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Common diagnostic challenges posed by North American blastomycosis as seen in a patient from Toronto, Canada

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Blastomycosis is a thermal dimorphic fungus endemic to the Ohio and Mississippi River valleys, and the Great lakes regions. Once inhaled a patient may present with a wide variety of clinical and radiographic manifestations, simulating other fungal, bacterial and neoplastic diseases and often leading to misdiagnosis. We describe a case of North American blastomycosis in a 42-year-old female living in southern Ontario. This case shows how the sporadic nature of this disease can lead to delayed diagnosis. This paper discusses the organism involved, epidemiology, etiology, clinical and radiographic presentations, diagnostic methods, treatment and prognosis.
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KEY WORDS: blastomycosis, Toronto, chiropractic, infection, back pain.

La balstomycose est un champignon dimorphe thermique qui persiste dans les vallées de l'Ohio et du Mississippi, ainsi que dans la région des Grands Lacs. Une fois qu'il inhale les champignons, le patient peut présenter une grande variété de signes cliniques et radiographiques qui ressemblent à ceux d'autres maladies fongiques, bactériennes et néoplasiques, ce qui peut entraîner une erreur de diagnostic. Nous décrivons ici un cas de blastomycose nord-américaine chez une femme de 42 ans qui habite le sud de l'Ontario. Ce cas montre comment le caractère sporadique de cette maladie peut retarder le diagnostic. Cet article traite des organismes touchés, de l'épidémiologie, de l'étiologie, des signes cliniques et radiographiques, des méthodes diagnostiques, des traitements et du pronostic.
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MOTS CLÉS : blastomycose, Toronto, chiropratique, infection, lombalgie.

Introduction

Blastomycosis is caused by the fungus *Blastomyces dermatitidis*, a thermal dimorphic fungus that exists in a mycelial form in the environment and later develops into a yeast form in the host body.[1–4] Since it can affect both immunocompetent and immunodeficient individuals, it is considered a primary pathogen as opposed to an opportunistic pathogen.[2]

The epidemiology of blastomycosis remains largely unknown. Since the disease is difficult to diagnose and is relatively uncommon, even in endemic regions, it is no longer on the list of reportable diseases to the public health authorities in Ontario.[2,5] This reduces the ability of epidemiologists to track its incidence and distribution.[5] In addition, there has been little success with attempts to develop specific and sensitive skin tests to define endemic areas.[6,7] Cases of blastomycosis often occur sporadically, although outbreaks are not uncommon.[1,2] The highest incidence of the disease is seen typically in men aged 25 to 50 who are exposed to the outdoors either recreationally or occupationally.[1–3,8]

Blastomycosis is endemic to both North America and

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Africa, and a number of cases have been reported in Central and South America. In North America, the disease is concentrated along the Mississippi and Ohio River basins, but can extend into Northern Wisconsin, Minnesota, and the Southern portion of the Canadian provinces bordering the Great Lakes.[1,3,7] Although prevalent in the moist, organically rich soil of wooded regions and near bodies of water, it is difficult to isolate from soil samples[4] making it almost impossible to accurately define the ecological niche of the fungus.[7]

Blastomycosis is most often caused by the accidental inhalation of *B. dermatitidis* conida from the soil. Once inhaled, the fungus is either cleared by alveolar macrophages or evades the host's defense mechanisms and is transformed from mycelia to yeast within the tissues. At this stage, a localized infection in the lung develops following an inflammatory pyogranulomatous tissue response that is distinctive to blastomycosis. If hiliar lymph node involvement occurs, lymphohematogenous dissemination occurs, allowing the yeast cells to spread to any of the organ systems.[1,3,4,7] The incubation period (from inhalation to the appearance of clinical disease) is estimated to be 21 to 106 days with an average of 45 days.[9]

Case report

A 42-year-old female presented to her family physician in January, 2000, with mild diarrhea, upper abdominal cramps, and generalized malaise of one month duration. An ultrasound examination subsequently revealed an enlarged gall bladder and cholecystitis was suspected. A surgical consult was performed at this time and a cholecystectomy ensued on April 28, 2000. One week following surgery, the patient's symptoms of diarrhea, upper abdominal cramping, lethargy, and a low-grade fever (38.5º) remained. A post-surgical ultrasound was performed over the right upper quadrant revealing a bile duct obstruction and a recommendation for endoscopic retrograde sphincterotomy was made; however, this test was not performed due to the patient's concerns regarding risks.

