Open Forum Infectious Diseases

BRIEF REPORT

Blastomycosis in New England: 5 Cases and a Review

John J. Ross,[1] Sophia Koo,[2] Ann E. Woolley,[2] and Richard A. Zuckerman[3]

[1]Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, USA, [2]Division of Infectious Diseases, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, USA, and [3]Dartmouth-Hitchcock Medical Center, Geisel School of Medicine at Dartmouth, Nashua, New Hampshire, USA

The geographic range of blastomycosis is thought to include New England, but documentation is sparse. We report 5 cases of infection with *Blastomyces dermatitidis* that were likely acquired in New England between 2011 and 2021. Our experience suggests that chart coding for the diagnosis of blastomycosis is imprecise and that mandatory reporting might help resolve uncertainties about the prevalence and extent of blastomycosis.

Keywords: blastomycosis; climate change; endemic mycoses; immunosuppression.

Blastomycosis is an invasive fungal infection endemic to parts of eastern North America. *Blastomyces dermatitidis*, the causative organism, is thermally dimorphic. At room temperature and in the environment, it grows as a mold, producing asexual spores (conidia) that may be inhaled, especially when soil is disturbed by logging, construction, or excavation. Inhaled conidia convert to yeast forms on phagocytosis by pulmonary macrophages. If the host immune response fails to clear the infection, respiratory symptoms develop after a typical incubation period of 4–6 weeks. Extrapulmonary dissemination may occur, with skin involvement being especially common [1].

Blastomycosis is hyperendemic in northwestern Ontario and central Wisconsin, and thought to be endemic throughout the Great Lakes region and the St Lawrence, Ohio, and Mississippi river valleys [1,2]. Precise delineation of its epidemiology is hampered by the lack of mandatory reporting in most jurisdictions, and by the fact that *B dermatitidis* is exceedingly difficult to culture from the environment [3]. It is presumed to be endemic in parts of New England, but the published literature is limited to 5 well-documented cases over a 68-year period [4–7]. We report 5 additional cases of blastomycosis likely acquired in New England between 2011 and 2021, strengthening the evidence for blastomycosis endemicity in these regions.

Received 14 November 2022; editorial decision 11 January 2023; accepted 18 January 2023; published online 20 January 2023

Correspondence: John J. Ross, MD, Brigham and Women's Hospital, 15 Francis St, PBB-B420, Boston, MA 02115 (jross4@bwh.harvard.edu).

Open Forum Infectious Diseases®

https://doi.org/10.1093/ofid/ofad029

METHODS

We performed a retrospective chart review of adults (age ≥18 years) with blastomycosis at 3 teaching hospitals in Boston, Massachusetts (Brigham and Women's Hospital, Brigham and Women's Faulkner Hospital, and Massachusetts General Hospital). Charts were identified via the Research Patient Data Registry (RPDR), using *International Classification of Diseases, Ninth Revision* (*ICD-9*) codes 116.x and *Tenth Revision* (*ICD-10*) codes B40*. The RPDR is a data warehouse containing inpatient and outpatient records from multiple hospital systems, including Epic electronic health records (EHRs), billing systems, and legacy EHR systems [8, 9]. The query tool primarily relies on *ICD-9* and *ICD-10* billing codes, although it also pulls in charts using associated longitudinal medical record (LMR) codes. Its accuracy has been validated for some commonly encountered inpatient diagnoses [10], although there is less data regarding its utility for less common diagnoses. All records were searched for the keywords "*Blastomyces*" and "blastomycosis," and discharge summaries, infectious diseases clinic notes and consults, and microbiology results were reviewed in both Epic and legacy EHR systems.

RESULTS

A total of 138 records were reviewed. Ten patients had infections with other fungi, including *Emmonsia*, *Blastoschizomyces*, *Spongipellis*, chromoblastomycosis, and paracoccidioidomycosis.

Seven patients had infection with the protozoan *Blastocystis hominis*, and 1 patient had a poorly differentiated malignant blastoma. Six cases of suspected but unconfirmed blastomycosis were excluded. Eighteen cases of culture-confirmed blastomycosis were identified. Ten were excluded because of residence in or travel to other areas endemic for blastomycosis in the past 5 years, 2 were excluded due to inadequate documentation of travel history, and 1 was excluded as having been previously reported [7]. In the remaining patients, it was not clear why the record had been tagged with an *ICD* code or LMR code for blastomycosis.

