Atypical mycobacteriosis in a lung transplant recipient


ABSTRACT: Although mycobacterial infections are more frequent in lung transplant recipients than in other solid organ recipients only occasional reports of infection from atypical Mycobacteria have been reported in patients receiving lung transplantation.

We present a case of pleural and cutaneous infection due to Mycobacterium fortuitum in a double-lung transplant recipient. The infection was rapidly responsive to therapy with a two drug regimen and no reduction of immunosuppression was necessary.


Mycobacterial infections are a serious complication in recipients of a solid organ transplant. Immunosuppression represents a well-known risk condition in these patients. Contamination from the donor organ or from the environment, reactivation of a pre-existing infection, and transmission from infected patients are all theoretical sources of disease. Only nine cases of mycobacterial infection in lung transplant recipients have been reported in the literature [1–5]. All but one of these infections was caused by Mycobacterium tuberculosis (MTB); the infection with atypical bacilli (ATB) was caused by Mycobacterium chelonae [1].

Twenty five lung transplants were performed between October 1993 and June 1996 in our institution. Immunosuppression initially consisted of triple drug therapy (azathioprine, cyclosporin, and prednisone). Acute rejection was treated with pulse intravenous methylprednisolone over 3 days.

In this article, we report a case of infection in a lung transplant recipient with Mycobacterium fortuitum, a fast growing Mycobacterium, usually nonpathogenic. Soil, natural water, dust, and various medical devices are the most common sources of contamination. Infection initially developed in the pleural space, and eventually involved the chest wall and the incision region of thoracotomy.

Case report

A 56 year old man underwent bilateral lung transplantation in December 1994 due to end-stage idiopathic pulmonary fibrosis. Surgical access was a transternal anterolateral bi-thoracotomy. Surgery lasted 7 h, after which the patient was treated in the intensive care unit. A total of four chest drainages were positioned and removed after the 4th, 5th, 7th and 8th days. After 3 weeks, the patient underwent a bronchoscopy for rejection-infection surveillance. No rejection and/or infection was diagnosed by transbronchial biopsy and bronchoalveolar lavage (BAL).

Twenty four hours after the bronchoscopy the patient developed conspicuous pleural effusion on the right side, with predominant lymphocyte cells (70%), elevated total protein count (43 g·L-1 in pleural fluid; 57 g·L-1 in serum), elevated lactate dehydrogenase (LDH) (2,103 IU·L-1 in pleural fluid; 282 IU·L-1 in serum), and low glucose levels (23 mg·dL-1). A culture revealed M. fortuitum.

The fluid was first removed by thoracentesis, but due to the persistence of the effusion, a pleural drainage was eventually inserted. No infection or swelling was evident in the surgical scar. A chest computed tomography (CT) scan performed at that time showed a normal lung parenchyma. The patient was discharged from hospital 2 weeks after the bronchoscopy in good general condition and without pleural drainage. A small effusion was still evident at that time. No specific therapy was initiated against Mycobacterium.

One month later, purulent secretions were collected from different sites of the surgical wound. A culture of the fluid revealed the presence of M. fortuitum. The patient was treated with syringe drainage of the fluid. In May a swelling in the left submamilla region was noted. A needle aspiration yielded a bloody, purulent, highly dense secretion. A culture was again positive for M. fortuitum. The microorganism appeared sensitive to ciprofloxacin, amikacin, clarithromycin, rifampin and isoniazid. Therapy with ciprofloxacin 500 mg b.i.d. and clarithromycin 500 mg b.i.d. was initiated: the immunosuppression was not tapered.

Six weeks later, the fluid in the submamilla region disappeared. The patient continued with a two drug regimen for 6 months, and he was then given clarithromycin alone, according to the experience of one drug regimen reported by WALLACE et al. [6]. This therapeutic regimen is still being followed (September 1996); the patient
In the literature, eight patients have been reported with infection due to MTB after lung transplantation [2–3]. Of these, two patients died of lung infection, one deteriorated due to tapering of immunosuppression, three recovered with medical treatment (but one recurred 2 yrs later), one patient required lobectomy associated with chemotherapy, and one suffered from tuberculous empyema necessitating drainage. Only one case of pulmonary disease caused by ATB (Mycobacterium chelonae) with a fatal outcome has been described, in a heart-lung transplant complicated by obliterative bronchiolitis [1]. Dromer et al. [5], who published the most consistent report on tuberculosis in lung transplant recipients, registered four cases of MTB infection among 61 patients (6.5%) submitted to lung or heart-lung transplant. In their study, the mean time of presentation was 7.5 months (range 3–13 months) after operation. Radiological features are atypical and the concomitant presence of other pulmonary pathological evidence (rejection or other infection) renders radiological interpretation more difficult.

