Turkish Journal of Thoracic and Cardiovascular Surgery 2020;28(3):543-546
http://dx.doi.org/doi: 10.5606/tgkdc.dergisi.2020.19009

Case Report / Olgu Sunumu

Lung transplantation for graft-versus-host disease after allogeneic stem cell transplantation: A report of two cases

Allojenik kök hücre transferi nakli greft-versus-host hastalığında akciğer nakli: İki olgu sunumu

Erman Bağatur Öztürk[1], Mustafa Vayvada[2], Atakan Erkılıç[3], Ahmet Erdal Taşçı[2]

Institution where the research was done:
University of Health Sciences, Kartal Koşuyolu Thoracic and Cardiovascular Surgery Training and Research Hospital, Istanbul, Turkey

Author Affiliations:
[1]Department of Thoracic Surgery, University of Health Sciences, Istanbul Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital, Istanbul, Turkey
[2]Department of Thoracic Surgery, University of Health Sciences, Kartal Koşuyolu Thoracic and Cardiovascular Surgery Training and Research Hospital, Istanbul, Turkey
[3]Department of Anesthesiology and Reanimation, University of Health Sciences, Kartal Koşuyolu Thoracic and Cardiovascular Surgery Training and Research Hospital, Istanbul, Turkey

ABSTRACT

Allogeneic peripheral stem cell transplantation is an effective treatment of malignant and non-malignant hematological diseases. However, it is associated with several complications, such as graft-versus-host disease, and also various complications involving different organ systems. Late-onset non-infectious lung complication is one of them. This pathology may also affect the different anatomical regions in the lung as parenchymas, bronchi, or vessels and may manifest with different clinical presentations. Lung transplantation can be an effective treatment in patients with pulmonary complications after allogeneic stem cell transplantation and also in patients who do not respond to treatment adequately and with a limited life expectancy. Herein, we report two rare cases who underwent lung transplantation after allogeneic stem cell transplantation.

Keywords: Allogeneic stem cell transplantation, lung transplantation, non-infectious pulmonary disease.

ÖZ

Malign olan ve olmayan hematolojik hastalıkların tedavisinde allojenik periferik kök hücre nakli etkili bir tedavidir. Ancak, greft-versus-host hastalığı gibi bazı komplikasyonlar ve çeşitli organ sistemlerini etkileyen komplikasyonlar ile ilişkilidir. Geç başlangıçlı non-enfeksiyöz akciğer komplikasyonu bunlardan biridir. Bu patoloji, akciğerlerin parankimler, bronşlar ve damarlar gibi anatomik bölgelerini de etkileyebilmekte ve farklı klinik tablolar ile kendini gösterebilmektedir. Akciğer nakli, allojenik kök hücre nakli sonrası pulmoner komplikasyon gelişen hastalarda ve aynı zamanda tedaviye yeterli düzeyde yanıt vermeyen ve yaşam beklentisi sınırlı olan hastalarda etkili bir tedavi yöntemi olabilir. Bu yazıda, allojenik kök hücre nakli sonrası akciğer nakli yapılan iki nadir olgu sunuldu.

Anahtar sözcükler: Allojenik kök hücre nakli, akciğer nakli, non-enfeksiyöz akciğer hastalığı.

Lung transplantation (LTx) is the most effective treatment modality for end-stage lung diseases. To date, approximately 65,000 LTx procedures have been administered worldwide of which approximately 4,500 have been reported annually. The mean life expectancy in these patients undergoing LTx has been estimated as 4.7 years for single LTx and 7.6 years for double LTx. The main reasons for diseases requiring LTx include chronic obstructive pulmonary disease, idiopathic pulmonary fibrosis, and cystic fibrosis.[1] Lung transplantation due to lung involvement after allogeneic bone marrow transfer is limited.[1] Herein, we

Received: November 28, 2019 *Accepted:* March 19, 2020 *Published online:* July 28, 2020