Concurrently, chest radiographs were performed and revealed consolidation of the right lower lobe suggestive of pneumonia (Figure 1). The patient received antibiotics and a chest radiograph was repeated once the course of antibiotic treatment was complete. Follow-up radiographs revealed no resolution of consolidation over the right

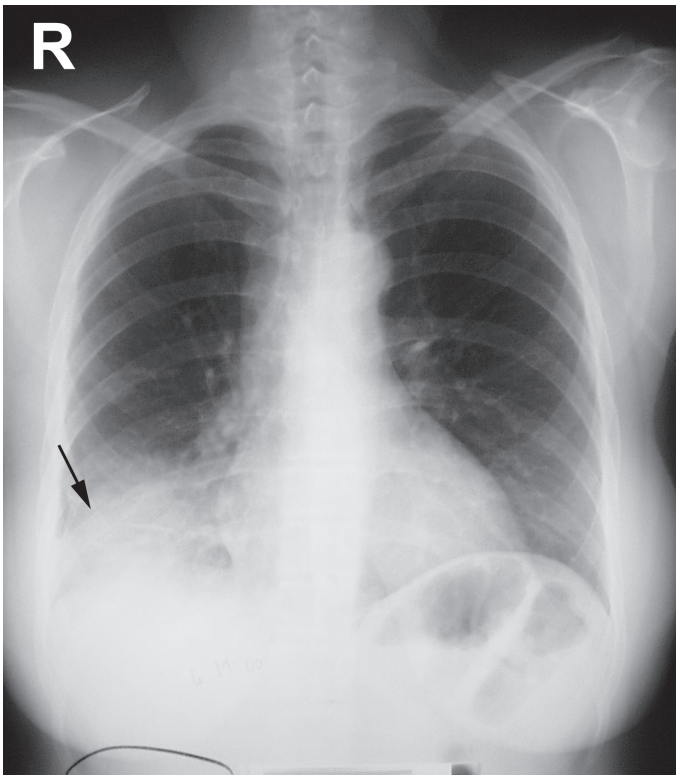

Figure 1 Initial chest radiograph showing right lower patchy consolidation (arrow).

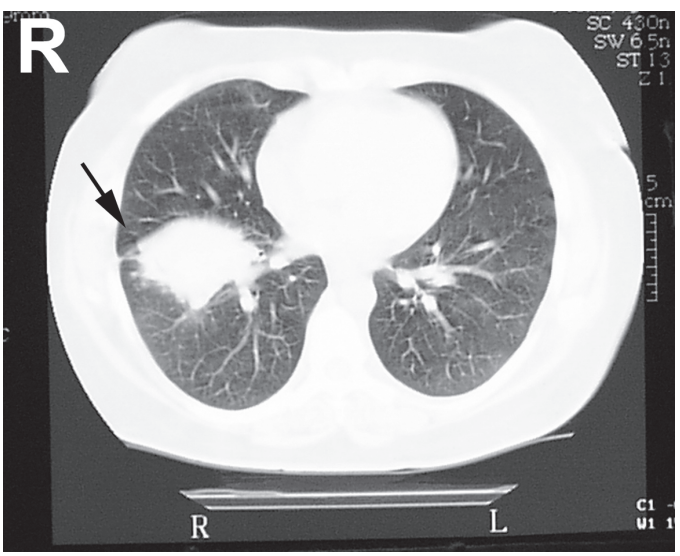

Figure 2 Initial CT scan showing a mass-like lesion in the right lower lobe (arrow).

lower lobe. She was subsequently referred to a respirologist, who recommended a computed tomography (CT) scan of the lungs. The CT scan, performed at the beginning of June, revealed a well-circumscribed oval mass in the lower lobe of the right lung measuring 5 cm at its greatest diameter (Figure 2).

With the suggestion of potential malignancy, a bone scan was performed which was negative. On June 21st and 23rd, 2000 needle biopsies were performed for cytologic analysis and reported negative for malignant cells. The respirologist recommended a partial right lobectomy but this was declined by the patient. The patient continued to experience a low-grade fever and malaise with a total weight loss of 10 to 12 pounds.

