Recurrent polymyositis-associated lung disease after lung transplantation

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Abstract

The association between interstitial lung disease and polymyositis/dermatomyositis is well known. It severely affects patients' quality of life, worsens prognosis and represents a major risk factor for premature death. Current treatment is unclear and therapeutic options are based on case series. We report the case of a 15-year old female diagnosed with end-stage lung disease associated to polymyositis who received a double lung transplant after 20 days of extracorporeal membrane oxygenation. She died 9 months later and microscopic post-mortem findings revealed recurrence of interstitial lung disease. This is the first time that recurrence of polymyositis-associated lung disease following lung transplantation is described in the literature.

Keywords: Polymyositis • Extracorporeal membrane oxygenation • Pulmonary fibrosis • Lung transplantation

INTRODUCTION

According to data from the International Society for Heart and Lung Transplantation registry, only 1.3% of lung transplants (LTx) were performed for connective tissue disease (CTD)-related lung dysfunction, mostly corresponding to systemic sclerosis and scleroderma overlap syndromes. A minority of cases was associated to polymyositis/dermatomyositis (PM/DM) [1].

PM/DM-related interstitial lung disease (ILD) was first recognized in 1956. It severely affects patients' quality of life, worsens prognosis and represents a major risk factor for premature death. Reported incidence rates vary between 5 and 65% depending on whether clinical, radiological, functional or histological criteria are used. The pulmonary compromise exhibits three patterns based on the clinical symptoms: those with acute onset and accelerated evolution to terminal respiratory failure leading to death in 4–6 weeks (15–25% of cases), those with chronic insidious respiratory symptoms (60%) and those without pulmonary symptoms but presenting with abnormal chest radiographs or pulmonary function tests (22%). The current treatment for myositis-associated ILD is unclear and based on case series. Corticosteroids are the primary approach, although other immunosuppressive agents are often required, and LTx has been suggested for those who develop refractory end-stage ILD [2]. Improvements in artificial lung devices such as extracorporeal membrane oxygenation (ECMO) support makes it possible to successfully bridge selected patients to LTx with promising results.

We present the first case in the literature of recurrence of PM-associated ILD following lung transplantation.

CASE REPORT

The patient was a 15-year old girl diagnosed with idiopathic inflammatory PM and confirmed ILD. Initial therapy included a prednisolone and methotrexate regimen but was discontinued after 5 months because it was ineffective. Azathioprine was then started. After 6 months following the diagnosis of PM, the patient was admitted for progressive dyspnoea and respiratory failure, elevation of creatine phosphokinase (CPK) and proximal muscle weakness. She was diagnosed with bronchiolitis obliterans organizing pneumonia. In the seventh and eighth months, the patient presented with bilateral pneumothoraces requiring pleurodesis and pulmonary resection. During the 10th month, the patient was admitted again for rapidly progressive respiratory failure and pulmonary hypertension. The case was referred for LTx.

When mechanically ventilated in our intensive care unit, high pressures were necessary, reflecting the restrictive respiratory pattern due to severe ILD (Fig. 1). Adequate oxygenation was not achieved (PaO\textsubscript{2}/FiO\textsubscript{2} ratio <80) despite maximal ventilatory support, leading us to start veno-venous ECMO (right femoral/ right jugular veins) as a bridge to lung transplantation. Right ventricular dysfunction developed and inhaled prostaglandins were used. Bleeding on the cannulation site occurred and transfusions of blood products were necessary. In the 11th month of diagnosis and after 20 days on ECMO, bilateral lung transplantation was performed with the patient under cardiopulmonary bypass (CBP). ECMO support was successfully withdrawn during surgery when CBP was established. The donor was a previously healthy 52-year old hypertensive woman with no known history of lung disease.
The cause of death of the donor was a subarachnoid haemorrhage. Histopathology of explanted lungs revealed interstitial fibrosis in a ‘patchwork’ pattern indicative of usual interstitial pneumonia (UIP).

On day 7 after LTx, the patient was weaned from mechanical ventilation and discharged to the ward on postoperative day 10. The post-transplant immunosuppressive regimen consisted of tacrolimus, mycophenolate mofetil, methylprednisolone and basiliximab.

Eight months after LTx, the patient was re-admitted for respiratory compromise. CPK levels remained normal; the trans-bronchial biopsy excluded allograft rejection and cultures ruled out an active pulmonary infection. Nevertheless, thoracic computed tomography scan (CT) showed bilateral extensive and diffuse compromise with ground-glass opacity (Fig. 2). Rapid deterioration led to mechanical ventilation, which again reflected a severely restrictive pattern. The patient again required veno-venous ECMO therapy but died 16 days later after an episode of electromechanical dissociation with ominous neurological compromise. Post-mortem macroscopic and microscopic graft examinations were made revealing advanced pulmonary fibrosis with UIP, suggesting a recurrence of the primary disease despite an immunosuppressive regimen.

DISCUSSION

The lung is the most common extra-muscular organ involved in PM/DM. Pulmonary compromise is present in more than 40% of patients, causing significant morbidity and mortality. Paradoxically, less than 5% of patients present with ventilatory muscle weakness leading to respiratory failure. Although the prognosis of ILD associated to PM/DM is not severe (94, 90 and 87% survival at 1, 3 and 5 years, respectively), predictors of poor outcome have to be recognized in order to make an early therapeutic approach, which may include LTx. ECMO may serve as a bridge to transplantation in refractory pulmonary disease. Recognized predictors include acute presentations, neutrophilic alveolitis, initial diffusion lung capacity for carbon monoxide less than 45%, forced vital capacity less than or equal to 60%, DM, microangiopathy and digital infarcts in DM, amyopathic DM and histological UIP [2, 3].

A recent review evaluated survival rates among 284 patients who received LTx for CTD-related lung disease. The cumulative survival was less when compared with a cohort of patients transplanted for chronic obstructive pulmonary disease, with a difference that peaked at 1 year (72.7 vs 83.1%, P < 0.001) and similar to those with LTx due to idiopathic pulmonary fibrosis (72.7 vs 77.7%, P = 0.049). An increased risk of mortality was most prominent at 6 months after transplantation. Differences in survival between the CTD sub-groups beyond 30 days of LTx did not reach statistical significance [4]. However, information about the prognosis of patients with myositis-associated lung disease after LTx is lacking.

The frequency of recurrent disease after LTx is low. It was described as 1% in a population of 1394 patients. Sarcoidosis was the most recurrent disease; however, no cases of recurrent myositis-related ILD were found [5].

To date, no cases of recurrent myositis-associated ILD after LTx have been reported. In the case we have described, the patient died 9 months after transplantation and recurrence was suggested based on CT findings and histopathological graft studies. Further case series are required to establish the prognosis and risk factors for poor outcome following LTx in this subgroup of patients.

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REFERENCES

The Registry of the international Society for Heart and Lung Transplantation:

