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A Case Report of a 74-Year-Old Immunocompromised Host Diagnosed with Pulmonary Blastomycosis and Pulmonary Hemorrhage

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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
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Patient: Male, 74-year-old
Final Diagnosis: Blastomycosis
Symptoms: Cough • hemoptysis • shortness of breath
Medication: —
Clinical Procedure: Bronchoscopy
Specialty: Critical Care Medicine

Objective: Rare disease

Background: Blastomycosis is a rare opportunistic disease caused by inhalation of the fungus *Blastomyces dermatitidis*. Blastomycosis can occur in all individuals but is most commonly seen in immunocompromised hosts. If left untreated or not caught early enough, blastomycosis can progress to fulminant multilobar pneumonia, acute respiratory distress syndrome (ARDS), and even death.

Case Report: A 74-year-old immunocompromised man in northeast Ohio presented to the Emergency Department with shortness of breath and hemoptysis. The patient had a negative evaluation for a gastrointestinal bleed and was found to have significant blood collection in the larynx and trachea. A bronchoscopy demonstrated right upper lobe hemorrhage and an infection with *Blastomyces* species. The patient was started on amphotericin B 5 mg/kg every 24 h for severe blastomycosis. The patient continued to have pulmonary hemorrhage and progressed to multilobar pneumonia and ARDS. Ultimately, the patient died due to respiratory distress after being hospitalized for 5 days.

Conclusions: Blastomycosis can present with multiple clinical manifestations, including pulmonary hemorrhage, in severe disease. Diagnostic delay of blastomycosis is common owing to a nonspecific patient presentation. Blastomycosis is an opportunistic infection; therefore, the fungus can be more commonly seen within immunocompromised hosts. The combination of diagnostic delay and immunocompromised hosts leads to an increased mortality rate from blastomycosis infections.

Keywords: Blastomycosis • Hemorrhage • Immunocompromised Host

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Background

Blastomycosis is a rare systemic disease caused by the dimorphic fungus *Blastomyces dermatitidis* [1]. *B. dermatitidis* exists in nature as a mycelial phase and converts to a yeast phase at body temperature (37°C) [2]. In North America, blastomycosis usually emerges in defined geographic regions surrounding the Great Lakes and the Ohio River and Mississippi River valleys. Blastomycosis is an opportunistic infection most commonly caused by inhalation of conidia into the lungs after exposure to contaminated soil [3]. Patients with blastomycosis can experience a range of clinical manifestations, involving asymptomatic infection, lung involvement that can mimic acute bacterial pneumonia, chronic presentations that imitate lung cancer or tuberculosis, and disseminated disease, which can often lead to diagnostic delay [1,2]. Respiratory failure is the most common cause of death in cases of pulmonary blastomycosis [4]. Blastomycosis has been reported to mimic other fungal infections, such as histoplasmosis and tuberculosis [3,5-7]. In more severe cases of histoplasmosis and tuberculosis, pulmonary hemorrhage has been identified as a significant life-threating complication [8]. However, little to no conclusive clinical data exists on blastomycosis-related pulmonary hemorrhage.

Blastomycosis was first described in Baltimore in the 1890s as a skin infection caused by a protozoan organism. However, it was later discovered that almost all cases of blastomycosis originate through pulmonary entry, whereas cutaneous lesions occur secondarily [8]. The most common extrapulmonary site affected is the skin, followed by bone, genitourinary system, and central nervous system manifestations [9]. In the immunocompetent individual, acute pulmonary blastomycosis can be mild and self-limiting, not requiring any treatment. However, treatment should be considered in all infected individuals to prevent extrapulmonary dissemination.

Pulmonary blastomycosis treatment is determined based on disease severity. There is no complete guideline to decipher the severity of blastomycosis, but severity should be determined by clinical judgment. For severe disease, the current blastomycosis guidelines from the Infectious Disease Society of America recommend amphotericin B liposomal 3 to 5 mg/kg daily or amphotericin B deoxycholate 0.7 to 1 mg/kg daily for 1 to 2 weeks, or until clinical improvement is observed. Step-down therapy consists of itraconazole 200 mg orally 3 times daily for 3 days, followed by 200 mg orally twice daily, for a total treatment duration of 6 to 12 months [1].

