CASE REPORTS

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The experience of bilateral lung retransplantation after prolonged extracorporeal oxygenation

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Abstract

Background. *Transplantation is the only effective method of helping patients with irreversible damage of the lung function when the possibilities of other treatment methods have been exhausted. At the same time, a chronic graft rejection is the main cause of the loss of the donor organ function in the long-term period, developing in more than 50% of patients within 5 years after surgery. Given irreversible lung damage with loss of lung functions, the only effective treatment method for this patient population is retransplantation,*

which is associated with high risks of complications and a long rehabilitation of the patient in the postoperative period.

Objective. *Demonstration of the first Russian experience of bilateral lung retransplantation in a patient after a long-term extracorporeal oxygenation.*

Results. *The article presents the description of the first experience of bilateral lung retransplantation in Russia performed in a patient with a chronic rejection 4.5 years after the primary transplantation performed for end-stage lung lesions in non-Langerhans cell histiocytosis. In the 96-day period of waiting for a donor organ, the patient's gas-exchange lung function was compensated by using veno-venous extracorporeal membrane oxygenation.*

Conclusions. *Retransplantation is an effective method of treatment for patients with irreversibly damaged lung function, but still remains an operation associated with high risks of complications and unfavorable outcome.*

Keywords: lung transplantation, non-Langerhans cell histiocytosis, rejection, bronchial stenosis, extracorporeal membrane oxygenation

Conflict of interests Authors declare no conflict of interest

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ECMO, extracorporeal membrane oxygenation
MLV, mechanical lung ventilation

Introduction

Lung transplantation is associated with high risks of complications, but is the only effective method of helping patients with damage to the lung function when the potentiaal of other treatment methods have been

exhausted [1]. In more than half of cases, patients develop chronic graft rejection within 5 years after transplantation, which leads to subsequent loss of the donor lung function [2]. In these cases, patients are indicated for lung retransplantation. Despite the existing risks associated with immunosuppression and repeated surgical intervention on the chest organs, the number of such operations in the world increases annually. Demonstration of clinical cases and exchange of experience will improve the treatment results for such patients [3].

Case Report

In 2013, at the age of 35, the patient began complaining of shortness of breath at moderate physical activity. The examination revealed cystic abnormalities in the lungs. In autumn of 2013, a video-assisted thoracoscopic biopsy of the right lung was performed. The results of the study confirmed the clinical diagnosis of pulmonary non-Langerhans cell histiocytosis. The administered therapy included: prednisolone, cyclophosphamide, alogliptin, a course of alprostadil. From 2016, the condition progressively worsened, respiratory failure increased. From January 2018, the patient received a continuous oxygen therapy, and in December 2018 he was included in the waiting list for lung transplantation. Lung transplantation was performed on January 13, 2019. Primary graft dysfunction was observed on the first day after surgery. In order to maintain the gas exchange and hemodynamics, extracorporeal membrane oxygenation (ECMO) was performed for three days. On the 40th day of the postoperative period cicatricial stenosis of the intermediate bronchus and the upper lobe bronchus on the left was diagnosed (Fig. 1) and in February 2020 was performed stenting with 12.0 mm diameter silicone endoprostheses. After achievement of stable satisfactory lumen of the bronchi the stents were removed in September 2020.

For 2 years, the patient remained in a stable condition, there were no signs of respiratory failure; he had an active lifestyle, received immunosuppressive therapy (tacrolimus and prednisolone).

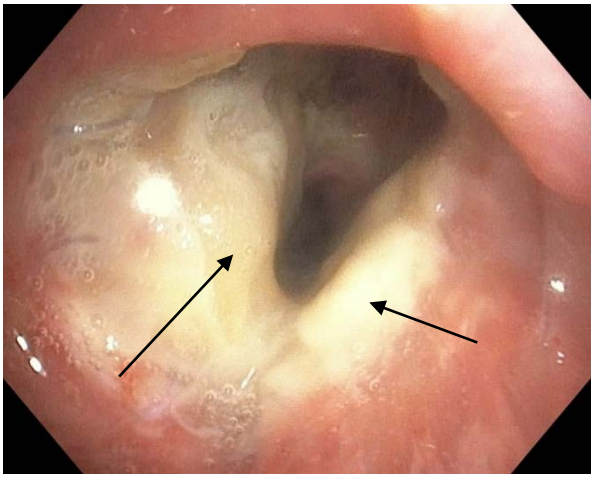

Fig. 1. Endoscopic photo. Fiberoptic tracheobronchoscopy demonstrating cicatricial stenosis of the bronchus (indicated by arrows)

Since the end of 2022, the patient developed and began to experience worsening respiratory failure. In this regard, in May 2023, he was admitted at the N.V. Sklifosovsky Research Institute for Emergency Medicine. A chronic graft rejection and grade 3 respiratory failure were diagnosed. The patient was transferred to the Intensive Care Unit and included in the Urgent Waiting List for a donor lung. As far as an adequate gas exchange was impossible to be ensured by mechanical lung ventilation (MLV), a venovenous ECMO system was connected through the femoral access. The waiting time for a donor organ was 99 days, of which the patient received ECMO for 96 days. Blood gas parameters on ECMO were as follows: pH 7.419, pCO_2 45.2 mm Hg, pO_2 39.6 mm Hg. On August 28, 2023, lung retransplantation was performed.

