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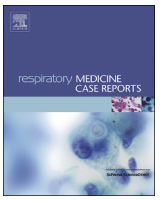

Case Report

Lung transplantation for cystic fibrosis complicated by cirrhosis: A case report

Miho Yamaguchi, Masaaki Sato *, Kentaro Kitano, Chihiro Konoeda, Jun Nakajima

Department of Thoracic Surgery, The University of Tokyo Graduate School of Medicine, 7-3-1 Hongo, Bunkyo-Ku, Tokyo, 113-8655, Japan

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ABSTRACT

A 16-year-old girl with a genetic diagnosis of cystic fibrosis was referred to us for consideration of lung transplantation. She had been hospitalized repeatedly for pneumonia and pneumothoraxes and her respiratory function had worsened progressively. Although she also had liver cirrhosis, she was considered a candidate for lung transplantation because her liver disease was compensated and only slowly progressive. After bilateral lung transplantation from a brain-dead donor, she developed ascites that was well controlled with diuretics. Otherwise, her post-operative course was uneventful and she was transferred to another hospital for rehabilitation 39 days after lung transplantation.

1. Introduction

Lung transplantation, a means of prolonging the lives of individuals with end-stage respiratory diseases, has the potential to dramatically improve quality of life and life expectancy. Cystic fibrosis (CF) is one of the most common indications for lung transplantation in Western countries [1]. The consequent increased life expectancy of patients with CF has resulted in accumulation of new information on non-pulmonary complications of CF, such as CF-associated liver disease (CFLD). CFLD is caused by mucus plugging intrahepatic bile ducts in patients with CF, leading to liver fibrosis and eventual liver cirrhosis and failure. CFLD affects 27%–41% of patients with CF [2–4]. End-stage liver disease is generally considered a contraindication to lung transplantation, except for simultaneous liver–lung transplantation. However, it is also recognized that CFLD progresses relatively slowly, leaving the possibility of lung transplantation only in selected patients with liver cirrhosis [5,6].

In this report, we describe successful lung transplantation in a patient with CF complicated by CFLD.

2. Case report

A 16-year-old girl with a history of recurrent pneumonia and pneumothoraxes was referred to our hospital as a potential candidate for lung transplantation.

She had a genetic diagnosis of CF and was being treated with Dornase Alfa and tobramycin inhalation. By the age of 7 years, she was being hospitalized once or twice a year for pneumonia. At age 12, home oxygen therapy was introduced. At age 14, she was hospitalized for right pneumothorax and severe pneumonia and required mechanical ventilation and a right open thoracotomy to treat her pneumothorax. Since then, her sputum culture had been positive for methicillin-resistant *Staphylococcus aureus* (MRSA). Thereafter, she had required hospitalization every few months.

* Corresponding author.
E-mail address: SATOM-SUR@h.u-tokyo.ac.jp (M. Sato).

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Her chest radiograph and computerized tomography (CT) showed bilateral multiple cystic changes, predominantly in the right lung, and some mosaic pattern with low attenuation areas (Fig. 1A and B). Her respiratory function tests on referral showed a vital capacity of 0.94 L (47% of predicted vital capacity), forced expiratory volume in 1 second (FEV1) of 0.52 L (31.9% of predicted FEV1), and FEV1% of 56.5%.

Findings on CT images and ultrasound suggested liver cirrhosis (Fig. 2A); however, no tissue diagnosis was made. She had no other potential causes of liver cirrhosis; thus, her liver cirrhosis was considered to denote CFLD. However, she had no evidence of esophageal varices or portal hypertension. Her total Child–Turcotte–Pugh score was 6 (albumin, 31 g/L; no hepatic encephalopathy; no ascites; total bilirubin, 5.1 μmol/L; prothrombin time -international normalized ratio, 1.13). Thus, her liver cirrhosis was classified

