Pitfalls and Challenges of Lung Transplant in a Patient With Kartagener Syndrome and Scoliosis

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Abstract

We present a 22-year-old woman with Kartagener syndrome and scoliosis who died 112 days after single lung transplant. The classic thoracic involvement of situs inversus totalis and the asymmetric arrangement of the thoracic vascular structures might be a pitfall for surgeon. Anatomic obstacles have forced the surgeon to perform a single transplant. The period of primary graft dysfunction in a single transplanted lung patient was a challenge; supporting the patient with a high flow and long period of extracorporeal membrane oxygenation might lead to a vanishing bronchus. Immotile cilia, a feature of Kartagener syndrome, were another challenge and patient needed several daily aspiration bronchoscopies. Vanishing bronchus is a gradual process with high mortality rates; commonly, stenosis is at the non anastomotic bronchial tree because of insufficient nourishment of the bronchial cartilages. Several repeat bronchoscopic balloon dilatations accompanied with medical treatment were unsuccessful.

Key words: Bronchiectasis, Extracorporeal membrane oxygenation, Immotile cilia, Vanishing bronchus

Introduction

Kartagener syndrome (KS) is an uncommon, congenital, genetic disorder characterized by bronchiectasis, situs inversus totalis thoracis et abdominalis, immotile cilia, chronic sinusitis, and infertility.1,2 Lung transplant is a treatment option for terminal-stage bronchiectasis. We present a case of KS, to highlight the importance of related anatomic variations pitfall that may influence the decision for patient selection and may complicate the course of the operation.

Case Report

A 22-year-old woman with KS and respiratory insufficiency, who required oxygen support 24 hours a day, was evaluated for a lung transplant. Pulmonary function test revealed a forced expiratory volume in 1 second, 27%; forced expiratory volume, 58%, and diffusing capacity of the lungs for carbon monoxide, 23 ymmetric thoracic cavities because of scoliosis apart from saccular bronchiectasis bilaterally. On echocardiography, she had a pulmonary artery systolic pressure of 50 mm Hg. In the right side of the heart catheterization, pulmonary artery wedge pressure was 10 mm Hg, and cardiac index was calculated as 3.2 L/min/m2; systolic, diastolic, and mean pulmonary artery pressures were 45 mm Hg, 32 mm Hg and 38 mm Hg.

Her medical history was clear except for osteoporosis, sinusitis, and scoliosis. Body mass index was calculated as 21.9 kg/m2 (height, 1.49 cm; weight, 51 kg) (total lung capacity predicted, 4.04 L). The results of a panel reactive antibody test were negative. A quantitative ventilation-perfusion scan revealed right-sided predominance: perfusion left lung (43%) and right lung (57%). As KS increases the propensity for chronic infections at multiple sites, our patient had Pseudomonas aeruginosa colonization in the tracheobronchial system. She had undergone an endoscopic operation for maxillary sinusitis after listing for a lung transplant.

After 4 months on the transplant waiting list, a donor who fulfilled all standard donor criteria was accepted for the patient. The donor’s characteristics were as follows: age, 30-year-old; female; weight, 65 kg; height, 1.63 cm; (total lung capacity predicted,
4.96 L), identical blood type; clear chest radiograph; no history of smoking, thoracic trauma, and malignancy with PaO$_2$/FiO$_2$ ratio of 386 mm Hg. Bilateral lung transplant was the planned surgery, and a clamshell approach was the chosen incision. As our patient had a pulmonary artery systolic pressure of 50 mm Hg, under the assistance of centrally cannulated extracorporeal membrane oxygenator (ECMO), left lung transplant was performed (ischemic-time: 312 min). On the right hemithorax after pneumonectomy, it was surprised that pulmonary artery was severely distorted and malpositioned due to dextrocardia and scoliosis. A possible implantation would have resulted in kinking of pulmonary artery and atrial cuff. Therefore, a left single lung transplant and right pneumonectomy were performed.

The patient was discharged from operating room to the intensive care unit with venoarterial ECMO, which was constituted peripherally through the left femoral vein and artery for ongoing hemodynamic instability, and to save excess blood from the single transplanted lung. T- and B-cell crossmatch were negative. She received standard triple regimen, intravenous tacrolimus, mycophenolate mofetil, and prednisolone without any induction. She experienced grade 3 primary graft dysfunction on second day and chest infiltrations on a chest radiograph grew in time (Figure 1A).