The donor of the lungs for retransplantation was a 43-year-old man with brain death caused by acute cerebrovascular accident of the

hemorrhagic type. According to fibrotracheobronchoscopy, the mucous membrane of the tracheobronchial tree was not hyperemic, the sputum was mucous, pathological neoplasms were absent. According to chest X-ray, pathology was not detected. Respiratory index (PaO_2/FiO_2) was 545. Oncological diseases, blood borne infections were not detected.

The greatest technical difficulties during lung retransplantation surgery were the stages of pneumolysis due to the pronounced adhesion process, and the mobilization of the elements of the pulmonary roots, especially the pulmonary arteries.

The preservation period was 5 hours 40 minutes for the right lung, 9 hours 10 minutes for the left lung. The donor organ preservative was Perfadex plus solution. (XVIVO Perfusion AB, Sweden). The patient was weaned from ECMO on the 3rd day after lung retransplantation.

On the 5th day after surgery, hemorrhagic discharge was seen through the drains; the computed tomography results prompted the diagnosis of a clotted hemothorax on the left. A 2 cm skin incision was made in the second intercostal space on the left along the midclavicular line, the port was made, through which a video system was inserted. At pleural cavity revision, blood clots were found, the source of bleeding was not identified. The clotted hemothorax of 1000 ml in volume was evacuated. There was no data on ongoing intrapleural bleeding. The pleural cavity was washed with antiseptic solutions. Drainage was performed through the access made.

On the 16th day, bilateral pneumonia was diagnosed in the Intensive Care Unit. A bacteriology culture revealed *Klebsiella pneumoniae*. Taking into account the drug sensitivity test results, meropenem 2 g intravenously 3 times a day, polymyxin B 50 mg intravenously 3 times a day, tigecycline 100 mg intravenously once a day were administered.

On the 28th day of the post-transplant period, intensive air flow through the pleural drains was noted; fibrobronchoscopy revealed partial failure about 5 mm of the left bronchial anastomosis (Fig. 2). Stenting of the bronchus was performed with a self-expandable covered stent (Fig. 3). After stenting, the airway leak-tightness was achieved.

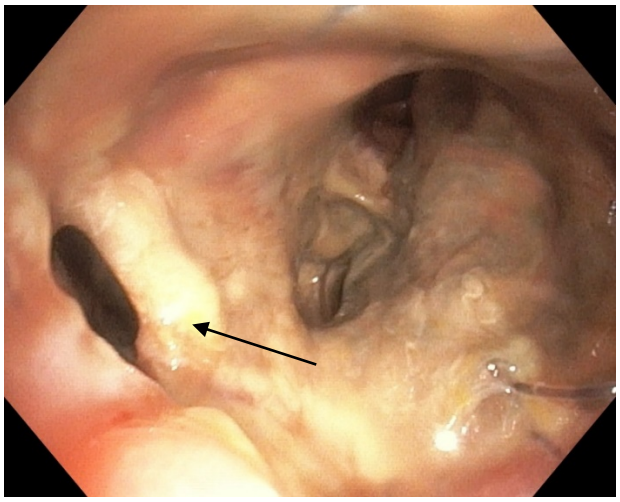

Fig. 2. Endoscopic photo. Fiberoptic tracheobronchoscopy demonstrating a partial failure of the left bronchial anastomosis (indicated by the arrow)

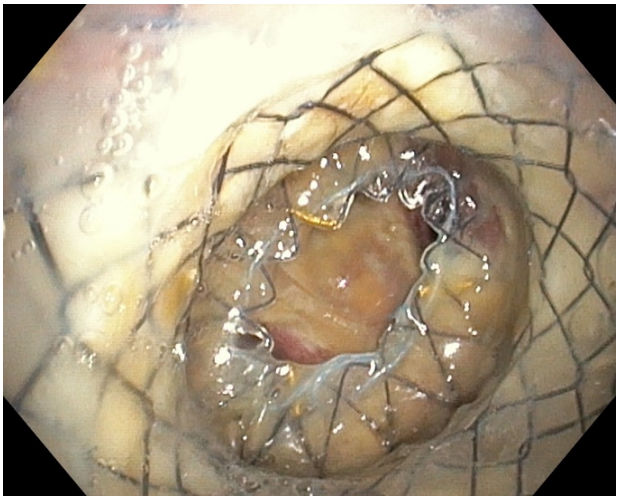

Fig. 3. Endoscopic photo. Fiberoptic tracheobronchoscopy demonstrating the state of the left bronchial anastomosis after stenting

