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Review

Challenges in Diagnosis and Management of Nontuberculous Mycobacteria in Solid Organ Transplantation

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Abstract

Nontuberculous mycobacteria (NTM) infections are relatively rare but carry significant morbidity in solid organ transplant (SOT) recipients. Given the rarity of disease and diagnostic limitations, a high index of suspicion is required for accurate diagnosis and initiation of appropriate treatment. We discuss the challenges in diagnosis and management of NTM infections specific to the SOT population.

Keywords

Nontuberculous mycobacteria; solid organ transplant; infectious complications

1. Introduction and Epidemiology

Nontuberculous mycobacteria (NTM) are ubiquitous in the environment and have been isolated from soil and water from both natural and treated sources. With increased awareness and

improvement in microbiologic techniques and detection, an explosion in the number of identified species has occurred over recent years, with now greater than 150 species described. Despite the breadth of species in this group, the majority of infections are caused by a relatively small number of species, most commonly *Mycobacterium avian complex* (MAC), *M.kansasii, M. marinum, M.haeophilum, M.xenopi* and the rapid growing mycobacteria (RGM) including *M.abscessus, M. chelonae and M. fortuitum* [1]. A total of approximately 25 NTM species have been previously reported to cause NTM disease in solid organ transplant (SOT) recipients [2]. Most infections occur as a result from exposure to the environment. There exists regional variation in species and consequently regional variation in predominant pathogens. Outbreaks related to environmental or nosocomial exposure have been described. A recent nosocomial outbreak of 126 patients with *M. abscessus,* which included 70 SOT recipients, was associated with a contaminated water source [3]. An outbreak of *M. chimaera* infection has affected patients requiring cardiopulmonary bypass utilizing Sorin 3T heater cooler devices, but no infections in heart or lung transplant recipients have been reported to date [4]. Although the vast majority of NTM infections are secondary to environmental exposure, there is now also report of possible person to person transmission involving *M.abscessus* in cohort of cystic fibrosis patients [5].

NTM infections across the general population are on the rise [6]. Incidence of disease in the SOT population is difficult to definitively determine. NTM infections are not communicable and although reporting of extra-pulmonary infection is mandated in at least one state, Oregon, this has not been required on a national level. A large single center study of SOT recipients of all organ types noted an incidence of NTM infection, defined as any positive culture for NTM, of 1.5% [7]. Incidence of NTM infection varies based on transplanted organ, with the highest being in lung transplant patients. Prior reports suggest incidence of 0.04% in liver transplant patients, 0.16-0.38% in kidney transplant patients, 0.24-2.8% in heart transplant recipients, and 0.46-8% in lung transplant patients [1].

SOT patients are at increased risk of NTM infections due to impairments in cellular immunity from immunosuppression. Lung transplant itself is a risk factor for NTM infection [8]. This may be related to multiple factors unique to this patient population: structural lung disease which is a known risk factor for NTM infection, direct exposure of allograft to the environment, a relatively high net state of immunosuppression in these patients, and the unique state of airway injury associated with chronic rejection manifesting as bronchiolitis obliterans. Among the lung transplant population, risk factors for NTM infection include cystic fibrosis (CF) as underlying diagnosis, use of anti-thymocyte globulin for induction immunosuppression, NTM disease or colonization pre-transplant, and single lung transplant [9].

2. Clinical Manifestations

Late presentation of NTM disease after SOT is common, with median onset ranging from 10-20 months post-transplant across different organ types [10]. NTM infections can have protean manifestations in the SOT population. Presentations can vary based on type of organ transplanted. Fever and constitutional symptoms can be absent due to underlying immunosuppression. Disseminated disease is common, and the most commonly isolated organisms in this setting include *M abscessus* and *M. chelonae* [2, 11]. In a recent systematic review of renal transplant patients with NTM, disseminated disease was the most common manifestation, affecting 40% of

patients [12]. Cutaneous disease, either localized or disseminated, is the most commonly reported manifestation of NTM in heart transplant recipients [11]. Skin lesions present as erythematous or violaceous subcutaneous nodules which often progress to form abscesses or ulcerations. Osteoarticular disease presenting as tenosynovitis or arthritis is also possible. RGM species (*M.abscessus, M.chelonae, M. fortuitum*) are the most common cause for NTM soft tissue and joint infections in SOT recipients [2]. Pleuropulmonary disease is the most commonly reported manifestation of NTM in lung transplant patients and also a significant cause of disease in heart transplant recipients [11]. Symptoms include cough, often productive of sputum, and dyspnea. The most common organisms to cause pulmonary disease include MAC, *M.kansasii, M.abscessus* and *M.xenopi* [2].