CASE REPORTS

Case 1

A 67-year-old man from northern Vermont was admitted to hospital with left lung infiltrates. Six years prior, he had undergone left-sided single lung transplantation for chronic obstructive pulmonary disease, and was on immunosuppressive

therapy with tacrolimus, azathioprine, and prednisone. Two months before admission, the Winooski River flooded his property, and he inhaled aerosolized silt while mowing his lawn. One month later, he developed progressive dyspnea and malaise. He was found to have a 4-cm lung nodule and was treated with oral doxycycline, without improvement. When his dyspnea worsened, he was admitted to a local hospital, started on imipenem and vancomycin, and transferred to a tertiary care center, where isavuconazole was added. His respiratory status deteriorated thereafter, requiring mechanical intubation. Urinary antigen testing was strongly positive for both *Histoplasma* and *Blastomyces*. A 1-cm firm, pink nodule with a central hemorrhagic crust was noted on his chin. This was biopsied, and cultures grew a mold identified as *B dermatitidis*. His pulmonary infiltrates worsened, and he developed refractory hypotension with multisystem organ failure. He was treated with comfort measures only, and died soon thereafter. Autopsy showed extensive pulmonary infection by broad-based budding yeast forms consistent with *Blastomyces*, involving the entire right lung in a bronchopneumonia pattern and the transplanted left lung diffusely.

Case 2

A 64-year-old man presented with 2 months of fever, dyspnea, dry cough, and pleuritic chest pain. Prior to his illness, he was able to walk up to 7 miles daily, but now became short of breath walking up a short incline. Three years previously, he had undergone orthotopic heart transplantation for nonspecific lymphocytic cardiomyopathy, and was on immunosuppressive therapy with mycophenolate, prednisone, and tacrolimus. He lived in northern Maine within sight of the Saint John River, which formed the Canadian border, and had formerly worked in a paper mill and as a potato harvester. Chest computed tomography (CT) showed bilateral lower lobe nodular opacities, subcarinal lymphadenopathy, and a moderate left pleural effusion. Thoracentesis was performed, with drainage of 1.2 L of exudative fluid. Gram stain and bacterial, mycobacterial, and fungal cultures were negative. Aspiration of a subcarinal lymph node was performed under endobronchial ultrasound guidance. Pathology showed broad-based budding yeast consistent with blastomycosis. Cultures grew *B dermatitidis*. Urinary *Blastomyces* antigen was positive at 1.66 ng/mL, and *Histoplasma* urine antigen was negative. He was treated with itraconazole for 1 year, with resolution of pulmonary infiltrates, and conversion of his urinary *Blastomyces* antigen to negative.

Case 3

A 57-year-old woman with type 2 diabetes and nonalcoholic steatohepatitis with cirrhosis presented with a 4-week history of skin nodules, followed by numbness over the lower abdomen, buttocks, and genital region, unsteady gait, and bowel and bladder incontinence. She had recently had a dry cough which persisted for several months, but had largely resolved prior to her acute illness. She lived in a low-lying area of northern Vermont, near the Missisquoi River and Lake Champlain. Physical examination was notable for eroded violaceous plaques on the right arm and left breast, weak rectal tone and perianal saddle anesthesia, and weakness and reduced sensation in the left lower leg. Magnetic resonance imaging of the brain and spine revealed enlargement and abnormal T2 signal within the conus medullaris, and enhancing lesions in the right frontal lobe and right internal capsule. CT chest was notable for an enlarged right axillary lymph node, atelectasis and infiltrates in the right lower lobe, and small bilateral pleural effusions. Lumbar puncture was notable for a minimal lymphocytic pleocytosis; bacterial, mycobacterial, and fungal cultures were negative. *Blastomyces* urinary antigen was weakly positive; urinary *Histoplasma* antigen was negative. Punch biopsy of a nodule on the right forearm showed granulation tissue with mixed inflammation and fungal forms consistent with blastomycosis; fungal cultures grew *B dermatitidis*. She was treated for disseminated blastomycosis with liposomal amphotericin B, but developed acute kidney injury after a week of therapy. She was switched to voriconazole, which she continued for the next 14 months. Two years after diagnosis, her imaging abnormalities and symptoms had resolved, aside from residual urinary incontinence.

Case 4

A 39-year-old previously healthy man was admitted to hospital with a 10-day history of painful skin nodules over the upper and lower extremities, torso, and neck, and 3 days of dyspnea, dry cough, and left-sided pleuritic chest pain. Prior to admission, he had been treated with oral ciprofloxacin and then amoxicillin-clavulanic acid without improvement. He lived in northern Vermont a block away from the Winooski River and was an avid outdoorsman who hiked and skied. CT chest of the chest revealed a 6-cm left upper lobe mass abutting the mediastinum, with associated mediastinal lymphadenopathy. Skin and CT-guided lung biopsies were performed, and the patient was discharged on doxycycline awaiting pathology and culture results. Skin and lung biopsies revealed broad-based budding yeasts, consistent with blastomycosis. Fungal cultures from the skin biopsy grew *B dermatitidis*, but cultures from the lung biopsy were negative. *Blastomyces* antibody was positive. He was treated with liposomal amphotericin B for 2 weeks, then transitioned to oral itraconazole, which he took for 10 months. At the completion of therapy, his skin lesions had healed, and chest CT showed only scarring and bronchiectasis at the site of the previous lung mass. Urinary *Blastomyces* antigen was negative at conclusion of treatment (this had not been previously obtained).

