Mold Infections in Solid Organ Transplant Recipients

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KEYWORDS

• Antifungal • Aspergillosis • Invasive fungal infections • Fusariosis • Mucormycosis • Transplant

KEY POINTS

- Mold infections in solid organ transplant (SOT) recipients are a significant cause of morbidity with a high 12-week mortality of 29%.
- The most common and serious mold infections in SOT recipients include invasive aspergillosis, mucormycosis, fusariosis, scedosporiosis, and phaeohyphomycosis.
- Diagnosis of mold infections can be challenging and usually requires histopathologic and/or microbiologic criteria, often obtained by biopsy and culture of affected tissues. Blood cultures are positive in about half of the patients with disseminated *Fusarium* species or *Lomentospora prolificans* infections.
- Treatment of mold infections often necessitates combined antifungal therapy and surgical excision or debridement for localized disease.

INTRODUCTION

Mold infections are an important cause of morbidity and mortality in the solid organ transplant (SOT) population. These infections carry a significant clinical and economic burden.[1–3] Mold infections include invasive aspergillosis (IA) and other emerging fungal pathogens, such as mucormycosis (zygomycosis), *Fusarium*, *Scedosporium*, and the dematiaceous fungi (dark molds), among others. Diagnosis and management of these patients are challenging, often requiring invasive diagnostic methodologies and a multidisciplinary approach to treatment. IA is the most common mold infection and second most common invasive fungal infection (IFI) (after *Candida*) in SOT recipients, accounting for 19% to 25% of all IFIs, with non-Aspergillus molds making up 7% to 10%.[4–7] Risk factors for infection include immunosuppressive therapy, loss of skin or mucosal integrity, and risks specific to organ transplant type, such as chronic lung disease or anatomic disruptions.[6,8] The 12-week overall mortality of mold infections in SOT recipients is overall high at 29% but varies by organ transplant type, with the

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highest mortality in liver transplant recipients.[5,9] This article reviews the epidemiology, risk factors, microbiology, diagnostic, and treatment approach to mold infections in SOT recipients.

ASPERGILLOSIS

IA is generally acquired via inhalation of conidia, making pulmonary infection the most common site of infection. Infections may be localized (pulmonary or extrapulmonary including surgical wound infections) or disseminated. Lung transplant recipients can be at risk for tracheobronchitis or infection of the bronchial anastomosis. IA occurs in 1% to 15% of SOT recipients.[10] Mortality in a recent series of SOT recipients was reported at 22%, which appears improved from historical cohorts, wherein mortality has been as high as 92% in some SOT populations.[11–13] The most common species causing human disease is *Aspergillus fumigatus*; *Aspergillus flavus*, *Aspergillus niger*, and *Aspergillus terreus* are also frequently encountered.

Diagnosis of IA, like other IFI, requires microbiologic and/or histopathologic criteria to define proven infection by European Organization for Research and Treatment of Cancer/Mycoses Study Group revised definitions.[14] Acquisition of adequate specimens is crucial for early diagnosis; bronchoscopy with bronchoalveolar lavage (BAL) is recommended for patients with suspected invasive pulmonary aspergillosis (IPA) with consideration of transbronchial biopsy or percutaneous needle biopsy depending on radiographic site of lesion.[15] Staining shows narrow septate hyphae with acute angle branching (**Fig. 1**). Recommended radiographic imaging should include chest computerized tomography (CT) scan for suspected IPA. Typical CT findings include nodules, consolidative lesions, or wedge-shaped infarcts. The classic halo sign, a nodule surrounded by a perimeter of ground glass opacity reflecting hemorrhage, may be seen particularly in neutropenic patients. An air crescent, or cavity in a mass or nodule, is usually a late CT finding.[15] Biomarkers such galactomannan (GM) and (1-3)-β-D-glucan from the serum may be considered but have low sensitivity in SOT recipients. Serum GM sensitivity has been reported to be only 20% to 30% in SOT populations.[16,17] However, testing of BAL for GM may improve sensitivity to 67% to 100% in SOT recipients.[10] Molecular testing with Aspergillus polymerase chain reaction (PCR) shows promise with high sensitivity for diagnosis of IA in some studies,

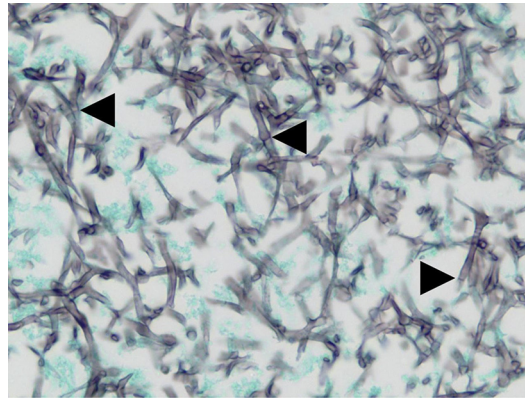

Fig. 1. *Aspergillus* narrow septate hyphae (*arrowheads*) (GMS stain, oil magnification ×1000). (*Courtesy of* Dr Daniel Rhoads and Dr Wissam Dahoud, UH Cleveland Medical Center, Cleveland, OH; with permission.)