LUNG TRANSPLANTATION FOR SILICOSIS

SİLİKOZİSDE AKCİĞER TRANSPLANTASYONU

SILICOSIS

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Öz

Amaç: Silikozis, silika tozu inhalasyonunundan kaynaklanan bir meslek hastalığıdır. Akciğer transplantasyonu açısından, silikozis iyi belgelenmiş bir hastalık değildir. Bu yazıda silikozisden etkilenen hastaların perioperatif seyri ve sonuçları bildirilmektedir. Gereç ve Yöntem: Silikozis tanısı ile 5 hastaya tek akciğer transplantasyonu yapıldı, aynı dönem boyunca akciğer transplantasyonlarının % 6.4'ünü oluşturdu (5/77). Tüm hastalar erkek olup, yaş aralığı 34-41'dir.Beş hastanın ikisi diş teknisyeni, bir tanesi taş ocağı çalışanı, geri kalan iki hasta kot kumlama işçileri idi. Tüm hastalarda istirahat sırasında oksijen ihtiyacı duyan nefes darlığı vardı. Bulgular: Dört hastada sağ, bir hastada sol tek traflı akciğer tranplantasyonu gerçekleştirildi. Tüm hastalara anterior torakotomi uygulandı. Bir hastada sağ ana pulmoner arteri kontrol altına almak için sternuma transvers insizyon yapıldı. Ameliyat sırasında hemodinamik instabiliteye bağlı olarak iki hastada arteriovenöz ekstrakorporeal membran oksijenasyon desteği gerekti. Perioperatif mortalite yoktu. İki olgu ilk 24 saatte ekstübe edildi ve bir hastada uzamış entübasyon nedeniyle trakeostomi açıldı. Üç hasta 9, 21 ve 28. günlerde hastaneden taburcu edildi. Tartışma: Akciğer transplantasyonu, son dönem silikoz için tek küratif tedavi yöntemidir. Native akciğerin pnömonektomisi son derece zor olabilir. Yoğun plevral adezyonlar ve fibrotik hiler lenf düğümleri, preoperatif toraks BT taramasında değerlendirilmelidir.

Anahtar Kelimeler

Silikozis; Akciğer; Trasnplantasyon

Abstract

Aim: Silicosis is an occupational disease caused by inhalation of silica dust. In terms of lung transplantation, silicosis has not been a well-documented disease. This article reports the perioperative course and the outcome of patients affected by silicosis. Material and Method: Single lung transplantation was performed in 5 of 77 patients diagnosed with silicosis, who comprised 6.4% of all lung transplantations during the same period. All the patients were males, with an age range of 34–41 years. Of the five patients, two were dental technicians, one was a quarry worker, and the remaining two patients were jeans sandblasting workers. All the patients had dyspnea that required oxygen during rest. Results: Unilateral lung transplantation was performed in four patients for the right lung and in one patient for the left lung. All the patients were approached by anterior thoracotomy. In one patient, a sternum transverse incision was made to take control over the right main pulmonary artery. Arteriovenous extracorporeal membrane oxygenation support was required for two patients due to hemodynamic instability during the operation. There was no perioperative mortality. Two cases were extubated in the first 24 hours, and tracheostomy was performed in one patient because of prolonged intubation. Three patients were discharged from the hospital on days 9, 21, and 28. Discussion: Lung transplantation is the only curative treatment for end-stage silicosis. Removal of the native lung may be extremely difficult. Dense pleural adhesions and fibrotic hilar lymph nodes must be assessed at the preoperative CT scan of the thorax.

Keywords

Silicosis; ECMO; Lung Transplantation

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Introduction

Silicosis, an occupational disease caused by inhalation of silica dust, results in progressive and permanent lung damage [1]. There is no specific treatment for silicosis, and lung transplantation remains the only option for patients presenting with end-stage lung disease. According to the annual report of the International Society for Heart and Lung Transplantation, silicosis constitutes only 2.2% of patients undergoing lung transplantation [2]. In this article, we report the perioperative course and the outcome of five patients with silicosis who underwent lung transplantation since our program began.