At this time, the patient presented to the H.K. Lee Walk-in Chiropractic Clinic with mid-back pain. She presented with a series of chest radiographs and CT scans which prompted a list of differentials that included bacterial pneumonia, bronchogenic carcinoma, tuberculosis and histoplasmosis; however, she did not receive chiropractic treatment until October due to time constraints as a result of the extensive medical testing she was undergoing.

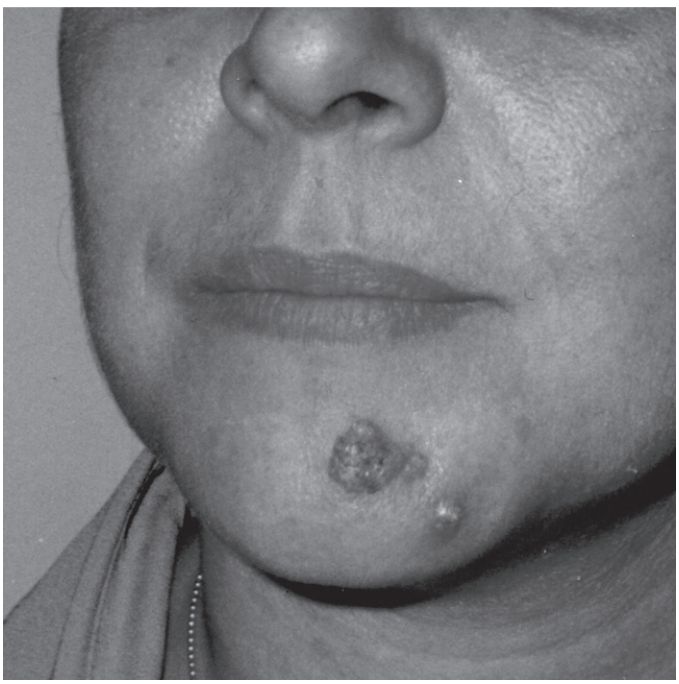

Figure 3 Note the veruccous plaque on the chin.

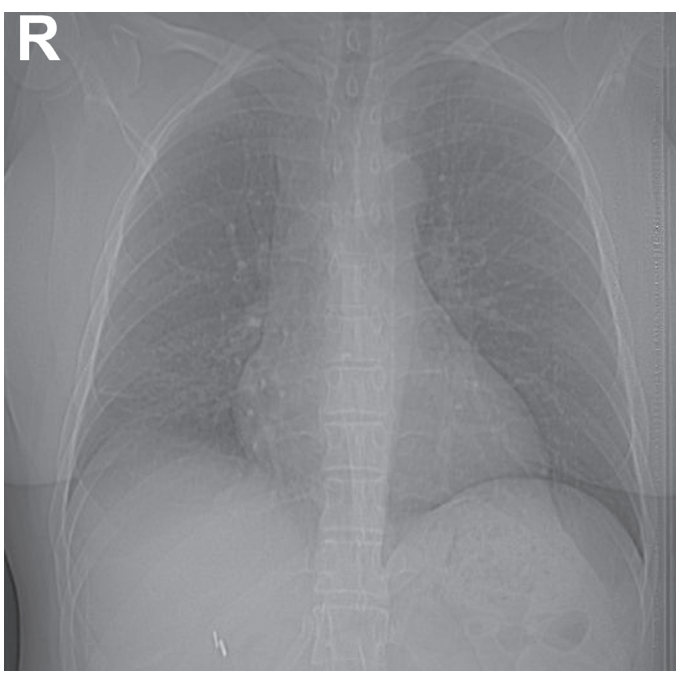

Figure 4A PA Chest radiograph 2 months following initiation of itraconazole therapy reveals substantial resolution of right lower lobe consolidation.

