Review of Cutaneous Blastomycosis Seen in Wisconsin

Nina Punyamurthy, BA; Kimberly Katz, MD; Alan Vu, MD; Nathan Duncan, BS; Karolyn A. Wanat, MD

ABSTRACT

Introduction: Blastomycosis is a fungal infection caused by *Blastomyces dermatitidis* that is hyperendemic in Wisconsin. It commonly presents as a pulmonary infection and frequently disseminates to the skin. Studies evaluating the presentation and diagnosis of blastomycosis with skin as a presenting sign have not been thoroughly evaluated, and understanding the most accurate way to diagnose this infection is important for earlier therapeutic intervention.

Methods: This is a retrospective chart review study of a single institution. Subjects were identified through a search of ICD-9 (*International Classification of Diseases, Ninth Revision*) and ICD-10 (*International Classification of Diseases, Tenth Revision*) codes for blastomycosis in the clinical record and pathology database. Patients were included if diagnosed with cutaneous blastomycosis infection or involvement of the skin from systemic infection from January 1, 2009, to June 1, 2021.

Results: Twenty patients with a diagnosis of cutaneous involvement of blastomycosis were identified; 65% (n = 13) were male. Median age of diagnosis was 55.5 years. Fifty-five percent of patients were White, 35% were Black or African American. In addition to residence in an endemic area, 50% (n = 10) had exposure risk factors. Fifty percent of patients (n = 10) initially presented with a skin concerns; 65% (n = 13) had extracutaneous involvement. Diagnosis was made by histopathology alone in 55% (n = 11), culture plus histopathology in 35% (n = 7), and culture alone in 5% (n = 1) of cases.

Conclusions: Our study highlighted similarities to those previously performed. Half of the patients (n = 10) who had cutaneous involvement of blastomycosis did not demonstrate clinically significant pulmonary involvement. Histopathology and culture remain critical in diagnosing cutaneous blastomycosis.

Author Affiliations: Medical College of Wisconsin (MCW), Milwaukee, Wisconsin (Punyamurthy); Department of Dermatology, MCW, Milwaukee, Wisconsin (Katz, Vu, Duncan); Department of Dermatology, Section of Dermatopathology, MCW, Milwaukee, Wisconsin (Wanat).

Corresponding Author: Karolyn Wanat, MD; email kwanat@mcw.edu; ORCID ID 0000-0001-6262-2559

INTRODUCTION

Blastomycosis is a fungal infection caused by *Blastomyces dermatitidis*. This dimorphic fungus is endemic in the Ohio and Mississippi River valleys, Great Lakes region, and southeastern United States and hyperendemic in several areas in northern Wisconsin and Michigan.[1] It most commonly presents as a pulmonary infection caused by the inhalation of spores found in soil. After inhalation, the mold converts to the yeast form and multiplies in the lungs. Up to 50% of infected individuals remain asymptomatic,[2] and both immunocompetent and immunosuppressed hosts can develop severe pulmonary infection progressing to acute respiratory distress syndrome.[1] Dissemination of *Blastomyces* species to other organs can occur, with the skin being the most common site involved (up to 59% of cases),[3] followed by osteoarticular involvement (25%), the genitourinary tract (<10%),[4] and central nervous system (5%-10%).[3-5] The skin lesions seen in blastomycosis can have variable presentations, including crusted verrucous lesions, thick plaques, painful ulcers, and tender subcutaneous nodules. Lesions are most commonly described on exposed areas on the head and extremities but can occur anywhere on the body.[1] Cutaneous infection caused by direct inoculation of the skin is also possible, though only reported in a small number of cases.[6]

Studies evaluating the presentation and diagnosis of blastomycosis with skin as a presenting sign are lacking, and understanding the spectrum of cutaneous manifestations and most

accurate way to diagnose this infection are important for earlier therapeutic intervention.

METHODS

This is a retrospective chart review study of a single institution approved by the Institutional Review Board. Subjects were identified through a search of ICD-9 (*International Classification of Diseases, Ninth Revision*) and ICD-10 (*International Classification of Diseases, Tenth Revision*) codes for blastomycosis in the clinical record and pathology database. Eligible charts were then reviewed for inclusion and exclusion criteria. Patients were included if diagnosed with cutaneous blastomycosis infection or involvement of the skin from systemic blastomycosis infection and had confirmation of diagnosis through histopathology or microbiological confirmation from January 1, 2009 to June 1, 2021. Data collected included demographic information (age, gender, ethnicity), specimen site, other organ involvement, organism type, comorbid medical conditions, past medical history, immunosuppression status, medications, travel history, relevant exposures, history of smoking, occupation, hobbies, general disease presentation, constitutional symptoms, medical or surgical treatment, treatment duration, time to resolution of infection, and whether histopathology and culture were obtained. Descriptive analyses were used in Excel to examine demographic characteristics and risk factors.

