A Unique Case of Coexisting Anaplasmosis and Blastomycosis

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ABSTRACT

Introduction: In presenting this case of tick-borne illness in a patient with known disseminated blastomycosis, we aim to discuss the clinical reasoning and decision-making process when treating a septic presentation in a complex patient with multiple exposures and risk factors, from identifying and addressing the most devastating differentials to selecting appropriate empiric anti-infective regimens.

Case Presentation: We present the case of a 60-year-old male with a medical history of diastolic heart failure, cirrhosis, sarcoidosis, hypertension, splenectomy, and recently diagnosed disseminated blastomycosis, who developed sepsis following a recent tick exposure.

Discussion: While a review of the literature revealed a paucity of cases of coexisting fungal and tick-borne illness, each is independently well-studied. Several reported commonalities exist between *Blastomyces* and *Anaplasma*, including endemic regions and at-risk populations.

INTRODUCTION

Anaplasmosis and blastomycosis are both endemic to the Upper Midwest region of the United States and share a range of overlapping risk factors and clinical features. Anaplasmosis is typically transmitted by *Ixodes* ticks and is associated with wooded areas of the northeastern and north-central states that harbor white-tailed deer. Blastomycosis is a fungal infection often associated with proximity to waterways or forested areas in the Ohio and Mississippi River valleys, as well as the Great Lakes region.[1-3] While both infections are well-described clinical entities that often present with nonspecific findings and febrile illness, there exists a dearth of data regarding the presentation of a co-infection. We present a case of a patient with known disseminated blastomycosis who, following a fishing expedition to northern Wisconsin, developed new-onset fevers and underwent further infectious workup.

CASE PRESENTATION

A 60-year-old male with a history of diastolic heart failure, cirrhosis, sarcoidosis, hypertension, splenectomy, and recently diagnosed disseminated blastomycosis presented with sepsis. In the 2 weeks prior to admission, he had traveled to northern Wisconsin and removed 2 ticks from his right upper extremity. He denied any rashes or other skin changes over the bites and had been taking itraconazole as prescribed for his blastomycosis.

On presentation, the patient was febrile to 104 °F, systolic blood pressure was 80 mmHg, heart rate was 91 beats per minute, and he required supplemental oxygen to maintain appropriate saturations. Computed tomography (CT) of the chest revealed interval improvement in the destructive pulmonary nodules and bilateral opacities related to his blastomycosis and was otherwise unremarkable. Sepsis resolved with fluid resuscitation, and he was initiated on empiric cefepime and vancomycin. Infectious Disease was consulted and recommended adding doxycycline and azithromycin to cover tick-borne illnesses and atypical pneumonia. Following the initiation of doxycycline, he defervesced within 24 hours and did not develop any further fevers during his hospitalization. Vancomycin, cefepime, and azithromycin were discontinued given his response to doxycycline. He also continued on itraconazole to cover for his underlying disseminated blastomycosis.

With the patient's rapid response to doxycycline, known tick

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Figure 1. Computed Tomography of the Chest From Admission With Disseminated Blastomycosis

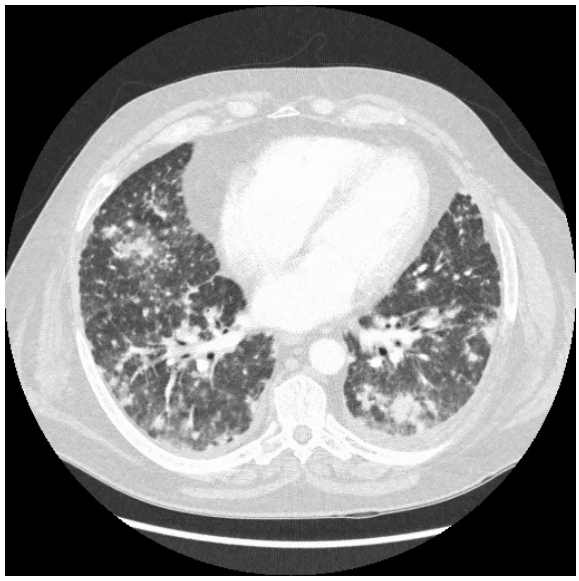
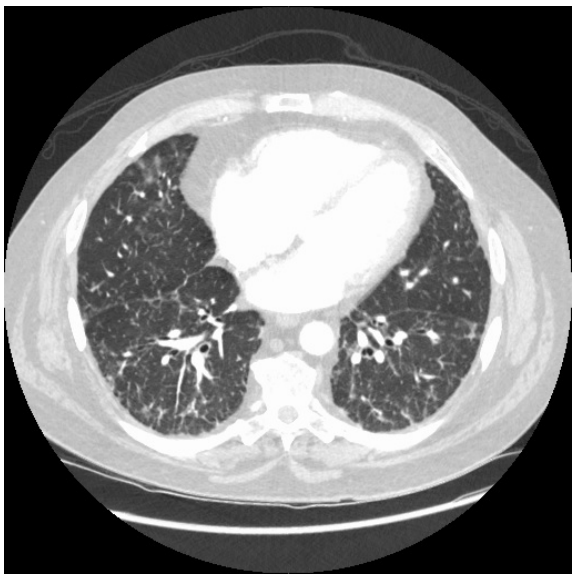


