Case Report

Atypical blastomycosis in a pregnant woman

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ABSTRACT

Blastomycosis is a rare fungal infection that frequently involves the skin. Atypical presentations are important to identify, especially in pregnant patients, to initiate appropriate therapy and prevent complications. Uniquely, we describe a case of atypical blastomycosis that presented with painful cutaneous abscesses in a pregnant patient, with dissemination to the central nervous system. The case was successfully treated with liposomal amphotericin B transitioned to voriconazole after delivery without complications for the patient or fetus.

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Introduction

Blastomycosis is a rare fungal infection that typically involves the lungs, with frequent dissemination to the skin (Saccente and Woods, 2010). Cutaneous lesions are most commonly painless ulcers and verrucous plaques, with pustules observed in the minority of cases. Pregnancy predisposes patients to a partial immunosuppression state, but central nervous system (CNS) involvement is exceptionally rare in pregnant patients with blastomycosis.

In this case report, we present an atypical presentation of blastomycosis during pregnancy with exquisitely tender abscesses and dissemination to the CNS.

Case

A 25-year-old woman who was 26 weeks pregnant was admitted with multiple skin abscesses. She first noticed a small erythematous papule on her right thigh 3 weeks prior to admission, which progressed with worsening tenderness and pain with weight bearing. Similar lesions began to develop on her left thigh and upper back. She was placed empirically on oral clindamycin with no improvement.

The patient was evaluated at our dermatology clinic 2 weeks after the development of the first lesion, at which point three of the four abscesses were incised and drained. Bacterial cultures at that time tested negative.

A few days later, the patient was admitted for worsening pain and failure to respond to outpatient therapies. She was started on intravenous vancomycin without significant improvement. At the time of our evaluation in the hospital, the patient was found to have four 2- to 3-cm, erythematous, firm, tender nodules on her left and right thighs and upper back (Figs. 1 and 2). A punch biopsy specimen of one of the lesions was obtained and sent for histopathologic evaluation and culture (Fig. 3). Within the dermis, diffuse abscess with associated fungal organisms was noted. Staining with Grocott methenamine-silver and periodic acid Schiff with diastase digestion highlighted the thickened capsule and broad-based budding, consistent with Blastomyces species. Fungal cultures obtained at the time of the biopsy tested positive for budding yeast forms suggestive of Blastomyces.

During her admission, the patient was found to have coughing, headache, dysarthria, and left-sided weakness. Magnetic resonance imaging was performed and demonstrated multifocal abnormally increased T2 and T2 flair signal throughout the brain that was most confluent within the pons and medulla (Fig. 4), suggestive of dissemination. In addition, a chest x-ray was performed, and showed a patchy opacity in the right upper lobe, suggestive of pulmonary involvement.

The patient was initiated on liposomal amphotericin B, which resulted in prompt improvement of her cutaneous lesions, cough, and neurologic symptoms. Treatment was continued for 60 days until preterm vaginal delivery at 35 weeks, at which time the patient was switched to voriconazole to complete a 12-month course. While on amphotericin B, the patient’s creatinine, potassium, and magnesium levels were monitored on Mondays, Wednesdays, and Fridays, and a complete blood cell count was obtained weekly.
Fig. 1. Left thigh showing 2 to 3 cm erythematos, firm, exquisitely tender nodule.

Fig. 2. Hematoxylin and eosin staining that shows diffuse dermal abscess formation with fungal organisms and a thickened capsule, with evidence of broad-based budding.

Fig. 3. Grocott methenamine-silver staining that highlights broad-based bud fungal organisms.
throughout therapy. The patient was maintained on magnesium and potassium supplementation during this portion of her treatment. Once switched to voriconazole, monitoring included weekly liver function tests and voriconazole troughs for 1 month, followed by monthly monitoring.

The patient has shown complete resolution of her symptoms at 9-month follow-up, and the child is healthy without complications.