On the 49th day after surgery, the patient in a stable condition was transferred from the Intensive Care Unit (ICU) to hospital ward. Rehabilitation was aimed at both restoring the respiratory function of the lungs and restoring the musculoskeletal system due to muscle atrophy associated with a long ICU stage of treatment. It included walking with a gradual distance increase between episodes of rest, stationary bike exercises, and gymnastic exercises aimed at developing the muscles of the upper and lower extremities. On the 62nd day, the patient was discharged in a satisfactory condition for outpatient follow-up.

Three months and 21 days after lung retransplantation, in December 2023, the patient was admitted for planned stent removal from the left main bronchus. Previously undiagnosed cicatricial stenosis was detected in the right main and intermediate bronchi. When removing the stent from the left main bronchus, bleeding was detected, which source was the pulmonary artery in the area of contact with the bronchial defect. The left main bronchus was obturated with a balloon obturator, and the right main bronchus was intubated using a bronchoscope.

An anterolateral thoracotomy was performed in the fifth intercostal space on the left. Pneumolysis was performed using blunt and sharp methods. The left pulmonary artery, pulmonary veins, and left main bronchus were isolated one by one, and tourniquets were applied to the vessels. An attempt was made to suture the bronchus, a bronchoarterial fistula was diagnosed, attempts to separate it turned unsuccessful. Pneumonectomy was performed for vital indications. During rigid endoscopy after pneumonectomy, a silicone endoprosthesis was positioned in the lumen of the right main and intermediate bronchi with the fenestration opposite the ostium of the right lung upper lobe bronchus.

On the 7th day after pneumonectomy, the patient was transferred from the Intensive Care Unit to hospital ward. In the Thoracic Surgery

Department, prevention of infectious and thromboembolic complications and rehabilitation were performed. Laboratory blood parameters and the hemostasis system (international normalized ratio, activated partial thromboplastin time) were monitored. Stabilization of the patient's condition was achieved: the patient was physically active, oxygen saturation was 98-99% without oxygen support. Despite the treatment, the patient died 2 months after pneumonectomy due to pulmonary embolism. This happened 5 months and 11 days after lung retransplantation.

Discussion

Currently, the number of retransplantations performed worldwide is steadily increasing. According to International Society for Heart & Lung Transplantation they account for approximately 4% of all lung transplants per year. This surgery is performed in terms of active immunosuppression, persistent infection, technical difficulties associated with repeated surgical intervention, which entail vascular, bronchial complications, dangers of the postoperative period, long-term stay on mechanical ventilation or the use of ECMO [4]. In our case, additional complications in patient management were caused by the long-term use of ECMO, which was undertaken as a “bridge to retransplantation”.

A long-term use of ECMO is a significant factor in mortality and morbidity in critically ill patients [5]. Ilhan Inci, Jonas Peter Ehrsam et al. reported that patients for this method should be carefully selected, taking into account risk factors: the recipient age over 35 years, the interval between transplants less than 1 year, primary graft dysfunction as an indication for retransplantation, and venoarterial type of ECMO [6]. According to data obtained by specialists from University Hospital of Zurich, a careful patient selection provides up to 67% 1-year survival [7]. In our clinical case, this was the only effective method to prolong the patient's

life, so the decision was made to continue using ECMO as a bridge to retransplantation with careful monitoring of the patient's parameters.

The fact of long graft ischemia also raised great concerns. It is generally accepted that the implantation of a donor lung after 6 hours of ischemia is associated with a high risk of its primary dysfunction. However, according to the study by Johns Hopkins University, no correlation was found between long total graft ischemia and the primary graft dysfunction or survival after lung transplantation [8]. Our clinical case confirms the possibility of transplanting a viable lung after 9 hours of pharmacological cold preservation.

Conclusion

Despite the high risks of complications, with the coordinated work of the entire team, performing lung retransplantation can be a method of treating patients with irreversible lung damage when other options have been exhausted. In this case, a long-term extracorporeal membrane oxygenation can be used as a "bridge to retransplantation". The period of cold ischemia of the graft for more than 6 hours in our clinical example did not lead to a primary graft dysfunction. In conditions of a donor organ shortage, it may be necessary to revise the periods of acceptable graft ischemia to increase the availability and efficiency of organ use.

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