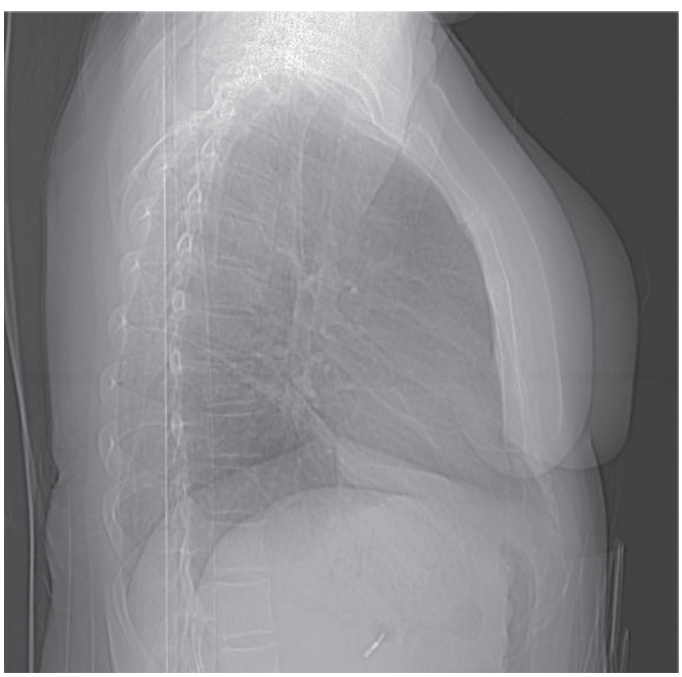

Figure 4B Lateral view shows residual fibrosis in the major fissure.

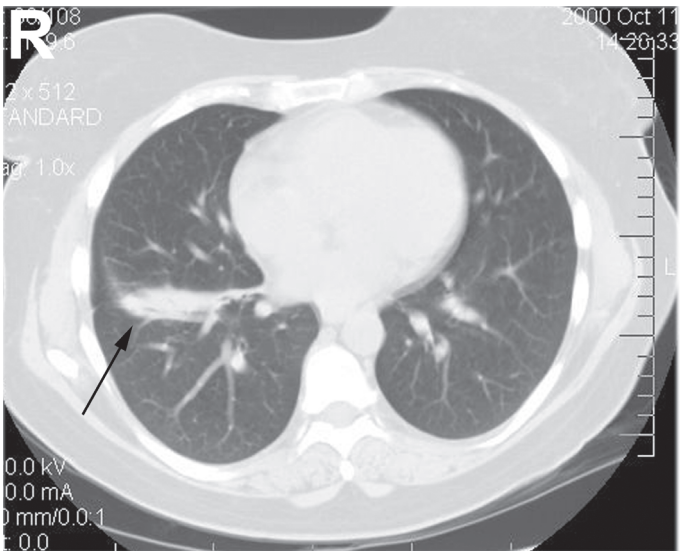

Figure 5 Chest CT scan 2 months post-treatment reveals a visible decrease in the size of the lesion with residual fibrosis in the major fissure (arrow).

In early August, a rapidly growing cutaneous lesion developed on her chin (Figure 3). A biopsy of the skin lesion confirmed the diagnosis of blastomycosis. The patient was prescribed Sporanox (200 mg/day) and one week later, the low-grade fever resolved and the size of the chin lesion also diminished considerably. Follow-up CT scan and radiographs performed in October 2000 revealed that the pulmonary lesion had diminished substantially (Figures 4 and 5).

In early October, the patient returned to the clinic for chiropractic treatment. Her mid-back pain was diagnosed as thoracic spine facet irritation with myofascial hypertonicity secondary to a viscerosomatic response from the mycotic respiratory infection. Treatment directed at the thoracic spine consisted of spinal manipulative therapy, spinal mobilizations and soft tissue therapy. Her thoracic discomfort improved rapidly.

Discussion

Clinical picture

Gilchrist first described blastomycosis in 1894 and since then it has been erroneously thought to have existed as two separate forms, pulmonary and cutaneous. In 1951, the work of Schwartz and Baum confirmed that blastomycosis is a primary pulmonary infection that may lead to systemic dissemination.[3] The clinical picture of blastomycosis is widely variable as it may present with a number of pulmonary or extrapulmonary manifestations. Typically, in about 75% of cases there is isolated lung involvement, but dissemination is common in up to 30% of the cases.[1]

Since blastomycosis remains a relatively uncommon fungal infection with a number of non-specific complaints, diagnosis is often delayed.[2] According to Davis and Sarosi,[7] blastomycosis can be asymptomatic or present with a wide variety of clinical signs and symptoms that may resemble a flu-like illness, acute or chronic pneumonia, tuberculosis, lung cancer or an infectious adult respiratory distress syndrome (ARDS).

