Case Report

Experience of the first lung transplantation performed in public sector in India

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ABSTRACT

Lung transplantation is the only modality that offers a long-term solution for end-stage lung diseases. Few centers in India have an active lung transplant program. Preoperative and postoperative considerations in lung transplantation may be different in the developing countries when compared to the developed world. In the early posttransplant period, infection could be the major consideration in developing countries, unlike graft rejection, that is usually the primary concern in the developed world. Herein, we report the first lung transplantation from a public sector hospital in India. The patient was a 33-year-old female, who underwent bilateral lung transplantation at our center, but succumbed to surgical and infectious complications in the early posttransplant period.

KEY WORDS: Interstitial lung disease, lung transplantation, pneumonia

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INTRODUCTION

Lung transplantation is the only definitive form of therapy for end-stage lung diseases that cannot be managed despite optimal treatment. Worldwide, about 4000 lung transplants are performed annually.[1] Chronic respiratory disorders are among the leading causes of morbidity and mortality in several developing countries including India.[2] However, only a few centers perform lung transplantation in India.[3,4] At present, there is a lack of a fully functional lung transplantation program in any public sector hospital in India. This is likely due to the logistic hurdles, which have to be overcome for the establishment of a successful transplant program. The transplant procedure itself is technically challenging and requires special surgical training. The postoperative care of the transplant recipient and management of immunosuppressive therapy also requires considerable expertise. In addition, postoperative complications are more frequently encountered in developing countries with incipient lung transplant programs.[5,6] Further, the transplant surgery and posttransplant care are an expensive affair, another major consideration in resource-constrained settings. Herein, we describe the first lung transplantation performed in a public sector hospital in India and discuss the challenges faced during the process.

CASE REPORT

A 33-year-old female with a diagnosis of chronic hypersensitivity pneumonitis presented with progressively increasing dyspnea [Figure 1]. She had been treated with high-dose glucocorticoids and azathioprine in the past. Despite optimal medical management, she continued

Access this article online

Quick Response Code:

Website: www.lungindia.com

DOI: 10.4103/lungindia.lungindia_74_18

How to cite this article: Prasad KT, Sehgal IS, Dhooria S, Agarwal R, Singh RS, Singh H, *et al.* Experience of the first lung transplantation performed in public sector in India. Lung India 2019;36:66-9.

to remain symptomatic and was enlisted for lung transplantation after a detailed assessment [Table 1].

The donor was a previously healthy, nonsmoking, blood group matched, 22-year-old brain dead male with a history of traumatic brain injury. He was mechanically ventilated on the assist-control mode of ventilation with an inspired oxygen fraction (FiO_2) of 0.21. His chest radiograph and flexible bronchoscopy were unremarkable, and he was considered fit for lung donation.

Table 1: Details of recipient assessment performed at baseline

Assessment	Result
History	
Prior thoracic surgery	Nil
Substance abuse	Nil
Previous pregnancies or blood transfusion	Two pregnancies
Comorbidities	Nil
NYHA functional class	IV
Oxygen requirement at rest	2 L/min by nasal prongs
Clinical examination	
Height (cm)	161
Body mass index (kg/m^2)	19.3
Chest deformity	Nil
Routine laboratory investigations	
ABO grouping and Rh typing	B-positive
Hemoglobin (g/dL)	14.2
Total leukocyte count, (per mm^3)	14,500
Platelets (per mm^3)	308,000
Prothrombin time (s)	14
Activated partial thromboplastin time (s)	26
Urea (mg/dL)	25
Creatinine (mg/dL)	0.6
Bilirubin (mg/dL)	0.7
Aspartate transaminase (U/L)	26
Alanine transaminase (U/L)	46
Alkaline phosphatase (U/L)	104
Albumin (g/dL)	3.2
Fasting blood sugar (mg/dL)	98
Arterial blood gas analysis	
pH	7.399
PaO_2 (mmHg)	83.6
$PaCO_2$ (mmHg)	48.4
Bicarbonate (mmol/L)	29.2
FiO_2	0.32
Pulmonary assessment	
Spirometry	Could not perform
6-min walk test	Could not perform
Cardiac assessment	
Electrocardiogram	Sinus tachycardia
Transthoracic echocardiogram	
Tricuspid regurgitation	Moderate
Tricuspid insufficiency pressure gradient (mmHg)	34
Size of cardiac chambers	Normal
Left ventricular ejection fraction (%)	62
Assessment for infectious diseases	
Tuberculin sensitive test	Negative
HIV serology and VDRL test	Negative
HBsAg and anti-HCV	Negative
Cytomegalovirus and toxoplasma serology (IgG and IgM)	Negative
Others	
Psychiatric assessment	Satisfactory
Social support assessment	Satisfactory
Preanesthesia assessment	Satisfactory