Case 5

A 58-year-old man with type 2 diabetes and binge alcohol use presented with friable skin nodules on the right arm and left flank that had enlarged over a period of several weeks.

He worked as a handyman in the Greater Boston area, where he had lived for the past 20 years, and he resided 2 blocks away from the Charles River. His only recent travel outside of Massachusetts had been to the Bronx. He had been born in Mexico, and previously resided in California. Skin biopsies revealed acute and chronic dermal inflammation, with occasional large ovoid yeasts with broad-based budding. Fungal cultures grew a mold identified as *B dermatitidis* at the University of Texas Health Science Center. Chest CT revealed a 1-cm left upper lobe nodule that had not been present on CT imaging obtained 1 year prior during a bout of coronavirus disease 2019 (COVID-19) pneumonia. He took oral itraconazole for 3 months with improvement, and was subsequently lost to follow-up.

DISCUSSION

We report 5 cases of blastomycosis in patients from New England, with several factors supporting local acquisition. Four cases are from northern Vermont and northern Maine. These states are contiguous with the Canadian provinces of Quebec and New Brunswick, which are known endemic regions for blastomycosis [11, 12]. All prior reports of blastomycosis in New England have come from Vermont or Maine [4–7]; none of the patients in these previous reports were documented to have traveled elsewhere. There is an additional case of blastomycosis in a resident of northern Maine who had undergone basic training in Louisiana and fought in Vietnam 3 years prior to his blastomycosis diagnosis [13], and another case in a Vermont logger who had traveled to Tennessee 4 months before his illness [14]. None of the patients that we report had traveled to or resided in other areas endemic for blastomycosis in the past 5 years.

All the patients that we report lived in close proximity to lakes and rivers, a classic risk factor for blastomycosis. Waterways with forest cover provide ideal conditions for the growth of *B dermatitidis*, which requires damp acidic soil with a high content of decaying organic material and animal feces [3]. Blastomycosis outbreaks have been associated with a variety of water exposures, including raccoon hunting in a Virginia swamp [15], school field trips to a beaver pond [3], and construction and excavation sites located along lakes and rivers [16, 17].

One of the patients that we report had a unilateral lung transplant 6 years prior to the development of disseminated blastomycosis. It is difficult to completely exclude blastomycosis infection acquired from the transplanted lung, but this seems less likely in view of the interval after transplantation, the lack of recent intensification of the patient's immunosuppressive regimen, and his recent exposure to aerosols from floodwaters. Floods have been associated with outbreaks of blastomycosis [18, 19], and linked to spikes in *B dermatitidis* DNA detection from soil samples [20]. Rain, dew, and mist also help to liberate infectious *Blastomyces* conidia [21].

Limitations of this study include the unclear sensitivity of the RPDR database for detecting cases of blastomycosis, the smaller amounts of data that could be retrieved from legacy EHR systems, and the fact that the bulk of our patient population is drawn from Massachusetts, which may limit our ability to capture cases of blastomycosis from other New England states.

A recent analysis of a large dataset of Medicare fee-for-services beneficiaries showed that blastomycosis is being diagnosed more often outside of traditional areas of endemicity [22]. One possible explanation is the increased use of immunosuppressive therapies, which has led to a recent spike in blastomycosis cases in Quebec [11]. Another is climate change. Extreme precipitation events are becoming more common in the northeastern United States and elsewhere [23], and the associated flooding may create favorable conditions for the transmission of *Blastomyces*.

Our experience suggests that the use of *ICD-9-CM* and *ICD-10-CM* diagnosis codes to determine areas of endemicity for blastomycosis may be subject to limitations. Coders may confuse blastomycosis with other fungal diseases, and even with protozoal infections such as *Blastocystis*. As well, patients treated for blastomycosis in 1 state may have acquired it while resident in another. Mandatory reporting might help clarify the current distribution of blastomycosis in North America. At present, blastomycosis is only reportable in 6 states and 2 Canadian provinces [1]. Jurisdictions in New England and elsewhere should consider making blastomycosis a reportable disease, particularly in view of the potential impacts of iatrogenic immunosuppression and climate change on the epidemiology of blastomycosis.

