Blastomycosis in Wisconsin: Beyond the Outbreaks

Katrina Thompson, Alana K. Sterkel, Erin G. Brooks

ABSTRACT

In the summer of 2015, many individuals visiting the Little Wolf River in Waupaca County were exposed to the pathogenic fungus, *Blastomyces*. Over time, 59 confirmed and 39 probable cases were reported to the Wisconsin Department of Health Services (W-DHS), making this one of the largest outbreaks in recent state history. Though most instances of blastomycosis are not associated with common source outbreaks, cases such as this highlight the need for vigilance regarding this preventable cause of death. In the state of Wisconsin, an average of 118.6 cases (range, 84-174) of confirmed blastomycosis are diagnosed annually; the majority of these cases are sporadic rather than outbreak-associated. In the current study, we review characteristics of blastomycosis cases diagnosed at our academic medical center, as well as examine statewide W-DHS data, in order to familiarize pathologists with the epidemiologic and histologic characteristics of this disease. *Acad Forensic Pathol.* 2017 7(1): 119-129

AUTHORS

Katrina Thompson MD, University of Wisconsin Hospital and Clinics - Department of Pathology and Laboratory Medicine

Roles: Project conception and/or design, data acquisition, analysis and/or interpretation, manuscript creation and/or revision, approved final version for publication, accountable for all aspects of the work, principal investigator of the current study, writing assistance and/or technical editing.

Alana K. Sterkel PhD, University of Wisconsin Hospital and Clinics - Department of Pathology and Laboratory Medicine

Roles: Project conception and/or design, data acquisition, analysis and/or interpretation, manuscript creation and/or revision, approved final version for publication, accountable for all aspects of the work, writing assistance and/or technical editing.

Erin G. Brooks MD, University of Wisconsin Hospital and Clinics - Department of Pathology and Laboratory Medicine

Roles: Project conception and/or design, manuscript creation and/or revision, approved final version for publication, accountable for all aspects of the work, principal investigator of the current study, general supervision, general administrative support, writing assistance and/or technical editing.

CORRESPONDENCE

Katrina Thompson MD, 1111 Highland Ave, Madison WI 53705, KThompson5@uwhealth.org

ETHICAL APPROVAL

As per Journal Policies, ethical approval was not required for this manuscript

STATEMENT OF HUMAN AND ANIMAL RIGHTS

This article does not contain any studies conducted with animals or on living human subjects

STATEMENT OF INFORMED CONSENT

No identifiable personal data were presented in this manuscript

DISCLOSURES & DECLARATION OF CONFLICTS OF INTEREST

This work was presented at the 2016 NAME Annual Meeting. The authors, reviewers, editors, and publication staff do not report any relevant conflicts of interest

FINANCIAL DISCLOSURE

The authors have indicated that they do not have financial relationships to disclose that are relevant to this manuscript

KEYWORDS

Forensic pathology, Blastomycosis, *Blastomyces*, Wisconsin, Outbreak

INFORMATION

ACADEMIC FORENSIC PATHOLOGY: THE OFFICIAL PUBLICATION OF THE NATIONAL ASSOCIATION OF MEDICAL EXAMINERS

©2017 Academic Forensic Pathology International • (ISSN: 1925-3621) • <https://doi.org/10.23907/2017.014>

Submitted for consideration on 8 Dec 2016. Accepted for publication on 20 Dec 2016

INTRODUCTION

The *Blastomyces* genus is comprised of two pathogenic dimorphic fungal species: *B. dermatitidis* and *B. gilchristii*. Both species are endemic east of the Mississippi river from Wisconsin to Louisiana and as far east as northern Maine (1). The organism is known to reside in the soil, but becomes aerosolized around lakes and rivers. In addition to humans, it can infect many different hosts including animals such as dogs. Inhalation is the most common way to acquire blastomycosis; transmission from person to person is uncommon, but can be seen, particularly transplacentally between mother and fetus or between partners during sexual intercourse (2). Rarely, direct inoculation of the skin has occurred during autopsies when pathologists have injured themselves and unintentionally contaminated the wounds with infected patient tissue (3). The clinical manifestations can be quite variable, ranging from asymptomatic to rapidly severe and fatal respiratory distress. Many factors are thought to contribute to clinical severity including inoculation level, time to treatment, and underlying health and immune status. Disseminated disease can also arise and may involve sites such as the skin, bone, genitourinary tract, and central nervous system (4). Although not a nationally notifiable disease, blastomycosis is endemic in the state of Wisconsin and has been designated as a reportable disease since two major outbreaks occurred in 1984 (5). Other states in which blastomycosis is a reportable disease include Arkansas, Louisiana, Michigan, and Minnesota (1).

