

# A Young Man Who Could Not Walk

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## ABSTRACT

Infections affecting the central nervous system caused by *Blastomyces dermatitidis* are rare but curable. We describe a case of a 24-year-old man who presented to the emergency department with progressive bilateral lower extremity weakness over 1 month. On the day of admission, he had minimal muscle strength and was hyperreflexic in the lower extremities. Sensation, however, was intact. Skin examination revealed annular, raised, crusted lesions on his face and legs. A magnetic resonance imaging (MRI) scan showed marrow replacement of the T7 and T8 vertebral bodies and an epidural mass with cord compression. A chest radiograph showed an infiltrate, and a subsequent needle biopsy revealed yeast resembling *B dermatitidis*. A skin biopsy was then obtained, and the culture grew out *B dermatitidis*. He received 4 weeks of amphotericin B lipid complex (total of 6 grams), followed by oral itraconazole. After 1 week on antifungals, he was able to walk with a walker and the skin lesions virtually resolved. At 5 months he was ambulatory and riding a bicycle daily. Blastomycosis should be included in the differential diagnosis of epidural masses.

## INTRODUCTION

Blastomycosis is a fungal infection that can affect multiple organ systems.<sup>1</sup> The dimorphic organism, *Blastomyces dermatitidis*, can be found in soil in the mold form, and infects humans by inhalation of spores to the lungs, where it converts to the yeast form. There,

it spreads hematogenously to the skin, bone, and other organs. Bone infections involving the thoracic spine have been reported previously.<sup>2</sup> We describe a patient with a very unusual presentation of blastomycosis who presented to our emergency department because he was unable to walk. Diagnosis was ultimately made by needle biopsy of the skin and lung.

## CASE REPORT

A 24-year-old African American man presented to our emergency department (ED) with a 1-month history of progressively worsening bilateral leg weakness. Initially, he noticed weakness in his right leg. At a subsequent ED visit, he received a diagnosis of right knee arthritis based on X-rays and was sent home. His symptoms progressively worsened and appeared in both legs. On the day of admission, he reported that he could not walk or get out of bed. The patient denied change in bowel or bladder habits, fever, chills, or cough, but did report some drenching night sweats. His medical history was not otherwise significant, except for several skin lesions on his head, torso, and legs. The skin lesions had been present for several months and did not resolve with topical treatment. He was from central Milwaukee, and resided in an approximately 85-year-old 2-story wood frame house on a small city lot. This house included a front porch with lattice-enclosed crawl space beneath. This site is not near a waterway and there was no evidence of nearby recent excavation. He did not report any significant occupational (he had been a grocery store clerk, and was then unemployed) or recent travel history.

Physical examination revealed a temperature of 98.8° F, blood pressure of 108/64, heart rate of 80, and respiratory rate of 16. Significant findings included multiple areas of red, annular, raised crusted lesions. One lesion was on his right submandibular region and was 4 cm in diameter. There were other lesions on the left posterior thigh (Figure 1) and left lower back. On neurologic exam, the patient was unable to walk. Both the legs were externally rotated. He had hyperreflexia of both lower

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extremities, right greater than left. He had 3-4 beats of sustained clonus of both ankles. Motor strength was absent for the right leg, and barely detectable for the left leg. He was unable to move his toes. Sensation, however, was intact. Plantar reflex showed down-going toes bilaterally. On rectal exam, there was good sphincter tone, and no masses were palpated. Patient had no point tenderness of the thoracic, lumbar, or sacral spine.

Laboratory data included a hemoglobin level of 14.6 gm/dL, and a white blood cell count of 9.5 K/ $\mu$ L. The absolute neutrophil count was 6.4 K/ $\mu$ L with a normal differential. The erythrocyte sedimentation rate (ESR) was 48 mm/hr. An MRI of the thoracic and lumbar spine was obtained, and showed partial marrow replacement of the T8 vertebral body and near complete marrow replacement of the T7, L2, and L3 vertebral body. An adjacent epidural mass of 6.8 cm in length and 10 mm in thickness was noted (Figure 2). There was a moderate degree of mass effect and partial flattening of the cord. Edema in the cord was consistent with cord compression. No abscess was noted. Chest radiograph showed an infiltrate in the upper left lobe (Figure 3). Computed tomography (CT) scan of the chest, abdomen, and pelvis also confirmed the abnormal findings in the lung and spine.

At this time, the presumptive diagnosis was neoplasm. Needle biopsy of the spine was attempted, but a specimen was unobtainable. A lung biopsy was then performed, which showed granulomatous disease, and the differential diagnoses expanded to include fungal and mycobacterial infections. The lung and skin biopsy ultimately showed fungal elements on periodic acid-Schiff stain smear (Figure 4). The skin culture was grown in mycosel media, and at 37° broad based budding yeast consistent with *B dermatitidis* was confirmed. Serology studies, including immunodiffusion for *B dermatitidis*, were positive at the time of diagnosis.

