Sporotrichoid *Mycobacterium marinum* Infection after Lung Transplantation for Alpha-1 Antitrypsin Deficiency

Shyam R. Javvaji1*, Srimanasi Javvaji2 and Marc E. Grossman2

1School of Medicine, University of Texas-Medical Branch, USA
2Department of Dermatology, Columbia University Medical Center, USA

Abstract

*Mycobacterium marinum* is a ubiquitous salt and fresh water organism, which in humans, causes cutaneous nodules, ulceration, tenosynovitis, osteomyelitis and rarely disseminated infection. There have been only 9 reported cases of *M. Marinum* infection in transplant recipients; we herein report the 10th case of a 52 year old female with alpha-1 antitrypsin deficiency that had undergone single lung transplantation. We review the literature of *M. marinum* infection in transplant recipients and ATS/IDSA guidelines for optimal therapy for this unusual infection.

ABBREVIATIONS

IVIG: Intravenous Immunoglobulin

INTRODUCTION

*Mycobacterium marinum* is a ubiquitous salt and fresh water non-tuberculous photochromogenic mycobacterium that naturally infects at least 150 species of frog fish, freshwater eels, and oysters [1,2]. *M. marinum* infections in humans usually arise from skin contact with contaminated water found in fish tanks, ponds, and swimming pools. The infection typically manifests as cutaneous nodules or ulceration but can spread to deeper structures causing tenosynovitis, osteomyelitis, and rarely disseminated disease. There have only been 9 reported cases of cutaneous *M. marinum* infection in transplant recipients; only one of which was a lung transplant recipient [2-10]. We report a case of cutaneous *M. marinum* infection in a transplant patient, the second case described with lung transplantation for alpha-1 antitrypsin deficiency.

CASE PRESENTATION

In March of 2012, a 52-year-old white female presented to the lung transplant clinic with shortness of breath and multiple subcutaneous nodules along her right forearm. She had alpha-1 antitrypsin deficiency with a single right lung transplant two years prior, for which she was taking tacrolimus, prednisone, and mycophenolate mofetil. Her transplant course was complicated by early acute cellular rejection three months after transplantation, primary graft dysfunction with donor specific antibodies requiring IVIG and rituximab, and infection with aspergillus and methicillin-resistant *Staphylococcus aureus* from her donor.

During her clinic visit, concern for allograft dysfunction and antibody mediated rejection resulted in hospital admission. She was found to have minimal acute rejection on transbronchial biopsy. She received IVIG during her hospitalization with no increase in immunosuppression given her subcutaneous nodules and concern for infection.

One month prior to this admission, she began to notice small, tender bumps on her right forearm that became increasingly painful. On exam she had a 4 cm mildly erythematous, tender, irregular mass of the distal extensor forearm with two proximal 1 cm subcutaneous nodules in a sporotrichoid distribution. On further questioning, the patient revealed that prior to the onset of her skin lesions; she had cleaned the filter of her fresh water fish tank, and had incurred a minor self-healing laceration. She subsequently developed painful sporotrichoid nodules of her forearm.

The differential diagnosis of these nodules included atypical mycobacterial infection, alpha-1 antitrypsin deficiency panniculitis, sporotrichosis, and traumatic fat necrosis. Excisional biopsy of one nodule showed a lymphohytic and neutrophilic microabscess, with red beaded acid-fast bacilli. Tissue culture on Lowenstein-Jensen agar confirmed *Mycobacterium marinum*. Pulmonary involvement was excluded, as AFB stain of transbronchial biopsy and bronchiolar lavage was negative. In addition, she had no findings on CT of her chest that were consistent with pulmonary mycobacterial infection.

Treatment was initiated with clarithromycin 500mg twice daily and ethambutol 900mg daily. At 6 week follow up, the patient developed several new nodules on the hand and forearm. All original nodules had decreased in size. The patient was continued on the same antibiotic regimen. At 6 month follow up, she had significant improvement of all skin lesions.