METHODS

A retrospective search of the University of Wisconsin Hospital and Clinics electronic databases including PowerPath (Sunquest Informational Systems), McKesson Information Systems, and Healthlink (Epic) was conducted for tissue samples, autopsies, cultures, and clinical information for patients positive for blastomycosis. Cases were retrieved from years 2003-2015 using search terms “blastomycosis,” “*Blastomyces*,” and “*B. dermatitidis*.” Until 2014, forensic pathology autopsy reports at our institution were maintained in a separate nonelectronic database; this separate forensic

report database was manually searched for confirmed blastomycosis cases from 2003-2014. Data were compiled concentrating on age at diagnosis, gender, race/ethnicity, comorbidities, method of diagnosis, morbidity and mortality due to *Blastomyces* infection, and date of initial diagnosis. Finally, statewide blastomycosis epidemiologic data provided by the Wisconsin Department of Health Services (W-DHS) from the years 2003-2015 were reviewed; a confirmed case of blastomycosis as defined by W-DHS required either isolation of *Blastomyces* spp. or visualization of the characteristic broad-based budding yeast from a patient sample.

RESULTS

University of Wisconsin Hospital and Clinics Data

Between 2003 and 2015, 82 confirmed cases of blastomycosis were diagnosed from culture and/or tissue samples obtained at the University of Wisconsin Hospital and Clinics (average annual number of cases, 6.31). Of these, 42 were diagnosed via culture only, 20 via tissue samples only (skin, lung, or other), and 20 via both culture and tissue samples. Demographics, comorbidities, and date of diagnoses are reported in **Table 1**. Review of medical records revealed that ten patients died due to blastomycosis, two of which were autopsied. **Table 2** outlines specific demographics, comorbidities, and date of diagnosis of those who died due to blastomycosis. The fatality rate of blastomycosis cases diagnosed by tissue was 12.2%. Autopsy findings were reviewed in both cases.

Autopsy Case 1:

An immunocompetent 21-year-old man without significant medical history participated in a Little Wolf River (Waupaca County, WI) rafting trip in July of 2015. He was diagnosed with blastomycosis in August, but declined antifungal treatment until November of 2015, at which point he was hospitalized with severe respiratory distress. He was ultimately placed on extracorporeal membrane oxygenation and antifungal medication. He developed metabolic abnormalities that led to acute toxic metabolic encephalopathy and he died.

At autopsy, the lungs were markedly heavy and consolidated, with multifocal hemorrhage (**Image 1**). Following formalin fixation, a focal miliary pattern of granulomas was evident (**Image 2**). Microscopic sections revealed diffuse interstitial and intra-alveolar organizing fibrosis, with scattered hyaline membranes and type II pneumocyte hyperplasia (**Image 3A**). All lung lobes were involved by this exuberant diffuse alveolar damage and organizing pneumonia. There were also geographic areas of intra-alveolar hemorrhage, necrosis, cavitation, and acute thromboemboli within distal vessels. Admixed with the areas of organizing fibrosis were numerous histiocytes and giant cells containing round, encapsulated, broad-based budding yeast that appeared morphologically consistent with blastomycosis (**Images 3B and 3C**).

Autopsy Case 2:

An immunocompromised 68-year-old man with a history of renal transplantation secondary to diabetic nephropathy was admitted six months prior to death due to diffuse viral (varicella zoster and cytomegalovirus) and fungal (*Aspergillus*) pneumonia. His medical history was significant for type 2 diabetes mellitus, hypertension, congestive heart failure, atrial fibrillation, and a prosthetic aortic valve. Complications during hospitalization resulted in an above-the-knee amputation for staphylococcal osteomyelitis. He developed fever and dyspnea, and went into cardiac arrest. Although successfully resuscitated, he subsequently developed acute respiratory and multiorgan failure and died.

