Using local epidemiology to make a difficult diagnosis: a case of blastomycosis

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ABSTRACT

An otherwise well 21-year-old man from Northwestern Ontario presented to our emergency department in Winnipeg, Manitoba, with a 2-month history of cough, progressively increasing dyspnea, hemoptysis and a 15-kg weight loss. His symptoms were worsening despite antibiotic treatment for presumed bacterial pneumonia. His past history included work as a seasonal labourer clearing brush. He was not hypoxic on room air, but his chest radiograph revealed a miliary pattern and bilateral infiltrates. A Mantoux test for tuberculosis was non-reactive, and the sputum gram stain was unremarkable. Empiric therapy was initiated for blastomycosis and the diagnosis was confirmed with a calcofluor stain of the sputum. Although blastomycosis is rare in most regions in North America, there is an unusually high incidence of blastomycosis in Northwestern Ontario. This case highlights the intolerance and utility of knowledge of the local epidemiology in establishing difficult diagnoses of regional importance, such as fungal pneumonias.

Key words: community acquired pneumonia; *Blastomyces dermatitidis*; blastomycosis; fungal pneumonia

RÉSUMÉ

Un homme âgé de 21 ans du Nord-Ouest de l'Ontario et auparavant en bonne santé a été reçu à notre département d'urgence à Winnipeg, Manitoba pour des antécédents de toux, de dyspnée progressive, d'hémoptysie et de perte de poids de 15 kg. Ses symptômes avaient empiré malgré une antibiothérapie pour une pneumonie bactérienne présumée. Ses antécédents personnels comprenaient un emploi comme travailleur saisonnier au nettoyage de broussailles. Il ne souffrait pas d'hypoxie à l'air ambiant, mais ses radiographies pulmonaires révélaient un motif miliaire et des infiltrats bilatéraux. Une épreuve de Mantoux de dépistage de la tuberculose était non réactive et la coloration de Gram des expectorations était sans particularités. Un traitement empirique fut amorcé pour une blastomycose et le diagnostic fut confirmé à l'aide d'une coloration au calcofluor des expectorations. Bien que la blastomycose soit rare dans la plupart des régions de l'Amérique du Nord, on constate un nombre exceptionnellement élevé de tels cas dans le Nord-Ouest de l'Ontario. Le présent cas met en évidence l'utilité de la connaissance de l'épidémiologie locale pour établir des diagnostics difficiles d'importance régionale comme les pneumonies à levures.

Case history

A 21-year-old man from Northwestern Ontario presented to an emergency department (ED) in Winnipeg, Manitoba, with a 2-month history of cough, progressively worsening dyspnea, hemoptysis and a 15-kg weight loss. The hemoptysis was characterized by blood-streaked white sputum. The patient usually worked as a seasonal labourer. His

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most recent work was on a construction project clearing brush and digging ditches. Eight weeks prior to presentation to our ED, he quit working because of progressively worsening dyspnea. Two weeks prior to presenting to our ED, he presented to medical attention and was found to be afebrile with unremarkable vital signs. A chest radiograph at that time revealed a left lower lobe consolidation, and a presumptive diagnosis of community-acquired pneumonia was made. The patient was prescribed a standard course of azithromycin, but his dyspnea worsened and, upon presentation to our ED, he was unable to walk more than 10 metres without stopping to rest.

On examination, he appeared unwell but not toxic. His vital signs included an oral temperature of 38.2°C, respiratory rate of 16 breaths/min, blood pressure of 100/63 mm Hg, heart rate of 103 beats/min, and a room air pulse oximetry reading of 97%. Physical findings included dullness to chest percussion and bronchial breath sounds in the right upper and left lower lung zones with decreased air entry was noted in the left lower lung zone. The remainder of the physical examination was unremarkable.

His chest radiograph was consistent with his physical examination findings and revealed right upper and left lower lobar opacities and a small left-sided pleural effusion (Fig. 1). A complete blood count revealed a white blood cell count of 25×10^9 cells/L with 23% neutrophils. Hemoglobin and serum creatinine were normal. A sputum gram stain revealed many polymorphonuclear cells, but no micro-organisms. The patient was started on empiric broad-spectrum antibacterial therapy and also on the antifungal agent, amphotericin B. Subsequently, the calcofluor stain of the sputum confirmed the presumed diagnosis of blastomycosis (Fig. 2), and the Mantoux test, performed on admission, was interpreted as non-reactive at 48 hours.

Within 72 hours of admission, the patient's dyspnea had resolved and he was able to walk comfortably within the hospital corridors. Unfortunately, the patient suffered acute renal failure with a maximum creatinine of 474 μmol/L (normal rage 44–106 μmol/L). Amphotericin B was discontinued and, within one week, his serum creatinine normalized. He was started on a 6-month course of itraconazole (400 mg once daily) and transferred back to his home community in markedly improved condition.