Correspondence: Erman Bağatur Öztürk, MD. SBÜ, İstanbul Mehmet Akif Ersoy Göğüs Kalp Damar Cerrahisi Eğitim ve Araştırma Hastanesi, Göğüs Cerrahisi Kliniği, 34303 Küçükçekmece, İstanbul, Türkiye
Tel: +90 212 - 692 20 00 e-mail: drermanb@gmail.com

Cite this article as:
Öztürk EB, Vayvada M, Erkılıç A, Taşçı AE. Lung transplantation for graft-versus-host disease after allogeneic stem cell transplantation: A report of two cases. Turk Gogus Kalp Dama 2020;28(3):543-546

©2020 All right reserved by the Turkish Society of Cardiovascular Surgery.

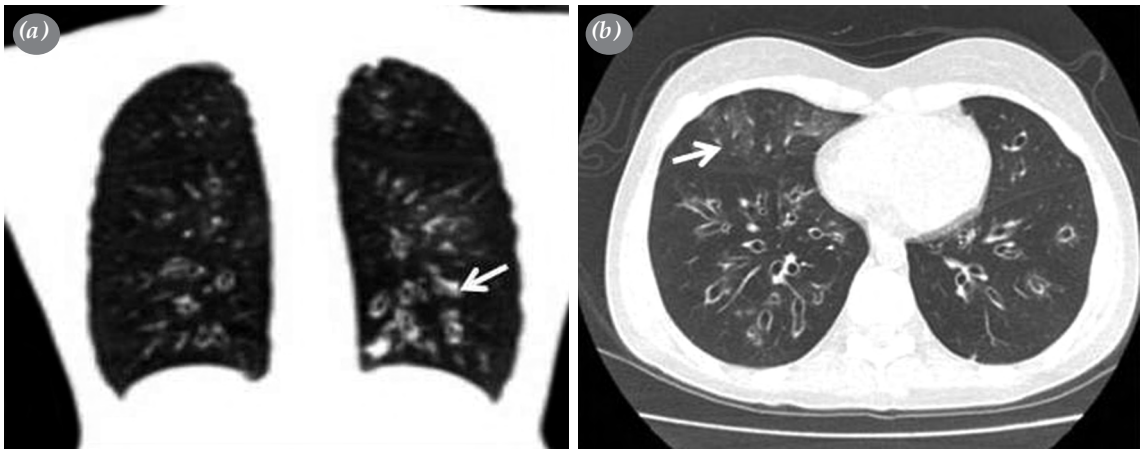

Figure 1. (a) Bilateral diffuse bronchiectasis areas (white arrow) and **(b)** ground-glass views on coronal reformatted axial images of thoracic computed tomography (white arrow).

report two cases who underwent LTx after allogeneic stem cell transplantation (ASCT), which is a relatively rare procedure.

CASE REPORT

Case 1- A 23-year-old female patient was diagnosed with acute myeloid leukemia (AML) in 2015 at an external center where she was admitted with complaints of fever, weakness, and loss of appetite. The standard treatment approach (cytosine arabinoside + idarubicin) and reinforcement (cytosine arabinoside) after remission were administered and the patient was cured. One year later, when her disease recurred, allogeneic peripheral stem cell transfer from an unrelated donor was administered, and successful results were obtained. The patient was admitted to the hospital with complaints of cough and shortness of breath within two or three months following the ASCT. The patient was admitted to our center after medical treatment. On her physical examination, she had respiratory distress, decreased bilateral breathing sounds, and generalized rales and rhonchi. At the time of admission, the pulmonary function test (PFT) results were as follows: forced vital capacity (FVC): 21%, forced expiratory volume in one sec (FEV1): 13%, and FEV1/forced vital capacity (FVC): 63%. Thoracic computed tomography (CT) showed diffuse areas of tubular bronchiectasis in both lungs (Figure 1a, b). Based on all these findings, the patient was placed on the organ transplant waiting list based on by the decision of the Lung Transplant Scientific Advisory Board with the diagnosis of diffuse bronchiectasis. Bilateral LTx was performed on June 9th, 2019 with the appropriate donor. The procedure was uneventful. The patient was transferred to the intensive care unit. She was extubated on postoperative Day 3 and followed with medical support and triple immunosuppressive regimen (calcineurin inhibitor,