3. Diagnosis

NTM infection post-transplant is relatively rare; as such, it is crucial to maintain a high index of suspicion so timely diagnosis can be made and appropriate treatment started. If NTM disease is suspected, tissue or fluid sample of affected area (i.e. bronchial lavage or skin biopsy) should be submitted to the lab for histopathology, fluorochrome staining and mycobacterial culture. Culture should be performed in both liquid media and solid media. Some NTM species require specialized media, temperatures, or longer duration of incubation for growth; an awareness of this and potentially alerting the microbiology lab of suspicions can be paramount in making the appropriate diagnosis (Table 1). For example, *M. haemophilum* requires media supplementation for growth, and *M. marinum* and *M. haemophilum* grow at temperatures lower than the standard incubation temperatures. Furthermore, the required incubation period varies depending on species. RGM typically grow within 7 days, whereas slow growers take longer, up to 8-12 weeks for *M. genavense* [13]. Given this slow growth, awaiting identification and susceptibilities can delay treatment decisions. More advanced molecular techniques such as DNA probes, PCR, and high-performance liquid chromatography are used to rapidly identify some NTM species once growing on media [13].

Diagnosis of NTM disease is fairly straightforward when NTM is isolated from a sterile site. However, diagnosis of disease is more challenging when NTM is isolated from a non-sterile site, such as sputum or bronchoaveolar lavage fluid. In the lung transplant population a positive culture is not always indicative of disease. Colonization of the airway by NTM is common in lung transplant patients, comprising 75-89% of cases with positive culture in two single center studies. Only 11-25% of lung transplant patients with positive cultures had disease that required treatment [9, 14]. Similarly, another small single center study found the same percentage of pulmonary colonization amongst all organ types (75%) [8]. Joint American Thoracic Society (ATS) and Infectious Disease Society of America (IDSA) guidelines suggest that the following criteria are required to diagnose pulmonary NTM disease: positive cultures from at least two separate expectorated sputum samples or one BAL specimen, clinical symptoms associated with NTM disease, and characteristic radiographic findings of NTM pulmonary disease such as bronchonodular or fibrocavitary changes [13]. Although there are limited data for applying these criteria to the immunocompromised patient, it is reasonable to use them as a framework for diagnosis of NTM disease in SOT patients. It needs to be recognized, however, that following these guidelines too strictly may miss cases of invasive disease in this population. There are

circumstances, particularly in the setting of potentially virulent organisms, such as *M.abscessus* in the setting of lung transplant where treatment may be warranted even in the absence of fulfilling all ATS criteria for disease. In any instance, burden of infection, radiographic changes and clinical symptoms should be taken into account for treatment decisions and treatment often individualized.

Table 1 NTM with special growth requirements.

Specialized growth media	
M. genavense	iron-containing compound
M. genavense	mycobactin J
M. avian subs. *paratuberculosis*	mycobactin J
M. ulcerans	egg yolk
Specialized growth temperatures	
M. haemophilum	28-30º C
M. ulcerans	25-33º C
M. chelonae	28-33º C
M. marinum	28-30º C
Duration of incubation	
M. ulcerans	8-12 weeks
M. genavense	8-12 weeks

Any clinically significant NTM isolate should be identified to the species level because, with the exception of MAC, this portends important information regarding prognosis and treatment. Furthermore, in certain cases, sub-speciation can be critical to optimal management. For example, *M. abscessus* complex is made up of subspecies *abscessus*, *bolletii,* and *massiliense.* Isolation of these various subspecies imparts important prognostic and treatment information since *M.a.massiliense*, which tends to be macrolide susceptible, portends a better prognosis than the other two subspecies [15]. In *M. abscessus* complex, a surrogate to this sub-speciation is molecular testing for the presence of a functional *erm*(41) gene. This gene is typically functional in *M. abscessus* subspecies *abscessus* and *bolletii,* but not in *massiliense.* The *erm*(41) gene confers inducible resistance to macrolides, such that the initial macrolide testing may appear susceptible but if incubated over a longer time period the organism will display macrolide resistance.