Discussion

North American blastomycosis is an uncommon granulomatous fungal infection caused by the thermally dimorphic fungus, *Blastomyces dermatitidis*. This organism exists in a mycelial form in the soil of warm, moist, wooded areas.[1] When the mycelia are disturbed, the conidia are inhaled. At body temperature, *B. dermatitidis* becomes a thick-walled budding yeast.[2] Although pulmonary manifestations are the hallmark of blastomycosis, hematogenous dissemination results in extra-pulmonary blastomycosis affecting other body systems including the skin, bones and, rarely, the central nervous system.[3–5] Mortality is uncommon and occurs predominantly in older adults with chronic illnesses.[6]

B. dermatitidis is distributed in the United States east of the Mississippi from Wisconsin to the Gulf of Mexico,[7] and in the eastern Canadian provinces as far west as Northwest-

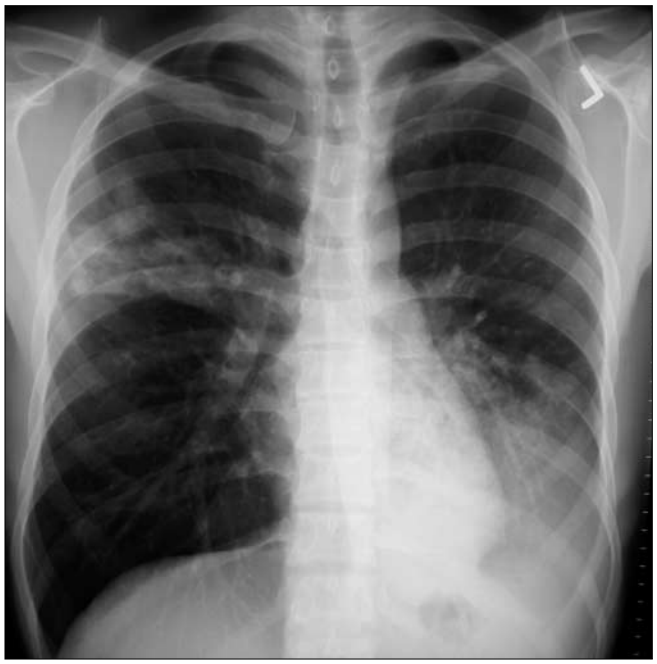

Fig. 1. Chest radiograph revealed right upper and left lower lobar opacities and a small left-sided pleural effusion.

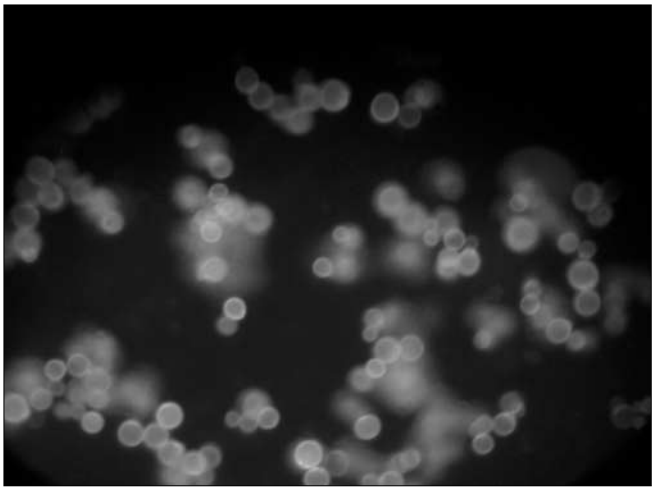

Fig. 2. Calcofluor stain of the sputum demonstrating broad-based budding yeast compatible with *B. dermatitidis.*

ern Ontario and Manitoba.[8,9] The annual incidence of blastomycosis varies greatly according to geographic region. In Wisconsin and Mississippi, the annual incidence is approximately 1.4 cases per 100 000 individuals.[10,11] In some regions of Canada, higher rates have been reported. For example, an annual incidence rate of 7.1 cases per 100 000 individuals has been reported in the Kenora, Ontario district,[9] and one study reported a rate of more than 117 cases per 100 000 individuals in a small region within this district.[6]

The incubation period of blastomycosis ranges from 30 to 45 days.[12] The most frequent symptoms of pulmonary blastomycosis are a productive cough with or without hemoptysis (93%), fatigue (82%), dyspnea (77%), fever (73%), weight loss (68%), night sweats (68%) and chest pain (58%).[6,8] Radiographic manifestations are varied, ranging from distinct lobar consolidations indistinguishable from a bacterial pneumonia to widely disseminated small lung nodules throughout both lung fields indistinguishable from miliary tuberculosis.[13] Given the clinical similarities between pulmonary blastomycosis and the more common pulmonary tuberculosis, the diagnosis of blastomycosis will not be made if cases are presumed to be tuberculosis. Confirmation of the diagnosis of blastomycosis rests upon either visualization of the broad-based budding yeast in sputum or tissue, or culture of *B. dermatitidis*. Serologic assays are available but they have insufficient specificity and sensitivity to establish the diagnosis of acute blastomycosis.

