



Knee-Deep in Trouble: The Conundrum of Disseminated Coccidioidomycosis, Azole Intolerance, and Pregnancy

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Introduction

Coccidioides immitis transmission occurs through inhalation of spores in endemic areas such as the southwest USA, Mexico, and Central America. About 60% of infections are asymptomatic. Symptomatic cases often resemble community-acquired pneumonia and typically resolve without antifungal treatment. Extrapulmonary dissemination occurs in less than 1% of symptomatic cases and is typically treated with azole therapy. Pregnancy is a well-established risk factor for both the development of acute disseminated infection as well as the reactivation of infection in patients with a history of extrapulmonary disease. In such cases, therapy tends to be lifelong. We present a case demonstrating the reactivation of *C. immitis* in a pregnant patient intolerant of conventional azole therapy.

History of Illness

- The patient is a 41-year-old G4P1021 Mexican woman presenting with increasing left knee pain and swelling while 19 weeks pregnant.
- Has a known history of coccidioidomycosis septic arthritis of the left knee, first diagnosed in 2013
- Intolerant to fluconazole due to fixed drug eruption
- Intolerant to voriconazole due to life-threatening hepatitis.
- 2014 started on posaconazole for long-term suppressive therapy
- Multiple lapses in treatment due to pregnancy, lack of insurance, prescription expiration, possible GI side effects to posaconazole, and additional social factors
- Most recently was lost to follow-up due to the COVID-19 pandemic and has been off posaconazole therapy for 3-4 years,

Physical Exam

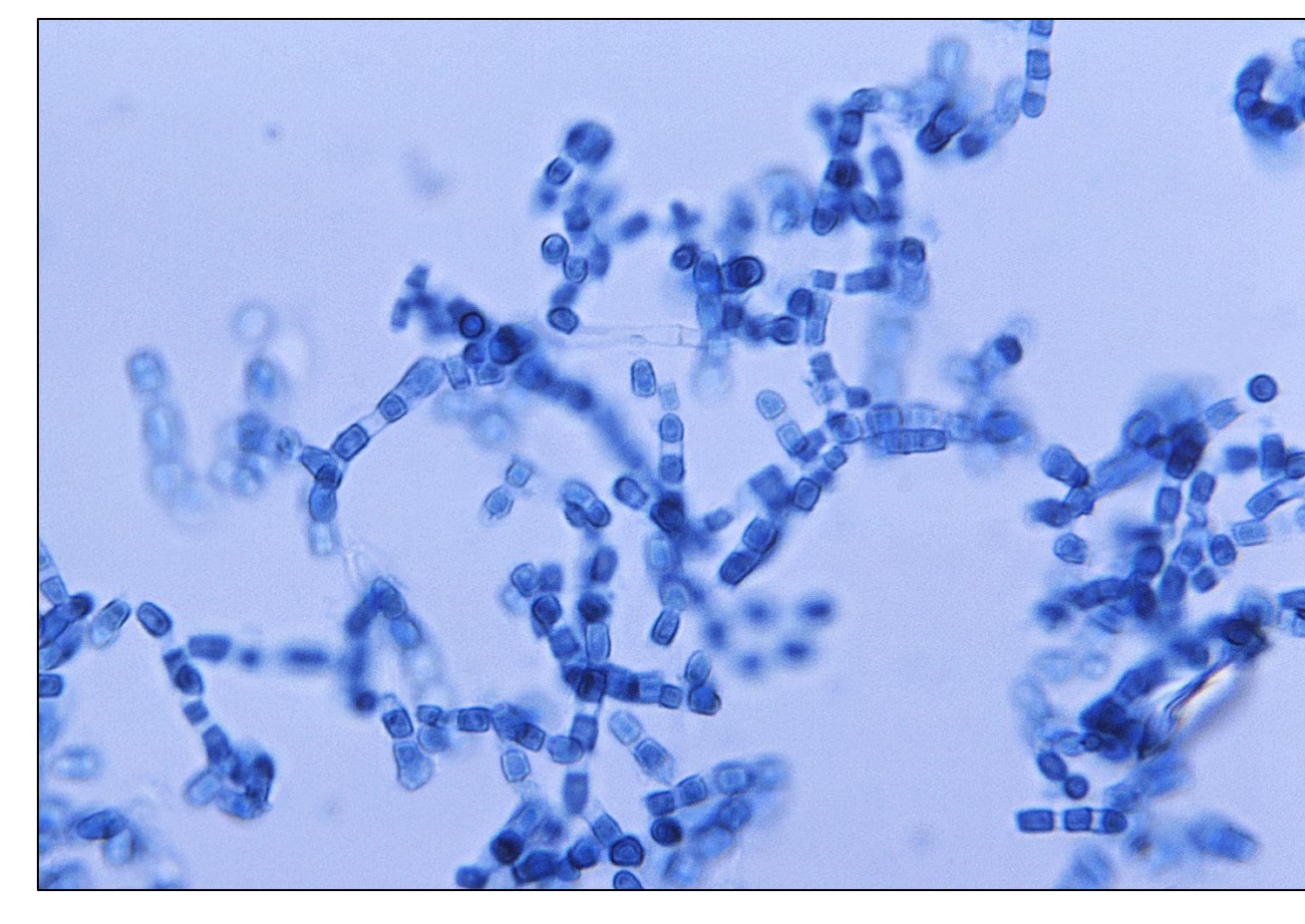
- Cardiovascular- RRR, no murmurs, rubs, or gallops
- Respiratory- No respiratory distress, CTA B/L
- Abdomen: +BS x4, soft, non-tender, **striae gravidarum, uterus size consistent with pregnancy**
- Extremities: no edema, no cyanosis, no clubbing, **mild edema localized to the left knee, tender to palpation, warm to touch, no erythema**

Investigative Studies

- Synovial fluid aspiration of the left knee
 - Growth of *Coccidioides* Species

Coccidioides sensitivities

Medications	MIC
Amphotericin B	0.06
Fluconazole	8
Isavuconazole	0.5
Itraconazole	0.125
Posaconazole	0.125
Voriconazole	0.25



Discussion and Conclusion

- Goals of care suppression of active infection without harm to the patient or her unborn baby
- Azoles are considered first-line therapy for disseminated infection, but unfortunately, they are teratogenic in the first trimester but safe in the second and third trimesters.
 - Liposomal amphotericin B is the drug of choice in the first trimester.
 - Consequently, the patient was hospitalized for 56 days on amphotericin B
- Sensitivity testing of isolates is essential to ensure treatment efficacy. Posaconazole is an unconventional therapy for *C. immitis*, but testing did confirm sensitivity despite previous lapses in treatment,
 - Caregivers were forced to choose Posaconazole, which has been largely unstudied for use in pregnancy
 - Social obstacles were overcome by receiving approval for the Merck Noxafil (posaconazole) patient assistance program to cover the cost of the medication.
- Encouraging pharmacotherapy adherence is crucial for chronic suppression of disseminated disease.
- The patient's baby is due at the end of October and has not reported complications since hospitalization.

References

- When symptomatic, most patients experience a primary lung disease clinically indistinguishable from community-acquired pneumonia. In these cases, patients' symptoms often resolve without targeted antifungal therapy (<https://www.ccm.org/content/89/8/451>).
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- *Coccidioides immitis* picture. <https://phil.cdc.gov/Details.aspx?pid=12196>