We present a case of a patient who was infected with pulmonary blastomycosis in his bilateral lungs. The patient presented with massive hemoptysis that developed into pulmonary hemorrhage as the fungal infection progressed. The patient was categorized as having severe disease and was given a lipid formulation of amphotericin B 5 mg/kg every 24 h.

Case Report

A 74-year-old man presented to the Emergency Department (ED) in northeast Ohio for shortness of breath and hemoptysis/cough that began 2 weeks prior. The patient also reported midsternal chest pain, which was present for several days intermittently. The patient reported feeling weak and was hypoxic at home, per the Emergency Medical Services. No black or tarry stools were reported. The patient had a past medical history of anemia, chronic hepatitis C, chronic kidney disease stage 4, diabetes mellitus, and hypertension. His past surgical history included a renal transplant in 2019. The patient was taking the following medications for his kidney transplant: tacrolimus 5 mg in the morning and 4 mg in the evening, 1 tablet of sulfamethoxazole 400 mg-trimethoprim 80 mg every Monday, Wednesday, and Friday, prednisone 5 mg daily, and mycophenolate 500 mg twice daily.

On arrival to the ED, pertinent physical examination findings included the lungs, which had coarse breath sounds bilaterally. The patient's vital signs were as follows: the patient was afebrile with a temperature of 36.4°C, blood pressure was 162/69 mmHg, heart rate was 99 beats/min, respiratory rate was 18 breaths/min, and oxygen saturation was 92% on 5 liters with a nasal cannula. The patient weighed 91.6 kg.

Pertinent laboratory values included white blood cells of 17.5×10^9/L, neutrophils of 84.1%, serum creatinine of 2.2 mg/dL, hemoglobin of 6.2 g/dL, hematocrit of 20.1%, and platelet count of 218×10^9/L. The patient's chest X-ray on admission read as "right upper lobe consolidation consistent with pneumonia." A fecal occult blood test came back positive.

On admission, the patient was diagnosed with right upper lung pneumonia and possible gastrointestinal hemorrhage. The patient was started on empiric antibiotics, including ceftriaxone 1000 mg i.v. every 24 h and doxycycline 100 mg i.v. twice daily for community acquired pneumonia (CAP). The patient was placed on ipratropium-albuterol and budesonide with 1 unit of packed red blood cells, transfused.

The following day (day 2 of admission), the General Surgery team was consulted to perform an esophagogastroduodenoscopy, which showed no evidence of bleeding for an upper gastrointestinal source, but a significant amount of blood was found in the larynx and trachea.

Therefore, the patient was intubated for airway protection. Subsequently, the Pulmonology team was consulted and

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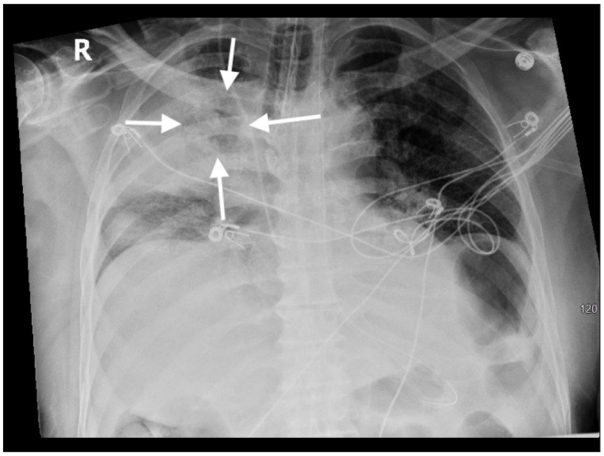

Figure 1. Chest X-ray on day 3 of admission. Arrows point to persistent right upper lobe consolidation.

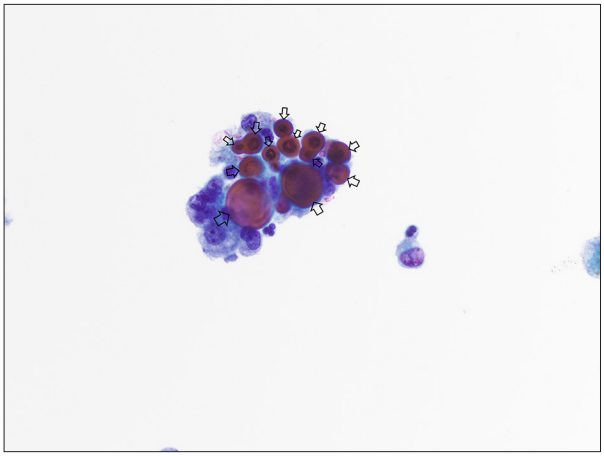

Figure 2. Papanicolaou stain that characterizes the broad-based budding fungus consistent with *Blastomyces*.

