapulmonary tissues such as skin and joints. In addition, case studies have shown the involvement of the peritoneum through hematogenous spread [4]. Recent case studies have illustrated disseminated coccidioidomycosis with meningitis and central nervous system (CNS) involvement in pregnancy. However,

the pregnancy was terminated due to preterm premature rupture of membranes [5]. Older studies have shown disseminated coccidioidomycosis in subsequent pregnancies that were treated exclusively with Amphotericin B, but no ventriculoperitoneal shunt [6]. To date, there are no reported cases of recurrent disseminated coccidioidomycosis with meningitis or CNS involvement in the setting of two subsequent pregnancies requiring a ventriculoperitoneal shunt. In this case report, we present a case of a 29-year-old G4P1021 with disseminated coccidioidal meningitis in her last pregnancy. She developed episodes of phonophobia, photophobia, and neck pain in the following pregnancy and had meningitis and hydrocephalus requiring a ventriculoperitoneal shunt with multiple hospital visits throughout her pregnancy.

## Case presentation

A 29-year-old G4P1021 was admitted to the OBGYN service at 8 weeks and 0 days by last menstrual period for nausea with emesis, headache, night sweats, and neck pain for one day. The presentation was concerning for recurrence of coccidioidomycosis, which had complicated her last pregnancy two years prior. At that time, she had been diagnosed with disseminated coccidioidomycosis

\* Corresponding author. 1501 N Campbell Avenue, Room 8327F, Tucson, AZ 32207, United States.

E-mail address: [chaurdonghsu@obgyn.arizona.edu](mailto:chaurdonghsu@obgyn.arizona.edu) (C.-D. Hsu).

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with respiratory, skin, and meningeal involvement in her third trimester, and was treated with high-dose fluconazole. She had a recurrence of symptoms two years later but was symptom free at the time of her positive urine pregnancy test 2–3 weeks before admission. At that point, she had stopped taking the fluconazole. Pertinent obstetric history included a spontaneous abortion, medical abortion, and the pregnancy complicated by coccidioidomycosis with an induction of labor at term for oligohydramnios. The patient also had a history of anemia, asthma, chronic migraines, hepatitis C antibodies, and former tobacco use. The patient was not native to the Southwest region of the U.S. but lived there for 10 years at the time of Valley Fever diagnosis.

On admission, the patient was afebrile with no leukocytosis. A lumbar puncture performed in the emergency department was consistent with a fungal infection. The patient was started on Amphotericin B for presumed recurrence of coccidioidomycosis. Sonography on hospital day 2 dated the pregnancy at 8 weeks and 3 days, and an MRI of the brain without contrast showed no intracranial abnormalities. On hospital day 7, a peripherally inserted central catheter (PICC line) was placed so that the patient could continue receiving the Amphotericin B at an outpatient center through the first trimester. The patient was discharged on hospital day 10, with no further complaints of headache, neck pain, nausea, and vomiting, or night sweats. Serology was positive for coccidioidomycosis immunodiffusion (IMDF) Ab IgM and IgG, and Complement Fixation (CF) titers came back as <1:2, while CSF CF was negative. The patient followed up with OBGYN outpatient at 13 weeks and 0 days and continued to report no symptoms. She stated that she had finished her course of Amphotericin B and switched back to fluconazole after her first trimester.

At 30 weeks, the patient was again admitted to the hospital for complaints of headache with phonophobia and photophobia, emesis, and neck pain and swelling, similar to her previous admission. At that time, MRI showed ventriculomegaly with communicating hydrocephalus that was new from her last imaging, believed to be secondary to the coccidioidomycosis infection. Following a therapeutic lumbar puncture, the patient reported that her headache and nausea had resolved. She was discharged on hospital day 3 with plans to install ventriculoperitoneal (VP) shunt following delivery. However, the patient was seen in the emergency room again for the same presentation at 34 weeks and was admitted once more at 37 weeks and 2 days. A repeat MRI of the brain at her third hospital admission showed an interval increase in hydrocephalus and cerebral edema. The patient underwent another lumbar puncture, with subsequent resolution of symptoms. There were no signs of intraamniotic infection or fetal compromise therefore the patient had no indication for induction of labor.

