Late Respiratory Infection after Lung Transplantation
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Background: Aiming to improve outcome of lung transplantation (LTx) patients, we reviewed risk factors and treatment practices for the LTx recipients who experienced respiratory infection in the late post-LTx period (>1 month after LTx).

Methods: We analyzed the clinical data of 48 recipients and donors from 61 LTx, who experienced late respiratory infections. Late respiratory infections were classified according to the etiology, time of occurrence, and frequency of donor-to-host transmission or colonization of the recipient prior to transplantation.

Results: During the period of observation, 42 episodes of respiratory infections occurred. The organisms most frequently involved were gram (−) bacteria: Acinetobacter baumannii (n=13, 31.0%), Pseudomonas aeruginosa (n=7, 16.7%), and Klebsiella pneumoniae (n=4, 10.0%). Among the 42 episodes recorded, 14 occurred in the late post-LTx period. These were bacterial (n=6, 42.9%), fungal (n=2, 14.3%), viral (n=4, 28.5%), and mycobacterial (n=2, 14.3%) infections. Of 6 bacterial infections, 2 were from multidrug-resistant (MDR) A. baumannii and one from each of MDR P. aeruginosa, extended spectrum β-lactamase (+) K. pneumoniae, methicillin-resistant Staphylococcus aureus and Streptococcus pneumoniae. Infection-related death occurred in 6 of the 14 episodes (43%).

Conclusion: Although the frequency of respiratory infection decreased sharply in the late post-LTx period, respiratory infection was still a major cause of mortality. Gram (−) MDR bacteria were the agents most commonly identified in these infections.

Key Words: Lung Transplantation; Respiratory Tract Infections

Introduction
Since the first human lung transplantation (LTx) in 1963, significant progress has been made in this field. From the registry of the International Society for Heart and Lung Transplantation (ISHLT), 3519 LTx for end-stage lung disease were performed in 2010. The median survival for LTx recipients, however, is 5.5 years, disappointing compared to that of other solid organ recipients.

Morbidity and mortality throughout the post-LTx period result primarily from infection; respiratory infections including pneumonia account for approximately 35% of deaths in the first year. Among solid organ transplant recipients, LTx recipients are most susceptible to infection. Several factors unique to the lung may explain this.

The various etiologies of respiratory infection in LTx
patients include opportunistic, hospital- and community-acquired microorganisms, which differ during the time to occurrence. Donor-to-host transmission is one of important risk factors in early respiratory infection following LTx7.

In the late post-LTx period (>1 month after LTx), the incidence of infectious episodes decreases markedly, despite patients returning to their normal activities at home or work. However, in this late phase, respiratory infection still presents a potentially fatal risk. Better understanding of post-transplantation susceptibility and of patterns of infectious exposure in the patient’s environment is urgently required to avert this risk.

The aim of this study is to evaluate the epidemiology of respiratory infection in LTx recipients at our center. In particular, we analyzed the time to occurrence of infection, colonization of the recipient with a relevant infectious agent, donor-to-host transmission of these agents, and the relationship of late-phase respiratory infection to mortality.

Materials and Methods

We analyzed the medical records of 48 LTx recipients treated at our institution between January 2006 and June 2012 for demographic data, primary respiratory disease, microbiological testing before and after transplantation, and episodes of infection throughout the post-transplantation observation period. This study was reviewed and approved by Institutional Review Board at Gangnam Severance Hospital, Yonsei University College of Medicine (IRB no. 3-2012-0223).

1. Pre-transplant screening

Before LTx, sputum samples were cultured for bacteria and fungi, and broncho-alveolar lavage (BAL) fluids from recipient was analyzed by fibrobronchoscopy, Pre-transplant evaluations also included serology for cytomegalovirus (CMV), Epstein-Barr virus, hepatitis A, B and C, herpes virus, and human immunodeficiency virus.

2. Antimicrobial prophylaxis

Postoperative antimicrobial prophylaxis was guided by culture from donor and recipient. For the patients without known colonization, antibacterial prophylaxis was given as either a single agent, piperacillin-tazobactam or a combination of ceftriaxone, isepamicin and metronidazole. Systemic antimicrobial drugs were administered for 7 days if surveillance culture from donor and recipient were both negative. If the cultures were positive, antibacterial prophylaxis was maintained for at least 2 weeks as indicated by the antibiogram. All patients underwent prophylaxis for fungi with fluconazole daily for one year and for Pneumocystis jirovecii infection with sulfamethoxazole-trimethoprim. Based on CMV serology, patients at high and moderate risk for CMV infection (recipient [−]/donor [+]) and recipient [+]/donor [+] or [−], respectively) were maintained prophylactically with intravenous ganciclovir for two weeks, followed by oral valganciclovir for up to 6 months or one year.

3. Immunosuppressive therapy

Methylprednisolone was used to induce immunosuppression and was followed by maintenance therapy with steroids, calcineurin inhibitor and an antimetabolite. Maintenance immunosuppressive drugs consisted of prednisone, tacrolimus and mycophenolate mofetil.

4. Post-transplant surveillance

Post-transplant evaluation included pulmonary function tests, imaging, periodic sputum cultures, and CMV antigenemia testing. If respiratory infection or rejection was suspected, the patient underwent a chest computed tomography scan, fibrobronchoscopy with alveolar lavage for bacterial and fungal cultures, indirect immunofluorescence tests for viral and P. jirovecii infections and mycobacterial polymerase chain reaction, and transbronchial biopsies to assess rejection and infection. Diagnosis of respiratory infection was made if a patient met any of the following criteria: fever (body temperature ≥37.8°C), cough, dyspnea, purulent expectora-