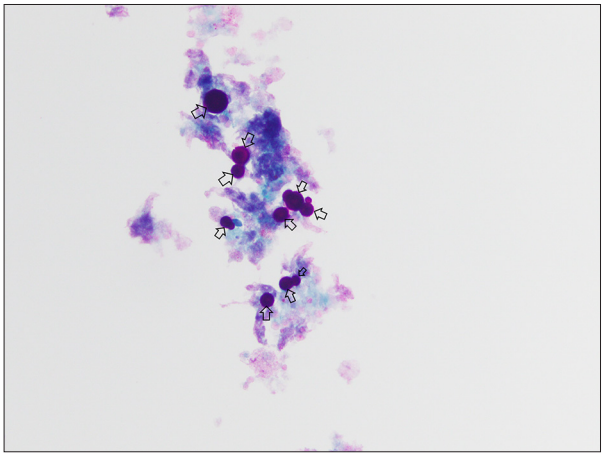

Figure 3. Periodic acid-Schiff stain that highlights the broad-based budding fungus consistent with *Blastomyces*.

completed a bronchoscopy the same day. The bronchoscopy showed bleeding that was localized to the right upper lobe in the posterior segment. A bronchoalveolar lavage (BAL) was performed, in which a specimen was taken from the patient's lung. Cold saline was used to attempt hemostasis, resulting in subpar control; thus, thrombin was injected into the airway, resulting in moderate control. Inhaled tranexamic acid was started to halt the hemorrhage. The patient remained intubated after the bronchoscopy. The patient was transferred to the Medical Intensive Care Unit for close monitoring. Overnight, the patient had visible blood out of his endotracheal tube and was transfused 1 unit of packed red blood cells.

On day 3 of admission, a repeat bronchoscopy revealed no new bleeding, and old blood clots were suctioned out of the right middle lower and left upper and lower lobes. The Infectious Disease team was consulted and expanded antibiotics to vancomycin and piperacillin-tazobactam owing to persistent right upper lobe consolidation on the chest X-ray (**Figure 1**) in the setting of an immunocompromised host. Later in the afternoon, the laboratory called with preliminary results for *Blastomyces* species from the BAL specimen. Thus, the decision was made to start the patient on amphotericin B 5 mg/kg daily for severe blastomycosis.

During the night of day 4 of admission, the patient became hypotensive at 92/54 mmHg, hypoxic with oxygen saturation of 88% on the ventilator, had increased serum creatinine to 2.7, and had bright red blood suctioned from his endotracheal tube. The patient was having massive hemoptysis and developed acute respiratory distress syndrome (ARDS), as defined by the Berlin Criteria (PEEP 7 and PO2/FiO2 ratio of 0.6) [10]. The decision was made to paralyze the patient and increase his sedation to prevent further coughing/hemoptysis.

During the morning of day 5 of admission, a repeat bronchoscopy was performed. Endobronchial blocker placement was completed by the pulmonologist. The patient's left lung was actively and profusely bleeding, into which thrombin was then injected. The pulmonologist recommended interventional radiology to embolize the right upper lobe artery. The family declined the procedure owing to the patient's poor prognosis. The chest X-ray showed the patient had progressed to multilobar pneumonia and continued to have acute hypoxic and hypercapnic respiratory failure. It was determined by the patient's family to withdraw care, and the patient ultimately died due to respiratory distress. Complete cytology results 2 days later were consistent with *Blastomyces* species. Papanicolaou and periodic acid-Schiff stains were completed, which highlighted and characterized that a broad-based budding fungus was growing in the BAL culture, consistent with blastomycosis (**Figures 2, 3**).