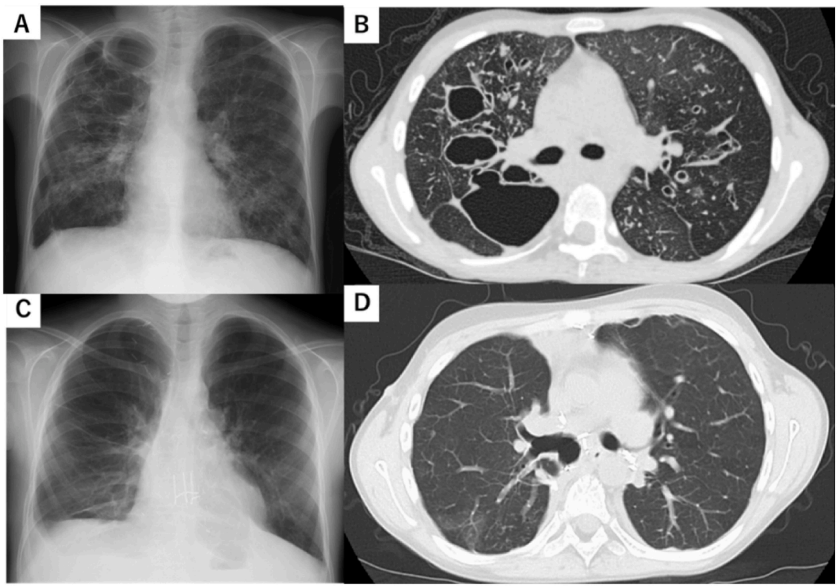

Fig. 1. Chest radiograph and CT images before and after bilateral lobar lung transplantation. (A) Preoperative radiograph and (B) CT image showing multiple pulmonary cysts. (C) Radiograph and (D) CT image 6 months after lung transplantation showing no abnormalities in either graft. CT, computed tomography.

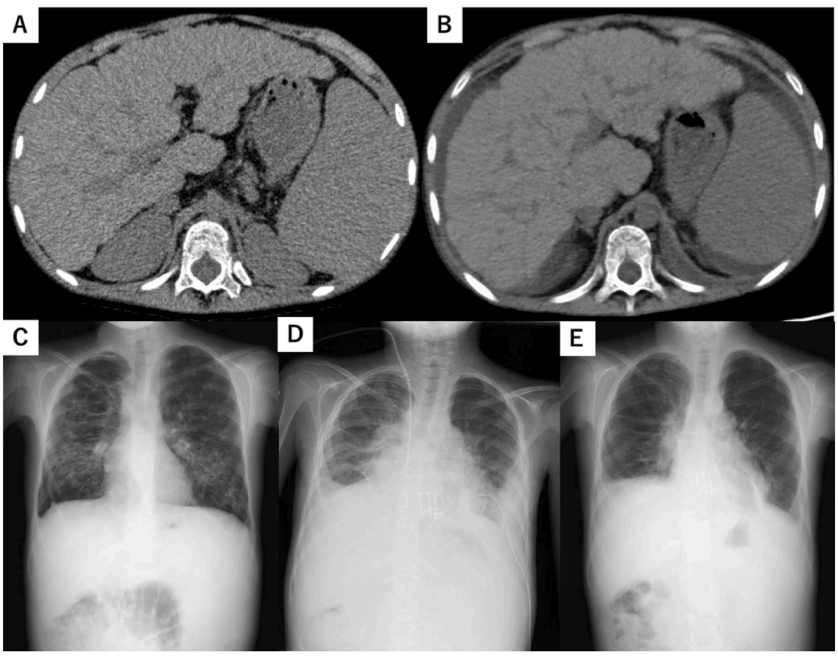

Fig. 2. Liver cirrhosis before and after lung transplantation. (A) Preoperative abdominal CT image showing cirrhosis and splenomegaly and (B) abdominal CT image on POD16 showing ascites. Compared with preoperatively (C), an abdominal radiograph (D) on POD 18 showed an increase in ascites. The ascites improved after starting diuretics.

as Child–Pugh class A (well-compensated disease). We consulted experts on CF in Toronto regarding indications for lung transplantation in patients with CFLD. After receiving positive opinions, we placed our patient on the waiting list.

After listing, her condition continued to deteriorate; she was rarely discharged home because of repeated bouts of MRSA pneumonia. Considering the average waiting time for lung transplantation is 3 years in Japan, it seemed unlikely that lung transplantation would occur. However, 5 months after listing, a brain-dead male donor with MRSA pneumonia emerged. Because he had a history of median sternotomy, was on a left ventricular assisting device, and both of his lower lobes had completely collapsed due to pneumonia, all the other transplant centers in Japan declined his lungs. Both upper lobes and the right middle lobe appeared intact on CT imaging and their total volume best matched our patient's small thorax. Thus, we performed bilateral lobar lung transplantation. The relevant technical details are that the donor's bilateral lower lobes were removed in a back-table procedure, followed by bronchial anastomoses between the main bronchi on the right side, leaving the lower lobe stump with suture reinforcement, and, on the left side, between the recipient's main bronchus and the donor's left upper lobe bronchus.