The type and duration of blastomycosis therapy is based on the clinical status of the patient. Seriously ill patients should receive parenteral amphotericin B. Once clinically stable, long-term therapy with an oral azole antifungal agent such as itraconazole may be initiated.[14] The empiric initiation of antifungal therapy depends on local epidemiology. This patient had symptoms consistent with either pulmonary tuberculosis or blastomycosis, so we were able to confidently initiate empiric blastomycosis therapy because he was not immunocompromised, his Mantoux test was negative, and he came from an area with an high incidence of pulmonary blastomycosis.

Conclusion

This case demonstrates the utility of local epidemiology in establishing a difficult diagnosis like acute pulmonary blastomycosis. Emergency physicians practising in Northwestern Ontario and Manitoba, or treating patients from these regions, should be aware of the high incidence of blastomycosis in this region and consider this diagnosis in patients who present with symptoms more commonly associated with pulmonary tuberculosis. In addition, practitioners assessing patients from these endemic areas, regardless of where they present, should maintain blastomycosis in the differential diagnosis of a non-resolving pneumonia, particularly if other etiologies have been excluded.[15]

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References

1. Dixon DM, Shadomy HJ, Shadomy S. In vitro growth and sporulation of *Blastomyces dermatitidis* on woody plant material. Mycologia 1977;69:1193-5.
2. Medoff G, Painter A, Kobayashi GS. Mycelial-to-yeast phase transitions of the dimorphic fungi *Blastomyces dermatitidis* and *Paracoccidiodes brasiliensis*. J Bacteriol 1997;169:4055-60.
3. Laskey W, Sarosi GA. Endogenous activation in blastomycosis. Ann Intern Med 1978;88:50-2.
4. Saiz P, Gitelis S, Virkus W, Piaseki P, Bengana C, Templeton A. Blastomycosis of long bones. Clin Orthop 2004;421:255-9.
5. Lemos LB, Guo M, Bilaga M. Blastomycosis: organ involvement and etiologic diagnosis. A review of 123 patients from Mississippi. Ann Diagn Pathol 2000;4:391-406.
6. Dwight PJ, Naus M, Sarsfield P, Limerick B. An outbreak of human blastomycosis: the epidemiology of blastomycosis in the Kenora catchment region of Ontario, Canada. Can Commun Dis Rep 2000;26:82-91.
7. Medoff G, Kobayashi GS. Systemic fungal infections: an overview. Hosp Prac (Off Ed) 1991;26:41-52.
8. Kepron MW, Schoemperlen C, Hershfield ES, Zylac CJ, Cherniack RM. North American blastomycosis in Central Canada: a review of 36 Cases. CMAJ 1972;106:243-6.
9. Crampton TL, Light RB, Berg GM, Meyers MP, Schroeder GC, Hershfield ES, et al. Epidemiology and clinical spectrum of blastomycosis diagnosed in Manitoba hospitals. Clin Infect Dis 2002;34:1310-6.
10. Centers for Disease Control. Blastomycosis – Wisconsin, 1986–1995. MMWR Morb Mortal Wkly Rep 1996;45:601-3.
11. Chapman SW, Lin AC, Heindricks KA, Nolan RL, Currier MM, Morris KR, et al. Endemic blastomycosis in Mississippi: epidemiological and clinical studies. Semin Respir Infect 1997;12:219-28.
12. Chapman SW. *Blastomyces dermatitidis*. In: Mandell GL, Bennet JE, Dolin R, editors. Principles and practice of infectious diseases. 5th ed. Philadelphia: Churchill Livingston; 2000. p. 2353-65.
13. Patel RG, Patel B, Petrini MF, Carter RR 3rd, Griffith J. Clinical presentation, radiographic findings and diagnostic methods of pulmonary blastomycosis: a review of 100 consecutive cases. South Med J 1999;92:289-95.
14. Chapman SW, Bradsher RW Jr, Campbell GD Jr, Pappas PG, Kauffman CA. Practice guidelines for the management of patients with blastomycosis. Infectious Diseases Society of America. Clin Infect Dis 2000;30:679-83.
15. Hannah EL, Bailey AM, Hajjeh R, Gershman K, Lindsley M, Hoffman RE. Public health response to 2 clinical cases of blastomycosis in Colorado residents. Clin Infect Dis 2001;32:e151-3.

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