Table 1. Patient Demographics, N = 20

Patient Variable	% (n)
Age and sex	
Median age	55.5 years
Male	65 (13)
Female	35 (7)
Race and ethnicity	
White	55 (11)
African American	35 (7)
Unknown	10 (2)

Table 2. Patients With Blastomycosis, N = 20

Patient Variable	% (n)
Other organ involvement	
Pulmonary	50 (10)
Osteoarticular	25 (5)
Central nervous system	10 (2)
At least 1 environmental exposure listed below	50 (10)
Outdoor leisure activity	25 (5)
Hunting/fishing	5 (1)
Proximity to construction	5 (1)
Diagnostic method	
Histopathology alone	55 (11)
Culture and histopathology	35 (7)
Culture alone	5 (1)
Bronchoalveolar lavage with culture	5 (1)

RESULTS

Twenty patients with a diagnosis of cutaneous involvement of blastomycosis were identified. The gender distribution was 65% male (n = 13). The mean age at time of diagnosis was 52.25 years, and the median age was 55.5 years (age range 19 - 88). Fifty-five percent of patients were White, 35% were Black or African American, and 10% were unknown or not reported (Table 1). All of the patients lived in Wisconsin. In addition to residence in an endemic area, 50% (n = 10) had exposure risk factors, including proximity to construction, hunting, fishing, or other outdoor leisure activities (Table 2). Fifty percent of patients (n = 10) initially presented with a skin concern. The morphology of cutaneous lesions was variable, with 40% (n = 8) of patients presenting with verrucous or crusted papules and plaques, 25% (n = 5) with violaceous papules or nodules, and 20% (n = 4) with an ulcerated lesion. Pustules and abscesses also were present in a minority of patients (n = 3). Forty percent (n = 8) of patients presented with pulmonary symptoms, including cough, hemoptysis, or shortness of breath. One patient first sought medical care for headaches, dizziness, and falls, and another presented initially for arthralgias. At time of presentation, 45% (n = 9) of patients also had constitutional symptoms of fever, chills, or weight loss. A majority of patients (65%, n = 13) had extracutaneous involvement. Organ systems involved included the lung (50%, n = 10), osteoarticular involvement (25%, n = 5), and central nervous system (10%, n = 2). Diagnosis was made by histopathology of skin biopsy alone in 55% (n = 11), culture plus histopathology in 35% (n = 7), and culture alone in 5% (n = 1) of cases (Table 2). In 4 of the cases in which diagnosis was made by histopathology alone, culture was obtained and did not demonstrate fungal organisms; in the other cases, culture was not performed. One patient was diagnosed with disseminated blastomycosis through bronchoalveolar lavage with culture alone and had resolution of cutaneous symptoms after starting antifungal therapy.

Twenty percent (n = 4) of patients with cutaneous blastomycosis were immunosuppressed. One patient had a history of kidney transplant, 1 with autologous stem cell transplant, and 2 with sarcoidosis and on systemic immunosuppressants (prednisone and/or mycophenolate mofetil). All 20 patients received antifungal therapy with a triazole. Itraconazole was used most (80%, n = 16), followed by voriconazole (25%, n = 5). Two patients were started initially on itraconazole and later switched to either voriconazole or posaconazole. Additionally, 35% (n = 7) of patients also received amphotericin B. Surgical debridement was utilized in 30% (n = 6) of patients. Seventy percent (n = 14) of patients had complete resolution of infection, while the remaining patients were either lost to follow-up or died due to unrelated causes before confirmation of infection resolution. There was no evidence of disease sequelae in any of the cases.

DISCUSSION

Our study highlighted several similarities to those previously performed. Interestingly, 75% of the patients in this study did not have an underlying source of immunosuppression, which is similar to prior studies where disseminated blastomycosis is commonly seen in those who are immunocompetent. This is in stark contrast to histoplasmosis and coccidioidomycosis in which immunosuppression is often a prerequisite for disseminated disease.[7] This difference may be due to the risk of systemic dissemination being determined by pathogen-related factors in blastomycosis, rather than host immune defenses as with other organisms.[7] Our patients had similar lung and cutaneous involvement, and half of the patients (n=10) in this study did not demonstrate clinically obvious pulmonary involvement. As pulmonary involvement is the most common source of infection, we hypothesize that even if not being the cause for presentation, patients have subclinical pulmonary involvement. The rate of osteoarticular and central nervous system involvement in this study were also similar to those in previous reports.[7] Interestingly, 3 patients in this study had a history of incarceration, though this may be related to environmental exposure of the site rather than incarceration itself.

