Diagnosing Fungal Infections in Neutropenic Patients

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Fungal infections are among the most serious complications in neutropenic patients. A major problem that has compromised management of fungal infections is healthcare professionals’ inability to recognize the infections when they occur. No adequate diagnostic tools exist to detect many of the fungal infections. Early diagnosis of disseminated candidiasis is a challenge because only 35%–50% of neutropenic patients have positive blood cultures (Bodey, 1997), and radiologic tests have low specificity in that patient population. For example, a routine chest x-ray can be negative, yet a computed tomography (CT) scan of the chest can be positive for pneumonia the next day. Therefore, fungal infections often are advanced before diagnostic confirmation; thus, overall outcomes are poor. A great effort has been invested in developing serologic tests to detect circulating antigens of fungi.

A study of the epidemiology of sepsis revealed that the annual number of cases of sepsis caused by fungal organisms increased 207% between 1979 and 2000 (Zaoutis et al., 2005). The increase in invasive fungal infections is related to more people receiving immunosuppressive therapy for hematologic malignancies, allogeneic hematopoietic stem cell transplantation, and broad-spectrum antibiotics. Invasive therapies such as central venous catheterization, mechanical ventilation, parenteral nutrition, and gastrointestinal procedures also have contributed to an increase in fungal infections.

Candidiasis

Candida species are the leading cause of invasive fungal infections in hospitalized patients and the fourth most common isolate recovered from cases of nosocomial bloodstream infections in the United States. Recent data from the Surveillance and Control of Pathogens Epidemiologic System regarding nosocomial bloodstream infections in U.S. hospitals identified a crude mortality rate of 40% for nosocomial candidemia, with 38% of the deaths directly attributable to the underlying disease (Wenzel & Edmond, 2001).

Most bloodstream infections with Candida species are caused by Candida albicans, Candida glabrata, Candida tropicalis, or Candida parapsilosis (Fridkin, 2005). The remaining infections tend to be caused by Candida krusei, Candida lusitaniae, or Candida guilliermondii. All four of the major species produce biofilms that can form on central venous catheters. Antifungal drugs have a reduced ability to penetrate the biofilms and eradicate the organisms. Candida parapsilosis also can colonize skin, leading to nosocomial spread by the hands and persistence in hospital environments.

Candida infections often involve disease outside the bloodstream. For example, disease may spread from the gastrointestinal tract to catheters and then to other organs. Patients with hepatosplenic candidiasis will be febrile and have abdominal pain and hepatosplenomegaly. Serum alkaline phosphatase levels usually are elevated greatly, disproportionately to other liver function tests. Hepatosplenic candidiasis can be diagnosed by CT scan or magnetic resonance imaging of the abdomen, which reveals multiple lesions in the liver or spleen. Treatment for the infection requires two to three weeks of therapy before patients show any response. The use of prophylactic fluconazole has greatly reduced the incidence of hepatosplenic candidiasis. Pulmonary nodules also can be detected by CT scan, and fungal skin lesions can be diagnosed by skin biopsy.

Candida albicans accounts for approximately 50% of the cases of hematogenously disseminated candidiasis,