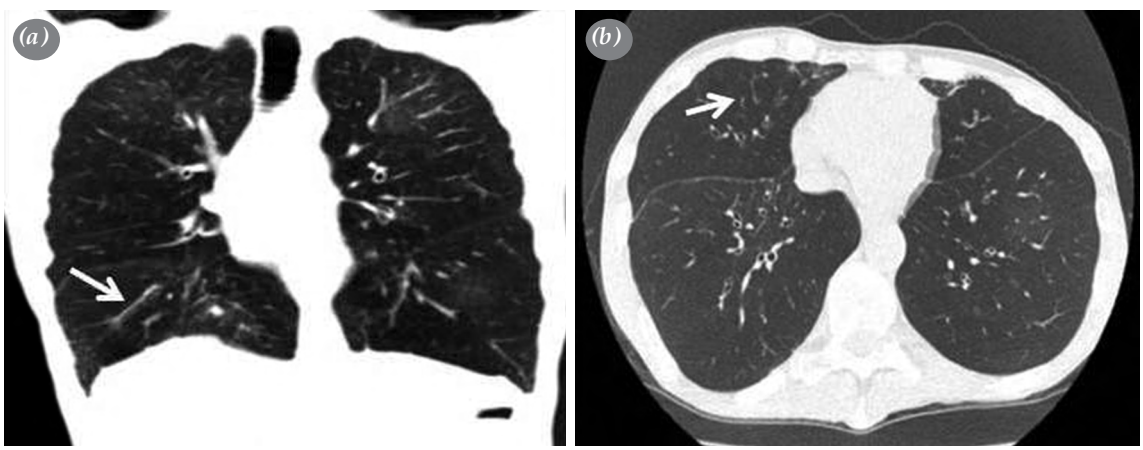

Figure 2. (a) Bilateral peribronchial thickening (white arrow) and **(b)** ground-glass views on coronal reformatted axial images of thoracic computed tomography (white arrow).

corticosteroid, mycophenolate mofetil). The patient was discharged on postoperative Day 13 without any complications. The patient is still being followed without any complication in the outpatient setting. A written informed consent was obtained from the patient.

Case 2- A-46-year-old male patient was diagnosed with AML in 2000 at an external center where he presented with complaints of fatigue, loss of appetite, and skin rash. When the disease recurred in 2003, ASCT from an unrelated donor was administered, and successful results were obtained. In the following months after treatment, graft-versus-host disease (GVHD) was diagnosed, and medical treatment was initiated. In 2012, the patient was diagnosed with organized pneumonia with increasing dyspnea and medical treatment was initiated. The patient was admitted to our clinic with severe respiratory distress, since his complaints did not regress despite medical treatment and regular follow-up. On his physical examination, bilateral breathing sounds were heard deeply. The expiration time was long and diffuse rhonchi were heard. At the time of admission, the PFT results were as follows: FVC: 26%, FEV1: 15%, and FEV1/FVC: 59%. Thoracic CT showed peribronchial thickening, bronchiectasis, and ground-glass opacities (Figure 2a, b). Based on all these findings, the patient was included in the LTx waiting list by the decision of the Lung Transplant Scientific Advisory Board for LTx. The patient underwent bilateral LTx on April 11th, 2019 with the appropriate donor. The procedure was uneventful, and the patient was transferred to the intensive care unit. Photographs of histopathological examination is shown in Figure 3. The patient was extubated on postoperative Day 2 and was taken to the ward on the same day. He was followed with necessary medical support and triple immunosuppressive regimen (calcineurin inhibitor, corticosteroid, mycophenolate mofetil). The patient was discharged on postoperative Day 18. However, he developed pancytopenia during his routine follow-up after discharge and was hospitalized in coordination with the hematology clinic and given medical treatment. The patient's general condition and laboratory parameters improved, and he was discharged. The patient is still being followed without any complication in the outpatient setting. A written informed consent was obtained from the patient.

