Tracheobronchial Aspergillosis following Primary Cutaneous Aspergillosis in a Lung-Transplant Recipient

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Abstract

Invasive aspergillosis, a major problem during the post-transplant period, typically presents with pneumonia or tracheobronchitis in lung transplant recipients. In contrast, primary cutaneous aspergillosis is very rarely observed in lung-transplant recipients. In this report, we describe a case of tracheobronchial aspergillosis following primary cutaneous aspergillosis in a lung-transplant recipient. Early diagnosis of tracheobronchial aspergillosis is important because occult tracheobronchial aspergillosis can be potentially lethal. Our report suggests that surveillance bronchoscopy may facilitate identification of occult tracheobronchial invasion in lung-transplant recipients with primary cutaneous aspergillosis.

Key words: aspergillosis, lung transplantation


Introduction

Lung transplantation is an optional treatment for patients with various end-stage lung diseases. From the first human lung transplantation in 1963 (1), the survival of lung transplant recipients has improved with the advance of surgical techniques. However outcomes after lung transplantation remain inferior to other types of solid organ transplantation. Infectious complications contribute substantially to morbidity and mortality following lung transplantation and account for up to 25 percent of all post-transplant death (2).

Lung-transplant recipients receiving long-term immunosuppressive therapy have a predisposition to Aspergillus infections, and the incidence of aspergillosis after lung transplantation is greater than that after other transplantation (3, 4). Aspergillosis in lung-transplant recipients commonly manifests as tracheobronchitis, pneumonia, and disseminated disease (5). However, cutaneous aspergillosis is rarely observed in lung-transplant recipients (6, 7). We report a case of tracheobronchial aspergillosis following primary cutaneous aspergillosis in a lung-transplant recipient.

Case Report

A 43-year-old woman with lymphangioleiomyomatosis (LAM) underwent bilateral lung transplantation in March 2009. The patient developed bilateral pneumothorax and empyema during the early postoperative period but did not show any symptoms of transplant rejection. She received deflazacort (24 mg/d), tacrolimus (target serum level, 10-20 ng/mL), and mycophenolate mofetil (target serum level, 3-5 mcg/mL) for immunosuppression. After transplantation, she received fluconazole (50 mg/d), cotrimoxazole (80/400 mg), and valganciclovir. Fluconazole and the other prophylactic agents were discontinued at 3 and 6 months after transplantation, respectively. Four months after transplantation, a painful skin nodule appeared at a catheter-insertion site on her left wrist (Fig. 1). Skin biopsy and fungal culture revealed cutaneous aspergillosis (Fig. 1). She had no fever or respiratory symptoms, and no significant abnormalities were observed in the chest radiograph at that time. We initially prescribed itraconazole (400 mg/d), and the skin lesion showed signs of improvement. However, 6 months after transplantation, she experienced dyspnea with sputum pro-
Figure 1. Gross and microscopic finding of cutaneous aspergillosis. (A) Four months after transplantation, an erythematous skin nodule appeared at a previous catheter-insertion site on her left wrist. (B) Skin biopsy showed proliferating aspergillus hyphae in deep dermis (Hematoxylin and Eosin staining, ×200).

Figure 2. Radiologic and bronchoscopic finding of tracheobronchial aspergillosis. (A) 6 months after transplantation, she experienced dyspnea with sputum production. Plain chest X-ray showed focal infiltration on the right lower lung field. (B) After starting mechanical ventilation, surveillance bronchoscopy revealed a fungal mass combined with an ulcerative lesion.

