Fungal Infections in Transplant and Oncology Patients

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KEYWORDS

• Invasive fungal infection • Transplant • Solid-organ transplant
• Hematopoietic stem cell transplant • Oncology • Fungus

Invasive fungal infections (IFIs) in oncology and transplant populations have been associated with significant morbidity and mortality. Research in this area remains in flux; as epidemiologic patterns shift, more is being learned about optimal treatment and the unique risks that predispose these special populations to such potentially devastating infections. This article highlights recent advances and important factors to consider when treating transplant and oncology patients with IFIs.

EPIDEMIOLOGY OF IFIS

Despite high associated morbidity and mortality, the epidemiology of IFIs in high-risk populations has not previously been well defined. Incidence estimates have been primarily based on single-center, retrospective studies.[1–3] The Transplant Associated Infections Surveillance Program (TRANSNET), a network of 23 transplant centers in the United States, prospectively studied the epidemiology of IFIs among solid-organ and stem cell transplant populations over a 5-year period (March 2001 to March 2006) and provided the first true approximation of the burden of fungal disease among transplant populations in the United States. Based on TRANSNET data, the overall incidence of IFIs in the hematopoietic stem cell transplant (HSCT) population was 3.4%, somewhat lower than previous estimates (DP Kontoyiannis, unpublished data, July 2009). In addition, invasive aspergillosis (IA) surpassed invasive candidiasis (IC) as

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the most common IFI encountered in the HSCT population: *Aspergillus* accounted for 43% of infections and *Candida* accounted for 28%, followed by other or unspecified molds including *Fusarium* and *Scedosporium* (16%), and zygomycetes (8%). Pneumocystosis, endemic fungal infections, and cryptococcosis were rarely encountered in the HSCT population. Consistent with previous reports,[4–7] mortality was high and 1-year survival was low for HSCT patients with IFI. Fusarium infections and IA were associated with the lowest 1-year survival (6% and 25%, respectively); however, survival among patients with zygomycosis (28%) and IC (34%) was not substantially better.

Among solid-organ transplant (SOT) recipients, *Candida* infections were significantly more common than *Aspergillus* infections. This distribution held true for all solid-organ groups except lung transplant recipients. In lung transplant recipients, *Aspergillus* was the most common fungal pathogen, and, when coupled with other molds, invasive mold infections were responsible for 70% of IFIs (PG Pappas, unpublished data, July 2009). This distribution has also been shown in other studies of SOT recipients.[8,9] Less common overall, but seen more frequently than in the HSCT population, were infections due to *Cryptococcus* and endemic fungi, causing 8% and 5% of IFIs, respectively. Zygomycetes were responsible for 2% of infections (PG Pappas, unpublished data, July 2009). The mortality associated with IFIs in the SOT population is high, but lower overall than in HSCT and oncology patients.

There are no recent, multicenter studies describing the incidence and clinical outcome of IFIs among the general oncology population, and it is difficult to obtain an accurate estimate of the frequency of fungal infections in this population from the published literature because most reports do not provide sufficient information regarding the patients' underlying disease. In general, compared with patients with solid tumors, patients with hematologic malignancies are at increased risk for fungal disease and response to IFI treatment is lower.[10] A 1992 international autopsy survey of patients with cancer identified fungal infections in 25% of patients with leukemia, 12% with lymphoma, and 5% with solid tumors. Overall, *Candida* was the most common fungal pathogen, responsible for 58% of fungal infections, whereas 30% of fungal infections were caused by *Aspergillus*.[11] A more recent single-center survey of autopsies performed on patients with hematologic malignancy confirmed the increased risk for IFI among patients with leukemia. Consistent with trends among transplant populations, the prevalence of IFI remained high and constant throughout the study period (1989–2003); although the rate of IC decreased, the prevalence of invasive mold infections increased.[12]

TYPES OF IFIS

Aspergillus

Aspergillus fumigatus is the most frequent species of *Aspergillus* causing clinical disease, perhaps due to specific virulence factors unique to the organism.[13] However, other species, most commonly *Aspergillus flavus*, *Aspergillus terreus*, and *Aspergillus niger*, are also implicated in invasive infections in humans. *A terreus* has been associated with amphotericin B resistance and a higher mortality[14] than other *Aspergillus* species, although the data to support this claim were primarily gleaned from patients treated with amphotericin B as initial therapy and before use of triazoles as first-line treatment of IA.[15]

In immunocompromised hosts, *Aspergillus* most commonly presents as invasive pulmonary aspergillosis, often with subsequent dissemination.[16–18] In lung transplant recipients, *Aspergillus* may also cause tracheobronchitis and bronchial anastomotic infection. However, pulmonary infections can present with fever, hemoptysis, cough,