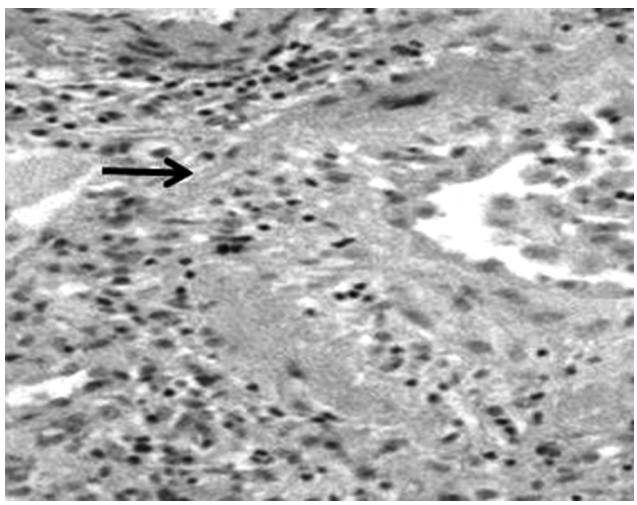

Figure 3. Lymphocytic infiltration around the outer layer of bronchiole smooth muscle and compression of bronchial lumen in subepithelial area with a collection of fibrous tissues (black arrow) (Histopathological image of graft-versus-host disease with hematoxylin-eosin ×200).

DISCUSSION

Late-onset non-infectious lung complications are seen in approximately 6 to 20% of the ASCT patients receiving treatment various hematological diseases.[2,3] This largely arises from GVHD which is an immunological reaction that may affect solid organs in approximately 30% of the ASCT cases.[2] The main underlying mechanism of damage to the solid organs is thought to be the recipient's immune cells interacting with cytotoxic T-lymphocytes. This pathology of the lung can be seen in various anatomical regions, such as bronchus, parenchyma, vein, or pleura and can be characterized by high morbidity and mortality rates.[3]

Bronchiolitis obliterans syndrome is the most common lung complication and is characterized by chronic inflammation, thickening of the fibers, and obliteration of the lumens of the terminal or respiratory bronchioles.[3] The diagnosis is made based on the PFT, thoracic CT, and biopsy.[3,4] Less common pulmonary complications are interstitial lung diseases.[4]

The most important pathology is organized pneumonia which is characterized by intra-alveolar mixed granulation tissue development and chronic interstitial inflammation. Thoracic CT typically reveals a ground-glass opacity and/or consolidation in the peribronchovascular area. In our cases, thoracic CT showed the findings of peribronchial thickening, bronchiectasis areas, and a ground-glass appearance, consistent with the definitions described in the literature.[5,6]

The main treatment in these patients with pulmonary GVHD is a systemic corticosteroid, as

well as extracorporeal photopheresis, azathioprine, mycophenolate mofetil, and bronchodilators. Recently, corticosteroids are recommended in the diagnosis and treatment guidelines.[7] Steroid and ruxolitinib treatment were administered for our first case; however, clinical conditions and PFT results deteriorated. In our second case, although the dose and duration of the treatment were unable to be determined exactly, steroid treatment was administered, and as the patient responded treatment inadequately, he was put on the waiting list of LTx. Altogether, we believe that the development in immunosuppressive drugs in forthcoming years would be very effective in the treatment of this condition.