Notes

Patient consent. The study was approved by the Partners Institutional Review Board (protocol number 2022P000881). Informed consent was waived due to the lack of use of identifiable health information and the logistical difficulties in obtaining informed consent in a retrospective chart review study.

Potential conflicts of interest. All authors: No reported conflicts.

References

1. Mazi PB, Rauseo AM, Spec A. Blastomycosis. Infect Dis Clin North Am **2021**; 35: 515–30.
2. Ashraf N, Kubat RC, Poplin V, et al. Re-drawing the maps for endemic mycoses. Mycopathologia **2020**; 185:843–65.
3. Klein BS, Vergeront JM, Weeks RJ, et al. Isolation of *Blastomyces dermatitidis* in soil associated with a large outbreak of blastomycosis in Wisconsin. N Engl J Med **1986**; 314:529–34.
4. Thompson WF. Blastomycosis of bone: report of a case. J Bone Joint Surg Am **1953**; 35:777–81.
5. Monaco WE, Batsis JA. A case of disseminated blastomycosis in Vermont. Diagn Microbiol Infect Dis **2013**; 75:423–5.
6. DeWitt CM, Shea K, Greene LA, Pierson JC. Atypical blastomycosis in a pregnant woman. Int J Womens Dermatol **2018**; 5:131–3.
7. Restrepo D, Haramati A, McCluskey SM, Branda JA. Case 22–2022: a 34-year-old woman with cavitary lung lesions. N Engl J Med **2022**; 387:261–9.

8. Murphy SN, Gainer V, Chueh HC. A visual interface designed for novice users to find research patient cohorts in a large biomedical database. AMIA Annu Symp Proc **2003**; 2003:489–93.
9. Weiss ST, Shin MS. Infrastructure for personalized medicine at Partners HealthCare. J Pers Med **2016**; 6:13.
10. Barr CJ, Barbalace RJ, Wessinger SJ, et al. Validation of a hospital-based joint registry: quantification of errors and maximizing utility. J Arthroplasty **2012**; 27:1766–71.
11. Carignan A, Boudhrioua C, Moreira S, et al. Changing patterns of disease severity in *Blastomyces dermatitidis* infection, Quebec, Canada. Emerg Infect Dis **2021**; 27: 2810–17.
12. Ross JJ, Keeling DN. Cutaneous blastomycosis in New Brunswick. CMAJ **2000**; 163:1303–5.
13. Ohler RL. North American blastomycosis: the second reported occurrence in Maine. J Maine Med Assoc **1970**; 61:135–8.
14. Paul DS, Kaminsky DA. A New England logger with a diffuse pneumonia. Chest **2000**; 117:244–7.
15. Armstrong CW, Jenkins SR, Kaufman L, et al. Common-source outbreak of blastomycosis in hunters and their dogs. J Infect Dis **1987**; 155:568–70.
16. Baumgardner DJ, Burdick JS. An outbreak of human and canine blastomycosis. Rev Infect Dis **1991**; 13:898–905.
17. Baumgardner DJ, Egan G, Giles S, Laundre B. An outbreak of blastomycosis on a United States Indian reservation. Wilderness Environ Med **2002**; 13:250–2.
18. De Groote MA, Bjerke R, Smith H, Rhodes LV III. Expanding epidemiology of blastomycosis: clinical features and investigation of 2 cases in Colorado. Clin Infect Dis **2000**; 30:582–4.
19. Bethuel NW, Siddiqui N, Edmonds L. Pulmonary blastomycosis in rural upstate New York. Ann Thorac Med **2020**; 15:174–8.
20. Jackson KM, Pelletier KC, Scheftel J, et al. Analysis and modeling of *Blastomyces dermatitidis* environmental prevalence in Minnesota using soil collected to compare basal and outbreak levels. Appl Environ Microbiol **2020**; 87:e01922-20.
21. McDonough ES, Wisniewski TR, Penn LA, et al. Preliminary studies on conidial liberation of *Blastomyces dermatitidis* and *Histoplasma capsulatum*. Sabouraudia **1976**; 14:199–204.
22. Mazi PB, Sahrmann JM, Olsen MA, et al. The geographic distribution of dimorphic mycoses in the United States for the modern era [manuscript published online ahead of print 11 November 2022]. Clin Infect Dis **2022**. doi:10.1093/cid/ciac882
23. Huang H, Winters JM, Osterberg EC, Horton RM, Beckage B. Total and extreme precipitation changes over the northeastern United States. J Hydrometeorol **2017**; 18:1783–98.