A novel case of disseminated blastomycosis in China

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To the Editor: A 25-year-old male patient was admitted to the First Affiliated Hospital, School of Medicine, Zhejiang University with complaints of fever, cough, and knee pain. He was an overseas student and had been back from the USA for 3 weeks, with no remarkable medical history before admission. He was initially diagnosed with a cold and given non-steroidal anti-inflammatory analgesics and oral antibiotics in a clinic. However, his symptoms were not alleviated. Swelling and pain in his left knee became worse so that normal walking was not possible. Gradually a red rash with mild pain above the epidermis appeared in the lower limbs. Then, the patient presented to a municipal hospital in Hangzhou, China, and underwent a chest computed tomography (CT) scan, which revealed high-density areas in both the left lower lobe [Figure 1A] and left hilum [Figure 1B]. Laboratory tests indicated the following results: white blood cell (WBC) count 11.6 × 10⁹/L, neutrophils 88.2%, and C-reactive protein (CRP) 70.3 mg/dL. Community-acquired pneumonia was considered first, and empirical anti-bacterial treatment (moxifloxacin injection, 400 mg per day) was administered. The patient did not improve despite the use of moxifloxacin injections for 1 week but did have an elevation in liver enzymes (alanine transaminase [ALT] 191 U/L and aspartic transaminase [AST] 121 U/L), higher CRP 218.5 mg/dL, AST 214 U/L, and ALT 93 U/L. The T-SPOT.TB assay, (1, 3)-β-D-glucan assay, galactomannan assay, and Cryptococcus capsular polysaccharide antigen latex agglutination test all showed negative results. Ultrasonography revealed no organic lesions in the liver and gallbladder. We initially considered the diagnosis to be the hematogenous spread of a gram-positive bacteria, for example, methicillin-resistant Staphylococcus aureus, and prescribed linezolid injection of 600 mg every 12 h initially. The histologic section of the bronchus mucous membrane was obtained from the former hospital for examination, and yeast spores with thick and doubly refractile cell walls were found [Figure 1F]. An articular puncture was performed right after transferring, and a total of approximately 25 mL of light brown bloody fluid was obtained. The joint effusion and skin pus drawn from the ruptured rash were sent for culture and smear. The fluorescence-stained microscopic examination revealed round spores scattered in both the joint effusion and skin pus [Figure 1G]. After reviewing the literature and taking all these clinical characteristics into account, we considered that this was probably a case of an imported, disseminated fungal infection endemic to North America and that it could be blastomycosis or coccidioidomycosis. To confirm our speculation, the skin pus was sent for pathogen detection based on next-generation sequencing (NGS) technology (PMseq™, BGI, Shenzhen, China), and 57 sequences uniquely corresponding to Blastomyces dermatitidis were identified. One week later, white and glabrous...
fungal colonies gradually appeared on a Sabouraud medium cultured with skin pus [Figure 1H]. Hence, the diagnosis of disseminated blastomycosis was established. On the third day after transferring, we started this patient on empirical anti-fungal treatment with oral posaconazole suspension, 400 mg twice per day for 12 days and subsequently, 200 mg three times per day because of further elevated liver enzymes (ALT 886 U/L). A follow-up chest CT scan revealed significant radiographic resolution after a 10-day anti-fungal therapy. Clinical symptoms, such as cough and knee joint pain, greatly improved, clusters of pustules on lower the limbs shrunk, and the ruptured pustules began to crust. The patient was discharged after 3 weeks with continuation of posaconazole prescribed. Follow-up monthly visits showed improved physical ability, further absorption of pulmonary effusions, and slightly elevated liver enzymes. The patient took posaconazole continuously for approximately 9 months.

Blastomycosis is endemic to some regions of North America, especially the areas near the St. Lawrence-Great Lakes and Mississippi river systems. Sporadic cases have also been reported in Africa and India. The fungus *B. dermatitidis* lives in soil and rotten wood near lakes and rivers and can cause pulmonary blastomycosis when inhaled, and it can also lead to cutaneous, osseous, genitourinary tract, and central nervous system infections by dissemination. It can also occur in immunocompromised and immunocompetent populations. The clinical manifestations of pulmonary blastomycosis can range from asymptomatic to acute respiratory distress syndrome.

The radiographic findings also show high variability. Blastomycosis has been described as “the great pretender” because it can mimic a broad variety of diseases, such as pneumonia, tuberculosis, and malignancy. Because it lacks specificity, it remains difficult to obtain a prompt diagnosis and often causes antibiotic overuse, especially in remote non-endemic areas. With the rapid development of globalization, frequent population migration calls for physicians’ deeper understanding of foreign endemic diseases. Nine cases were reported previously in China,[1-4] most of whom were male (7 out of 9) with a median onset age of 29 years, ranging from 17 to 68 years. This could be partly explained by young men being more likely to participate in outdoor activities than young women and elderly people. None of the cases were immunocompromised except for a 68-year-old male patient with diabetes. Except for the two cases that were not reported, five cases had a history of living or traveling in the areas where the disease is endemic, while the other two had never traveled far before the onset of the disease, suggesting that blastomycosis could be present sporadically in China. The median delay in final diagnosis was 2.5 months. Seven cases were misdiagnosed as common respiratory infections at first and were treated with antibiotics over long time periods, ranging from 1 to 8 months, and three of these patients received anti-tuberculosis therapy afterward in view of suspected tuberculosis. The other two cases were misdiagnosed as malignancy. Culture of *B. dermatitidis* provides a definitive diagnosis of blastomycosis; however, it is time-consuming. Direct histopathological or cytopathological examinations help to facilitate prompt diagnosis of the disease. In the present case, we used an NGS-based
pathogen detection method to facilitate early diagnosis and timely anti-fungal therapy. Treatment recommendations for blastomycosis are based on the disease severity, site of infection, immune status, and pregnancy.\cite{5} In mild to moderate disseminated blastomycosis, oral itraconazole is first recommended, while amphotericin B is required in moderate to severe cases. Some reports, though limited, showed successful use of posaconazole for the treatment of blastomycosis.\cite{6} In the present case, posaconazole was prescribed on account of the patient’s liver function and the accessibility of drugs. It achieved great success in a short period of time. Follow-up visits also showed good tolerance of the drug. Posaconazole might be an effective and safe alternative treatment option for disseminated blastomycosis.

**Declaration of patient consent**

We certify that we have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

**Conflicts of interest**

None.

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