Anti-HCV: Antibody against hepatitis C virus, FiO_2: Fraction of inspired oxygen, HBsAg: Hepatitis B surface antigen, HIV: Human immunodeficiency virus, NYHA: New york heart association, $PaCO_2$: Arterial partial pressure of carbon dioxide, PaO_2: Arterial partial pressure of oxygen, VDRL: Venereal disease research laboratory

During explantation of the donor lungs, secretions were noted in both the main bronchi and swabs were sent for bacterial culture. The recipient's thoracic cavity was accessed by clamshell incision (transverse thoracosternotomy), and both lungs were transplanted sequentially. Induction immunosuppression was initiated intraoperatively with intravenous basiliximab (20 mg infused over 30 min during lung implantation) and intravenous methylprednisolone (500 mg infused before perfusion of each lung). The surgery was completed in 10 h. The patient was shifted to an Intensive Care Unit for postoperative care. Immunosuppression was continued using intravenous methylprednisolone (125 mg every 6 h) and oral tacrolimus (0.1 mg/kg/day). Histopathological examination of the explanted recipient lung showed airway-centric fibrosis consistent with a diagnosis of chronic hypersensitivity pneumonitis.

She continued to require FiO_2 of 0.4 for 24 h after the surgery, and the chest radiograph revealed the bilateral diffuse alveolar opacities [Figure 2a]. Echocardiography showed a normal ejection fraction. Primary graft dysfunction, antibody-mediated rejection, and hospital-acquired infection were considered. The results of the direct crossmatch (performed with blood samples obtained from the donor and recipient preoperatively) were negative. The patient was started on intravenous colistin (5 million units infused every 12 h and 2.5 million units nebulized every 12 h) and intravenous vancomycin (500 mg every 6 hourly). She was extubated on the second postoperative day and was administered preemptive noninvasive ventilation (NIV).

The culture from bronchial swabs sent from the donor lungs intraoperatively, blood culture from the recipient, and bronchoalveolar lavage fluid from the recipient grew multidrug-resistant (MDR) *Klebsiella pneumoniae* sensitive

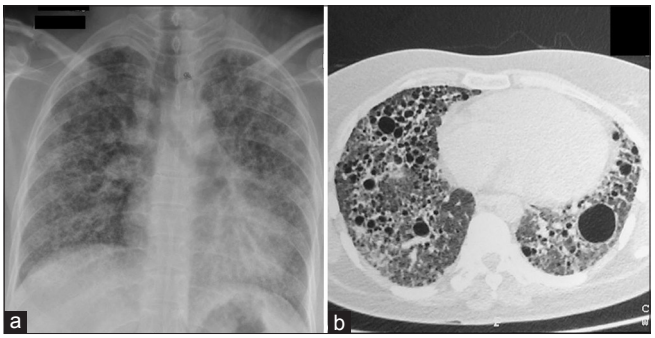

Figure 1: (a) Preoperative chest radiograph showing bilateral extensive reticulonodular opacities obscuring cardiac borders. (b) Preoperative high-resolution computed tomography scan of the chest showing bilateral intra and interlobular septal thickening, patchy areas of consolidation, ground glass opacities, and presence of variable-sized cysts

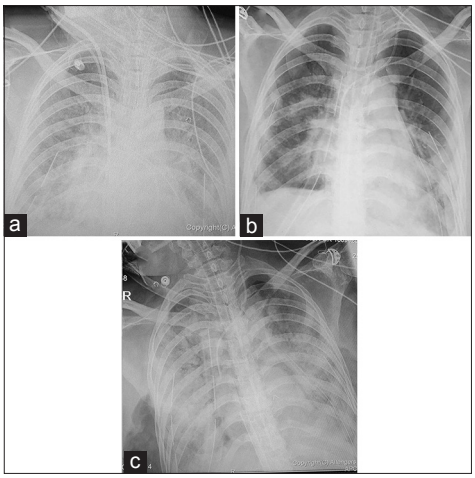

Figure 2: (a) Chest radiograph on the first postoperative day showing bilateral diffuse alveolar opacities. (b) Chest radiograph 12 days after transplantation showing partial clearing of the alveolar opacities. (c) Chest radiograph 14 days after transplantation showing reappearance of extensive bilateral alveolar opacities. Evidence of air collection within the subcutaneous soft tissue can also be noted at both sides of the chest

to colistin. As the fever was persistent and the respiratory failure was not improving, intravenous tigecycline (initial dose of 100 mg followed by 50 mg every 12 h) was added, and vancomycin was stopped. Tacrolimus and basiliximab (second dose) were withheld, and immunosuppression was maintained with oral prednisolone (40 mg/day). Blood culture grew MDR *K. pneumoniae* despite 7 days of appropriate antibiotics. She also developed bilateral empyema due to MDR *K. pneumoniae*. Intravenous fosfomycin (8 g every 8 h) was added, and intrapleural irrigation was performed with colistin (0.5 million units in each pleural cavity every 12 h) that resulted in partial clearing of the lung opacities [Figure 2b]. She was weaned off NIV and was administered oxygen using high-flow nasal cannula and subsequently through nasal prongs (2 L/min).

