

# Novel cases of blastomycosis acquired in Toronto, Ontario

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## Abstract

BLASTOMYCOSIS, A POTENTIALLY FATAL FUNGAL DISEASE, is well known from defined areas of endemicity in Ontario, primarily in the northern part of the province. We present 2 unusual cases that appear to extend the area of endemicity into urban southern Ontario, specifically Toronto. Both patients presented to a dermatology clinic with skin lesions. Chest radiography, history and general physical evaluation indicated no disease at other body sites. Both cases appeared to represent "inoculation blastomycosis" connected with minor gardening injuries and a cat scratch respectively. Atypical dissemination could not be completely excluded in either case. Neither patient had travelled recently to a known area of high endemicity for blastomycosis, nor had the cat that was involved in one of the cases. Physicians must become aware that blastomycosis may mimic other diseases, including dermal infections, and may occur in patients whose travel histories would not normally suggest this infection.

### Case 1

The patient was a 59-year-old immunocompetent woman with no history of recent travel to known areas of endemicity for blastomycosis. She had, however, been gardening in a ravine area of western Toronto near a stream.

In March 1998 a lesion developed over the patient's right lateral malleolus, gradually increasing in size. She described the initial lesion as being similar to a pimple. Approximately 2 months later, similar lesions developed on 2 fingers. Several biopsies revealed no distinctive features. A variety of antimicrobial agents were administered without effect. She was referred to a dermatology centre.

Dermatological examination indicated a large, erythematous, scaling plaque on the right lateral malleolus and verrucous, indurated lesions on the left index and right ring fingers. The areas surrounding the plaques were slightly violaceous, and pressure led to purulent discharge. Samples were obtained for repeat biopsy. Histopathologic findings were interpreted as compatible with a deep fungal infection; culture yielded *Blastomyces dermatitidis*. The results of chest radiography were reported as normal.

The diagnosis of blastomycosis was confirmed, and the patient was started on oral itraconazole 200 mg once daily. Shortly thereafter, a generalized erythematous eruption developed, which histologic examination revealed to be compatible with mild inflammation, not suggestive of a drug reaction. Some swelling of the ankles occurred subsequently, possibly indicating a reaction between itraconazole and nifedipine. The patient had not previously admitted to taking the latter drug. The swelling disappeared after the dose of nifedipine was decreased. After 4 months of itraconazole therapy, the lesions resolved completely. At the time of writing there had been no further symptoms.

### Case 2

A 23-year-old woman from Etobicoke, Ont., had a 2-year history of a slowly enlarging lesion over the right anterior shoulder. The lesion had first appeared in December 1996, about 2 months after her cat had scratched her. There had been no associated systemic symptoms or significant previous medical problems. Her travel history included a vacation in Bermuda 1 year before the ap-

## Review

## Synthèse

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pearance of the lesion, a visit to a small town in Saskatchewan 28 months before and travel in northwest Europe 30 months before. The cat had been purchased in the Toronto area in 1994 and had subsequently never left Etobicoke, a Toronto suburb. The cat appeared healthy at the time of the scratching incident and remained so afterward.

Physical examination of the patient revealed a well-defined 5 × 2 cm erythematous plaque with focal areas of crusting and a raised border, accompanied by scattered satellite pustules. The differential diagnosis included Majocchi's granuloma and a deep fungal infection. Histopathologic examination of a punch biopsy sample showed marked pseudoepitheliomatous hyperplasia and a diffuse inflammatory infiltrate of lymphocytes and neutrophils, with focal suppurative granuloma formation. Periodic acid – Schiff staining showed large, round fungal cells with prominent cytoplasmic retraction. Fungal culture yielded *B. dermatitidis*. The results of chest radiography were normal.

The patient was treated with oral itraconazole 200 mg once daily. After 8 weeks she appeared cured, and therapy was discontinued. At the time of writing there had been no recurrence of the infection.

## Background

Blastomycosis is an uncommon, though regularly seen, life-threatening<sup>1</sup> disease caused by a dimorphic fungal pathogen, *B. dermatitidis*. Infection ordinarily derives from inhalation of inoculum from contaminated environmental material. Such cases usually begin as a mild to severe pneumonia-like illness. This primary infection may be followed after some weeks or months by dissemination to other body sites. The dermis is the site at which secondary lesions most frequently occur; sites of less frequent occurrence include bones, joints, the urogenital system, the central nervous system and the liver.<sup>1,2</sup> Uncommonly, blastomycotic skin lesions similar to those acquired through dissemination may be acquired by traumatic injection of environmental inoculum directly into the dermis; this is referred to as "inoculation blastomycosis."<sup>1</sup>

Blastomycosis is one of several environmentally acquired fungal diseases with defined areas of endemicity. The following areas of North America are well established as areas of endemicity for this disease: northern Ontario north and west of Lakes Superior and Huron, as well as contiguous boreal Manitoba<sup>3,4</sup> and, rarely, adjacent Saskatchewan; areas near the east shore of Lake Huron,<sup>5</sup> the south shore of the St. Lawrence River, especially in Quebec; the Mississippi and Ohio river basins; and montane areas of the US southeast.<sup>1,2</sup> Kane and colleagues<sup>3</sup> performed epidemiologic studies of cases reported by southern Ontario institutions and found that at least 75% of the cases involved infections acquired in the northern Ontario area of endemicity; travel histories were incomplete for the remainder of the cases. To our knowledge, no cases of blastomycosis have been definitively shown to have been acquired in or near the major population areas of industrial southern Ontario.

