Pulmonary Resection For Bronchial Polyp After Lung Transplant in a Cystic Fibrosis Patient

Małgorzata Olszowiec-Chlebna,1 Teresa Ruszczyk-Bilecka,1 Joanna Jerzyńska,1 Paweł Majak,1 Tomasz Grzelewski,1 Łukasz Pryt,2 Iwona Stelmach1

Abstract

Many clinical conditions should be considered in the differential diagnosis of life-threatening events in cystic fibrosis patients after a lung graft transplant. We report on a 17-year-old boy who underwent a lobectomy owing to an inflammatory endobronchial polyp complicated by massive airways bleeding 12 months after having had a bilateral sequential lung graft for cystic fibrosis. This unusual complication underscores the requirement for flexible bronchoscopy in patients with recurrent infection at any stage after transplant. Early diagnosis may prevent life-threatening complications.

Key words: Cystic fibrosis, Lung transplant, Complications

Introduction

Despite improvements in surgical techniques and immunosuppressive medicines, airway complications remain an important cause death after a lung transplant.1,2,3 Nevertheless, a wide range of other clinical conditions must be accounted for in the differential diagnosis of life-threatening events after a lung graft. We present a case of a cystic fibrosis patient who, during the first year after a bilateral sequential lung graft experienced a pulmonary thromboembolism, and life-threatening recurrent bleeding from an inflammatory endobronchial polyp and ultimately right lower lobectomy.

Case Report

A 17-year-old boy underwent a bilateral sequential lung transplant in September 2010 because of terminal respiratory insufficiency caused by cystic fibrosis. A bilateral sequential lung transplant was conducted via bilateral anterolateral thoracotomy on extracorporeal membrane oxygenation at the Vienna Transplant Center.

His postoperative course was complicated by 2 mild rejection episodes and reactive depression. The immunosuppressive treatment included tacrolimus, prednisolone, and mycophenolate mofetil. Before the lung graft, he had a forced expiratory volume in 1 second (FEV1) of 0.43 L (13% of predicted), and a forced vital capacity of 0.81 L (21% of predicted). The lungs were infected with multiresistant *Pseudomonas aeruginosa* and *Staphylococcus aureus*. The patient also had diabetes mellitus since 2009 and was treated with subcutaneous insulin. He had a central venous catheter (Vital-Port Vascular Access System; COOK MEDICAL INC., Bloomington, IL, USA) surgically implanted 2 years before the transplant.

The results of pretransplant serologies for hepatitis C virus, hepatitis B virus, human herpesvirus types 1 and 2 were negative, whereas serologies for *cytomegalovirus* and Epstein-Barr virus were positive. During 4 months after the bilateral sequential lung transplant, the patient developed 2 episodes of significant lower respiratory infection. He was treated with IV ciprofloxacin and colistin or tobramycin inhalation owing to *Pseudomonas aeruginosa* detected in the bronchoalveolar lavage. The patient recovered from each infection with an FEV1 of 20% to 24% predicted. His nutritional status also improved.
Despite our efforts, he and his family were convinced that he was cured of cystic fibrosis. Despite recommendations and warnings, they did not attend follow-up medical appointments. Six months after the bilateral sequential lung transplant, the patient reported to the outpatient visit complaining of general malaise, dyspnea, weight loss, and blurred vision. On auscultation, fine crackles were noted over both lungs, and on eye examination, detachment of the retina in the left eye was found. The results of his serum glucose were $> 27.75$ mmol/L, and glycated hemoglobin was greater than 0.16 proportion of total hemoglobin; he had lost 8 kg.

