



Case Reports

From Syphilis to Surprise: Unmasking Disseminated Blastomycosis in a 20-Year-Old Male

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BACKGROUND

Blastomycosis is a systemic endemic fungal infection caused by *Blastomyces dermatitidis*, a dimorphic fungus, that predominantly affects the lungs but can disseminate to other organs, mimicking many diseases, making diagnosis challenging. We present a case of disseminated blastomycosis in a male, initially misdiagnosed as syphilis due to a false positive biopsy result for *Treponema pallidum*. This case highlights the importance of considering atypical presentations of fungal infections, even in the presence of laboratory findings and outside of the normal geographic regions they may be found.

CASE PRESENTATION

A 20-year-old Marshallese speaking male who had recently moved to Washington from Indiana, presented to the emergency department with progressive right knee pain. He had no known past medical history, no prior trauma to his knee, recent travel, hiking, and denied a history of sexually transmitted infections or sexual activity in the past year. Review of systems was positive for night sweats, a nonproductive cough for 2 weeks, reduced appetite, and nausea. He also reported a chronic left lower extremity wound for the past 2 years, and noticed it was spreading from his bilateral knuckles to mid-humerus and bilateral lower extremities 3 months prior. Due to his progressing rash, he followed up with his dermatologist. At the dermatology clinic, he underwent a 6mm punch skin biopsy taken from a 12cm lesion on his left thigh and a 6mm punch biopsy from his right dis-

Abstract

Blastomycosis is a systemic endemic fungal infection caused by *Blastomyces dermatitidis*, a dimorphic fungus, that predominantly affects the lungs but can disseminate to other organs, mimicking many diseases, making diagnosis challenging. We present a case of disseminated blastomycosis in a male, initially misdiagnosed as syphilis due to a false positive biopsy result for *Treponema pallidum*. This case highlights the importance of considering atypical presentations of fungal infections, even in the presence of laboratory findings and outside of the normal geographic regions they may be found.

tal forearm. He was subsequently sent to the hospital due to concern for tuberculosis versus non-tuberculosis mycobacterial infection versus *Treponema pallidum* infection.

On presentation, he was febrile with a temperature of 102°F; the remainder of his vital signs were within normal limits. Labs on admission were significant for leukocytosis at 14.8 K/uL. On examination, he had a 25cm x 15cm wound on his superolateral left thigh and a diffuse, psoriasiform rash on the extensor surfaces of his upper and lower extremities. He was also found to have a swollen, erythematous right knee that was warm to touch with pain to passive range of motion. He was started on empiric antibiotics of ceftriaxone 2 grams every 24 hours and vancomycin 1 gram every 8 hours.

He underwent an MRI which demonstrated a large joint effusion with synovitis, marrow edema, peri-articular muscular edema, and a tracking interosseous fluid collection into the distal femoral metaphysis consistent with an intraosseous abscess up to 6.7 cm in length. The arthrocentesis of the right knee joint showed 21,126 nucleated cells/uL with 89% neutrophils and 390,000 red blood cells/uL, suggestive of an inflammatory effusion, possibly related to the infectious process. Additional lab results for HIV and *T. pallidum* antibody were negative. C-reactive protein was found to be 24.2 mg/dL, with an ESR >130 mm/hr ([Table 1](#)).

Orthopedic surgery was consulted, and he was taken to the operating room for right knee arthrotomy with anterior and posterior synovectomy, partial excision, and debridement of the abscess in his right distal femur. During the procedure, he was found to have gross purulence in

Table 1. Lab values on admission

Lab Test	Lab Result	Reference Range
WBC	14.8 k/uL	3.8-11 k/uL
Total hemoglobin	11.7 g/dL	13.2-17 g/dL
Hematocrit	36.7%	39.0-50.0%
Platelets	476 K/uL	150-400 K/uL
Absolute Neutrophils	12.14 K/uL	1.9-7.4 K/uL
% Neutrophils	82.1%	40%-70%
% Lymphocytes	10.3%	15%-48%
% Monocytes	6.4%	0-12%
% Eosinophils	0.0%	0-7%
% Basophils	0.3%	0.2%
% Immature Granulocytes	0.9%	0-1%
Peripheral Smear	Moderate normocytic anemia. Mild thrombocytosis.	
Sodium	128 mmol/L	135-145 mmol/L
Potassium	3.4 mmol/L	3.5-5.0 mmol/L
Chloride	97 mmol/L	99-109 mmol/L
Carbon Dioxide	20 mmol/L	21-28 mmol/L
Glucose	107 mg/dL	65-99 mmol/dL
Creatinine	0.7 mg/dL	0.7-1.3 mg/dL
Alkaline Phosphatase	150 U/L	35-115 U/L
ALT	89 U/L	10-65 U/L
AST	42 U/L	10-45 U/L
CRP	24.2 mg/dL	0.0-1.5 mg/dL
ESR	>130 mm/hr	0-15 mm/hr
Lactate	1.9 mmol/L	0.6-2.0 mmol/L
Treponema Pallidum Ab total	Non-Reactive	
Treponema Pallidum Ab, IgG (FTA-ABS)	Non-Reactive	
Rapid Plasma Reagin	Non- Reactive	
Fungitell, serum	< 37 pg/mL	< 80 pg/mL
HIV-1 P24 Ag	Non-Reactive	
HIV 1 and 1 Ab, rapid	Non-reactive	
Hepatitis A Ab Total	Positive	
Hepatitis B Surface Antibody Qual	Non-Reactive	
Hepatitis A IgM Ab	Negative	
Hepatitis C Ab	Negative	
QuantiFERON TB Gold	Negative	

the joint and bone. Fungal smear from surgical specimen was positive for budding yeast. Histoplasma and Blastomyces urine antigen, cryptococcal antigen, and 1,2-Beta D-Glucan were obtained. He then started on voriconazole. However, he began to develop hallucinations and QT prolongation requiring transition to Isavuconazonium.