In the zones where blastomycosis is endemic, the disease is predominantly encountered in rural or wilderness areas, where the etiologic agent may colonize soil or plant litter in riparian sites.<sup>4</sup> An at least partial association with sites mod-

ified by the activities of animals, especially beavers,<sup>6</sup> has been suggested. Blastomycosis acquired in urban areas is uncommon. Of the 12 well-documented blastomycosis outbreaks that occurred in North America between 1954 and 1991, only 1 was in an urban area.<sup>7</sup> This outbreak, in which 5 residents of a Chicago suburb were infected, was possibly associated with heavy dust raised during local road construction.<sup>8</sup> Sporadic cases within major cities are also extremely uncommon. In Toronto, where autochthonous blastomycosis has not heretofore been documented, this pattern may be changing. In addition to the cases reported here, 2 cases of blastomycosis involving immigrant children who had not left Toronto during the previous 5 years are under separate investigation (unpublished data), and other possible autochthonous cases are being investigated.

It should be noted that a widely reproduced distribution map<sup>1,2,4</sup> shows blastomycosis as highly endemic on the north shores of Lakes Erie and Ontario, including the major population centres of urban southern Ontario. No data supporting this map, which is at least 3 decades old, are known to us. Certainly, it does not reflect data collected or trends observed by 2 of us (J.K., R.C.S.) at the Central Public Health mycology reference laboratory in Toronto, which has had access to material from all culture-positive blastomycosis cases in the greater Toronto area and most other parts of Ontario since 1946. The map may be an artifact of the historic concentration of academic medical facilities in southern Ontario. Most of the authors who have reproduced the map in recent years have noted in accompanying text that Canadian data differ from what is shown.<sup>1,2,4</sup>

Many southern Ontarians spend portions of the summer at cottages in northern areas of the province or on Lake Huron. Blastomycosis contracted in such areas and diagnosed in urban areas must be distinguished from blastomycosis acquired directly in those urban areas. In general, the prevalence of indigenous blastomycosis in an area may not be accurately reflected by hospital records, which lack detailed travel and residence histories.

## Comments

The singular feature that characterized the 2 cases above, apart from the involvement of people with no travel to known areas of high endemicity, was that they presented as skin lesions with no sign of accompanying systemic symptoms. It may be difficult to distinguish inoculation blastomycosis from the variant of disseminated blastomycosis in which pulmonary infection is transitory and subclinical. The latter type of case has long been known.<sup>1</sup> For example, in one recent case (unpublished) seen by 1 of us (R.C.S.), the patient had a bone lesion and no history of pulmonary symptoms; however, CT scans of the lungs revealed a small, healed lesion compatible with previous pulmonary blastomycosis. Although such scans of asymptomatic body sites are not commonly done, the question of whether skin lesions are connected with disseminated blastomycosis may be of serious practical concern. In disseminated cases, the possibility of additional lesions, including undetected internal lesions, is an indication for extended treatment. Itraconazole 200 mg daily for 6 months is the standard treatment regimen of choice. If involvement of the central nervous system is detected, if severe systemic symptoms develop, or if the patient is immunosuppressed, treatment with amphotericin B may be indicated. Because pulmonary investigations in the present cases consisted only of radiographic examinations, pulmonary involvement cannot be definitively excluded. Both cases, however, had features compatible with inoculation blastomycosis. Development of the lesion in case 2 was preceded by a cat scratch, and case 1 involved sites at which the patient reported receiving minor scratches and punctures during gardening. Case 1, however, with its widely scattered lesions originating as papules, is also reminiscent of dissemination from subclinical pulmonary blastomycosis. Unfortunately, this matter cannot be resolved without performing arduous or invasive tests, which are unwarranted. The second case, with its rapidly cured, traumatically engendered single lesion, is more typical of injection blastomycosis. It was of interest, however, that the patient had travelled to a small town in Saskatchewan, near Saskatoon, an area where autochthonous blastomycosis may be endemic but rare,<sup>9</sup> more than 2 years before her lesion appeared at the site of a cat scratch. Laskey and Sarosi<sup>10</sup> presented 2 cases in which spontaneously resolving pulmonary blastomycosis was followed by disseminated blastomycosis 32–33 months later. Their cases both featured pulmonary symptoms severe enough to occasion radiographic examination on initial presentation, with characteristic signs of a pneumonic process. In general, the cases followed a pattern of relatively severe, reactivating blastomycosis, a disease course quite distinct from that seen in our patients. Continuing pulmonary infection was confirmed in their cases by culture of *B. dermatitidis* from sputum. Although no single piece of evidence absolutely rules out a similar, delayed reactivation in the second case that we have reported, there

are at least 6 factors that, taken in combination, make it exceedingly improbable: the patient's denial of having suffered a noteworthy pulmonary problem during the whole period in question, which was supported by negative radiographic results; occurrence of the disease only at a trauma site where soil inoculation might have occurred; the slowly progressing, localized, rapidly resolving nature of the infection; the relative rarity of greatly delayed cases of blastomycotic reactivation; the long period elapsed since travel to the Saskatchewan area of endemicity; and the rare occurrence of the organism in the area visited. Soil contact via trauma in an area of emerging endemicity — as confirmed by the presence of other cases — is a much more parsimonious causal explanation in this case.