Cutaneous lesions in disseminated blastomycosis are classically reported as verrucous or ulcerative.[8] The verrucous lesions begin as papules and progress into plaques, often with heaped up borders. The ulcerative form, in contrast, begins as erythematous nodules or pustules that then ulcerate and heal over and may reulcerate. While we do not have data on lesion morphology for 3 of the patients, the remainder of patients in our subset had typical presentations of blastomycosis (Figures 1 and 2).

Histopathology and culture remain critical in diagnosing cutaneous blastomycosis, along with a high degree of clinical suspicion. In this study, culture had an overall yield of 63.6% for growth of fungal organisms; however, for the specimens that did not grow fungal organisms, histopathology allowed for diagnosis with the presence of broad-based budding yeast. While previous studies have demonstrated that culture is the most sensitive diagnostic method for blastomycosis,[9] our study highlights scenarios where histopathology was required for diagnosis as culture did not grow. Histopathology and bedside diagnostics, such as performing microscopy using potassium hydroxide and exfoliative cytology, also remain crucial in earlier diagnosis as this can be visualized before the culture has resulted in growth.[10] When evaluating a patient with clinical concern of cutaneous blastomycosis, performing both culture and histopathology on tissue specimens is essential. This study demonstrates that both culture and histopathology should be utilized to aid in timely diagnosis if blastomycosis is suspected. Limitations of the study include small sample size, retrospective nature, and partial or incomplete data for patients lost to follow-up.

Figure 1. Verrucous Plaques on the Face (A) and Lower Extremity of the Same Person

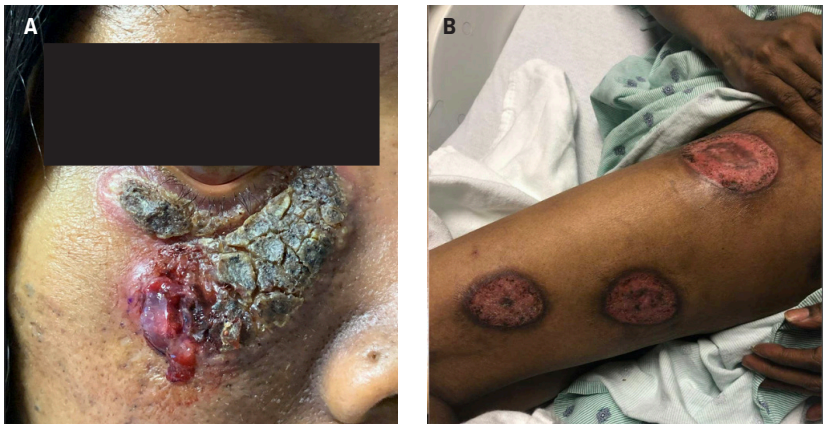
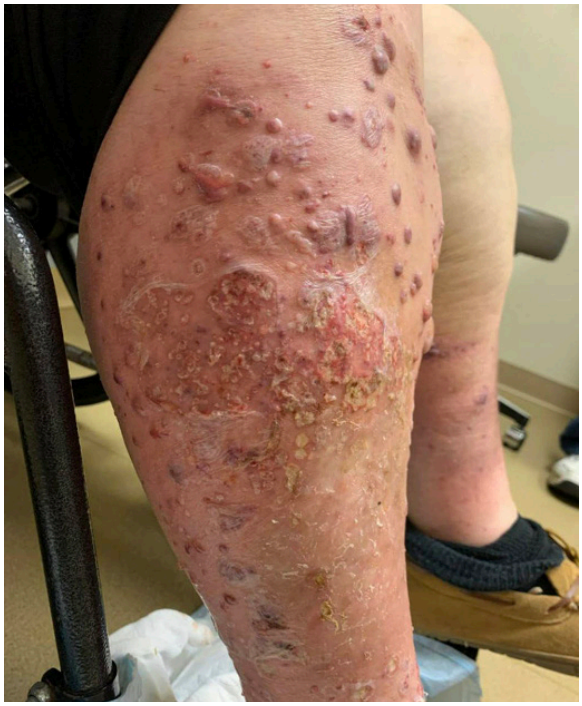


Figure 2. Numerous Pustules, Superficial Erosions, and Ulcers with Fibrinous Tissue Involving Nearly the Entire Right Lower Leg



CONCLUSIONS

This study highlights the most common presentations of blastomycosis infection of the skin seen in Wisconsin, which is similar to that demonstrated by previous studies. Diagnosis of this systemic infection can be achieved through skin histopathology, bedside diagnostics, and culture. As the complications of invasive

blastomycosis can result in hospitalizations, surgery, bacteremia, and even death, understanding demographic information of these patients and methods of early detection allow us to better understand and treat these types of infections.

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