Clinically, blastomycosis can be categorized as, acute pulmonary, chronic pulmonary, and disseminated blastomycosis.

Acute pulmonary blastomycosis is characterized by a flu-like illness presenting with fever, arthralgia, myalgia, headaches and productive or non-productive cough. A number of patients with the acute pulmonary form experience spontaneous resolution of the primary lesion; however, endogenous reactivation may occur and result in either pulmonary or extrapulmonary disease.[1,4]

The chronic pulmonary form is characterized by symptoms that last for greater than 3-weeks duration. Patients typically present with a 2 to 6 month history of night sweats, fever, weight loss, productive cough and chest pain. Routine chest radiographs taken before a diagnosis of blastomycosis is made may reveal mass-like lesions that are often misdiagnosed as malignancies.[1]

The presentation of disseminated blastomycosis is highly variable with extrapulmonary involvement with or without primary lung involvement.[1] The most common extrapulmonary sites in order of decreasing frequency are, skin, bone, male genitourinary, and central nervous system.[2]

Cutaneous lesions may be either verrucous or ulcerative.[8] The verrucous lesions begin as small papules and, if left untreated, become raised plaques with irregular borders, characterized by crusting over a subcutaneous abscess.[6] This particular manifestation was seen in our patient (Figure 3). The ulcerative lesions have sharp, heaped up borders with a base of exudate[6], and it is thought that cutaneous lesions may represent a marker for multiorgan system involvement.

Of specific importance to chiropractors is that bone may be affected in 25% of the extrapulmonary cases[8] and involvement usually takes the form of lytic osteomyelitis.[10] The persistent joint and bone pain associated with this particular manifestation of blastomycosis may be the main reason why patients seek out medical care. Skeletal involvement can be widespread and include, the vertebrae, pelvis, sacrum, skull, ribs, and long bones.

In approximately 5 to 10 percent of cases, the nervous system is involved either in the form of meningitis or cranial abscesses. Other areas affected include the reticuloendothelial system, the mouth and oropharynx, the eyes, breast tissue and the endocrine system.[8]

Radiographic features

The radiographic appearance of blastomycosis is highly variable and no one characteristic pattern exists,[11] making differential diagnosis from other fungal, bacterial or neoplastic disease difficult. Most often, the initial radiographic presentation tends to be localized airspace disease characterized by patchy and confluent airspace opacities with indistinct borders, in a segmental, subsegmental, or nonsegmental distribution.[2] Due to its radiographic appearance and clinical presentation of fever, chills and productive cough, the initial diagnosis of blastomycosis is often overlooked in favour of a diagnosis of bacterial pneumonia.[12]

Blastomycosis may present itself in other patterns such as, focal masses, interstitial, nodular, reticulonodular and miliary.[2,10,12] Infiltration of the lung may be unilateral or bilateral, with or without regional lymph node enlargement;[10] however, lymph node involvement tends to be more common in histoplasmosis.[7] Cavitation, calcification and pleural effusion may also occur, but remain rare.[7,10]

When blastomycosis presents itself as a focal mass, the initial concern is that it may represent bronchogenic carcinoma, prompting additional tests such as needle biopsy, and even a lobectomy;[7] however, although pulmonary blastomycotic lesions may pose a challenge to differentiate from bronchogenic carcinoma, the diagnosis is suggested by the presence of air bronchograms.[10]

There have been attempts to associate acute clinical presentation with airspace disease and chronic presentation with more mass-like lesions.[1] However, others have found a variety of presentations regardless of stage of disease.[11,12]

Diagnosis

At the present time, the most definitive diagnostic method is the demonstration of *B. dermatitidis* using histologic or mycologic techniques.[7] Of these techniques, digestion of the sample with a 10% potassium hydroxide (KOH) solution is the gold standard.[1] A number of serological tests, such as complement fixation, immunodiffusion, and enzyme immunoassay, are also available, however, they all vary in terms of diagnostic accuracy, sensitivity and specificity.[10] The clinical suspicion of blastomycosis must be high in order to requisition the diagnostic test procedures.

