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Title: Living-donor lobar lung transplantation for rapidly progressive interstitial pneumonia associated with clinically amyopathic dermatomyositis: Report of a case

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Abstract (105 words)

Diffuse interstitial pneumonia (IP) associated with collagen disease is a rare indication for lung transplantation. The manifestations of collagen disease are variable and dermatomyositis (DM) is often considered a contraindication for lung transplantation because of active myositis and a high incidence of malignancy. Furthermore, clinically amyopathic dermatomyositis (C-ADM) is associated with rapidly progressive IP resulting in a poor prognosis. Bilateral living-donor lobar lung transplantation was performed in a 52-year-old female with rapidly progressive IP associated with C-ADM, and the postoperative course was uneventful. To our knowledge, this case represents the first living-donor lobar lung transplantation for a patient with rapidly progressive IP associated with C-ADM.

Text

Introduction

Collagen diseases, such as dermatomyositis (DM) and systemic sclerosis (SSc), often cause interstitial pneumonia (IP) which leads to severe pulmonary dysfunction. However, very few cases receiving lung transplantation for DM have been reported, and outcomes were often unsatisfactory. Furthermore, clinically amyopathic dermatomyositis (C-ADM) is associated with rapidly progressive IP, resulting in a poor prognosis.

Herein, we report bilateral living-donor lobar lung transplantation in a patient with rapidly progressive IP associated with anti-CADM-140 antibody positive C-ADM.

Case Report

A 52-year-old female was diagnosed with DM in August 2010, when she developed Gottron's papule with slight interstitial shadow in the bilateral peripheral lungs on chest computed tomographic scan. After diagnosis of IP associated with DM, steroid therapy was initiated with intravenous methylprednisolone, followed by oral steroid medication; however, she began to develop dyspnea on effort and IP worsened. Continuous supplemental oxygen inhalation and cyclosporine were initiated in September 2010. Although the symptom of DM was controlled with treatment including cyclophosphamide and intravenous immunoglobulin, her respiratory status further deteriorated due to IP progression.

The patient was transferred to Kyoto University Hospital on November 2, 2010. On admission, her vital capacity was 1.12 L (42.6% predicted) and arterial blood gas demonstrated a pH of 7.43, PaO₂ of 96.8 mmHg, and PaCO₂ of 40.3 mmHg with 3L/min oxygen administered via a nasal cannula. Muscle strength was normal in all extremities on physical examination. There was no sign of esophageal dysmotility. A chest computed tomographic scan demonstrated severe fibrosis of the bilateral lungs (Figure 1) and after admission, subcutaneous and mediastinal emphysema (Figure 2) developed with worsening dyspnea. The level of serum creatine kinase was 28 IU/L. Antinuclear, anti-Jo-1 antibodies were negative. Although the results of serum levels of a few tumor markers were elevated (CEA: 19.6, CYFRA: 5.1,

NSE: 25.99, preoperative evaluation including a 2-deoxy-18F-fluoro-glucose-positron emission tomography scan did not demonstrate any evidence of coexisting malignant diseases. Anti-CADM-140 antibody, recently reported to be found specially in C-ADM, was detected in her serum on admission and she was diagnosed as having rapidly progressive IP associated with anti-CADM-140 antibody positive C-ADM.

Her life expectancy was estimated to be quite limited without lung transplantation. On November 17, 2010, she underwent living-donor lobar lung transplantation with a left lower lobe from her daughter (22-year-old) and a right lower lobe from her son (20-year-old), who desired to be lung donors and were considered eligible by medical and psychological preoperative evaluations. The surgical aspects of the donor lobectomy, donor backtable preservation technique, and recipient bilateral pneumonectomy and lobar implantation have been previously described by Starnes' group¹. We performed simultaneous lung lobe donation from both donors with three teams including the recipient team. Ischemic times of right lower and left lower lobes were 196 and 115 minutes, respectively.

The postoperative course was uneventful. The patient was completely weaned from a ventilator on POD 4. 4. We did not have any trouble managing immunosuppression after transplantation with regard to renal function. The patient was discharged from the hospital on POD 59. Six months after transplantation, her vital capacity was 1.77 L (68.1% predicted) and arterial blood gas in room air demonstrated a pH of 7.43, PaO₂ of 101.7 mmHg, and PaCO₂ of 41.8 mmHg. Seven months postoperatively, she has resumed her normal life without oxygen inhalation or recurrence of IP, and is able to perform daily activities.