The incidence of mycobacterial infection among solid organ transplant recipients differs according to the organ and to the different authors. In renal transplants, Mycobacterial infections were documented in 0.8% of recipients by Delaney et al. [7], who emphasized that the majority are diagnosed in the first 12 months post-transplantation. Lung, bones, skin, peritoneum, allografts, and miliary form are the most frequent sites of infection in these patients. In their experience, about 60% were MTB and 40% ATB. In a series of 487 renal recipients, Hall et al. [8] identified 22 cases of mycobacterial infection (4.5%), including 21 MTB and 1 ATB. Four cases of ATB infection have been reported by the Mayo Clinic [9] in recipients of kidney (2), heart (1), and liver (1) transplant.

Common manifestations of ATB infection in solid organ recipients include: cutaneous lesions of the extremities, tenosynovitis, and joint infections [9]. Surgery, reduction of immunosuppression and chemotherapy with antitubercular drugs, depending on the extent of the infection, the form of presentation and the site, are all associated with a good outcome in many cases. ATB can often be isolated from secretions of these patients, but in the majority of cases these are considered to be saprophytes, and this was the initial interpretation in the present case. ATB are ubiquitous organisms that are part of the normal environmental flora. Individuals may have airways colonized with atypical mycobacteria without evidence of infection. The American Thoracic Society (ATS) has proposed criteria for the diagnosis of atypical mycobacterial pulmonary infections, distinguishing definite infection from probable infection [10]. Pleural effusions are rare in nonimmunosuppressed hosts and are described in 5–20% of cases [11–13].

In the present case, the organism was first identified in pleural fluid, of which the cellularity and biochemical data appeared consistent with tuberculosis. We speculated that, from this first site of infection, the agent moved through the soft tissue to the chest wall and to the surgical wound, finally establishing the infection in the submammalian area.

The common incubation period for this infection ranges 1–6 months [14]. Considering the very early identification of this agent in the pleural fluid (3 weeks after the operation) we can hypothesize that: 1) the patient had been infected during the operation (some interesting possibilities are iatrogenic manoeuvres, such as chest tube drainage or intraoperative bronchoscopy, or infection of the pleural space from contaminated ice used in the preservation of the graft); 2) the patient was already colonized before transplantation, and the heavy postoperative immunosuppression acted as a reactivating factor; or 3) the donor lung was the source of infection, however, the clear aspect of the lung parenchymal on high resolution CT scan tends to dismiss this final option.

We do not know the importance of the role played by medical therapy, chest tube drainage and serial needle aspiration of the cutaneous lesions in the subsidence of the infection, although the natural history strongly supports the usefulness of the chemotherapy. Indeed, it was only after the use of antitubercular chemotherapy that all infected foci progressively disappeared, and the patient definitely recovered.

Clarithromycin and ciprofloxacin were selected among the sensitive drugs as the least toxic agents. Isoniazid and amikacin were excluded because of the risk of liver and kidney toxicity. Rifampin was excluded because of the well-known effect on the half-life and serum concentration of cyclosporin.

In normal patients, the degree of symptomatology often plays a role in determining optimal management of mycobacterial infection, but in those patients with debilitating symptoms a prolonged and multiple-drug regimen may be necessary. In individuals with localized disease, surgical resection can be curative [15], but in the present patient a definitive response was only evident following medical therapy.

In conclusion, we emphasize the possibility that atypical bacilli can become pathogenic in lung transplant patients. Depending on the patient's general condition and symptoms, a carefully selected chemotherapy, without reduction of immunosuppression, can be considered as an appropriate therapeutic option, with curative intent.

**References**