Material and Method

Between July 2009 and July 2015, unilateral lung transplantation was performed in five patients (four patients for the right lung and one patient for the left lung) presenting with end-stage lung disease caused by silicosis. These patients constituted 6.4% (5/77) of the total number of patients who were operated on during the same period. Diagnosis was made by radiological findings on CT scan and history of exposure. The results of spirometry, arterial blood gas values, 6-min walking test, and ventilation–perfusion scintigraphy are presented in Table 1. Echocardiography showed no right side enlargement and tricuspid jet in any of these patients.

Table 1. Characteristics and preoperative evaluation

Patients No	1	2	3	4	5
Gender	M	M	M	M	M
Age	34	38	41	34	43
Occupation	dental prosthesis technician	jeans sandblasting worker	jeans sandblasting worker	dental prosthesis technician	quarrier
Exposure (year)	10	3	4	2	15
İnterval (year)	4	4	6	1	4
FEV1 % (L)	17 (0.61)	37 (1.48)	26 (0.97)	none	27 (0.83)
FVC (L)	42 (1.81)	35 (1.68)	48 (1.48)	none	81 (0.81)
FEV1/FVC	33	81	108	none	100
PaO2 mmHg	49	57	51	57	53
PaCO2 mmHg	45	49	44	51	50
V/Q scan (right/left)	78/22	44/56	47/53	48/52	42/58
6 MWT(meter)	250	170	200	230	310
PASP by RHC (mmHg)	37	none	none	36	80

FEV1, Forced expiratory volume at timed intervals of 1.0 second; FVC, Forced vital capacity; PaO2, arterial partial pressure of oxygen; PaCO2, arterial partial pressure of carbon dioxide; V/Q scan ventilation/perfusion lung scan; 6MWT, six-minute walk test; PASP, pulmonary artery systolic pressure;RHC, right heart catheterization

Patients were evaluated and listed for lung transplantation using the consensus committee criteria. However, pleural thickenings suggesting dense adhesions and extensive mediastinal fibrosis were reviewed in more detail for planning of the operation. In only one patient, standard anterior thoracotomy through the fifth intercostal space was the choice of incision that was extended to the contralateral side to split the sternum. Extreme care was undertaken using electro and argon beam cautery to control the bleeding from the chest wall during pneumolysis. However, pleural adhesions necessitate a longer time to remove the native lung, in addition to the hilar dissection that is an obvious challenge for surgeons. Thus, the recipient operation was started at the earliest time point possible to have more time for pneumonectomy and subsequent hemostasis before implantation of the donor lung. None of the patients underwent rethoracotomy due to hemorrhage.

Piperacillin–tazobactam was given as empirical antibiotic therapy for prophylaxis and in the early postoperative period. The antibiotic therapy was changed or was continued based on the donor culture results and postoperative early bronchoscopic findings. Immunosuppression therapy consisted of tacrolimus, mycophenolate mofetil, and steroids. The target whole-blood trough level of tacrolimus was 12–16 ng/mL. Steroid treatment was initiated at the time of graft reperfusion at a dose of 500 mg and then at 1 mg/kg per day during the first week.

Results

The characteristics and preoperative evaluation results of the patients are given in Table 1, and the operation and results are summarized in Table 2.

