Persistent and nonprogressive cutaneous blastomycosis in a pregnant adolescent

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INTRODUCTION

Blastomycosis is a fungal infection endemic to the Great Lakes region and Mississippi River Valley,[1] although it is found worldwide. Although asymptomatic infections have been recognized, blastomycosis is usually a respiratory syndrome with rare cases of fulminant respiratory failure from acute respiratory distress syndrome. Dissemination to skin, bone, and other organs without obvious lung disease is not uncommon.[2]

Six distinct species of *Blastomyces* have been described,[3,4] with 4 that are pathogenic to humans. Of these, *Blastomyces dermatitidis* is more likely to cause disseminated disease and *Blastomyces gilchristii* is more often associated with pulmonary-only disease.[2] *Blastomyces percursus* and *Blastomyces helicus* are newly described human pathogens, and not much is known about how they present clinically.

Gestational blastomycosis is rare and presents a risk for disseminated disease in the mother and fetus because of the relative immunosuppression of pregnancy.[5-7] Systemic blastomycosis in pregnant patients may be fatal to the fetus, especially when left untreated.[5] We describe an adolescent patient with untreated cutaneous blastomycosis that remained in situ through 2 pregnancies.

CASE REPORT

A healthy 17-year-old white girl was noted to have an inflammatory breast lesion at the time of her initial obstetric visit. She described the lesion as being present intermittently over a year and self-treated sporadically with topical neomycin, polymyxin B, and bacitracin. She was otherwise healthy, despite a 2-month history of pleuritic chest pain occurring 2 years earlier that self-resolved. On examination, a 1-cm nondraining, centrally ulcerated red plaque was noted on the left medial breast. Through the remainder of her pregnancy, the breast lesion persisted, expanding to 3 cm in size, despite applying mupirocin 3 times daily. Other than an urgent care visit for symptoms of a presumed upper respiratory infection at 30 weeks, the pregnancy proceeded normally, and the patient delivered a healthy baby at 38 weeks via cesarean section.

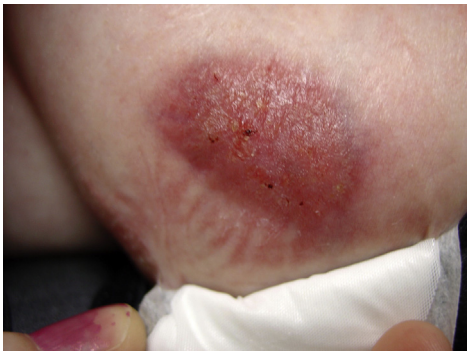

Fig 1. Cutaneous blastomycosis. Left medial breast plaque of female patient with persistent lesion.

In the postpartum period, the dermatology department noted a solitary 2-cm sharply demarcated, centrally eroded, erythematous plaque. A clinical differential diagnosis of the chronic inflammatory plaque included lichen planus, so treatment was started with topical desoximetasone 0.025%

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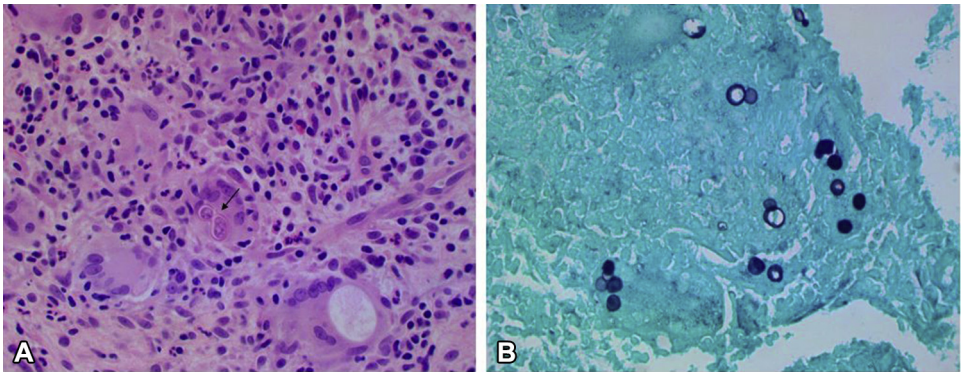