The Vital-Port was occluded. He was admitted to the Pediatric Medical University Hospital for 81 days. His hyperglycemia was aggressively treated, and nutritional supplementation improved his condition. He was treated successfully with recombinant tissue plasminogen activator. Because of an abnormal chest radiograph (and oxygen saturation value of 84.9%), a chest computed tomography was performed, which revealed thrombi in the left lower lobe of the pulmonary artery and in segmental arteries, bilaterally. The results of an echocardiography showed a thrombus (about $15 \times 7$ mm) localized in the right atrium at the tip of the Vital-Port. The next echocardiography revealed that the thrombus had moved to the right ventricle. Because of the high risk associated with cardiac surgery, initial therapy with low molecular weight heparin was begun, and then with clinical deterioration, tissue plasminogen activator was initiated. The Vital-port was instilled with alteplase before it was removed surgically. During 30 days, recanalization of the pulmonary arteries and dissolution of the intracardiac thrombus was achieved. During the hospitalization, fungemia with *Candida albicans* was diagnosed and treated with intravenous amphotericin B and caspofungin. Because of radiographic and laboratory evidence for *Mycoplasma pneumoniae* and *Pseudomonas aeruginosa* respiratory infections, the patient received several successive antibiotics. Infection due to Epstein-Barr virus, cytomegalovirus, and *Pneumocystis jiroveci* were ruled out.

On the 55th day in the hospital, massive, most probably pulmonary bleeding from the nose and mouth occurred (liters of blood) followed by cardiac arrest and prompt cardiopulmonary resuscitation. Leading doctors suspected GI bleeding. An urgent upper gastrointestinal endoscopy led to the additional diagnoses of hemorrhagic gastritis and duodenitis. The patient was extubated 4 days later. Owing to suspected aspiration, pneumonia, and blood loss, symptomatic treatment and antibiotics were administered. Eighty-one days later, the patient was discharged home from the hospital in good condition with the recommendation of subcutaneous low molecular weight heparin.

After 6 weeks (11 months after the bilateral sequential lung transplant), the patient attended a routine follow-up visit. During blood collection, he began to cough and experienced another episode of massive pulmonary bleeding. Cardiopulmonary resuscitation was performed, including the instillation of epinephrine into the bronchial tree, which stopped the bleeding. An urgent flexible bronchoscopy revealed massive granulation tissue overgrowing the tracheal bifurcation in place of transplant anastomosis and a large fibrin clot. Part of the granulation (and the fibrin clot) from both mainstem bronchi were removed. There was no evidence of pulmonary embolism, pulmonary infarction, or vascular fistula in computed tomography-angiography. Elective flexible bronchoscopy revealed a polyplike 4-mm lesion in the distal right lower lobe bronchus. The polyp was well-vascularized and had a necrotic surface (see Figure 1).

![Figure 1. Bronchoscopic Photographs of 4-mm Polipoid Lesion in the Right Lower Lobe Bronchus in 2 Different Shots](image)

The polyp is well-vascularized and has necrotic surface.

The patient was transferred to the Vienna Transplant Center for further treatment. At the Vienna General Hospital, a positron emission tomography with computed tomography was performed, which confirmed a 7-mm polyp in the right lower lung lobe lumen without enhancement and therefore, no sign of malignant disease. The first flexible bronchoscopy aimed at removing bronchoscopic polyp was done; however, massive bleeding occurred upon slight contact with tissue; therefore, local vasopressin and peripheral blood transfusion was administered and the intervention was stopped. Removal of the polyp...
was done 2 days later by dissecting the right lower lobe, and initially, hemorrhagic pneumonia was diagnosed by endoscopy. Unfortunately, neither gross histology nor microhistology revealed any evidence for the pathology of the polyp, that was suggested by endoscopy.

Cytologic studies of the removed lung and bronchoalveolar lavage disclosed no presence of cancer infiltration and atypical cells. Moreover, there was no evidence for lung rejection, Epstein-Barr virus, cytomegalovirus, and Pneumocystis jiroveci infection on histologic examination. Also, serology for herpes simplex virus, varicella-zoster virus, and polymerase chain reaction for cytomegalovirus and Epstein-Barr virus excluded viral infection. At the next follow-up visits, the patient was clinically well, with no infections related to the respiratory tract, and the sequential lung function tests of the boy improved (his FEV₁ was 57% to 70%, weight was 32 to 33 kg).