An additional challenge in diagnosis of NTM infection in SOT is the number of new species being discovered. It is inevitable that we isolate some of these new species in our SOT population and will be met with the challenge to determine the clinical significance of a positive culture and derive an effective treatment regimen for newly described organisms.

4. Outcomes and Management

These infections are often difficult to treat. Disease cure rates in the literature range from 32-44%, although a greater number do have some clinical improvement without complete resolution of infection on NTM therapy [11]. Outcomes in transplant patients with NTM disease are highly variable: depending on the extent of infection, susceptibility of the organism and level of immunosuppression of the host [9, 11, 12]. Early infection (within the first year post-transplant) has been associated with decreased survival in SOT patients, although NTM infection itself was listed as a cause of death in a minority [16]. Immunomodulatory effects of the infection, rejection, or development of secondary nosocomial infections are all thought to contribute to this mortality. Interestingly, there is no significant difference in survival between patients infected with *M.abscessus* or other non-*M.abscessus* NTM infections [16]. In lung transplant patients specifically, one study suggests increase in mortality associated with NTM isolation, although cause of death was more commonly related to a non-NTM infection [9]. Other studies in the lung transplant population did not show any increased mortality associated with NTM isolation, but one did suggest trend towards increased incidence of bronchiolitis obliterans syndrome (BOS) [14, 17].

Detailed specific drug regimens targeting individual NTM is outside the scope of this review; however, Table 2 provides recommended initial empiric regimens for the most commonly isolated organisms. Empiric regimens may differ based on site of infection. A key principle in the treatment of NTM infections is that a multi-drug regimen for prolonged period is required for cure and to avoid development of antimicrobial resistance. It is also important to recognize that there is discordance between *in vitro* drug susceptibilities and clinical response. For MAC, clinical response correlates only to macrolide *in vitro* susceptibility but other drug susceptibilities do not reliably predict clinical outcome. For many NTM species, laboratory determined susceptibility breakpoints have not been confirmed to be clinical meaningful. Therefore, it is necessary to approach interpretation of this data with an appreciation of the limitations. It is also worth noting the possibility of inducible macrolide resistance in RGM. A functional *erm* gene confers inducible macrolide resistance, and can be found in *M. fortuitum* and *M. abscessus* subspecies *abscessus* and *bolletii.* If present, these organisms can be resistant to macrolides even when they appear susceptible in the laboratory. To evaluate for inducible resistance, isolates either need to be held for two weeks to evaluate for phenotypic evidence or molecular diagnostics utilized to evaluate for presence of a functional *erm* gene.

Interactions between NTM therapy and immunosuppressive medications complicate the treatment of this disease (Table 3). Azithromycin is the preferred macrolide for treatment of NTM over clarithromycin since it is a less potent inhibitor of cytochrome P450 (CYP450) and thus, has less of an impact on calcineurin inhibitor (CNI) levels. Rifampin is a potent inducer of CYP3A4 resulting in decreased CNI and sirolimus levels which can lead to organ rejection. Rifabutin has less of this effect, and is thus the preferred rifamycin in SOT recipients. Close monitoring of drug levels, medication side effects, and allograft function during treatment for NTM infection is critical. Careful consideration should be given to the appropriateness of intermittent or three times a week therapy in this population given the potential for fluctuating levels of immunosuppression if thrice weekly antibiotics are administered and also the potential absorption issues associated with complications of lung transplantation.

Table 2 Initial Antibiotic regimens for treatment of common NTM infections*.

NTM Species	Recommended Regimen	Alternative Agents	Considerations
M.abscessus subsp. *abscessus* or *bolletii*	Cefoxitin or Imipenem Amikacin plus additional alternative agent +/-Azithromycin	Linezolid Tigecycline Clofazimine	Presence of Erm(41) gene confers inducible resistance to macrolides. Some experts still include Azithromycin as part of regimen.
M.abscessus subsp. *massiliense*	Azithromycin Cefoxitin or Imipenem Amikacin	Clarithromycin Linezolid Tigecycline Clofazimine	
MAC	Azithromycin Rifabutin Ethambutol +/- Amikacin	Clarithromycin Rifampin Amikacin	Amikacin should be included in initial regimen if pulmonary cavitary disease present, or considered in setting of severe or disseminated disease
M. chelonae	Azithromycin plus either Tobramycin, Linezolid, or Imipenem	Clarithromycin Amikacin Tigecycline	
M. fortuitum	Amikacin Ciprofloxacin Sulfonamides	Cefoxitin Imipenem Doxycycline	Isolates contain erm(39) gene which confers inducible resistance to macrolides so use these agents with caution.
M. haemophilum	Azithromycin Rifabutin Ciprofloxacin	Rifampin Clarithromycin Amikacin Sulfonamides Doxycycline	Variable susceptibility to doxycycline and sulfonamides
M. kansasii	Rifabutin Ethambutol Isoniazid	Rifampin Clarithromycin Azithromycin Moxifloxacin Amikacin Sulfomamides	