Table 2. The operation and postoperative evaluation results

No patients	Operation	Extracorporal support	ICU stay (days)	Hos.Stay (days)	Survi
1	Left	-	10	21	41 month
2	Right	A-V /V-V ecmo	14	28	28 month
3	Right	A-V ecmo	19	19	19 day
4	Right	-	4	9	3 month
5	Right	-	10	120	4 month

ICU, intensive care unit; AV, arterio-venous, V-V; veno-venous; ECMO, extracorporeal membrane oxygenation

Patient 1

Single lung transplantation of the left lung was performed in a 34-year-old male patient with a diagnosis of silicosis. This patient was the first successful lung transplantation case in our clinic. His symptoms, which had started 4 years earlier, included cough and shortness of breath. Silicosis was diagnosed based on clinical and radiological criteria. He worked as a dental technician for 10 years and had been exposed to silica particles. He had undergone inpatient treatment at various times since the year of diagnosis. He was admitted several times to the emergency department due to respiratory distress. He also required continuous oxygen support in the last year (5 L/min). The patient's preoperative pulmonary function test showed severe respiratory impairment (FEV1: 0.61 L 17%; FEV1/FVC: 33%; FVC: 1.81 L 42%). Echocardiography of both ventricles showed normal findings. Pulmonary artery systolic pressure (PASP) was measured as 27 mmHg. In the V/Q lung scan examination, the right lung perfusion was 73% and the left lung perfusion was 27%.

The donor was a 13-year-old male. Brain death had occurred as a result of subdural hematoma due to head trauma in a vehicle

accident. The duration of mechanical ventilation was 4 days, and PaO2/FiO2 was 550 mmHg in the arterial blood gas test. Bronchoscopy showed no purulent secretions.

Single lung transplantation was performed with left anterior thoracotomy. Preoperative PASP was measured as 40 mmHg using the Swan-Ganz catheter. The patient tolerated one lung ventilation, and hence there was no need for extracorporeal life support. Ischemia time was 6 h. The length of stay in the intensive care unit (ICU) was 10 days. On the 21st day, he was discharged from the hospital. After 8 months of follow-up, pneumonia was detected in the graft lung. Polymerase chain reaction using throat swabs and bronchial lavage samples showed the presence of H1N1 virus. The patient was treated with oseltamivir. Rejection was excluded using transbronchial biopsy. During the follow-up, several social and educational problems that have a significant effect on the post-transplantation course were identified. The patient showed chronic rejection at the end of the third year because he stopped taking the immunosuppressive drugs for a certain period of time.

Patient 2

A 38-year-old male jeans sandblasting worker was diagnosed with silicosis based on clinical and radiological findings. He was exposed to silica dust for 3 years. Single right lung transplantation was performed 4 years from the time of diagnosis. He required oxygen support at 2 L/min in the last year. Pulmonary function test results were as follows: FEV1: 1.48 L 37%; FVC: 1.68 L 35%; FEV1/FVC: 37%. In the 6-min walking test examination, he was desaturated and walked 170 m with oxygen support. The V/Q scan study revealed respiratory function of 44% in the right lung and 56% in the left lung. Echocardiography examination showed EF measured at 50% and mild suppression of the left ventricular function. PASP was normal. Hence, right heart catheterization was not performed.

The donor was a 24-year-old male who was diagnosed with brain death due to head trauma. The duration of mechanical ventilation was 4 days, and PaO2/FiO2 was 667 mmHg in the arterial blood gas evaluation. Chest radiography and bronchoscopic findings were normal. Right anterior thoracotomy was planned for single lung transplantation. During the operation, arteriovenous extracorporeal membrane oxygenation (ECMO) support was needed because of hemodynamic instability. An ECMO cannula was inserted into the femoral artery. A-v ECMO was converted to v-v ECMO at the end of the operation, and the patient was extubated on the second day. He was extubated from mechanical ventilation on the postoperative third day. He was monitored for 14 days in the ICU and was discharged on the 28th day. Since the patient did not have much familial and social support, he died due to graft rejection on the following 28th month.

Patient 3

A 41-year-old male patient was referred to the lung transplantation clinic due to a diagnosis of silicosis. The patient, who had been diagnosed 6 years earlier, was a jeans sandblasting worker for the past 4 years. He required 4 L/h of oxygen daily and walked 200 m in the 6-min walking test. Pulmonary function test results were as follows: FEV1: 0.97 L 26%; FVC 1.48 L 48%; FEV1/FVC: 108%. The V/Q scan examination showed respiratory function of 53% in the right lung and 47% in the left lung. Echocardiography showed EF measured at 65%, and PASP was 15–20 mmHg. Hence, right heart catheterization was not performed.