At autopsy, the lungs were markedly heavy, with focal consolidation and pulmonary bullae. Several small, white-tan nodules averaging 0.2-0.5 cm in diameter were scattered throughout the lung parenchyma. Acute antemortem thromboemboli were visualized within the small peripheral pulmonary arteries with corresponding wedge-shaped, tan colored distal infarcts. Microscopic sections revealed pneumonia, necrosis, and hemorrhage resulting in disruption of the alveoli. Numerous round, encapsulated, broad-based budding yeast, morphologically consistent with blastomycosis were also seen. Gross examination of the skin re-

Table 1: Demographics, Health Status, and Year of Diagnosis for Confirmed Blastomycosis

Average Age at Diagnosis	45 (range 3-86)
Sex	
Male	53 (65%)
Female	29 (35%)
Race	
Caucasian	58 (70%)
African American	4 (5%)
Asian	8 (10%)
Hispanic	3 (4%)
American Indian	1 (1%)
Unavailable	8 (10%)
Comorbidities	
None	31
Transplant (solid organ)	17
Underlying lung disease	9
Infections (HIV, tuberculosis, etc.)	6
Diabetes Mellitus	10
Other Causes of Immune Suppression	21
Year	
2003	7
2004	2
2005	5
2006	6
2007	6
2008	3
2009	10
2010	9
2011	4
2012	5
2013	5
2014	10
2015	10

Table 2: Demographics, Health Status, and Year of Diagnosis for Blastomycosis-Related Deaths

Average Age at Diagnosis	50 (range 21-76)
Sex	
Male	7 (70%)
Female	3 (30%)
Race	
Caucasian	5 (50%)
Asian	2 (20%)
Hispanic	1 (1%)
Unavailable	2 (20%)
Comorbidities	
None	1
Transplant (solid organ)	6
Underlying lung disease	1
Infections (HIV, tuberculosis, etc.)	2
Diabetes Mellitus	2
Other Causes of Immune Suppression	1
Year	
2003	1
2004	2
2007	1
2010	2
2011	1
2012	1
2014	1
2015	1

vealed scattered ring-like gray lesions averaging 0.5 to 1.0 cm in diameter concentrated over the back and anterior chest wall. Microscopic examination of those lesions revealed normal cutaneous architecture without evidence of intracellular inclusions.

Wisconsin Department of Health Services Data

Between 2003 and 2015, the average number of confirmed cases of blastomycosis reported annually in the state of Wisconsin was 118.6 (range, 84-174). The majority of cases were sporadic; however, in four

years (2006, 2009, 2010, 2015) there were blastomycosis outbreaks (**Figure 1**). The most recent outbreak of blastomycosis arose among individuals who visited the Little Wolf River in Waupaca County, WI during the summer of 2015. To date, there have been 59 confirmed and 39 probable cases of blastomycosis—including the previously described fatality—associated with this outbreak.

Beginning in 2008, W-DHS began requesting more in-depth demographic, clinical, diagnostic, and exposure documentation for reported cases of blastomycosis.

Image 1: Pulmonary blastomycosis results in markedly heavy lungs with numerous fibrous adhesions causing irregularity of the pleural surfaces. The patches of discoloration represent areas of hemorrhage and necrosis.

sis. Between 2008 and 2014, there were a total of 787 confirmed blastomycosis cases in Wisconsin. The majority of the patients were male (67%), and the median age of diagnosis was 46 years (range, 3-97 years). The symptoms most commonly reported were cough and/or fatigue (75%), fever/chills/night sweats (50%), and skin lesions (25%). In 44% of cases (n=346), inpatient hospitalization was required and the annual fatality rate was 5.6% (range, 3.2-11.2%). One caveat is that while reporting of blastomycosis is mandatory in

the state of Wisconsin, reporting of whether or not a confirmed case results in death is not. Thus, the above fatality rates only represent those deaths that were voluntarily reported.

DISCUSSION

The diagnosis of blastomycosis may not be clinically suspected as the disease manifestations can vary widely. One larger retrospective study found that

Image 2: White, firm, granulomatous lesions are common within *Blastomyces* infected organs. Within the lungs, granulomas can vary in size and may be either focal or diffuse in a miliary pattern (as seen above). Formalin fixation can increase tissue contrast, allowing for better visualization of small granulomas.

the diagnosis was correctly suspected at initial clinical evaluation in only 18% of patients (6). The most common misdiagnoses included lung tumor and/or metastatic disease, pneumonia, and tuberculosis (7). Given that the disease is often unsuspected, microbial culture samples may not be submitted, necessitating diagnosis by morphologic evaluation of tissue samples obtained via biopsy or autopsy. As shown in the current study, even in endemic states such as Wisconsin, the majority of blastomycosis cases are sporadic rather than associated with well-publicized outbreaks, and case history may not be particularly helpful in suggesting the diagnosis. Our data suggest that while the median age of blastomycosis diagnosis is 45 years, the disease should be considered in all age groups ranging from pediatric to geriatric and

that patients need not be immunocompromised to become infected. Of the patients at our institution infected with *Blastomyces*, 40% had no clinical history or comorbidity that would cause immunosuppression or opportunistic infection opportunities. The other 60% had some sort of immunosuppression either iatrogenic (e.g., solid organ transplant undergoing transplant rejection prevention, chemotherapy, or corticosteroid treatment for other underlying disorders), concurrent infections (e.g., human immunodeficiency virus, tuberculosis), or medical conditions (e.g., underlying lung disease or diabetes mellitus). Men are more likely to be affected than women; more than two-thirds of the patients were male in our study. This male predominance has also been noted in other studies; it is theorized that this is likely multifactorial and may be