Discussion

We report the case of a patient with lung transplant owing to cystic fibrosis who underwent pulmonary resection because of a presumed inflammatory endobronchial polyp complicated by massive airways bleeding. Although airway complications after lung transplant are encountered in approximately 10% to 15% of cases, with a mortality rate of 2% to 4%, one other rare conditions should be included in the differential diagnosis of life-threatening complications.4,5

It is generally believed that there is no systemic blood supply to the airways, which should decrease the chance of a massive hemorrhage. Unfortunately, the chest computed tomography angiography did not reveal any de novo bronchial artery supply to the lungs, possibly encouraged by repeated infection. In light of this case, interventional embolization of a systemic artery perfusing this polyp-like lesion could have been curative and thereby, would have spared him from the lobectomy. However, because other possibilities (eg, neoplasmatic diseases) were not ruled out, this attempt was not possible.

Reason studies have found no significant difference in survival between transplanted cystic fibrosis patients with preoperative diagnosis of diabetes mellitus and those without.6,7 On the other hand, it is obvious that noncontrolled hyperglycemia is a risk factor for bacterial and fungal graft infection and also, for thromboembolism, such as the one seen in our patient.8 The thrombolysis, as in this case, also has been reported in the literature.9 In the studies, the mortality rate because of thromboembolism is estimated at 43%.10

According to published data, there are only few pathologic processes that manifest as an endobronchial polyp (eg, benign neoplasms or suture granulomas).11 Our review of the literature shows that the only reported cases of endobronchial polyps in lung transplant recipients are associated with new cytomegalovirus infection.12 However, in our case, there was no evidence for any viral infection. The lesion in our patient had gross features connected with inflammatory polyps without atypical cells. In this case, repeated infection (ie, viral, fungal and bacteria) during first 8 months after bilateral lung transplant suggest that infection may have elicited formation of the polyp. Histologic examination of the removed lung established the diagnosis of hemorrhagic pneumonia. Another possibility is that there had been a massive hemorrhage, and the blood ended up in the right lower lobe alveolar space. Infection is one of the most important factors affecting survival after transplants in cystic fibrosis patients. The presence of multidrug-resistant pathogens, such as Pseudomonas aeruginosa, in the upper and lower respiratory tracts after transplant likely contributes significantly to the frequency and severity of infections in cystic fibrosis patients.3,5 Approximately 3% of cystic fibrosis lung graft recipients need pulmonary resection because of inflammatory complications5; fungal infections are present in 10% of lung grafts.3,13

We can speculate that chronic colonization of Pseudomonas aeruginosa was the risk factor for developing chronic bronchitis, and a bronchial reaction in the infected polyp formed in our patient; however, recurrent Pseudomonas infection is very common after transplant in cystic fibrosis, and bronchial polyps have never been reported. In the present case, there was an attempt to treat the endobronchial polyp in a stepwise manner, but the bronchoscopy was complicated by recurrent hemorrhage and the lobectomy was performed. Such resections offer important options in caring for postoperative lung graft recipients.4,5,14

There are many contributing factors for chronic airway inflammation in this case. Nonadherence (partly a nonaggressive surveillance and treatment protocol) of the bronchial denervation and failure to
adequately detect and treat repeated/chronic bronchial inflammation in this case may have lead to an unusually severe and chronic up-regulation of bronchial inflammation.\textsuperscript{15,16}

Persistent or recurrent infections cause many complications in cystic fibrosis patients that may require aggressive treatment. The presented case underscores the need for flexible bronchoscopy or lung biopsy in patients with recurrent infection, not only during the early phase after transplant. This would prevent life-threatening conditions, such as the massive hemorrhage that occurred twice in our case, which are not always complications of a lung transplant. Lastly, other procedures to spare the patient from a lobectomy (eg, an interventional embolization or sleeve resection) are possible; however, none could have been safely applied in this case.

References