The donor was a 27-year-old male who was diagnosed with brain death due to drug intoxication. Mechanical ventilation duration was 7 days, and arterial blood gas test showed PaO2/FiO2 of 549 mmHg. Right anterior thoracotomy incision was scheduled for the lung transplantation. Arteriovenous ECMO support was required in this patient due to cardiac arrest on induction. Femoral artery and vein were used for cannulation. We were not able to wean the patient from the ECMO and he died on the 19th postoperative day due to multiple organ failure. Unfortunately, there was no opportunity for an adequate evaluation of the neurologic status of this patient after the operation.

Patient 4

A 34-year-old male patient was admitted to the emergency room due to sudden onset of dyspnea and pneumothorax detected in both lungs. The patient was referred to the lung transplantation clinic after acute treatment. He had worked as a dental technician for 15 years; silicosis was diagnosed based on clinical and radiological findings. He needed 3 L/min of oxygen daily. Echocardiography results were as follows: EF 65%, PASP 20 mmHg. PASP 36 was measured at the right heart catheterization.

The donor was a 52-year-old male patient. Brain death had occurred in this patient due to cerebrovascular disease. Arterial blood gas test revealed PaO2/FiO2 of 450 mmHg. Bronchoscopy and radiological findings were clear. Single lung transplantation was performed via right thoracotomy. The postoperative course was uneventful. After ICU admission for 4 days, he was discharged on the ninth postoperative day. Bronchus intermedius narrowing was detected on the third month in a routine check-up bronchoscopy. There was no active complaint. Rigid bronchoscopy was planned for bronchial dilation to prevent progression of the narrowing. Active bleeding from the right main bronchus occurred during the operation. Despite the urgent thoracotomy, he died due to asphyxia and bleeding.

Patient 5

The patient was a 45-year-old male with a diagnosis of silicosis and had been followed up for 3 years. He depended on oxygen at 2 L/min daily for the past year. His occupation was ship blasting work for the past 15 years. The pretransplant evaluation results of the pulmonary function test were as follows: FEV1: 0.83 L 27%, FVC 0.81 L 100%; FEV1/FVC: 125%. Arterial blood gas results were measured as pCO2 of 53 mmHg and pO2 of 50 mmHg. He walked 352 m in the 6-min walking test. The V/Q lung scan examination showed right lung perfusion of 52% and left lung perfusion of 48%. PASP was measured at 25 mmHg on echocardiography, 80 mmHg on the right heart catheterization. Ejection fraction was 65%.

The donor was a 57-year-old male who was diagnosed with brain death due to a brain aneurysm. Arterial blood gas test showed PaO2/FiO2 of 392 mmHg. Bronchoscopy and radiological findings were clear. Single right lung transplantation was planned. We believed it would be difficult to perform pulmonary

artery dissection due to the hilar adhesions observed in the patient's preoperative chest CT evaluation. We performed transverse sternal incision in addition to right anterior thoracotomy. Pulmonary arterial bleeding occurred during the operation, and the intrapericardial right pulmonary artery was taken under control. Hemodynamics during the operation were stable. Ischemia time was 5 h. He was extubated 24 h after the operation and was later monitored for 10 days in the ICU. The patient required intermittent CPAP and was again intubated due to respiratory distress on the 15th day. Tracheostomy was performed. Despite being provided the maximum physical and mental support, the patient was extremely reluctant to cooperate with the transplantation team, and his condition never recovered so that he could be discharged from the hospital.

Discussion

Silicosis is a disease that affects not only the lung parenchyma but also the pleural spaces and the pulmonary and mediastinal lymphatics. Clinical expression of this disease varies significantly depending on the intensity and duration of exposure and host defense [3]. Thus, as with any other indications of lung transplantation, it is mandatory to make an individualized decision for silicosis patients.