Image 3: Microscopic lung sections showing: **A)** Diffuse interstitial and intra-alveolar organizing fibrosis, scattered hyaline membranes, intra-alveolar hemorrhage, and necrosis (H&E, x40), **B)** Histocytes and giant cells containing round, encapsulated, yeast (H&E, x400), and **C)** The characteristic broad-based budding (arrow) associated with *Blastomyces* (H&E, x1000).

attributable to the increased likelihood of men participating in outdoor activities, either recreationally or occupationally (2, 8).

Epidemiologic clues that should raise the suspicion for blastomycosis include travel or residence in an endemic/hyperendemic area, participation in outdoor activities involving exposure to soil and wetlands, and recent onset of pulmonary or flu-like symptoms (8). As the disease incubation period ranges from three weeks to three months, it may be challenging to correlate disease onset with a particular exposure (5). As shown by our study, there can be wide geographic variation

of blastomycosis incidence within a single state. For instance, our institution is located within Dane County, WI— a nonhyperendemic region. Annually, we diagnose six to seven cases of blastomycosis via culture or morphologic assessment of tissue, and our county's average annual incidence rate of blastomycosis is one per 100 000 persons. The hyperendemic counties of northern Wisconsin have an average annual incidence rate of greater than ten per 100 000 persons. Due to the nonspecific clinical presentation of blastomycosis, patients may be inappropriately treated with antibiotics, even in endemic states. Blastomycosis should thus be considered in the differential diagnosis of patients

Figure 1: Confirmed cases of blastomycosis in the state of Wisconsin between 2003 and 2015. Bars in black represent years with known outbreaks (2006, 2009, 2010, 2015).

expiring of pulmonary illness unresponsive to antibiotic therapy (8). As dogs have a relatively high rate of blastomycosis infection, a history of the recent death of a pet dog due to a pulmonary illness may indicate a possible common source *Blastomyces* exposure; however, blastomycosis is not transmitted between species (8, 9). Finally, there may be racial and/or ethnic predispositions to blastomycosis: a study of Marathon County found that of the 55 patients who contracted blastomycosis during the 2009-2010 outbreak, 45% were Hmong. This ethnic clustering was ultimately deemed to be multifactorial, but further investigation into a possible genetic predisposition is currently underway (10). Our data showed a predominance of infection within the Caucasian population (approximately 70%), which more likely is representative of our general population demographics rather than an ethnic predisposition.

Given that the clinical manifestations can be variable and case history noncontributory, having a good working knowledge of the morphology of blastomycosis and its mimics can be essential. Characteristically, blastomycosis is found in the yeast rather than hyphal form at human body temperatures. The yeast is round, 8-15 μm in diameter, encapsulated, and clear, with broad-based budding (9, 11). Alveolar macrophages assimilate the yeast in an attempt to destroy it, but in fact provide it a safe and environmentally controlled setting to replicate. The exact mechanism by which *Blastomyces* is able to evade the natural immune system is not fully understood, but surface proteins such as BAD-1 and α 1-3 glucan may play a significant role (2, 11, 12). The other two organisms that may resemble blastomycosis are *Paracoccidioides brasiliensis*, a dimorphic fungus endemic in Central and South America, and *Cryptococcus neoformans*, a ubiquitous environmental fungus found worldwide. *Paracoccidioides*, as compared to *Blastomyces*, has a thinner cell wall, more polymorphic shape, and may show circumferential small buds surrounding the parent yeast (the so-called “mariner’s wheel” appearance). *Cryptococcus* has a thick mucicarmine-positive mucoid capsule, as opposed to the thin or incomplete mucicarmine capsular staining that may occasionally be seen with *Blastomyces* (9).