Her chest radiograph showed focal infiltration on the right lower lung field (Fig. 2A). In spite of empirical antibiotic treatment, her condition worsened. Chest computed tomography (CT) showed a polypoid mass on the right main bronchus and multiple nodules on both lower lobes. We changed the antibiotic regimen and included empirical amphotericin B (35 mg/d). Mechanical ventilation was started to improve the aggravated dyspnea. Bronchoscopy revealed a fungal mass combined with an ulcerative lesion on both the second carina and the right lower lobe bronchus (Fig. 2B). Bronchoscopic biopsy revealed many septated hyphae with acute angle branching and BAL culture isolated *Aspergillus* species. *Acinetobacter baumanii* was also isolated in the quantitative BAL culture and blood culture. The patient received broad-spectrum antibiotics and antifungal agents against both pathogens. Her skin and lung lesions were gradually improved, but after 3 months of treatment, her renal function worsened due to long-term amphotericin B administration. We replaced amphotericin B with voriconazole (150 mg/d), and her renal function stabilized. The pneumonia and invasive aspergillosis were improved, and the patient was transferred to the general ward with noninvasive ventilator support. However, 9 months after transplantation, she presented with pelvic hematoma and hemoptysis. Pelvic CT revealed extraperitoneal pelvic mass with internal hemorrhage, which implied recurrent LAM, and 1 month...
later, she died of sudden asphyxia resulting from massive hemoptysis.

Discussion

Tracheobronchitis is a common form of aspergillosis in lung transplant recipients. It presents with three different patterns in the airway such as, obstructive bronchial aspergillosis, ulcerative tracheobronchitis and pseudomembranous tracheobronchitis (8-10). Depending on patterns of the disease, tracheobronchitis in lung-transplant recipients may produce symptoms such as cough, dyspnea, and wheezing. However, the patient may be asymptomatic for a considerable time, and the chest radiograph may be normal or show areas of atelectasis (11). Furthermore, Aspergillus is grown from sputum specimens in only 8 to 34 percent of patients (12). Therefore, early diagnosis may be difficult from a routine examination alone. The present patient did not show any definite symptoms of invasive aspergillosis in the early period of infection. There was no evidence of pre-existing aspergillus infection on surveillance bronchoscopy which was performed preoperatively and at 3 weeks after transplantation. Chest CT at 3 months also did not show any evidence of invasive aspergillosis. After the tracheobronchial aspergillosis progressed to the fulminant stage, we could identify foci of infection.

Cutaneous aspergillosis is a rare manifestation in lung transplant recipients and has been reported to occur in 4 percent of patients with documented Aspergillus infection (13). It may present either as primary or secondary infection. Primary cutaneous aspergillosis is caused by direct implantation of Aspergillus following trauma. On the other hand, secondary cutaneous aspergillosis usually presents with multiple lesions without any evidence of preceding trauma and is caused by hematogenous spread from the underlying infected organ. Cutaneous aspergillosis among solid-organ transplant recipients usually occurs as primary infection directly in the surgical wound or as nodules near a site of a break in the integument, such as catheter insertion site and pressure sore (14). The present patient had neither symptoms of disseminated aspergillosis nor did she show any abnormalities during routine examination. The cutaneous aspergillosis typically occurs at the site of intravenous catheter insertion as a single lesion. Therefore, we concluded that the skin lesion was caused by primary cutaneous aspergillosis.

Response to antifungal therapy in aspergillosis depends on several factors, including the immune status, the extent of infection and the species of Aspergillus. In the present case, tracheobronchial aspergillosis developed despite the clinical improvement of cutaneous aspergillosis with itraconazole therapy. There are some possible explanations. Unlike cutaneous aspergillosis, invasive pulmonary aspergillosis partially responds to itraconazole therapy. According to one prospective study, only 39 percent of invasive aspergillosis shows a complete or partial response with itraconazole therapy (15). Another possible cause of treatment failure is resistance to itraconazole (16). The strain from bronchus might be innately resistant to itraconazole although we did not have any data about the species of Aspergillus and DNA mapping. Owing to the paucity of reports on cutaneous aspergillosis in lung-transplant recipients, the significance of primary cutaneous aspergillosis as a risk factor for invasive pulmonary aspergillosis in these patients is not clear. However, our case showed that primary cutaneous aspergillosis may complicate other invasive aspergillosis in lung-transplant recipients. A substantial delay in the early diagnosis remains a major obstacle to the successful treatment of invasive aspergillosis. However, a routine examination including cultures of sputum specimens and chest X-ray lacks sensitivity. The role of chest CT may be limited in the early period of tracheobronchial aspergillosis. In conclusion, surveillance bronchoscopy may facilitate identification of the potentially fatal occult tracheobronchitis in lung-transplant recipients with cutaneous aspergillosis.

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References

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