Other tests were obtained, including a tuberculosis skin test; induced sputum for acid fast bacilli; serologies for aspergillus antibody, histoplasma, and coccidiomycosis; serum protein electrophoresis; and an HIV test. All were negative.

Our patient received lipid complex amphotericin B for a total of 6 grams over about 2 months. After several days of therapy, the patient improved dramatically and was able to move his toes and legs. After 1 week, the patient was able to walk with a walker. The skin lesions virtually resolved over several weeks. Repeat MRI of the lumbar and sacral spine was done 2 weeks after initial treatment, and the epidural mass had decreased in size to about 5 mm in maximum thickness. There was



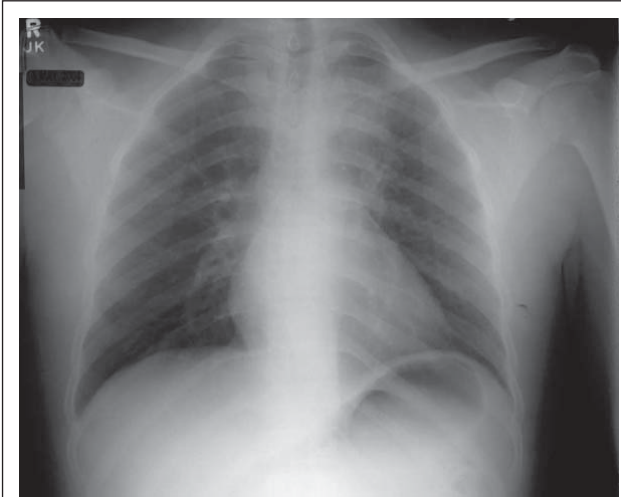
Figure 1. Lesion on left posterior thigh.



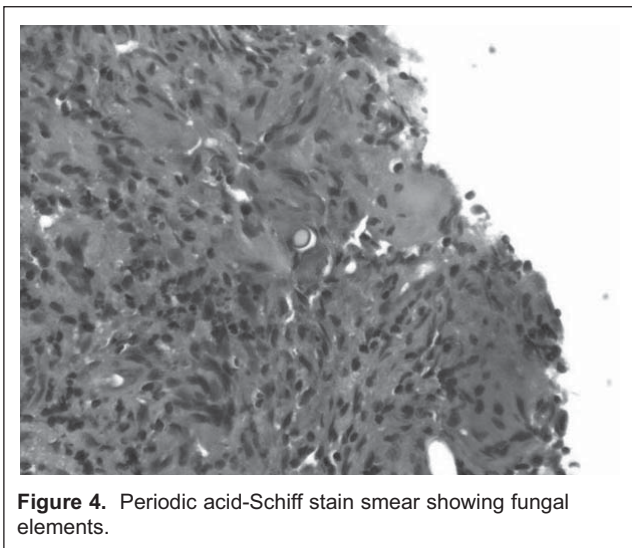
Figure 2. Patient's MRI results showing an epidural mass.

also moderate decrease in cord compression. Repeat chest radiograph showed residual scarring in the left upper lobe. After 2 months, the antifungal agent was switched to itraconazole 200 mg twice a day. Overall, the evidence suggested that he was responding to antifungal therapy and, thus, surgical management was not pursued.

As of 5 months since treatment onset, the patient remained on itraconazole, was ambulatory, had completed physical therapy and rode a bicycle 1-2 hours daily for exercise. He had gained 20 pounds since hospital discharge but still experienced some night sweats and chills. A repeat MRI showed fatty replacement of



**Figure 3.** Patient's chest radiograph showing an infiltrate in the upper left lobe.



**Figure 4.** Periodic acid-Schiff stain smear showing fungal elements.

thoracic vertebral bodies in the area of the previous fungal mass. There was some persistent edema of the thoracic cord, but no evidence of spinal cord compression. His chest X-ray revealed slight improvement in the left paratracheal and suprahilar opacities. His chemistry panel was normal.