Delaying of extubation was considered, and a tracheostomy was performed on fourth day. After improvement of lung functions, peripheral ECMO was weaned on ninth day. Two days later (on the 11th day), patient had fever (39.2°C), CO$_2$ retention and acidosis developed together with neutrophilia and high C-reactive protein; therefore, venous-arterial re-ECMO was initiated through the right femoral vein and the right femoral artery. As “red leg-blue head” syndrome developed, arterial cannula was switched to right subclavian artery. We broadened antibacterial and antifungal spectrum and bronchoalveolar lavage was performed. However, polymerase chain reaction for community-acquired respiratory viruses in the lavage fluid, mycobacterial polymerase chain reaction, and direct fluorescent antibody for Pneumocystis jiroveci were all negative. Donor-specific antibody was negative. The transbronchial biopsy from the left lower lobe revealed organizing pneumonia; there were no signs of acute rejection (ISHLT classification was A0Bx) and pulse corticosteroid therapy of 1 gram/day intravenous methylprednisolone for 3 days was initiated, followed by 1 mg/kg/day prednisolone. Seven days later (on the 18th day), graft dysfunction diminished, infiltration resolved, fever declined, and biomarkers decreased to normal ranges and ECMO was weaned again (totally 17 days ECMO). Weaning from mechanical ventilation and closing of tracheostomy was delayed until 40th day because of the prolonged need for cleaning bronchoscopies, as the secretions could not be expelled from trachea because of muscle weakness and remaining immotile cilia of the tracheal mucosa. During the mechanical ventilation period, between 20th day and 40th days, Pseudomonas aeruginosa, Blastoschizomyces capitatus, and Candida albicans, were microbiological agents isolated from bronchoalveolar secretions of tracheobronchial system, all of which were treated according to the antimicrobial resistance data and current guidelines.

From 42nd day, the patient was followed-up in the ward, and between 42nd and 54th days, we performed daily cleaning bronchoscopies for secretion retention (Figure 1B). During this period, we noticed that orifices of the left lung were getting narrowing (Figure 2A). On 54th day, reintubation was...
performed with bronchoscopic balloon dilatation of left lung orifices for low SaO₂ levels. Subsequently, several bronchoscopic balloon dilatations (8 more times) were performed with optimization of medical immunosuppressive treatment (Figure 2B). On 77th day, a retracheostomy was performed and with the assistance of bronchoscopic techniques, accompanying granulation tissue of left lung cartilages was mechanically removed. However, bronchial narrowing, which started from segmental bronchus, reached to the main bronchus, and this complication was diagnosed as vanishing bronchus (VB). Unfortunately, patient died on 112th day because of a vanishing bronchus.

**Discussion**

Patients with KS could have pitfalls and challenges for clinicians. Anatomic distortion and malpositioning as a result of asymmetric thoracic cavities, scoliosis, dextrocardia, and abnormal originating pulmonary vessels could be a pitfall. Therefore, the surgeon may be forced to perform single lung transplant with contralateral pneumonectomy depended on anatomic asymmetric arrangement of thoracic vascular structures and main bronchus. Su and associates reported 2 cases with severe scoliosis, both had successful double lung transplant and the authors stated that distorted thoracic anatomy and scoliosis was not a technical contraindication.³ Brioude and associates mentioned that the surgical procedure of KS patients does not seem to require specific technical modifications when performed with lungs provided by a normal donor.¹ Similarly, Graeter and associates performed a double lung transplant for KS and emphasized that no technical modifications were necessary.² Despite the successful experiences of these authors, we do not agree with them; anatomic obstacles may have seen. Scoliosis, dextrocardia, thoracic asymmetry with abnormal originating pulmonary vessels, together could be observed, and surgeons may have a difficult situation in case.

A single lung transplant could be a challenge for any lung transplant patient; during primary graft dysfunction and organizing pneumonia periods, 1 donor lung could be incapable for adequate gas exchanging. Therefore, accompanying ECMO support during this period may be needed according to arterial blood gas analyses. During intensive care unit follow-up of our patient, she had both grade 3 primary graft dysfunction and subsequent organizing pneumonia; so re-ECMO was initiated with high flow. Long-standing with high levels of ECMO flow may lead to insufficient bronchial nourishment and VB.