Figure 2. Computed Tomography of the Chest on Second Admission Showing Interval Improvement



bites, 2-week illness incubation period, and gradually rising fever curve, suspicion was high for tick-borne illness. Laboratory evaluation was negative for hemolysis, and no parasitemia was observed on blood smear. Prior to discharge, the removed ticks were brought into the hospital and sent to the lab for further evaluation. Due to his clinical improvement, he was discharged home on itraconazole and doxycycline while his full tick-borne illness panel was still pending. Serum *Anaplasma* polymerase chain reaction testing ultimately resulted as positive, and the patient responded well to a 14-day course of doxycycline.

DISCUSSION

Patients with known infections who present with fevers offer a diagnostic challenge. This case was further complicated by the patient's recent tick bites, as many tick-borne illnesses share endemic areas, symptoms, and risk factors with fungal infections, such as blastomycosis. *Blastomyces* is endemic to the Midwestern, south-central, and southeastern United States, while *Anaplasma phagocytophilium* is found in northeastern and north-central states.[4-7] Both infections most commonly affect middle-aged and elderly males, such as our patient, and both may present with nonspecific findings that make diagnosis a challenge.[5,8]

Patients with anaplasmosis often report a tick bite or exposure 1 to 2 weeks prior to symptom onset and typically present with fevers, myalgias, and headaches.[9] In contrast to ehrlichiosis and Lyme disease, which share a common vector with anaplasmosis, cutaneous manifestations at the site of the tick bite are uncommon.[6] Patients may develop transient leukopenia or thrombocytopenia, although these laboratory changes are variable and not always present. Blastomycosis, caused by the inhalation of fungal conidia, typically presents with mild flu-like symptoms, although pneumonia and even acute respiratory distress syndrome may develop in severe pulmonar blastomycosis. Disseminated blastomycosis appears most commonly with cutaneous and bony lesions, although other manifestations, such as central nervous system involvement, may develop.[10,11]

Our patient's disease timeline, symptom course, and recent tick bites were highly suspicious for tickborne illnesses – a suspicion compounded by his rapid response to treatment with doxycycline. While disseminated blastomycosis is known to cause fevers and similar presenting symptoms, he endorsed adherence to his antifungal medication, consistent with his reassuring CT findings. In addition, his improving skin lesions and lung imaging made worsening blastomycosis a less likely diagnosis. Although babesiosis was initially a concern given his asplenia, he did not have a clinical or laboratory picture suggestive of hemolysis, and no parasitemia was noted on an urgently processed blood smear. This left us with a high clinical suspicion for Lyme, ehrlichiosis, and anaplasmosis. As the laboratory tests for these conditions may take weeks to return a result, we treated the patient with doxycycline for empiric coverage of tick-borne illnesses. Doxycycline is the first-line treatment for all tick-borne illnesses endemic to the United States. It has a relatively benign side effect profile – making it a low-risk but effective treatment option – and was confirmed with pharmacy to not interact with itraconazole.[6]

Our patient demonstrated a robust response to doxycycline initiation, defervescing within 24 hours with no further febrile

episodes. In most cases, symptoms tend to improve rapidly following doxycycline administration.[6] In cases such as this, in which the response to therapy is a temporary confirmation of the diagnosis until laboratory results are available, the duration of antibiotic therapy can be determined after the diagnosis is made and response assessed.[6]

Funding/Support: None declared.

Financial Disclosures: None declared.

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