Blastomycosis in the Mountainous Region of Northeast Tennessee*

Rezhan Hussein, MD; Saad Khan, MD; Foster Levy, PhD; Jay B. Mehta, MBBS, FCCP; and Felix A. Sarubbi, MD

Background: **In the United States, cases of human blastomycosis are largely described in defined geographic areas, with Mississippi reporting the highest prevalence of disease in the southeast region. The infection is uncommonly recognized in mountainous areas, and our previous report of blastomycosis in the southern Appalachian mountains of northeast Tennessee appeared to be an exception to the usual disease distribution.**

Methods: **Our current retrospective study was undertaken to determine whether blastomycosis has persisted as an endemic fungal infection in our northeast Tennessee geographic area and whether epidemiologic features have changed over a 25-year time period.**

Results: **Results show that clinical aspects of the disease have remained fairly constant with few exceptions; mass-type pulmonary lesions have become more common, and itraconazole has emerged as the therapy of choice. Most notably, however, are the observations that blastomycosis persists as a major endemic fungal infection in our mountain region, more than half of all cases occurring during the period from 1996 to 2005 were found in a core area centered on two counties, Washington and Unicoi; three of five counties surrounding the core counties experienced rate increases compared to our previous study.**

Conclusions: **These findings suggest a further expansion of this endemic fungal disease beyond the core region.** ***(CHEST 2009; 135:1019–1023)***

Key words: blastomycosis; endemic; incidence rates; Tennessee

Abbreviation: CI = confidence interval

Human blastomycosis is a well-recognized systemic mycosis with an established geographic distribution that includes the states bordering the Mississippi and Ohio rivers, the midwest states, the Canadian provinces bordering the Great Lakes, and a limited area of New York and Canada bordering the St. Lawrence River.[1,2] The prevalence of blastomycosis in these regions is approximately 1 per 100,000 persons.[1] However, there are hyperendemic areas in these regions where the annual incidence rate for blastomycosis has been reported to reach 117 per 100,000 population in the Kenora region of Ontario, Canada[2] and 100 per 100,000 population in the Eagle River region of Vilas County, WI.[3] In the southeast United States, Mississippi is reported to have the highest prevalence of blastomycosis. Climatic and environmental factors, including sandy, acidic soil, decaying organic material, and high humidity, appear to promote the growth of the fungus and have been implicated as contributing to the elevated prevalence rate in Mississippi.[4]

In describing the distribution of blastomycosis in the midwestern and southern states, other authors[5,6]

*From the Divisions of Infectious Diseases (Drs. Hussein, Khan, and Sarubbi) and Pulmonary Medicine (Dr. Mehta), Department of Medicine, James H. Quillen College of Medicine, and the Department of Biological Sciences (Dr. Levy), East Tennessee State University, Johnson City, TN.

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Correspondence to: Felix A. Sarubbi, MD, Department of Medicine, James H. Quillen College of Medicine, East Tennessee State University, Johnson City, TN 37614; e-mail: felix.sarubbi@va.gov

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have documented the majority of cases in low-lying plain and river basin areas and have commented on the infrequency of cases from the mountainous areas of eastern Kentucky and western North Carolina. Interestingly, our previous publication[7] that described blastomycosis in northeast Tennessee appears to represent the only report of a substantial number of such cases occurring in a mountainous region. We previously recorded a significant increase in the number of blastomycosis cases in our geographic area for the period from 1980 to 1995, and this correlated with both population expansion and new construction projects. Since the reporting of blastomycosis from mountainous areas appears to be out of the ordinary and, in view of the continued growth in population as well as sustained property development in the northeast Tennessee region, we examined occurrences of this fungal infection for the period from 1996 to 2005 to assess regional trends in prevalence, to track the geographic progression of infection, and to determine whether the prior observations represented a time-limited episodic event or whether the disease has become established within northeast Tennessee.