The patient had a spontaneous rupture of membranes with spontaneous vaginal delivery and no complications at 38 weeks and 3 days. Apgar scores were 8 and 9, and baby girl was briefly admitted to the NICU for 1 day. A repeat serology was <1:2, and the patient was discharged on postpartum day 1. On postpartum day 9, she returned to the emergency room for a headache and underwent her therapeutic lumbar puncture, which relieved her symptoms. Almost 8 weeks after delivery, she had a ventriculoperitoneal shunt placed with subsequent Computed Tomography (CT) head demonstrating expected postsurgical changes and improvement in hydrocephalus. The patient returned to the emergency room for nausea and headache following placement of the ventriculoperitoneal shunt. However, CT of the head showed no significant findings, and the patient was believed to have CSF diversion syndrome. VP shunt settings were adjusted accordingly, and on subsequent follow-up, the patient reported no further symptoms. The patient was continued on high-dose fluconazole with close follow-up.

## Discussion

On initial presentation, the patient in our case presented with the combination of neck pain and headache. In a pregnant patient with this presentation, potential diagnoses include meningitis (bacteria, viral, or fungus), preeclampsia/eclampsia, cerebral venous thrombosis, and migraines, amongst other diagnoses. Interestingly, recent studies have looked at the role of novel biomarkers in preeclampsia, however, our patient's normal blood pressure, absence of end organ damage, and presentation at 8 weeks were reassuring that this was not a case of preeclampsia [7]. MRI was also used to evaluate and rule out other intracranial abnormalities. Additionally, initial lumbar puncture and patient's past medical history of disseminated coccidioidomycosis were suggestive of fungal meningitis, confirmed on follow-up serology.

Previous case reports have described meningeal involvement with coccidioidomycosis infection in pregnancy [8]. In addition, a recent case has shown hydrocephalus in coccidioid meningitis in a non-pregnant patient requiring VP shunts with multiple revisions [9]. Notably, VP shunts have been used in other pregnancy acquired infections such as Zika virus, in addition to de novo hydrocephalus developing during pregnancy [10,11]. A literature review found 8 case reports of pregnant women with obstructive hydrocephalus treated with VP shunts due to various causes not including coccidioid meningitis [11]. Therefore, our case is rare because the patient had two subsequent pregnancies with coccidioid meningitis requiring VP shunt and was able to deliver healthy babies in both pregnancies.

Regarding the patients' medical course, it is important to note the patient had no evidence of intraamniotic infection or fetal compromise throughout her pregnancies. On admission at 37 weeks and 2 days her symptoms and clinical presentation met no ACOG criteria for induction of labor prior to 39 weeks including no preterm premature rupture of membranes [12,13].

Patients with disseminated coccidioidomycosis in pregnancy have been found to have peritoneal, placental, and CNS involvement. In addition, the disseminated disease has also been associated with high maternal and fetal mortality, particularly in later trimesters [14]. Coccidioid meningitis is a devastating complication of disseminated coccidioidomycosis with minimal improvement in mortality over the last several decades [15]. If left untreated, disseminated coccidioidomycosis during pregnancy has mainly been fatal. Our case highlights the potential risk for the recurrence of disseminated coccidioid meningitis in subsequent pregnancy and the importance of aggressive treatment and management in pregnant patients with good outcomes of both mother and baby.

Our unique case is describing recurrent disseminated coccidioidomycosis with meningitis and hydrocephalus in two subsequent pregnancies requiring ventriculoperitoneal shunt. This is the first case in the literature that reported recurrent disseminated coccidioidomycosis meningitis and hydrocephalus in the subsequent pregnancy, requiring a later ventriculoperitoneal shunt with the successful outcome delivery of a healthy baby girl at term.

## Credit author statement

**Jonathan E. Blohm:** Investigation, Formal Analysis, Writing – Original Draft preparation, Writing – Review & Editing.

**Lee R. McMahon:** Investigation, Formal Analysis, Writing – Original Draft preparation, Writing – Review & Editing.

**Chaur-Dong Hsu:** Conceptualization, Writing – Review & Editing, Supervision, Project administration.

## Conflicts of interest

None.

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