On the 12th postoperative day, the patient developed acute onset hypotension with drainage of fresh blood in both the chest drains. During surgical re-exploration, the anterior wall of the right ventricle was found to be punctured by one of the sternal wires (which had cut through the bone) and was repaired successfully. However, postoperatively, the patient continued to deteriorate with increasing alveolar opacities and evidence of subcutaneous air collection on chest radiograph [Figure 2c]. She succumbed to refractory septic shock secondary to hospital-acquired pneumonia, 14 days after the initial surgery. Biopsy of the transplanted lung obtained during the surgical re-exploration did not show any evidence of graft rejection.

DISCUSSION

The index case highlights the challenges faced during lung transplantation in the early postoperative period. Although the surgery was technically successful, the patient succumbed to overwhelming infection, possibly acquired from the donor.

The common causes of hypoxemia with bilateral alveolar opacities in the immediate postoperative period include primary graft dysfunction, hyperacute/acute antibody-mediated rejection, hospital-acquired pneumonia, and pulmonary edema.[7] Worldwide, primary graft dysfunction is the most common cause of death in the early postoperative period (first 30 days following transplantation), and infections are the leading cause of death thereafter in the 1st year after transplantation.[1] However, in developing countries, the infection may play a more important role in the early postoperative period, as highlighted in the index case.

Donor colonization with bacteria is a common phenomenon. In fact, up to 90% of donor lungs utilized in lung transplantation have positive cultures from the lung.[8,9] Classically, the presence of purulent secretions on bronchoscopy and/or positive gram stain reports on tracheal secretions in donor are considered to be contraindications for lung donation.[10,11] However, more recently, donors are considered acceptable despite the presence of these factors if they have a good, stable, or improving lung function.[12,13] Since our donor did not have any purulent secretions during the initial bronchoscopy, we did not obtain samples for cultures. However, bronchial swabs obtained from the donor intraoperatively showed MDR *K. pneumoniae*, and the same organism was subsequently isolated from the blood, BAL fluid, and pleural fluid of the recipient. It is likely that the recipient acquired the infection from the donor lung. Although transmission of microorganisms from the donor is an uncommon event (<10%),[8,9,12,14] recipients of lungs from donors with bacterial colonization have been shown to have relatively poor outcomes.[11] Hence, it may be prudent to avoid harvesting lungs from a donor with positive microbial isolates from tracheobronchial secretions.

During the initial 48–72 h of the postoperative period, differentiating hospital-acquired infection from hyperacute or acute antibody-mediated rejection could be difficult as both these conditions present with rapid onset of hypoxemic respiratory failure with bilateral alveolar opacities as noted in the index case. Knowledge of donor-specific antibodies (DSA) or panel reactive antibodies (PRA) in the recipient could have been useful in this setting. PRA testing detects preformed antibodies in the host which react against the human leukocyte antigens obtained from pooled samples of blood donors. It is an index of the proportion of the general population to which the recipient is immunologically reactive. A pretransplant PRA level above 25% has been shown to be a predictor of death after lung transplantation.[15] We could not perform the test for DSA or PRA in the index case due to lack of availability. However, results of the direct crossmatch (performed after the surgery with samples obtained preoperatively) were negative.

Our patient showed partial improvement with broad-spectrum antibiotics. However, after she underwent surgical re-exploration for the unfortunate surgical complication (cardiac injury by migrated sternal wire), shock worsened further leading to her ultimate demise. Injury to heart or great vessels by migration of sternal wire suture is an uncommon but known complication of thoracic surgery.[16,17] This complication has been reported to occur up to 28 years after thoracic surgery and is thought to be related to wire migration due to respiratory movements of the thorax.[17]

Finally, we came across only two reports in the published literature from India detailing the outcome of five patients who underwent lung transplantation (single lung transplantation ($n = 2$), heart-lung transplantation ($n = 3$), and no reports of double lung transplantation were available).[3,4] There is an urgent need to initiate a lung transplant registry where all the lung transplant cases and their outcomes should be maintained so as to identify problems unique to our geographic locale.

CONCLUSION

In addition to early surgical complications, hospital-acquired infection in the immediate postoperative period, especially with MDR organisms could be an important cause of poor outcome of lung transplantation in a developing country. Strict adherence to infection control measures, adequate screening of donors with bronchoscopy and endotracheal cultures (wherever feasible), and a well-balanced immunosuppression protocol may help to prevent this disastrous complication.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient's spouse has given his consent for the diseased patient's images and other clinical information to be reported in the journal. He understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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