Review of the literature reveals that the number of patients who underwent LTx after ASCT is limited. There is no study reported before 1992.[8] major main studies reported in the literature are as follows: 12 LTx cases by Koenecke et al.,[9] seven LTx cases by Vogl et al.,[10] 12 pediatric LTx cases by Faraci et al.,[11] and 105 patients by Greer et al.[12] In these studies, the survival and complication rates of patients with LTx after ASCT and those with LTx for other reasons were comparable.

In conclusion, we believe that further studies about this subject would provide contributions to the diagnosis and treatment of these patients in the future. Besides, regular pulmonary function tests seem to be beneficial for early diagnosis and treatment in patients undergoing allogeneic stem cell transplantation, and lung transplantation is a favorable treatment option in patients with resistant pulmonary complications.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Chambers DC, Cherikh WS, Goldfarb SB, Hayes D Jr, Kucheryavaya AY, Toll AE, et al. The International Thoracic Organ Transplant Registry of the International Society for Heart and Lung Transplantation: Thirty-fifth adult lung and heart-lung transplant report-2018; Focus theme: Multiorgan Transplantation. J Heart Lung Transplant 2018;37:1169-83.
2. Patriarca F, Poletti V, Costabel U, Battista ML, Sperotto A, Medeot M, et al. Clinical presentation, outcome and risk factors of late-onset non-infectious pulmonary complications after allogeneic stem cell transplantation. Curr Stem Cell Res Ther 2009;4:161-7.
3. Chiodi S, Spinelli S, Ravera G, Petti AR, Van Lint MT, Lamparelli T, et al. Quality of life in 244 recipients of allogeneic bone marrow transplantation. Br J Haematol 2000;110:614-9.
4. Jagasia MH, Greinix HT, Arora M, Williams KM, Wolff D, Cowen EW, et al. National Institutes of Health Consensus Development Project on Criteria for Clinical Trials in Chronic Graft-versus-Host Disease: I. The 2014 Diagnosis and Staging Working Group report. Biol Blood Marrow Transplant 2015;21:389-401.e1.
5. Nakaseko C, Ozawa S, Sakaida E, Sakai M, Kanda Y, Oshima K, et al. Incidence, risk factors and outcomes of bronchiolitis obliterans after allogeneic stem cell transplantation. Int J Hematol 2011;93:375-82.
6. Hildebrandt GC, Fazekas T, Lawitschka A, Bertz H, Greinix H, Halter J, et al. Diagnosis and treatment of pulmonary chronic GVHD: report from the consensus conference on clinical practice in chronic GVHD. Bone Marrow Transplant 2011;46:1283-95.
7. Pipavath SN, Chung JH, Chien JW, Godwin JD. Organizing pneumonia in recipients of hematopoietic stem cell transplantation: CT features in 16 patients. J Comput Assist Tomogr 2012;36:431-6.
8. Calhoon JH, Levine S, Anzueto A, Bryan CL, Trinkle JK. Lung transplantation in a patient with a prior bone marrow transplant. Chest 1992;102:948.
9. Koenecke C, Hertenstein B, Schetelig J, van Biezen A, Dammann E, Gratwohl A, et al. Solid organ transplantation after allogeneic hematopoietic stem cell transplantation: a retrospective, multicenter study of the EBMT. Am J Transplant 2010;10:1897-906.
10. Vogl UM, Nagayama K, Bojic M, Hoda MA, Klepetko W, Jaksch P, et al. Lung transplantation for bronchiolitis obliterans after allogeneic hematopoietic stem cell transplantation: a single-center experience. Transplantation 2013;95:623-8.
11. Faraci M, Bertaina A, Dalissier A, Ifversen M, Schulz A, Gennery A, et al. Solid organ transplantation after hematopoietic stem cell transplantation in childhood: A multicentric retrospective survey. Am J Transplant 2019;19:1798-805.
12. Greer M, Berastegui C, Jaksch P, Benden C, Aubert J, Roux A, et al. Lung transplantation after allogeneic stem cell transplantation: a pan-European experience. Eur Respir J 2018;51:1701330.