**DISCUSSION**

*Blastomyces dermatitidis* is a dimorphic fungus endemic in the southeastern and south central states bordering the Mississippi River, as well as the Midwestern states<sup>1</sup> and Colorado.<sup>3</sup> During 1986-1995, 670 cases in Wisconsin were reported to the Division of Health, which translated into an incidence rate of 1.4 cases per 100,000 persons.<sup>4</sup> The mean annual incidence rate from 1984 to 1996 in Vilas County in northern Wisconsin was 40

cases per 100,000.<sup>5</sup> Our patient came from Milwaukee County, which had a mean annual incidence rate of 0.7 cases per 100,000 from 1999-2003. *B dermatitidis* has been isolated from areas in or near the soil in northern Wisconsin and other areas in relationship to blastomycosis outbreaks or case clusters.<sup>6</sup>

The most common clinical manifestation of this disease is pulmonary infection. Chest radiographs can show infiltrates suggestive of mass, an alveolar infiltrate, or other patterns. Other manifestations include skin, bone, and central nervous system (CNS) problems. One study showed that out of 534 blastomycosis cases, 369 cases (69%) involved lungs, 116 (22%) bone, 29 (5%) CNS, and 20 (4%) other.<sup>7</sup> The most common CNS infections are meningitis and epidural or cranial abscesses.<sup>8</sup> However, spinal cord compressions, spine instability, headaches, seizures, paraparesis, and coma can also occur.<sup>2</sup> Our patient essentially presented with paraplegia, a rare manifestation of blastomycosis.

The differential diagnoses of blastomycosis range from cancer to other infections. Acute pulmonary disease can look like a bacterial infection. Chronic pulmonary disease can look like tuberculosis or cancer. Skin lesions can appear like other fungal infections, or basal cell or squamous cell carcinoma. CNS lesions can appear as metastatic cancer on MRI. Hypercalcemia can appear like sarcoid.<sup>8</sup>

Because of the concern for spinal cord compression in our patient, an MRI was initially obtained to look for changes in the soft tissue, spinal canal, and cord.<sup>9</sup> A CT scan was obtained after the MRI to look for additional lesions in the chest or abdomen. After the MRI and CT were obtained, we continued to consider several pathological processes. These included metastatic cancer; fungal infections other than blastomycosis, such as actinomycosis; cryptococcosis; and tuberculosis (Potts Disease). Coccidiomycosis was unlikely, given our patient's location.

Diagnosis of this disease should include direct visualization of the single broad based budding yeast either in secretions, cultures, or histopathology. CNS lesions can be biopsied either with a needle or by excision. In our patient, interventional radiology was utilized to perform the bone and lung biopsy. Our patient did not require surgical intervention. A study done by Ward et al<sup>2</sup> suggested 3 general surgical indications for CNS blastomycosis: mass lesions, diagnostic biopsy, and osteomyelitis not responding to medication. Since 1995, several cases with CNS infections that did not receive surgical intervention but did well on medical management have been reported in the literature.<sup>10</sup>

Prior to antifungal agents, death from blastomycosis reached upwards of 60% of cases. Amphotericin B was discovered in 1956 and subsequent trials showed the cure rate without relapse ranged from 77% to 91%. Amphotericin B is a polyene that absorbs ergosterol, a part of the fungal membrane, and increases the permeability of the membrane. In effect, it pokes holes through the membrane, rendering it useless for regulating products into and out of the cell. The side effects of amphotericin B include infusion-related symptoms such as shaking chills and fever. Renal failure associated with azotemia, renal tubular acidosis, and electrolyte imbalance can stop treatment. Amphotericin B has remained first line for life-threatening infections,<sup>11</sup> despite the risk for permanent kidney damage and the need for kidney dialysis. Yamada et al<sup>12</sup> reported acute renal failure incidence as high as 49% and 65%.

Our patient used Abelcet, a lipid formulation of amphotericin B. This is basically a complex of amphotericin B and cholesteryl sulfate. In animal model studies, the half-life is greater, concentrations in liver tissue are higher, and concentrations in kidney tissue are lower compared to conventional amphotericin B. Also, nephrotoxicity is less than with conventional amphotericin B.<sup>12</sup>

This case suggested an unknown urban environmental source of *Blastomyces* exposure. Residing in close proximity to waterways and exposure to excavation has been associated with infection,<sup>13</sup> and excavation was suggested as the source of the only (small) outbreak in a large urban area.<sup>14</sup> This patient appeared to lack these or other geographic risk factors. His home was an older house with a front porch, similar to 2 urban sites associated with animal blastomycosis.<sup>15</sup> In a small study of houses within the limits of a small Wisconsin city, the presence of a front porch was associated with human blastomycosis cases, compared to controls, however this association was not found among 38 cases in Milwaukee County (D Baumgardner, E Knavel, unpublished data). There was no specific relationship to any environmental feature suggested by this present case report.

## CONCLUSION

Blastomycosis is a potentially fatal fungal infection with myriad presentations. Untreated patients with spinal cord lesions may progress to paraplegia. Patients who live in endemic regions for blastomycosis presenting with epidural masses should be worked up for fungal infections and appropriately treated. Lipid complex amphotericin B may be a reasonable frontline antifungal agent with less nephrotoxicity than regular amphotericin B.

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