Treatment

Upon diagnosis of blastomycosis, the primary consideration is whether to manage the disease with an antifungal agent or using clinical observation to monitor its course. The two single most important factors in determining the course of treatment are, the clinical presentation of the patient and the toxicity of the antifungal agents.[13] Clinical observation should be limited to individuals with a mild pulmonary form whose symptoms are improving at the time of diagnosis. Antifungal therapy is recommended for all other patients with symptomatic pulmonary disease or any extrapulmonary manifestations.[14] Amphotericin B, a highly antimycotic but extremely toxic agent, is commonly used as a treatment for systemic fungal infections.[7] It is recommended for patients who are afflicted with severe acute pulmonary manifestations, adult respiratory distress syndrome,[7] immunocompromised patients, and those with central nervous system involvement.[3] Oral azoles, such as ketoconazole, itraconazole or fluxonazole are recommended for mild to moderate acute, subacute or the chronic pulmonary and disseminated forms. Our patient was prescribed a course of Itraconazole for 6 months and experienced a complete resolution of the pulmonary and cutaneous lesions.

Prognosis

The prognosis for most patients with mild to severe pulmonary blastomycosis with or without dissemination is good, provided that antifungal therapy is initiated shortly after diagnosis.[11] A mortality rate of greater than 50% appears to be associated with blastomycosis presenting with impaired gas exchange as seen in respiratory distress or failure.[7]

Conclusion

Blastomycosis is thermal dimorphic fungus endemic to the Ohio and Mississippi River valleys, and the Great lakes regions. Once inhaled a patient may present with a wide variety of clinical and radiographic manifestations simulating other fungal, bacterial and neoplastic diseases often leading to misdiagnosis. Our case presents as a classic example of how delayed diagnosis may occur due to the sporadic occurrence of this entity.

Chiropractors should be aware of the possibility of a viscerosomatic pain referral pattern in a patient who presents with a lung lesion and back pain. Blastomycosis should be included in the differential diagnosis of a pulmonary lesion that appears as pneumonia or a mass-like lesion, especially in known endemic areas. This is of greater importance to chiropractors in Ontario as the incidence of cases has increased in the southernmost part of the province.[5]

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References

1 Goldman M, Johnson PC, Sarosi GA. Fungal Pneumonias:The Endemic Mycoses. Clinics In Chest Med 1999; 20(3):507–519.
2 Kuzo RS, Goodman LR. Blastomycosis. Seminars in Roentgenol 1996; 31(1):45–51.
3 Chao D, Steier KJ, Gomila R. Update and review of blastomycosis. JAOA 1997; 97(9):525–532.
4 Bradsher RW. Histoplasmosis and Blastomycosis. Clinical Infectious Diseases 1996; 22(Suppl 2):S102–S111.
5 Dwight PJ, Naus M, Sarsfield R, Limerick B. An Outbreak of human Blastomycosis: the Epidemiology of Blastomycosis in the Kenora Catchment Region of Ontario, Canada. Can Comm Dis Rep 2000; 26(10):82–91.
6 Body BA. Cutaneous Manifestations of Systemic Mycoses. Dermatologic Clinics 1996; 14(1):125–135.
7 Davis SF, Sarosi GA. Epidemiological and clinical features of pulmonary blastomycosis. Seminars in Respiratory Infections 1997; 12(3):206–218.
8 Bradsher RW. Clinical features of blastomycosis. Seminars in Respiratory Infections 1997; 12(3):229–234.
9 Klein BS, Vergeront JM, Weeks JR. Isolation of Blastomyces dermatitidis in soil associated with a large outbreak of blastomycosis in Wisconsin. N Engl J Med 1986; 314:529–534.
10. Areno JP, Campbell GD, George RB. Diagnosis of blastomycosis. Seminars in Respiratory Infections 1997; 12(3):252–262.
11. Patel RG, et al. Clinical Presentation, Radiographic Findings, and Diagnostic Methods of Pulmonary Blastomycosis : A Review of 100 Consecutive Cases. South Med J 1999; 92(3):289–295.
12. Koen AF, Blumberg LH. North American Blastomycosis in South Africa Simulating Tuberculosis. Clinical Radiol 1999; 54:260–269.
13. Bradsher RW. Therapy of blastomycosis. Seminars in Respiratory Infections 1997; 12(3):263–267.
14. Johnson P, Sarosi G. Current therapy of major Fungal Disease of the Lung. Infectious Disease Clinics of North America 1991; 5(3):635–645.