Although airway complications nearby anastomotic site(s) after a lung transplant continue to be a significant cause of morbidity, a severe form of bronchial stenosis can occur at a lobar/segmental nonanastomotic site, which generally defined as VB syndrome.⁴ Vanishing bronchus is associated with acute worsening of pulmonary functions with stepwise and slowly declining of SaO₂ and forced expiratory volume in 1 second levels leads to mortality. Vanishing bronchus is a slow and gradual process that can affect any section of the lower airway, and this complication was thought to be a result of abnormal airway healing in the backdrop of an ischemic airway.⁵ The majority of cases; actually, the most severe form, occurring on the right side, are at the segmental bronchus, nonanastomotic site bronchial stenosis, and named VB intermedius syndrome.⁵,⁶ Hayes and associates reported a case of VB in the left allograft in a lung transplant case for cystic fibrosis, as our patient had similarly on the left side bronchus.⁵

![Figure 2. (A). Bronchial Narrowing on Left Lower Lobe Basal Segments, (B). After Bronchoscopic Balloon Dilatation](image-url)
Consequently, long standing with high levels of ECMO flow was a challenge. As a result, it may lead to insufficient bronchial cartilage nourishment and enhances the possibility of VB. Systemic arterial blood supply was not being restored during lung transplant, and cartilage complications have been attributed to ischemia of donor bronchus. The major causative factor for ischemic airway and VB was long period of ECMO time in our patient (17 days). The role of microbiological factors in the development of VB has not been well defined. Hayes and Mansour reported an adolescent cystic fibrosis patient (16 years old) who underwent a double lung transplant with VB complication and cultured *Aspergillus fumigatus* on bronchoalveolar lavage fluid.\(^4\) Shah and associates documented 344 lung transplant patients, 7 patients had VB complication, and isolated microorganisms were methicillin-resistant *Staphylococcus aureus* (n = 1), *Pseudomonas aeruginosa* (n = 3), *Aspergillus spp* (n = 2), and Ebstein Barr virus (n = 1). Our patients’ bronchoalveolar lavage fluid cultures demonstrated *Pseudomonas aeruginosa*, *Blastoschizomyces capitatus*, and *Candida albicans* during intensive care unit follow-up; however, the role of microbiologic agents in VB remains unclear.

Presenting symptoms of VB are associated with narrowing of bronchial orifices; including shortness of breath, cough, and wheezing.\(^4,6\) On the chest radiograph and thoracic CT, collapse and atelectasis can be observed, if a totally obstructed lobe is present. Bronchoscopic observational findings are the main diagnostic tool. Depending of the affected area, bronchial structures can be noticed as concentrically narrowed defining the term *vanishing*. Bronchial weblike structures, extensive granulation tissue, and external bronchial compression should be excluded.

Several treatment procedures including lobectomy, balloon dilatations, bronchoplasty with stent replacement, brachytherapy, electrocautery, and mitomycin application are suggested.\(^5-7\) In a case series, Kesavan and associates evaluated 59 lung transplant patients and 3 of them developed VB complications.\(^6\) Two of them underwent a lobectomy and 1 patient underwent sequential balloon dilatation.\(^6\) Shah and associates retrospectively evaluated 344 lung transplant patients; 7 developed VB. Therapeutic interventions of these patients were as follows: bronchoscopic bronchoplasty (n = 5), bronchoplasty with metallic stent placement (n = 5), brachytherapy (n = 3), electrocautery (n = 3), and mitomycin application (n = 2).\(^6\) The effectiveness of these therapeutic options is still debatable; survival after diagnosis was limited; unfortunately, mortality occurs in most patients. Shah and associates reported 7 VB cases; complete bronchial atresia ultimately developed in 6 of them, and 5 deceased because of respiratory insufficiency.\(^6\)

As our patient had a single lung transplant and a diffuse nonanastomotic airway complication including both upper and lower lobes, obviously, she did not have a chance for anatomic resection. However, sequential balloon dilatations (8 times) accompanied with medical treatment had been performed with a limited success for short period of time. As the bronchi were extensively affected from the anastomosis down to the segmental orifices, stent placement was inappropriate. Retransplant could be a treatment option. However, same challenging factors such as anatomic malpositioning, primary graft dysfunction, and long ECMO periods could result in the same complications and found to be unfeasible as a surgical option.

Immotile cilia could be another challenging situation for a lung transplant patient with KS. As patients have defective cilia motility, this leads to an absence of clearance of tracheobronchial secretions and leads to secretion retention. This means they need several bronchoscopies after lung transplant.

**Conclusions**

Symptomatic narrowing and finally complete obstruction of the associated bronchus/segment is defined as VB and an unusual nonanastomotic airway complication after lung transplant. Although rejection and infection are the accompanied causative factors, ischemia of the bronchial cartilages may have a primary role. For KS patients, more care should be spent on patient selection by the meaning of anatomic and surgical pitfalls, single lung transplant, long-term, and high flow of ECMO and immotile cilia; therefore, physicians should be mindful of these complications to obtain successful outcomes.

**References**