While nonspecific, gross features supportive of blastomycosis infection include those pulmonary findings reported in the two previously described autopsy cases such as consolidation and hemorrhage; granulomatous lesions are often visible and can be either focal or diffuse (4). Pleural adhesions and hilar adenopathy are also common. Upon sectioning of the lungs, areas of edema, hemorrhage, and cavitory necrosis may be seen. Cutaneous manifestations are also common; the lesions are characteristically round, may be single or multiple, and vary in size from 0.5-1.5 cm in diameter. They tend to appear raised with a violaceous, verrucous, arciform border, while the center of the lesion is pustular and often has crust formation (**Image 4**) (13, 14). Histologically, lesions show hyperplasia of the epidermis with neutrophilic and granulomatous infiltrate of the dermis. The degree of histologic changes in skin can vary widely (as demonstrated in the second autopsy case) and lesions grossly consistent with blastomycosis infection may not be easily recognized histologically. The use of special stains such as such as Periodic acid–Schiff with/without diastase (PAS/PAS-D) or Grocott’s/Gomori Methenamine Silver (GMS), can be beneficial (**Image 5**). In general, most of the antemortem blastomycosis testing modalities are also available for postmortem samples. A comparison of testing options, including relative costs, turnaround times, and required samples is given in **Table 3**.

Image 4: Gross image of a verrucous cutaneous *Blastomyces* lesion. The lesions are characteristically round, pustular, and vary in size from 0.5-1.5 cm in diameter.

CONCLUSION

As blastomycosis is not a nationally notifiable disease, epidemiologic patterns of infection have yet to be fully characterized. Review of data from states with mandatory reporting, such as Wisconsin, can thus contribute greatly to the understanding of this disease. The average number of confirmed cases per year in our state is 118.6; in at least 44% of these, inpatient hospitalization is required; annually, 5-6% are fatal. These figures likely underestimate the actual disease morbidity/mortality as reporting of the disease

is mandatory in our state, but reporting of deaths is voluntary. Though most cases of blastomycosis are sporadic, the recent Little Wolf River outbreak illustrates that common source exposures continue to occur. It also reinforces the importance of timely institution of antifungal therapy, as the one fatality arose in an otherwise immunocompetent young man who initially refused treatment. Untreated blastomycosis has a reported mortality rate of approximately 60-78% (2, 17). As blastomycosis is often not suspected clinically, morphologic assessment of tissue with or without microbial cultures is essential to postmortem exam-

Image 5: Special stains available to better visualize *Blastomyces* in tissue section. **A)** Periodic acid-Schiff with diastase (PAS-D, x500), **B)** Grocott's/Gomori Methenamine Silver (GMS, x500).

Table 3: Summary of Common Postmortem Testing Available for *Blastomyces*

Test	Sample Type	Turn Around Time	Price Range	Known Limitations
Stained slides (H&E*, PAS-D†, GMS‡)	Tissue	Days	\$106-183	Infection burden affects visualization; exact identification sometimes difficult
Potassium hydroxide (KOH) mounts (Image 6)	Skin scraping, pus, bronchial secretions	Hours	\$50-60	Correct deep sampling important; high false negative rate
Culture	Tissue, blood, bronchial secretions, urine, CSF§	Weeks	\$75-85	Requires collection under sterile conditions
Antibody/Antigen	Blood, urine, CSF	Days	\$54-111	Consistency of sample and storage temp critical; cross-reactivity common (15, 16)
18/28S RNA Polymerase chain reaction (PCR)	Fresh and formalin-fixed tissue, blood, bronchial secretion, urine, CSF	Days	\$450-500	Primary visualization of fungi needed

* Hemotoxylin and Eosin

† Periodic acid–Schiff with/without diastase

‡ Grocott's/Gomori Methenamine Silver

§ Cerebral spinal fluid

Image 6: Potassium hydroxide (KOH) mount of *Blastomyces* with calcofluor white staining visualized under florescent light (aqua color is computer generated). Notice broad-based budding of yeast, which is characteristic of *Blastomyces*.

ination. At our academic institution, we diagnose six to seven cases of blastomycosis annually via culture or examination of biopsy and/or autopsy tissue. Overall, our study highlights the need for vigilance among pathologists regarding this preventable cause of death.

ACKNOWLEDGEMENTS

The authors would like to thank Dr. Gregory Gauthier from the University of Wisconsin for providing the cutaneous photo of *Blastomyces*.