Discussion

Lung transplantation for the treatment of respiratory failure caused by systemic diseases remains controversial. IP associated with collagen disease is a rare indication for lung transplantation. Because of various manifestations of collagen disease, each patient should undergo individual consideration. According to guidelines for the selection of lung transplant candidates proposed by the International Society of Heart and Lung Transplantation (ISHLT), evidence of quiescent systemic disease is

recommended, and any evidence of active vasculitis should preclude referral ². Shitrit et al. recently reported a review of the literature on lung transplantation for scleroderma. In their review of 54 patients with scleroderma, there was no difference in infection, rejection, and two- and five-year survival rates between patients with scleroderma and other lung transplant recipients ³.

It is well known that DM is often associated with malignancies and for this reason, there are very few reports of lung transplantation for DM ⁴. In performing lung transplantation for DM, two major issues should be carefully discussed. Firstly, DM should be well controlled irrespective of IP. Secondly, the possibility of coexisting malignancy should be excluded.

It is known that certain patients with DM may have the typical skin manifestations of DM but no evidence of myositis, a condition known as amyopathic DM. Sontheimer proposed the existence of a unique subgroup of patients with DM who have the clinical cutaneous features of DM but no evidence of clinical myositis symptoms for at least 2 years after the onset of skin manifestations, referred to as clinically amyopathic DM (C-ADM) ⁵. Some patients with C-ADM have been noted to develop rapidly progressive IP. Sato et al. have identified novel autoantibodies (Anti-CADM-140 autoantibodies) to an ~140 kd polypeptide in patients with DM and Anti-CADM-140 autoantibodies were detected specially in patients with C-ADM. In addition, anti-CADM-140 antibodies were associated with rapidly progressive IP ⁶. In a comparison between DM patients (including those with C-ADM) with anti-CADM-140 antibodies and those without anti-CADM-140 antibodies, the frequency of rapidly progressive interstitial lung disease was significantly increased in anti-CADM-140-positive patients compared with that in anti-CADM-140-negative patients ⁶. Nakashima et al. reported in their study of anti-CADM-140 antibody among 192 patients with various connective tissue diseases and 13 patients presenting with the anti-CADM-140 antibody. Among the 13 anti-CADM-140-positive patients, 12 patients (92%) had IP, seven (54%) developed acute progressive IP and six of seven died within six months of disease onset despite medical treatment ⁷.

In the present case, myopathic symptoms were absent because of nature of C-ADM. However, IP was progressive and clearly life-threatening. Selva-O'Callaghan et al. reported two cases of lung

transplantation for acute progressive IP associated with DM which were unsuccessful, but the cause of death could not be determined⁸. Recently, Kim et al. reported successful bilateral lung transplantation for a patient with the acute form of IP associated with DM from a cadaveric donor⁴. The patient did not show recurrent DM or IP at 11 months. Patients with the acute form of IP are often in a very unstable condition. Two of three reported patients with the acute form of IP died after cadaveric lung transplantation. Whether those patients were positive for anti-CADM-140 antibody remains unknown.

The evaluation of muscle weakness and immunosuppressant-responsiveness are very important factors for the success of lung transplantation for DM patients. In addition, for clinically amyopathic dermatomyositis (C-ADM) patients, it is crucial that transplant surgeons have the appropriate association of practice with rheumatologists and pulmonologists for reliable diagnosis and decision making for performing transplantation, because of this disease's nature of rapidly progression.

We previously reported the case of living-donor lobar lung transplantation for interstitial pneumonia associated with dermatomyositis⁹, which was not C-ADM. To our knowledge, this case represents the first living-donor lobar lung transplantation for a patient with rapidly progressive IP associated with C-ADM. Careful and prompt assessment is essential to make decisions whether lung transplant is an option for such acute progressive IP patients with anti-CADM-140-positive C-ADM, in order not to waste the opportunity to rescue. Thereafter, close post-transplant follow-up is mandatory to detect the possible occurrence of malignancy or recurrent of IP.

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Figure Legend

Figure 1. Chest computed tomographic scan on admission demonstrated severe fibrosis in the bilateral lower lobes.

Figure 2. Chest roentgenogram 11 days after chest computed tomographic scan demonstrated subcutaneous and mediastinal emphysema

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Figure 1.



Figure 2.