M. marinum	Azithromycin Ethambutol +/- Rifabutin	Rifampin Clarithromycin Azithromycin Sulfonamides Doxycycline Minocycline	Rifabutin can be considered for extensive disease.

*Based on ATS/IDSA and AST guidelines for treatment of NTM infections. Doses: Amikacin 10-15 mg/kg IV daily or three times per weak, Azithromycin 250-500 mg PO daily, Cefoxitin 8-12 g IV in divided doses daily, Ciprofloxacin 500 mg PO BID, Clarithromycin 500 mg PO BID, Clofazimine 50-100 mg PO daily, Doxycycine 100 mg PO BID, Ethambutol 15 mg/kg PO daily, Imipenem 1g IV BID, Isoniazid 300 mg PO daily, Levofloxacin 500-750 mg PO daily, Linezolid 600 mg PO daily, Minocycline 100 mg PO daily, Moxifloxacin 400 mg PO daily, Rifabutin 150 mg PO daily, Rifampin 600 mg PO daily, Trimethoprim/Sulamethoxazole 800-1600 mg sulfa component PO BID, Tigecycline 50 mg IV once or twice daily, Tobramycin 5mg/kg IV daily or three times per week.

Table 3 Interactions between antibiotics used to treat NTM and immunosuppressive agents.

Antibiotic	**Immunosuppressive agent**	**Interaction**
Macrolides (clarithromycin > azithromycin)	CNI	Increased CNI level
Rifamycins (rifampin > rifabutin)	CNI	Decreased CNI level
	Sirolimus	Decreased sirolimus level
	Steroids	Decreased effectiveness
Aminoglycosides	CNI	Increased risk of renal dysfunction
Levofloxacin	CNI	Increased CNI level
Imipenem	Cyclosporine (CsA)	Increased risk of neurotoxicity
Tigecycline	CsA	Increased CsA level

Whenever possible, a reduction in the intensity of immunosuppression should be employed as part of the treatment of NTM infection. However, similar to *Mycobacterium tuberculosis* in SOT patients, paradoxical Immune Reconstitution Inflammatory Syndrome (IRIS) has been described in a kidney patient with *M. kansasii* infection [18]. Therefore, a worsening in clinical status after initial improvement with appropriate antibiotic therapy and reduction in immunosuppression with the absence of positive culture results should prompt consideration of IRIS. In the case described by Lemoine et al, an increase in immunosuppression led to favorable response.

Optimal duration of therapy in this patient population is not clear. Guidelines recommend 12 months of therapy from date of culture clearance for pulmonary disease and at least 4-6 months for soft tissue disease or bone disease respectively. Ongoing disease surveillance with follow up

imaging and microbiologic testing whenever possible can be helpful in determining duration of therapy. In the setting of pulmonary disease, ATS/IDSA guidelines suggest monthly sputum samples for monitoring of infection, with the first negative sputum counting as day zero for the length of treatment [13]. Due to underlying immunosuppression, the duration of therapy may need to be longer in SOT patients than what is suggested in guidelines. It is reasonable to consider these recommended durations as the minimum in this patient population [11]. Relapse is possible after completion of therapy so patients should have ongoing clinical and possibly microbiologic monitoring.