Physicians in urban areas must be aware that blastomycosis should be included in the differential diagnosis of any atypical, nonhealing skin lesions, including those that are sequelae of scratches or that began as papules arising in areas not known to have been scratched. Other possibilities to be considered in similar cases are acid-fast bacteria, other subcutaneously infecting or dimorphic fungi, treponemes and malignancy. Although travel and residence histories can be used to raise the index of suspicion for blastomycosis, the present cases show that in urban southern Ontario, they cannot be used to rule out blastomycosis in patients who have not travelled. It should be stressed that dermal blastomycosis usually indicates current or recent systemic involvement. Skin lesions occur in a small proportion of acute primary blastomycosis cases and in up to 80% of cases of progressive (chronic) blastomycosis.<sup>11</sup> Lesions may be verrucous or ulcerative. Central clearing and scaling may occur in some lesions. The advancing border of the lesion will reveal the yeast forms of the etiologic agent in a 10% potassium hydroxide or sodium hydroxide wet preparation, which allows a rapid presumptive diagnosis, which should be confirmed by culture of a biopsy sample.

The documentation of 2 cases of blastomycosis indigenous to urban southern Ontario indicates either an emergence of the disease in this area or a long-undetected endemicity previously masked by the much greater number of cases imported to southern hospitals from the northern Ontario zone. Data are currently being collected to determine if there has been a significant increase in apparently indigenous cases of blastomycosis in the Toronto area over the past decade. In the meantime, it is crucial that the southern Ontario medical community be aware that for atypical lesions of the skin, bone, lung and other organs, the possibility of blastomycosis must be considered for all residents.

*Competing interests:* None declared.

*Contributors:* Drs. Lester and DeKoven were the primary physicians and providers of patient information for cases 1 and 2 respectively. They did extensive follow-up work when additional queries were raised by reviewers. Dr. Kane contributed to the laboratory diagnosis for both cases, initiated the report and collated the patient information from the 2 primary physicians. He was a co-strategist of queries to patients. He also ensured correct geographic knowledge of past blastomycosis cases compared with the present cases and maintained the collection of long-term data

about the endemicity of blastomycosis in Ontario. Dr. Simor contributed to the laboratory diagnosis in both cases and provided useful amendments to the article. Dr. Krajden coordinated the broader epidemiological analysis. He assembled the criteria for distinguishing inoculation from disseminated blastomycosis and interpreted the present cases in light of this information; he was instrumental in comparing these cases with reactivated blastomycosis. Dr. Summerbell was involved in reference laboratory confirmation of the identity of the organism, wrote and revised the manuscript and responded to reviewers' comments (after discussion with the other authors).

## References

- Rippon JW. *Medical mycology. The pathogenic fungi and the pathogenic actinomycetes*. 3rd ed. Philadelphia: WB Saunders; 1988.
- Kwon-Chung KJ, Bennett JE. *Medical mycology*. Philadelphia: Lea & Febiger; 1992.
- Kane J, Righter J, Krajden S, Lester RS. Blastomycosis: a new endemic focus in Canada. *CMAJ* 1983;129:728-31.
- DiSalvo A. The ecology of *Blastomyces dermatitidis*. In: Al-Doory Y, DiSalvo AF, editors. *Blastomycosis*. New York: Plenum Medical Books; 1992. p. 43-73.
- Bakerspigel A, Kane J, Schaus D. Isolation of *Blastomyces dermatitidis* from an earthen floor in southwestern Ontario, Canada. *J Clin Microbiol* 1986;24:890-1.
- Klein BS, Vergeront JM, Weeks RJ, Kumar UN, Mathai G, Varkey B, 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.
- DiSalvo A. The epidemiology of *Blastomyces dermatitidis*. In: Al-Doory Y, DiSalvo AF, editors. *Blastomycosis*. New York: Plenum Medical Books; 1992. p. 75-104.
- Kitchen MS, Reiber CD, Eastin GB. An urban epidemic of North American blastomycosis. *Am Rev Respir Dis* 1977;115:1063-6.
- Vallabh V, Martin T, Conly J. Blastomycosis in Saskatchewan. *West J Med* 1988;148:460-2.
- Laskey W, Sarosi GA. Endogenous activation in blastomycosis. *Ann Intern Med* 1978;88:50-2.
- Causey WA, Campbell GD. Pathologic features of blastomycosis. In: Al-Doory Y, DiSalvo AF, editors. *Blastomycosis*. New York: Plenum Medical Books; 1992. p. 189-220.

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