DISCUSSION

Mycobacterium marinum infection is rare in the general population, with a reported incidence of 0.27 cases per 100,000. M. marinum is even more uncommon in the transplant population with only 9 other reports of cutaneous infection in the literature: four kidney transplant patients, two dual kidney and pancreas transplant recipients, one liver, one hematopoietic stem cell, and one other lung transplant patient [2-10]. This lung transplant case occurred in a 52 year-old female with alpha-1 antitrypsin deficiency who underwent bilateral lung transplant 2.5 years prior to onset of M. marinum nodules of her left hand and forearm. She was treated with surgical excision and antibiotics for 6 months with resolution of her infection [2].

Most cases of M. marinum infection in transplant recipients result from exposure to aqueous environments like the immunocompetent host. Five of the nine transplant cases involved exposure to aquariums and fish containing ponds, two cases with direct contact with fish, and two cases where exposure was not reported [2-10].

These transplant recipients most commonly presented with sporotrichoid or ascending nodules of the upper extremities. Three of nine cases involved the lower extremities as well. The most extensive disease occurred in the patient with a hematopoietic stem cell transplant for acute myeloid leukemia reported by Jacobs et al [6]. He developed numerous tender subcutaneous nodules of his upper and lower extremities. On PET-CT the patient was found to have osteomyelitis of the proximal tibia, a hypermetabolic brain nodule, infectious foci of the right lung and right testes, and numerous intramuscular and intraosseous lesions. The patient was started on antibiotic therapy for one year with clarithromycin, rifampin, and ethambutol. Six month PET-CT showed improvement in multiple subcutaneous nodules and right tibial abscess [6].

Treatment of M. marinum infection in transplant recipients poses a challenge, because of immunosuppression and risk of extensive disease burden. In 2007, the ATS/IDSA published a statement regarding diagnosis and treatment of non-tuberculous mycobacteria with no specific recommendations for immunosuppressed patients diagnosed with Mycobacterium marinum. The authors’ recommended treatment with two active agents in cluding combinations of clarithromycin, ethambutol, and rifampin for 1-2 months after resolution of symptoms, typically a course of 3-4 months. According to their recommendations, the combination of clarithromycin and ethambutol provides the optimal balance of efficacy and tolerability for most patients. In cases of osteomyelitis or other deep structure infection, addition of rifampin is advised [11].

Of the non tuberculous mycobacteria, M. marinum in addition to M. abscessus, M. chelonae, M. fortuitum, and M. ulcerans are most common to cause localized cutaneous infection. M. abscessus is treated with oral clarithromycin or azithromycin combined with parenteral medications including amikacin, cefoxitin, or imipenem. M. chelonae is susceptible or intermediate in susceptibility to tobramycin (100%), clarithromycin (100%), linezolid (90%), imipenem (60%), amikacin (50%), cefazidine, doxycycline (20%), and ciprofloxacin (20%). M. fortuitum is treated with multiple oral antimicrobial agents including newer macrolides and quinolones, doxycycline, and minocycline, and sulfonamides. These organisms are usually treated for 4 months with multiple agents. Medical treatment for M. ulcerans, however, is poor. Treatment of choice is surgical debridement with skin grafting [11].

The treatment regimens reported in the literature for the 9 transplant recipients with M. marinum were various combinations of ethambutol, rifabutin, rifampin, minocycline, doxycycline, ciprofloxacin, moxifloxacin, INH, protonamide, and trimethoprim-sulfamethoxazole [2-10]. The average duration of antibiotic therapy was 6.6 months and median length of treatment was 5 months. In a study by Aubrey et al. looking at 63 patients with M. marinum infection, none of were reported to be transplant recipients, average duration of therapy with a variety of antimicrobials was not reported, but median duration of antibiotic therapy was 3.5 months [12].

Overall, when comparing Mycobacterium marinum infection in the general population versus immunosuppressed transplant recipients, both groups had similar clinical presentation and water exposure. Transplant cases required a longer course of antibiotics. As such, M. marinum in transplant recipients should follow the IDSA/ATA recommendation of treatment for 1-2 months after resolution of skin lesions with at least 2 active agents including a combination of ethambutol, clarithromycin, or rifampin [13].

REFERENCES