5. Prevention

A specific challenge is the management of transplant candidates who are colonized or infected with NTM organisms pre-transplant. This occurs most commonly in the lung transplant population as many of these transplant candidates have structural lung disease, such as CF or chronic obstructive pulmonary disease (COPD), which is a risk factor for presence of NTM. NTM infection incidence in the CF population is as high as 20% [19]. The transplant candidacy of patients infected with *M.abscessus* has been controversial. The presence of *M.abscessus* pre-transplant is associated with post-operative thoracic cavity infection including mediastinal and sternal wound infections [20, 21]. Patients with a positive culture pre-transplant are more likely to develop post-transplant disease [22, 23]. Despite the increase in post-operative morbidity, survival has not been significantly altered in single center studies [10, 23, 24]. As such, International Society of Heart and Lung Transplantation (ISHLT) guidelines suggest that *M.abscessus* is not an absolute contraindication to transplantation unless there is progressive disease despite therapy or when therapy is tolerated poorly [25]. In general, lung transplant candidates with *M.abscessus* infection should be started on therapy as soon as transplant is being considered with the goal to lessen burden of infection and assess tolerability of an effective anti-mycobacterial regimen [21, 22, 24]. If a patient is transplanted with positive AFB cultures for *M.abscessus*, experts recommend chest cavity irrigation with an anti-mycobacterial agent and close attention to surgical technique to avoid contamination. Post-operative management should include close monitoring of surgical wounds and pleural space, monitoring of BAL specimens for NTM, and continuation of peri-operative anti-mycobacterial antibiotics [26]. The significance of colonization with other NTM including MAC pre-lung transplant is also unclear. Practices vary from no treatment with monitoring to pre-transplant and/or peri-transplant anti-mycobacterial therapy. The American Society of Transplantation recommends that lung transplant candidates colonized or infected with MAC should be treated with multi-drug therapy prior to transplant [1].

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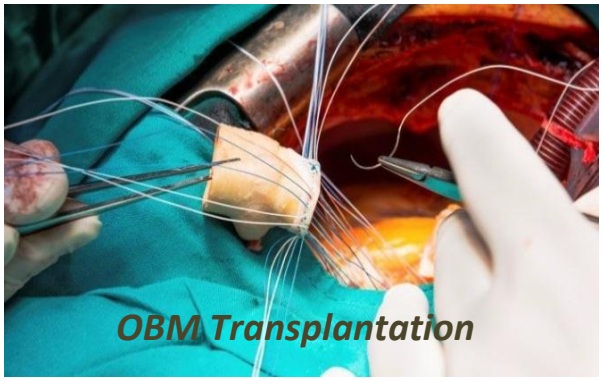
References

1. Keating MR, Daly JS, Practice AIDCo. Nontuberculous mycobacterial infections in solid organ transplantation. Am J Transplant. 2013; 13: 77-82.
2. Piersomoni C. Nontuberuculous mycobacteria infection in solid organ transplant recipients. Eur J Clin Microbiol Infect Dis. 2012; 31: 397-403.
3. Baker AW, Lewis SS, Alexander BD, Chen LF, Wallace RJ Jr, Brown-Elliott BA, et al. Two-phase hospital-associated outbreak of mycobacterium abscessus: Investigation and mitigation. Clin Infect Dis. 2017; 64: 902-911.
4. van Ingen J, Kohl TA, Kranzer K, Hasse B, Keller PM, Szafrańska AK, et al. Global outbreak of severe mycobacterium chimaera disease after cardiac surgery: a molecular epidemiological study. Lancet Infect Dis. 2017; 17: 1033-1041.
5. Aitken ML, Limaye A, Pottinger P, Whimbey E, Goss CH, Tonelli MR. Respiratory outbreak of mycobacterium ab-scessus subspecies massiliense in a lung transplant and cystic fibrosis center. Am J Respir Crit Care Med. 2012; 185: 231-232.
6. Adjemian J, Olivier KN, Seitz AE, Holland SM, Prevots DR. Prevalence of nontuberculous mycobacterial lung disease in U.S. medicare beneficiaries. Am J Respir Crit Care Med. 2012; 185: 881-886.
7. George IA, Santos CA, Olsen MA, Bailey TC. Epidemiology and outcomes of nontuberculous mycobacterial infections in solid organ transplant recipients at a midwestern center. Transplantation. 2016; 100: 1073-1078.
8. Longworth SA, Vinnard C, Lee I, Sims KD, Barton TD, Blumberg EA. Risk factors for nontuberculous mycobacterial infections in solid organ transplant recipients: a case-control study. Transplant Infect Dis. 2014; 16: 76-83.
9. Huang HC, Weigt SS, Derhovanessian A, Palchevskiy V, Ardehali A, Saggar R, et al. Non-tuberculous mycobacterium infection after lung transplantation is associated with increased mortality. J Heart Lung Transplant. 2011; 30: 790-798.
10. Knoll BM. Update on nontuberculous mycobacterial infections in solid organ and hematopoietic stem cell transplant recipients. Curr Infect Dis Rep. 2014; 16: 421.
11. Doucette K, Fishman JA. Nontuberculous mycobacterial infection in hematopoietic stem cell and solid organ transplant recipients. Clin Infect Dis. 2004; 38: 1428-1439.
12. Song Y, Zhang L, Yang H, Liu G, Huang H, Wu J, et al. Nontuberculous mycobacterium infection in renal transplant recipients: a systematic review. Infect Dis (Lond). 2018; 50: 409-416.
13. Griffith DE, Aksamit T, Brown-Elliott BA, Catanzaro A, Daley C, Gordin F, et al. An official ATS/IDSA statement: diagnosis, treatment, and prevention of nontuberculous mycobacterial diseases. Am J Respir Crit Care Med. 2007; 175: 367-416.
14. Knoll BM, Kappagoda S, Gill RR, Goldberg HJ, Boyle K, Baden LR, et al. Non-tuberculous mycobacterial infection among lung transplant recipients: a 15-year cohort study. Transplant Infect Dis. 2012; 14: 452-460.

