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Case Report

CASE REPORT

Unusual presentation of pulmonary blastomycosis complicated by amphotericin-induced refractory electrolyte abnormalities

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Abstract

Blastomyces dermatitidis is an endemic mold infection commonly seen in the midwestern of the USA and rarely affects pregnant women. The most common presentation is a pulmonary infection with variable degrees of severity. Of note, the clinical and radiographic findings of pulmonary blastomycosis can be mistaken for other pulmonary pathologies, thus earning the title of 'the great pretender'. The treatment of choice of infected pregnant patients is amphotericin B, which is known to produce electrolyte imbalances. However, it infrequently causes severe, prolonged and profound hypokalemia and hypomagnesemia. We present the case of a 27-year-old pregnant patient with pulmonary blastomycosis presenting with a lung mass suspicious of malignancy and treated with amphotericin B with subsequent prolonged refractory hypokalemia and hypomagnesemia. Keywords pulmonary blastomycosis pregnancy biopsy computed tomography angiography liposomal amphotericin B

INTRODUCTION

Blastomyces dermatitidis is an opportunistic pyogranulomatous infection endemic in the midwestern of the USA [1]. It is mostly obtained during outdoor activities, causing a primary lung infection, which in rare circumstances can disseminate to the skin, bones and the genitourinary system. The initial presentation of pulmonary blastomycosis is often mistaken for other infectious or non-infectious etiologies [2]. On very rare occasions, opportunistic fungal infections as the *Blastomyces dermatitidis* can occur on pregnant women, which are partially immunosuppressed [3]. This case highlights diagnostic and therapeutic strategies for blastomycosis, which was initially diagnosed as an inflammatory or malignant process in a pregnant woman and treated with amphotericin, as this is the only approved drug in pregnancy.

CASE REPORT

We describe the case of a 27-year-old woman, 24 weeks pregnant, who presented to the hospital with shortness of breath and productive cough for the last 3 months requiring frequent outpatient medical assessments. She did not have any recent travel, but she lives in Chicago. Physical examination revealed right basal crackles, but it was otherwise unremarkable. Initial workup revealed mild elevation of WBC at 11.4 $\times$ 10^3/μl along with an unremarkable chest X-ray. Patient declined computed

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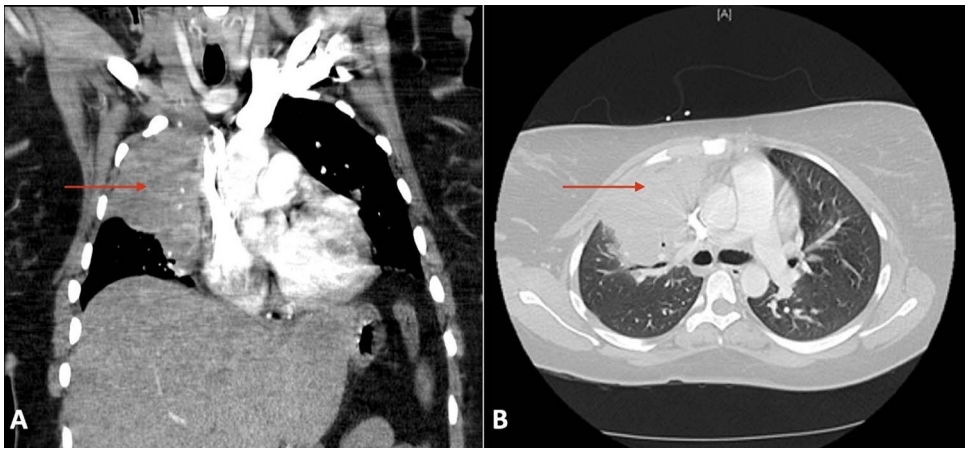

Figure 1: Chest CT angiography revealing large confluent airspace opacity in the anterior right upper lobe abutting the chest wall and mediastinum (red arrow). (**A**) Coronal view. (**B**) Axial view.

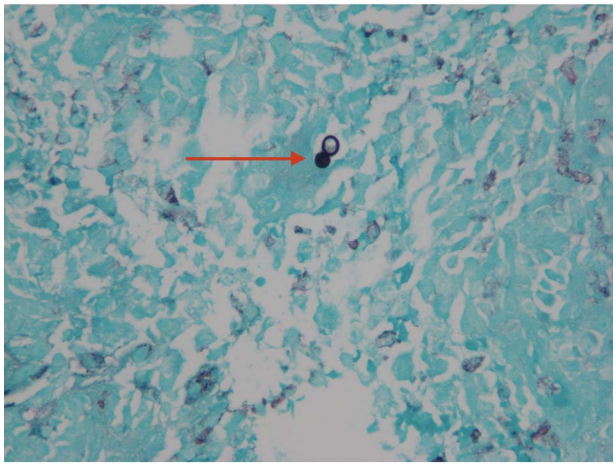

Figure 2: Histologic findings of core biopsy from the right-sided lung mass. Silver stain highlighting a body yeast with characteristics of Blastomyces dermatitidis (red arrow).