Our patient's early post-operative course was uneventful with successful extubation on post-operative day (POD) 4. She had an episode of acute rejection on POD 10 that was successfully treated with steroid pulses. Infection was well controlled with vancomycin and cefepime. Approximately two weeks after transplantation, she reported development of abdominal bloating. A CT scan taken on POD 18 showed encapsulated bilateral pleural effusions and ascites (Fig. 2B–D). Her serum albumin remained at approximately 3.0 g/dL without supplementation. Continued oral diuretics and bilateral chest tube drainage improved her condition (Fig. 2E). Although she had ongoing mild to moderate pancytopenia throughout her post-operative course, she had no episodes of bleeding and her surgical wounds healed in a timely manner, including the right bronchial stump. She was able to walk and climb stairs without oxygen supplementation and was transferred to another hospital on POD 39 for rehabilitation. Approximately 2 years after lung transplantation, her quality of life remains significantly improved compared with that before transplantation. Her graft lungs also recovered without problems (Fig. 1C and D). Although mild progression of her liver cirrhosis remains a concern and she is being followed up carefully, her liver function has not yet deteriorated to the point of necessitating liver transplantation.

3. Discussion

We here report successful bilateral lobar lung transplantation in a 16-year-old girl with CF complicated by liver cirrhosis as a result of CFLD. Given that she was at high risk of life-threatening pulmonary infection and respiratory failure, lung transplantation was the only option for prolonging her life. However, the presence of liver cirrhosis was a major concern because advanced irreversible failure of other vital organs is one of the exclusion criteria for lung transplantation [7]. Lung transplantation alone is rarely indicated in patients with CF and liver failure. Although simultaneous liver–lung transplantation may be considered [5], this is an unrealistic option in Japan because of the severe organ shortage in that country. There are no established guidelines concerning when, or in what order, lung transplants or simultaneous liver–lung transplants should be performed on CF patients [6]. Of note, liver damage caused by CFLD characteristically progresses relatively slowly, even when complicated by portal hypertension. Indeed, a study from the University of Toronto found no difference in five-year survival after isolated lung transplantation between CF patients with compensated liver cirrhosis and those without CFLD [8]. The Child–Pugh classification of the CFLD in this study was A or B; our patient had milder liver disease than did those patients. Thus, we considered that isolated lung transplantation was a viable option for our patient.

Another key to the success of lung transplantation in our patient is that we performed bilateral lobar transplantation using size-mismatched marginal donor lungs. The patient had been hospitalized repeatedly for pneumonia and pneumothorax and had an extremely poor prognosis. Living-related lobar lung transplant was considered; however, there were no suitable donors. In general, short-statured lung transplant candidates tend to have longer waiting times because size-matched deceased donor lungs for such patients are rarely available [9]. This is particularly true of patients with CF, for whom deceased lobar transplantation is a potential solution [9]. Salvage of the upper and middle lobes of infected donor lungs, as was successfully achieved in the present case, is an encouraging means of prolonging survival of short-statured patients and constitutes effective use of the limited donor organs available.

It is important to note that careful decision making and meticulous intra- and post-operative management of such vulnerable patients with liver disease are vital for achieving successful outcomes. In general, liver dysfunction has significant negative impacts on wound healing and post-operative recovery, being associated with increased morbidity and mortality after lung transplantation. Indeed, the present patient's refractory pleural effusion and ascites and persistent pancytopenia may have had detrimental effect on her post-operative course. Additionally, poor wound healing may have resulted in disruption of the right bronchial stump of the donor lung. Moreover, lung and liver diseases are known to frequently be associated with each other (e.g., alpha-1-antitrypsin deficiency) [5]. Thus, careful evaluation and individualized strategies and, ideally, in the absence of definitive evidence, expert opinions from highly experienced transplant surgeons, are extremely valuable in overcoming such challenges.

4. Conclusion

We here report a case of deceased-donor lobar lung transplantation in a patient with CF complicated by liver cirrhosis caused by CFLD. The liver damage associated with CFLD is often relatively mild; thus, exclusion of patients with CFLD from lung transplantation should be carefully considered.

Declaration of competing interest

The authors declare no conflicts of interest associated with this manuscript.

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