In the absence of a positive treponema antibody, an RPR was sent and resulted negative. The skin biopsy from his dermatologist appointment resulted and demonstrated pallidum stain highlights spirochetes in epidermis, consistent with syphilis. On hospital day five, doxycycline 100 mg twice per day was initiated per infectious disease recommendations in the setting of peni-

cillin shortage. On hospital day 7, the punch biopsy of his left thigh wound returned positive for blastomycosis dermatitis. Isavuconazonium was then switched to itraconazole 200mg twice per day with a duration of 6 to 12 months, and he began to show signs of improvement. At this point, a chest CT showed infiltrates in a bilateral, disseminated, miliary pattern, consistent with pulmonary blastomycosis. He tolerated the itraconazole well and was discharged on hospital day 13 in good condition with recommendations to continue itraconazole for 12 months and doxycycline for two weeks. Upon follow-up appointment 10 days post hospitalization, the patient remained stable with improvement of cutaneous blastomycosis. Per infectious disease, he was recommended to send a diluted



Figure 1. Left lower extremity skin findings on presentation.



Figure 2. Right upper extremities skin findings on presentation.

specimen for treponemal antibody; However, this was never obtained, and the patient did not follow up.

DISCUSSION

Blastomycosis is a dimorphic fungus that exists as both mold in the environment and as a yeast in tissues at body temperature. The most common species is *Blastomyces dermatitidis*. *B. Dermatitidis* is most found in moist acidic soil near lakes and rivers, and is endemic to mid-western, southeastern, and southcentral United States.¹ Unfortunately, the true prevalence and incidence of blastomycosis is not known, as it is a reportable infection in a select few U.S. states. The yearly incidence in these states is estimated to be less than 2 cases per 100,000 people and Wisconsin may have the highest incidence of any state, with yearly incidence ranging from 10-40 cases per 100,000 people.²

Differing from other mycosis, *B. Dermatitidis* often presents in immunocompetent hosts; however, immunocompromised individuals may present with more severe disease. Up to 50% of infected patients are asymptomatic. Symptomatic patients primarily manifest with pulmonary symptoms. After hematogenous spread from the lungs, around 20-50% of patients develop extrapulmonary disease. Men are more likely to have extrapulmonary disease.³

Cutaneous involvement is the most common extrapulmonary form of *B. Dermatitidis*. Skin involvement is estimated to be present in 40-80% of cases. Cutaneous involvement presents in two different forms, verrucous and ulcerative.⁴ The second most common extrapulmonary site is osseous. The prevalence is estimated to be anywhere from 6%-48% with an average prevalence of osteomyelitis in 25% of cases with extrapulmonary manifestations, but 75% of patients with osseous blastomycosis have pulmonary disease. Any bone can be involved, however, the most affected is the lower limb and axial skeleton.^{4,5} Our patient had osseous disease present in his distal femur. Genitourinary symptoms is the third most common extrapulmonary manifestation. This involvement can present as prostatitis or epididymo-orchitis. A prostate massage prior to urine collection improves the detection of genitourinary involvement.^{5,6}

Acquiring the infection can be either sporadically from the environment while disturbing the soil by either construction or outdoor recreational activities. In highly endemic areas, dogs, which are used for hunting, can develop fatal blastomycosis. Cats are less frequently infected, possibly due to less time spent with their nose to the ground.⁷ Blastomycosis is only infectious to humans through spores released by hyphae. The most common mode of transmission is through inhalation of Blastomycosis spores. In the lungs, the spores produce the yeast form of Blastomycosis. The risk factors for disseminated blastomycosis are immunocompromised state, HIV infection, solid organ or hematopoietic stem cell transplantation, and immunosuppressive medications such as TNF inhibitors and prolonged steroids and pregnancy.⁵

Another interesting aspect of this case is the suspicion of the Hook effect in retrospect, which led to delayed diagnosis of syphilis. The Hook effect, or Prozone phenomenon, is an immunologic phenomenon whereby antibodies' effectiveness to form immune complexes can be impaired due to extremely high concentrations of an antibody or an antigen. This results in false negative data. This phenomenon has limited studies, but those that have been done report this phenomenon is extremely rare, occurring in between 0.2-2% of the population with syphilis, and higher in those with HIV.⁸ The patient was ultimately found to have syphilis from evidence provided via a skin biopsy.

In conclusion, this case expresses the significance of considering disseminated blastomycosis in the differential

diagnosis of patients with systemic symptoms and skin lesions even while initial data may suggest alternative diagnosis such as syphilis. Atypical cases can make accurate diagnosis difficult, therefore, it is important to continue to broaden your diagnosis when laboratory results are misleading to ensure timely initiation of appropriate medical therapy.

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- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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- Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND

Disclosures/Conflicts of Interest

The authors declare they have no conflicts of interest

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SUPPLEMENTARY MATERIALS

Supplementary Table. Comprehensive work up

Download: <https://bhm.scholasticahq.com/article/132257-from-syphilis-to-surprise-unmasking-disseminated-blastomycosis-in-a-20-year-old-male/attachment/271422.html>