REFERENCES

- Centers for Disease Control and Prevention [Internet]. Atlanta: Centers for Disease Control and Prevention; c2015. Blastomycosis; [updated 2015 Dec. 5; cited 2016 Aug 31]. Available from: <http://www.cdc.gov/fungal/diseases/blastomycosis/index.html>.
- Bariola RJ, Vyas KS. Pulmonary blastomycosis. *Semin Respir Crit Care Med*. 2011 Dec; 32(6):745-53. PMID: 22167402. <https://dx.doi.org/10.1055/s-0031-1295722>.
- Larson DM., Eckman MR, Alber RL, Goldschmidt VG. Primary cutaneous (inoculation) blastomycosis: an occupational hazard to pathologists. *Am J Clin Pathol*. 1983 Feb; 79(2):253-5. PMID: 6823911. <https://doi.org/10.1093/ajcp/79.2.253>.
- Haque AK. Pulmonary pathology. Philadelphia: Churchill Livingstone/Elsevier; 2008. Chapter 12, Fungal diseases; p.219-44.
- Centers for Disease Control and Prevention (CDC). Blastomycosis--Wisconsin, 1986-1995. *MMWR Morb Mortal Wkly Rep*. [Internet]. 1996 Jul 19 [updated 1996; cited 2016 Aug 31]; 45(28):601-3. Available from: <http://www.cdc.gov/mmwr/preview/mmwrhtml/00043101.htm>.

- 6) Lemos LB, Baliga M, Guo M. Blastomycosis: The great pretender can also be an opportunist. Initial clinical diagnosis and underlying diseases in 123 patients. *Ann Diagn Pathol*. 2002 Jun; 6(3):194-203. PMID: 12089732. <https://doi.org/10.1053/adpa.2002.34575>.
- 7) Saccente, M., Woods GL. Clinical and laboratory update on blastomycosis. *Clin Microbiol Rev*. 2010 Apr; 23(2):367-81. PMID: 20375357. PMCID: PMC2863359. <https://dx.doi.org/10.1128/CMR.00056-09>.
- 8) Pfaff BL, Agger WA, Volk TJ. Blastomycosis diagnosed in a nonhy-perendemic area. *WMJ*. 2014 Feb; 113(1):11-8; quiz 19. PMID: 24712215.
- 9) Taxy JB. Blastomycosis: contributions of morphology to diagnosis: a surgical pathology, cytopathology, and autopsy pathology study. *Am J Surg Pathol*. 2007 Apr; 31(4):615-23. PMID: 17414110. <https://dx.doi.org/10.1097/01.pas.0000213389.47913.b8>.
- 10) Roy M, Benedict K, Deak E, et al. A large community outbreak of blastomycosis in Wisconsin with geographic and ethnic clustering. *Clin Infect Dis*. 2013 Sep; 57(5):655-62. PMID: 23735332. <https://dx.doi.org/10.1093/cid/cit366>.
- 11) Mycology Online [Internet]. Adelaide (Australia): University of Adelaide; c2016. Blastomyces dermatitidis; [updated 2016 July 18; cited 2016 Aug 31]. Available from: <http://www.mycology.adelaide.edu.au/mycoses/dimorphic/>.
- 12) Brandhorst TT, Rooney PJ, Sullivan TD, Klein BS. Using new genetic tools to study the pathogenesis of Blastomyces dermatitidis. *Trends Microbiol*. 2002 Jan; 10(1):25-30. PMID: 11755082. [https://doi.org/10.1016/s0966-842x\(01\)02258-2](https://doi.org/10.1016/s0966-842x(01)02258-2).
- 13) Balasaraswathy P, Theerthanath. Cutaneous blastomycosis presenting as non-healing ulcer and responding to oral ketoconazole. *Dermatol Online J*. 2003 Dec; 9(5):19. PMID: 14996392.
- 14) Busam KJ. Dermatopathology. 2nd edition. Philadelphia: Saunders Elsevier; c2015. Chapter 3, Infectious diseases of the skin p. 105-83.
- 15) ARUP Laboratories [Internet]. Salt Lake City: ARUP Laboratories; c2016. Blastomyces antibodies by CF and ID; [cited 2016 Aug 31]. Available from: <http://ltd.aruplab.com/Tests/Pub/0050626>.
- 16) MiraVista Diagnostics [Internet]. Indianapolis: MiraVista Diagnostics; c2016. Blastomyces quantitative EIA test; [cited 2016 Aug 31]. Available from: <http://miravistalabs.com/medical-fungal-infection-testing/antigen-detection/blastomyces-dermatitidis-quantitative-eia-test/>.
- 17) Sterkel AK. Subversion of innate immunity by blastomyces dermatitidis [dissertation]. Madison (WI): University of Wisconsin-Madison; 2014. 164 p.