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Discussion

Blastomycosis is a disease caused by the fungus *B. dermatitidis* and has varying clinical presentations and severity of illness. An estimated 1 to 2 cases of symptomatic *B. dermatitidis* infections requiring treatment with antifungal drugs occurs per 100 000 in the population each year in endemic areas in the United States [7-9]. Between 1990 and 2010, a total of 1216 deaths were attributed to blastomycosis in the United States, with an overall age-adjusted mortality rate of 0.21 per 1 million person-years [11]. Blastomycosis is a fungal infection that primarily affects the lungs when the fungal spores are inhaled from infected soil. Although there have been occurrences involving cutaneous inoculation of the fungus, almost all cases of blastomycosis are recognized as having a pulmonary origin. The severity of disease depends on the exposure intensity, host immunity, and presence of underlying pulmonary disease. Immunocompromised patients have up to a 40% mortality rate [2,12-14]. Immunosuppressed patients usually develop infections after exposure in the environment, just like immunocompetent patients.

Acute pulmonary blastomycosis can be misdiagnosed as a respiratory tract infection, including CAP. Consolidation is the most common chest radiographic finding and is indistinguishable from CAP. Left untreated, acute pulmonary blastomycosis can progress clinically to chronic pneumonia or ARDS [15]. Diagnostic delay is often seen with blastomycosis due to its uncommon nature and symptoms that mimic many other pulmonary disease developments. The clinical presentation of acute pulmonary blastomycosis is often nonspecific, with symptoms including: fever (54%), cough (73%), night sweats (31%), chills (28%), chest pain (41%), sputum production (50%), hemoptysis (23%), shortness of breath (38%), and weight loss of 5% (37%) [16,17]. When suspected, *B. dermatitidis* is relatively easy to culture and isolate, as colonization does not occur, establishing a definite diagnosis [18]. In areas where the infection is less prevalent, more invasive procedures, such as a bronchoscopy, can be used for diagnosis.

Pulmonary hemorrhage, also referred to as massive hemoptysis, is a potentially life-threatening condition comprised of bleeding from the pulmonary or bronchial vasculature. Owing to the high mortality associated with this condition, immediate evaluation and stabilization is imperative for the patient's survival. The usual source of pulmonary hemorrhage is the bronchial vasculature, causing up to 90% of massive hemoptysis [19]. Literature reviews have identified lung cancer, pneumonia/lung abscess, bronchiectasis, histoplasmosis, and tuberculosis as causes of pulmonary hemorrhage [3,5-7]. Since blastomycosis can mimic several of these pulmonary diseases and can have a high mortality rate, high suspicion for blastomycosis should be considered for a possible diagnosis in patients experiencing hemoptysis, decreasing hemoglobin, and bronchoscopy findings consistent with bleeding in endemic areas where blastomycosis can be found, especially in immunocompromised hosts.

In this case, a combination of laboratory, imaging, and bronchoscopy findings led to the diagnosis of blastomycosis. Complete cytology showed positive results for *Blastomyces* species (our hospital's laboratory does not differentiate the species), thus establishing the diagnosis of blastomycosis. Current clinical practice guidelines from the Infectious Disease Society of America recommend various treatment regimens, depending on the severity of disease. Definitive indications for antifungal therapy include acute diffuse pulmonary infection with moderate to severe symptoms, chronic pulmonary infection, disseminated infection, and central nervous system infection [1].

The patient in this case was immunocompromised and categorized as having severe pulmonary blastomycosis in both lungs and was initiated on amphotericin B 5 mg/kg daily.

Due to massive hemoptysis/pulmonary hemorrhage, severe fungal infection, and progression to ARDS, the patient died. The origin of this infection is unknown. Per conversation with a family member, the patient did not hunt, fish, or enjoy being outdoors.

This case report demonstrates the association between *B. dermatitidis* and its ability to cause pulmonary hemorrhage. Due to its life-threatening potential, blastomycosis should be considered as a possible diagnosis of pulmonary infection when clinically appropriate.

Limitations to this case report do exist. We cannot exclude the possibility of a chance association that a pulmonary hemorrhage occurred in this patient and was not directly caused by the blastomycosis infection specifically. Also, this case report was a retrospective design.

Conclusions

Blastomycosis has nonspecific symptoms and nonspecific radiographic findings that result in diagnostic delay. This can be time sensitive for immunocompromised patients since they are at an increased risk for mortality and have an increased chance for infection progression and severity. Little to no literature exists, to the best of our knowledge, considering pulmonary hemorrhage as a part of blastomycosis pathology. However, after reviewing the literature involving similar fungal infections, this case has led us to believe that pulmonary blastomycosis infections can cause complications of massive hemoptysis/pulmonary hemorrhage in severe disease.

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Declaration of Figures' Authenticity

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