NOTES

Disseminated Infection Due to *Bipolaris australiensis* in a Young Immunocompetent Man: Case Report and Review

K. L. Flanagan and A. D. M. Bryceson

From the Hospital for Tropical Diseases, London, United Kingdom

We report a case of disseminated infection due to *Bipolaris australiensis* in a 21-year-old immunocompetent Pakistani man. He presented with fever and jaundice. Examination revealed a mass in the right lung, mediastinal lymphadenopathy, a pericardial effusion, and abdominal masses obstructing and invading the common bile duct and right ureter. Histological examination and culture of a biopsy specimen of the hilar mass yielded the fungal pathogen *B. australiensis*. The patient was treated successfully with amphotericin B and itraconazole.

To our knowledge, we report the first case of systemic bipolaris infection in an immunocompetent host. *Bipolaris* species cause a variety of diseases in plants and animals (including humans) and are likely to become increasingly recognized as a cause of infection in immunocompromised patients.

Case Report

A previously well 21-year-old Pakistani man arrived in the United Kingdom in January 1994. He presented to another hospital on 24 January 1994 because of a 5-month history of recurrent fevers and a 3-week history of jaundice. He had been examined in Pakistan, but no cause for his fevers was found. He had a history of asthma, was not receiving any medication, and had no allergies. He did not have any risk factors for HIV infection. He was a smoker but rarely drank alcohol.

CT of the abdomen revealed an obstructed, infiltrated common bile duct and a right hydronephrosis and hydroureter that were caused by mass lesions. He underwent endoscopic retrograde cholangiopancreatography, and a stent was inserted. CT of the chest showed a mass lesion at the junction of the left upper lobe and lingula, and bronchoscopy and biopsy were performed. An eosinophilic infiltrate thought to represent a parasitic infection was found. Bacterial and mycobacterial stains and cultures of biopsy specimens were negative. Fungal cultures were not performed. Echocardiography revealed a large pericardial effusion.

He was admitted to our institution on 9 February 1994. Physical examination revealed sinus tachycardia and mild abdominal tenderness; the cardiovascular, chest, and neurological findings were otherwise normal. Laboratory tests at admission revealed the following values: hemoglobin, 11.1 g/dL (normal range, 13.5–17.5 g/dL); WBCs, 26.4 × 10⁹/L (4.0–11.0 × 10⁹/L) (neutrophils, 12.1 × 10⁹/L [2.5–7.5 × 10⁹/L]; lymphocytes, 5.5 × 10⁹/L [1.5–3.5 × 10⁹/L]; eosinophils, 7.2 × 10⁹/L [0.04–0.44 × 10⁹/L]; monocytes, 1.3 × 10⁹/L [0.2–0.8 × 10⁹/L]; platelets, 908 × 10⁹/L (150–400 × 10⁹/L); and erythrocyte sedimentation rate, 76 mm/h. Biochemical tests disclosed the following values: alkaline phosphatase, 2,130 U/L (normal range, 100–280 U/L); aspartate aminotransferase, 69 U/L (11–55 U/L); bilirubin, 85 μmol/L (3–17 μmol/L); albumin, 35 g/L (35–53 g/L); IgG, 34.9 g/L (8±18 g/L); IgA, normal; and IgM, normal. CD4 and CD8 T cell counts were normal, and serological testing for HIV was declined. Serological testing for *Aspergillus fumigatus*, *Aspergillus flavus*, and *Scedosporium apiospermum* was negative. Trephine biopsy of bone marrow revealed reactive eosinophilia, and cultures of bone marrow for bacteria, fungi, and *Mycobacterium tuberculosis* were negative.

Fungal infection with possible underlying lymphoma was the provisional diagnosis. Repeated CT of the chest on 11 February 1994 showed extensive mediastinal lymphadenopathy, a large pericardial effusion, and right-upper-lobe cystic changes suggesting proximal bronchiectasis. On 15 February 1994, CT-guided mediastinal biopsy failed; therefore, mediastinoscopy and biopsy were performed. Histological examination of biopsy material confirmed infection with single hyaline fungal cells and septate mycelium in a granulomatous inflammatory mass; there was no evidence of lymphoma or malignancy. The patient’s condition deteriorated with persistent fevers, abdominal pain, weight loss, and anemia for which a transfusion was required. Empirical treatment with intravenous amphotericin B (1 mg/kg) was started. Fungal cultures subsequently yielded a *Bipolaris* species that was later identified as *Bipolaris australiensis* susceptible to amphotericin B and itraconazole.

After a cumulative dose of 695 mg of amphotericin B had been administered, his condition improved with cessation of...
abdominal pain and fever and significant weight gain. Repeated CT scans showed a marked decrease in the severity of the mediastinal lymphadenopathy and pericardial effusion. An ill-defined hepatic lesion remained, and there was decreased dilation of the intrahepatic bile duct. The appearance of the renal tract had improved. After 920 mg of amphotericin B had been administered, he returned to Pakistan. He received a further 1,275 mg of amphotericin B followed by treatment with oral itraconazole (100 mg daily for 2 weeks). According to correspondence 8 months later, he was in good health. He had returned to his original weight of 75 kg and believed that the treatment had been successful.