Fig 2. Cutaneous blastomycosis. Microscopic sections of left medial breast punch biopsy. **A**, Irregular pseudoepithelial hyperplasia with exocytosis of inflammatory cells, and underlying dense mixed inflammatory infiltrate mixed with multinucleated giant cells, containing large, thick-walled yeast. **B**, Broad-based budding yeast cells. (**A**, Hematoxylin-eosin stain; **B**, Gomori methenamine-Silver stain. Original magnifications: **A**, and **B**, ×400.)

cream twice daily. The patient failed to follow-up until 4 months later, again pregnant and with a persistent breast lesion (Fig 1). At 25 weeks' gestation, a punch biopsy of the lesion was performed, and budding yeast characteristic of *Blastomyces* were identified by histopathology (Fig 2). Tissue cultures subsequently grew *Blastomyces*. DNA was extracted from the fungal culture and species typed by sequencing a portion of the ITS2 rDNA as previously described.[8] The isolate was determined to be *B dermatitidis*.

Extracutaneous physical examination and chest radiograph were unremarkable besides her pregnant state. One day of intravenous amphotericin B therapy (20 mg) was given, followed by intravenous amphotericin B (40 mg) 3 days weekly and topical ketoconazole 2% cream twice daily. After 4 weeks of treatment, amphotericin B was held because of uncontrolled electrolyte abnormalities. At 39 weeks' gestation, the patient delivered a healthy baby via cesarean section. Because the patient's skin lesions were noted as resolved, ketoconazole cream was discontinued after 9 months. The patient remains free of blastomycosis without clinical recurrence after 13 years.

DISCUSSION

The clinical presentation of blastomycosis is usually a mild-to-moderate respiratory illness but ranges from asymptomatic to acute respiratory failure. Moreover, blastomycosis presents as disseminated illness in up to 20% of cases but occasionally with minor or no respiratory manifestations.

This unusual blastomycosis case spanned 2 years from documentation of the lesion through the end of treatment. Despite the early discontinuation of systemic treatment due to electrolyte abnormalities, we believe that the patient's clinical response was more likely caused by the amphotericin B course, although incomplete, than the topical ketoconazole. Neither the 4-week course of amphotericin B nor topical ketoconazole would normally be considered standard treatment for blastomycosis, but in this case, it seems to have been effective, possibly because of the mild nonprogressive nature of the infection.

The diagnostic certainty of preceding pulmonary infection is low. Throughout the infection, the only suggestion of pulmonary disease was intermittent chest pain 2 years before documentation of the lesion and a single urgent care visit for shortness of breath and ticklish cough during the presence of the lesion. The shortness of breath and cough was presumably a self-limited viral upper respiratory infection, but the timing of the pleuritic chest pain is potentially suspicious for the initial infection, particularly if the 1-year history of the lesion is accurate. Because of the lack of pulmonary symptoms, chest radiographs were not obtained until after diagnosis of the skin lesion and were found to be normal.

The causative strain in this case was determined to be *B dermatitidis*. Previous studies have established that infections of *B dermatitidis* are more likely to cause disseminated disease and less likely to present as acute pulmonary disease.[2] *B dermatitidis* infections have also been found to take longer to diagnose, as measured from symptom onset.[2] This finding is probably attributable to the less-intense pulmonary involvement, which may be a result of the virulence mechanisms of *B dermatitidis* compared with other *Blastomyces* strains. In this case, delayed diagnosis was in part caused by the

lack of familiarity with cutaneous blastomycosis symptomology even within an endemic area (personal observations, J.L.A.).

One speculative explanation for the stable, nonprogressive nature of this infection is the potential for patient-acquired immunity. Previous research has shown that *Blastomyces* exposure likely provides future protection against blastomycosis.[9,10] Although there is no evidence to suggest that this patient was previously exposed or had known household members with previous exposure, she lived and was seeking health care within an endemic area for blastomycosis; therefore, she could have been previously exposed and acquired some level of protective immunity.

Here we describe a stable nonprogressive case of cutaneous blastomycosis in an adolescence girl through 2 pregnancies, without impact to the fetus, despite delayed treatment. Future genetic studies of patients with mild or nonprogressive cases of blastomycosis like the one described here could provide much insight into host immune response to fungal pathogens. We advocate for increased physician awareness that blastomycosis can present as disseminated illness with minor or no respiratory manifestations.

This study was conducted ethically under a Marshfield Clinic Research Institute Institutional Review Board approved protocol, with approval of a waiver of informed consent.

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