Compared with other indications of lung transplantation, patients with silicosis resemble those presenting with idiopathic pulmonary fibrosis (IPF) in terms of respiratory mechanics and pulmonary hemodynamics [4]. However, patients with silicosis are relatively young and robust with otherwise good physical condition and remain stable until advanced respiratory failure develops. Thus, patients can still be good candidates for transplantation even if spirometric values are significantly decreased. The right heart performance and pulmonary pressures also remain relatively stable along the course of the disease. Theoretically, the exposure of lungs to silica would be similar in both lungs, but the perfusion scan may reveal a significant difference. This gives important information for surgeons not only about the side to be removed but also about the possible need for perioperative extracorporeal support.

Despite the several postoperative advantages of a silicosis patient, extreme difficulty may be encountered during the removal of the native lung. We believe that this is the most crucial part of patient selection and probably the major determinant of the postoperative course. Excessive bleeding during pneumolysis is unavoidable, and requirement of extracorporeal support for any reason significantly increases blood loss resulting in perioperative hemodynamic instability.

Preoperatively, the CT scan of the thorax must be carefully assessed for dense pleural adhesions and fibrotic hilar lymph nodes. However, our experience shows that preoperative images do not correlate well with perioperative findings. Therefore, we believe that the surgical team must be prepared for the worst scenario when a patient with silicosis is considered for transplantation. We extensively use electro-thermal bipolar tissue sealing system and argon laser during pneumolysis and spend a longer time to achieve hemostasis after the removal of the native lung. Mediastinal dissection of the hilar structures is extremely dangerous in some cases because of fibrosis. Thus, another precaution we took in the present cases is an intrapericardial approach to the main PA for quicker and safer control. The intrapericardial space remains intact despite dense mediastinal fibrosis. When the native lung is removed, the rest of the operation becomes straightforward.

Perioperative heparinization for extracorporeal support increases bleeding and therefore has a negative effect on the postoperative course. However, it seems that ECMO is frequently used for patients undergoing lung transplantation for various indications. In a case series previously reported by Mao et al., four of five patients required ECMO [5]. Although we immediately put one of our patients on ECMO due to cardiac arrest upon induction, compared with the series of lung transplantations, the rate of ECMO use in our experience is still higher. Our experience suggests that those patients who likely require extracorporeal support perioperatively should be listed for transplantation with extreme caution. Regarding the postoperative hemodynamics following a single lung transplantation, we believe that double lung transplantation should be undertaken only in those patients presenting with limited pleuroparenchymal adhesions and mediastinal fibrosis.

In the long term, progressive fibrosis in the contralateral lung results in a refractory dry cough in some patients. Oral codeine is the drug of choice for these patients. Eventually, the contralateral native lung becomes totally fibrotic with zero perfusion without causing any clinical problem.

Depending on the end-stage lung disease, symptoms are worsened by poor living conditions and psychosocial status. In those cases, long-term survival may not be achieved unless these conditions are corrected after successful transplantation of the lung. Our patients, especially jeans sandblasting workers, had poor quality of life. When they applied to our transplant clinic, they had poor nutrition and condition. Immunosuppressive (anti-rejection) drugs are important to protect the transplant organ after lung transplantation. With the other patient who was a dental technician, we were faced with psychosocial problems. In the third year, rejection developed after the discontinuation of immunosuppressive drugs. Long-term survival cannot be achieved based solely on using correct surgical standards; it must also involve correcting poor living conditions and psychosocial situations.

Conclusion

Our limited experience suggests that lung transplantation is an acceptable option for patients with silicosis. However, the perioperative course might be technically challenging for the surgical team and therefore has to be carefully planned. The improvement of living conditions and poor physical condition is required to achieve long-term survival.

Competing interests

The authors declare that they have no competing interests.

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