**Mycological studies.** The biopsy specimen obtained at our institution was sent to the Department of Medical Mycology, St. Thomas’s Hospital (London), where it was divided and inoculated onto brain-heart infusion medium (Difco Laboratories, Detroit) and glucose-peptone agar (2% dextrose/1% mycological peptone [Oxoid, Basingstoke, Hants, England]) supplemented with 0.005% chloramphenicol. The plates were incubated at 30°C. Within 1 week, pure growth of phaeoid mold developed on both media. Microscopic examination revealed multicellular conidia on geniculate conidiophores characteristic of the genus *Bipolaris*. The isolate was referred to Dr. C. Campbell (Mycological Reference Laboratory, Bristol Public Health Laboratory, Bristol, United Kingdom) who formally identified it as *B. australiensis*. Antifungal susceptibility testing was performed at St. John’s Institute of Dermatology (London) by using a liquid double dilution technique. The MICs of amphotericin B and itraconazole were 0.25 and <0.25 μg/mL.

**Discussion**

A literature search suggested that this is the first case report of systemic bipolaris infection in an immunocompetent host. A similar case was reported by Karim et al. [1] in 1993. These investigators suggested that they reported the first case, but this is questionable since the patient had been receiving treatment with high doses of prednisolone (60 mg) for >6 months. Their patient was successfully treated with intravenous amphotericin B once the diagnosis was made 2 years after presentation.

*Bipolaris* species, previously classified in the genus *Drechslera* [2, 3], are a group of pigmented, phaeoid, filamentous fungi ubiquitous in the environment. They are recognized pathogens of plants but also cause infections, albeit rarely, in animals and humans. The term *phaeohyphomycosis* refers to soft-tissue and systemic infections caused by phaeoid fungi. In immunocompetent humans, *Bipolaris* species cause a variety of noninvasive infections. The first report of infection in a human was a fatal case of meningoencephalitis caused by *Bipolaris* (*Drechslera*) *hawaiiensis* [4]. *Bipolaris* (*Drechslera*) species have been well-recognized causes of allergic sinusitis since the first case was cited in 1984 by Sobol et al. [5]. In a review of 22 cases of allergic fungal sinusitis [6], *Bipolaris* organisms were the most common fungi isolated.

Eye complications including mycotic keratitis, corneal ulceration, and orbital cellulitis have been described [7–9]. Allergic bronchopulmonary disease due to *Bipolaris* species that is similar to allergic bronchopulmonary aspergillosis has been recognized [10], and serological testing reveals that patients with this disease have precipitins to *Bipolaris*. *Bipolaris* species can colonize prosthetic heart valves [11], and cases of subcutaneous phaeohyphomycosis [12] and osteoarthritis [13] have been reported. Disseminated infections have been described in immunocompromised patients. In a review of 27 episodes of fungemia in HIV-positive children [14], *Bipolaris* *spicifera* was responsible for 52% of the cases; the proposed portal of entry was permanent indwelling venous catheters.

Our case is the first report of disseminated bipolaris infection in an immunocompetent host. We postulate that the route of entry was the lung, possibly via colonization of the bronchietatic area. Why colonization led to systemic infection remains a mystery, but one report may provide a clue. In 1988, Dewey et al. [15] described a 13-kD maize mitochondrial protein that conferred susceptibility to *Bipolaris maydis* toxin. Expression of this protein by *Escherichia coli* showed that the mitochondrial gene product is responsible for susceptibility to the toxin. It has since been found that mutations in the maize mitochondrial T-urf 13 gene eliminated susceptibility to the fungal pathotoxin of *B. maydis* race T [16]. It is possible that human susceptibility to *Bipolaris* species in the apparently immunocompetent host is the result of a mitochondrial gene product or mutation or other subtle defects in the immunologic response.

The literature suggests that the use of amphotericin B alone [1, 17] or in combination with imidazoles [5, 11] is the recommended treatment for bipolaris infection. In reports of invasive phaeohyphomycosis, complete recovery following treatment has been described. However, long-term follow-up is necessary to confirm this finding, and as yet, there are too few reports to be certain of cure. *Bipolaris* species are likely to become increasingly recognized pathogens as the incidence of HIV infection rises and as more organ transplantations are performed with resultant use of immunosuppressive drugs. Early diagnosis and treatment are of the utmost importance since untreated disseminated infection with *Bipolaris* may be fatal.

**Acknowledgments**

The authors thank St. John’s Institute of Dermatology (London) and the Department of Medical Mycology, St. Thomas’s Hospital (London), for identification of the fungus.

**References**