Discussion

First described in 1894, blastomycosis is a rare fungal infection that typically involves the skin and lungs (Saccente and Woods, 2010). Blastomycosis is most common in the Ohio and Mississippi River Valleys, with cases also reported in the Northeast. Although most commonly a pulmonary infection, blastomycosis can disseminate to involve the skin and CNS as observed in our patient. In addition, in rare cases, primary cutaneous blastomycosis can be seen secondary to direct inoculation (Saccente and Woods, 2010).

Approximately 60% of patients with blastomycosis have skin involvement, with most resulting from dissemination. Typically, lesions are painless and are most frequently seen on the head, neck, and extremities (Saccente and Woods, 2010). Our patient’s presentation was atypical, because the skin lesions were exquisitely tender and painful. In addition, though papular, nodular, and pustular skin lesions can be seen, typical presentation is ulcers and verrucous plaques (Saccente and Woods, 2010).

Pregnancy itself predisposes mothers to partial immunosuppression, likely increasing the likelihood of initial infection and subsequent dissemination. In cases of blastomycosis during pregnancy, multisystem organ involvement is seen in 48% of cases, including 61% with skin involvement (Baker et al., 2017). CNS involvement occurs in ~5% of immunocompetent patients and appears to be more rare during pregnancy, with no cases in a recent case series of 23 patients (Baker et al., 2017).

When the disseminated infection involves the CNS, the Infectious Diseases Society of America considers this to be a severe disseminated infection. The Infectious Diseases Society of America published guidelines on the treatment of severe disseminated blastomycosis recommending initial treatment with liposomal amphotericin B for a minimum of 4 to 6 weeks and then switching to an azole agent for 12 months (Chapman et al., 2008). In the case of a pregnant patient, therapy with liposomal amphotericin B should be continued until delivery, following which the transition can be made to an azole agent.

Although standard amphotericin B has been implicated in renal failure, liposomal amphotericin (as used in our patient) has not been shown to pose such a risk and has better CNS penetration (Chapman et al., 2008; Wortmann et al., 2010). Additionally, amphotericin B is relatively safe to use during pregnancy and is the therapy of choice in neonates who show signs of infection (Chapman et al., 2008).

In contrast, the teratogenic risk of azole agents is too great to be used in a pregnant patient. The resulting phenotype has been compared with that seen in patients with Antley-Bixler Syndrome, which is caused by a mutation in FGF2 and leads to abnormal sterol metabolism or in CYP P-450. Because fluconazole is a selective inhibitor of CYP P-450, embryonic exposure can lead to similar birth defects that most frequently include craniosynostosis, dysmorphic facial features, and other skeletal anomalies (Lopez-Rangel and Van Allen, 2005). When severe disseminated blastomycosis in a pregnant patient is identified and treated appropriately, the patient and fetus can have a good outcome.

Conclusions

We report on an atypical presentation of disseminated blastomycosis during pregnancy. This case demonstrates exquisitely painful abscess formation and dissemination to the CNS, which are both rare presentations of a relatively uncommon infectious process. We highlight the importance of identifying this atypical presentation of blastomycosis to guide proper treatment, and prevent complications for both patient and fetus.

References

Baker T, Patel A, Halteh P, Toussi SS, DeLaMora P, Lipner S, et al. Blastomycosis during pregnancy: A case report and review of the literature. Diagn Microbiol Infect Dis 2017;88:145–51.

Chapman SW, Dismukes WE, Proia LA, Bradsher RW, Pappas PG, Thrhelld MG, et al. Clinical practice guidelines for the management of blastomycosis: 2008 update by the Infectious Diseases Society of America. Clin Infect Dis 2008;46:1801–12.

Lopez-Rangel E, Van Allen M. Prenatal exposure to fluconazole: An identifiable dysmorphic phenotype. Birth Defects Res A Clin Mol Teratol 2005;73:919–23.

Saccente M, Woods GL. Clinical and laboratory update on blastomycosis. Clin Microbiol Rev 2010;23:367–81.

Wortmann G, Zapor M, Ressner R, Fraser S, Hartzell J, Pierson J, et al. Liposomal amphotericin B for treatment of cutaneous leishmaniasis. Am J Trop Med Hyg 2010;83:1028–33.