15. Koh WJ, Jeon K, Lee NY, Kim BJ, Kook YH, Lee SH, et al. Clinical significance of differentiation of Mycobacterium massiliense from Mycobacterium abscessus. Am J Respir Crit Care Med. 2011; 183: 405-410.
16. Longworth SA, Blumberg EA, Barton TD, Vinnard C. Non-tuberculous mycobacterial infections after solid organ transplantation: A survival analysis. Clin Microbiol Infect. 2015; 21: 43-47.
17. Shah SK, McAnally KJ, Seoane L, Lombard GA, LaPlace SG, Lick S, et al. Analysis of pulmonary non-tuberculous mycobacterial infections after lung transplantation. Transpl Infect Dis. 2016; 18: 585-591.
18. Lemoine M, Laurent C, Hanoy M, Leporrier J, François A, Guerrot D, et al. Immune reconstitution inflammatory syn-drome secondary to mycobacterium kansasii infection in a kidney transplant recipient. Am J Transplant. 2015; 15: 3255-3258.
19. Adjemian J, Olivier KN, Prevots DR. Epidemiology of pulmonary nontuberculous mycobacterial sputum positivity in patients with cystic fibrosis in the United States, 2010-2014. Ann Am Thorac Soc. 2018; 15: 817-826.
20. Chernenko SM, Humar A, Hutcheon M, Chow CW, Chaparro C, Keshavjee S, et al. Mycobacterium abscessus infections in lung transplant recipients: the international experience. J Heart Lung Transplant. 2006; 25: 1447-1455.
21. Qvist T, Pressler T, Thomsen VO, Skov M, Iversen M, Katzenstein TL. Nontuberculous mycobacterial disease is not a contraindication to lung transplantation in patients with cystic fibrosis: a retrospective analysis in a Danish patient population. Transplant Proc. 2013; 45: 342-345.
22. Chalermskulrat W, Sood N, Neuringer IP, Hecker TM, Chang L, Rivera MP, et al. Non-tuberculous mycobacteria in end stage cystic fibrosis: Implications for lung transplantation. Thorax. 2006; 61: 507-513.
23. Zaidi S, Elidemir O, Heinle JS, McKenzie ED, Schecter MG, Kaplan SL, et al. Mycobacterium abscessus in cystic fibrosis lung transplant recipients: report of 2 cases and risk for recurrence. Transplant Infect Dis. 2009; 11: 243-248.
24. Lobo LJ, Chang LC, Esther CR, Gilligan PH, Tulu Z, Noone PG. Lung transplant out-comes in cystic fibrosis patients with pre-operative Mycobacterium abscessus respiratory infections. Clin Transplant. 2013; 27: 523-529.
25. Weill D, Benden C, Corris PA, Dark JH, Davis RD, Keshavjee S, et al. A consensus document for the selection of lung transplant candidates: 2014--an update from the Pulmonary Transplantation Council of the International Society for Heart and Lung Transplantation. J Heart Lung Transplant. 2015; 34: 1-15.
26. Rao M, Silveira FP. Non-tuberculous mycobacterial infections in thoracic transplant candidates and recipients. Curr Infect Dis Rep. 2018; 20: 14.



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