tomography (CT) chest due to concerns of radiation exposure and was discharged on oral antibiotics. Three weeks later, she developed worsening respiratory symptoms and basic blood work showed a WBC of 12×10^3, she declined chest CT again and was sent on oral antibiotics. One month later, she was admitted at our hospital with hemoptysis and severe dyspnea, chest X-ray showed a large right upper lobe airspace opacity, subsequent chest CT showed a mass like consolidation on the right upper lobe measuring up to 9 cm in diameter and an additional mass of 2.2 cm in diameter in the left lower lobe. Findings were concerning for neoplasm with a multifocal infectious process also considered in the differential given appearance (Fig. 1). She underwent an ultrasound-guided needle biopsy of the lung mass that showed pyogranulomatous inflammation with silver stain highlighting broad base budding yeast (Fig. 2). Subsequent biopsy cultures were positive for Blastomyces dermatitidis and Blastomyces antigens in urine were positive, with values of 1.73 ng/ml.

Liposomal amphotericin B (AmB) was initiated and the patient symptoms progressively improved over the course of a week. Her course was complicated by profound hypomagnesemia (0.6 mmol/l) and hypokalemia (2.2 mmol/l) despite aggressive IV and oral repletion along with high doses of amiloride (40 mg). Creatinine levels were within normal limits through her treatment. After finalizing her amphotericin regimen, electrolyte disturbances resolved, and the patient had a pregnancy to term without any abnormality on her newborn.

DISCUSSION

Blastomycosis is endemic to the midwestern, southeastern and south-central USA, with an incidence rate that can reach 2.88 hospitalizations per 100 000 persons-year [4]. The incubation period ranges between 3 and 15 weeks. Women are affected less frequently than men and pregnancy seems to be even less frequent. A 20-year retrospective observational study was able to find only 19 cases in pregnant patients, the age of affected women ranged from 17 to 39 years with the medium duration of pregnancy being 26 weeks. When untreated vertical transmission of the disease was reported [3]. The infection can range from asymptomatic to acute respiratory distress syndrome, with a wide variety of infiltrates seen on imaging studies. Given that pregnancy is considered a mildly immunosuppressed state, prompt diagnosis and treatment are warranted.

A combination of clinical suspicion and antigenic testing usually guides therapy. However, histology and cultures are the gold standard and may be required, given that Blastomyces antigenic testing has been shown to have cross reactivity with other fungal infections [1, 5]. Pulmonary blastomycosis has non-specific symptoms (fever, weight loss, shortness of breath, cough) and can present in an acute or chronic manner with different degrees of severity. The radiographic findings can be mistaken with pneumococcal pneumonia, tuberculosis and cancer, thus earning the title of the 'great pretender' [2, 6]. Delay in diagnosis has been related to multiple antibiotic courses, disseminated disease and increase in mortality [7–9]. Our patient underwent several antibiotic regimens and had a 3-month delay in diagnosis that likely allowed progression of the primary infection leading to CT chest finding of a large mass suspicious of malignancy. It is of note that initial Blastomyces urine antigen levels were low, despite the presence a 9 cm mass on CT.

Current guidelines recommend treating blastomycosis on pregnant patients with AmB since azoles have been reported associated with teratogenicity in animal models [9]. The length of treatment on severe disease goes between 6 and 12 months. Liposomal amphotericin is safer when compared to other formulations; however, nephrotoxicity and electrolyte imbalances remain a considerable side effect and are secondary to an increase in the permeability to cations in the distal renal tubules. This is reflected by hypokalemia and hypomagnesemia noted during surveillance laboratory blood work and replaced with supplementation as needed. Even when hypokalemia is expected, severe and persistent hypomagnesemia is not usually seen with AmB [10]. Our patient required a total of 2940 Meq of potassium and a 116 mg of magnesium before reaching stable serum levels. This replacement was required despite of supratherapeutic doses of amiloride.

After reviewing literature, we have found only one other case of a pregnant woman with pulmonary blastomycosis presenting as a primary lung malignancy by Austin et al. Also, we were unable to find a report on profound and prolonged hypokalemia and hypomagnesemia requiring aggressive repletion on this same population. This case highlights the importance of including blastomycosis in the main differential diagnosis of pulmonary processes on endemic areas and to frequently monitor electrolytes on patients requiring amphotericin.

ETHICAL APPROVAL

No ethical approval was required for this article.

CONSENT FOR PUBLICATION

Informed consent was obtained for this case. The patient consented and gave permission for publication of these data.

GUARANTOR

P.T. will be the proposed guarantor for this paper.

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CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflict of interest.

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