Materials and Methods

This research project was approved by the East Tennessee State University Institutional Review Board and the institutional review boards or the research committees at participating hospitals. The current study period extended from January 1996 through December 2005 compared to our previous study period, which included the years 1980 to 1995. The methods used to identify patients with infection caused by *Blastomyces dermatitidis* were similar to those used in our previous report.[7] We contacted the State of Tennessee Health Department Laboratory in Nashville, TN, and obtained a listing of patients who were confirmed as culture positive for *B dermatitidis*. Culture-positive patients from the northeast Tennessee region frequently received care at one of our major regional referral hospitals, including Johnson City Medical Center in Johnson City, Holston Valley Hospital and Medical Center in Kingsport, and Bristol Regional Medical Center in Bristol. These facilities serve the patient populations in northeast Tennessee, southwest Virginia, parts of western North Carolina, and southeast Kentucky. Additional patients were treated at James H. Quillen Veterans Affairs Medical Center and at North Side Hospital, both of which are in Johnson City. Furthermore, microbiology and pathology records at each of these five hospitals were reviewed for culture-proven cases as well as cases confirmed by the presence of typical, single, broad-based, budding yeasts with a thick, doubly-contoured cell wall observed in clinical specimens submitted for histologic, cytologic, or potassium-hydroxide digestion examination. While the majority of microbiology- or pathology-positive specimens from the participating hospitals involved hospitalized patients, we identified 14 cases involving outpatients who were referred to East Tennessee State University physicians for treatment. The medical records for all of these identified inpatient and outpatient cases were reviewed as were the records for patients coded for any type of blastomycosis infection.

The three cities comprising the Tri-Cities urban conglomerate and their 2005 population sizes include Johnson City (58,718), Kingsport (44,130), and Bristol (42,188). Between 1995 and 2005, these cities experienced population growth of 16%, 10%, and 5%, respectively. The racial composition of the Tri-Cities area is 90% white.

A standard data collection form was used to record clinical and epidemiologic data. Previously published criteria for ARDS[8] and immunosuppression[9] were used.

Comparisons of blastomycosis prevalences among eras within the region and counties and among counties were conducted using population census data for the rate denominators that were used to compute rate ratios and 95% confidence intervals (CIs). Significance was assessed using two-tailed χ^2 statistics with Yates correction. Temporal differences in the association of potential risk factors with blastomycosis were assessed using the χ^2 statistic in 2×2 contingency tables. Differences were considered significant if $p < 0.05$ and the CI did not encompass 1.

Results

Infection due to *B dermatitidis* was diagnosed in a total of 76 patients during the study period from 1996 to 2005, and 67 of these patients (88%) were culture positive. The general characteristics of patients from the previous and current studies are shown in Table 1. Immunosuppressed patients in the period from 1996 to 2005 included single cases of each of the following: HIV infection; chronic lymphocytic leukemia; systemic lupus erythematosus; rheumatoid arthritis; Sjögren syndrome from cytotoxic medication; and Ig deficiency. There were also three patients with lung cancer, two patients with CNS malignancy, two patients with unspecified malignancy, one patient with prostate cancer, and one patient with renal cell cancer.

Exposure-prone occupations for the 1996 to 2005 period were identified for 34 patients, and included farming (16 patients), construction work (13 pa-

Table 1—*Characteristics of Patients in Whom Blastomycosis Was Diagnosed in Northeast Tennessee

Characteristics	1980–1995 (n = 72)	1996–2005 (n = 76)
Gender		
Male	50 (69.4)	54 (71.1)
Female	22 (30.6)	22 (29.1)
Age, yr	52 (13–86)	59 (26–91)
White race	64 (88.9)	72 (94.7)
Immunosuppressed	9 (12.5)	15 (19.7)
Diabetes mellitus	16 (22.2)	15 (19.7)
ARDS	9 (12.5)	3 (3.9)
State of residence		
Tennessee	55 (76.4)	67 (88.2)
Virginia	13 (18.1)	7 (9.2)
Kentucky	3 (4.2)	1 (1.3)
West Virginia	0	1 (1.3)
North Carolina	1 (1.4)	0

*Values are given as No. (%) or average (range), unless otherwise indicated.