Received: 11 February 2021 | Accepted: 1 March 2021

DOI: 10.1111/1759-7714.13936

CASE REPORT

WILEY

Urgent lung transplantation for thymic neoplasm-associated severe constrictive bronchiolitis with bronchiectasis and radiotherapy-induced organizing pneumonia: A case report

Tomaž Štupnik[1,2] | **Marija Iča Dolenšek**[3] | **Jernej Mlakar**[4] | **Karmen Stanič**[5] | **Matevž Harlander**[2,6] | **Sabina Škrgat**[2,6]

[1]Department of Thoracic Surgery, University Medical Centre Ljubljana, Ljubljana, Slovenia

[2]Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia

[3]Department of Radiology, University Medical Centre Ljubljana, Ljubljana, Slovenia

[4]Institute of Pathology, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia

[5]Department of Radiotherapy, Institute of Oncology Ljubljana, Ljubljana, Slovenia

[6]Department of Pulmonary and Allergic Diseases, University Medical Centre Ljubljana, Ljubljana, Slovenia

Correspondence
Tomaž Štupnik, University Medical Centre Ljubljana, Zaloška 2, SI-1000 Ljubljana, Slovenia.
Email: tomaz.stupnik@kclj.si

Abstract

Here, we present the case of a 28-year-old woman who developed severe and progressive thymoma-associated constrictive bronchiolitis with bronchiectasis, despite undergoing thymectomy. The disease was further complicated by radiation-induced organizing pneumonia (RIOP), which developed after adjuvant radiotherapy (RT) for Masaoka stage II thymoma. The patient was successfully treated with an urgent lung transplantation (LTx) for irreversible respiratory failure.

KEYWORDS

end-stage lung disease, lung transplantation, radiation induced organizing pneumonia, thymic neoplasm-associated bronchiolitis

INTRODUCTION

Bronchiectasis is an irreversible dilation of the bronchi caused by numerous conditions. Bronchiectasis can also present as an uncommon (up to 1.5%) comorbidity of a thymic neoplasm and is usually associated with thymoma-associated immunodeficiency, a rare condition known as Good's syndrome (GS). Bronchiectasis without GS has also been reported, with pathological and computed tomography (CT) features of diffuse panbronchiolitis.[1]

Lung transplantation (LTx) is reserved for rare instances of severe bronchiectasis.[1] To the best of our knowledge, there have been no previous studies which have reported GS in association with thymoma-associated bronchiectasis.

Radiation-induced organizing pneumonia (RIOP) is a type of interstitial pneumonia characterized by infiltration of the lungs outside the radiation field, differentiating it from radiation pneumonitis.[2,3] Its management is symptom-oriented and steroid therapy is reserved for those with severe symptoms and extensive disease. The prognosis is excellent, and no deaths have been reported to date.[4]

CASE REPORT

A 28-year-old otherwise healthy female with a six-month history of a dry morning cough was diagnosed with a 3 cm nonmyasthenic thymoma. Slightly thickened bronchial walls and a diffuse moderate tree-in-bud pattern suggesting bronchiolitis were shown on high-resolution CT (HRCT) (Figure 1(a)). Her forced expiratory volume in the first second (FEV1) was 79%.

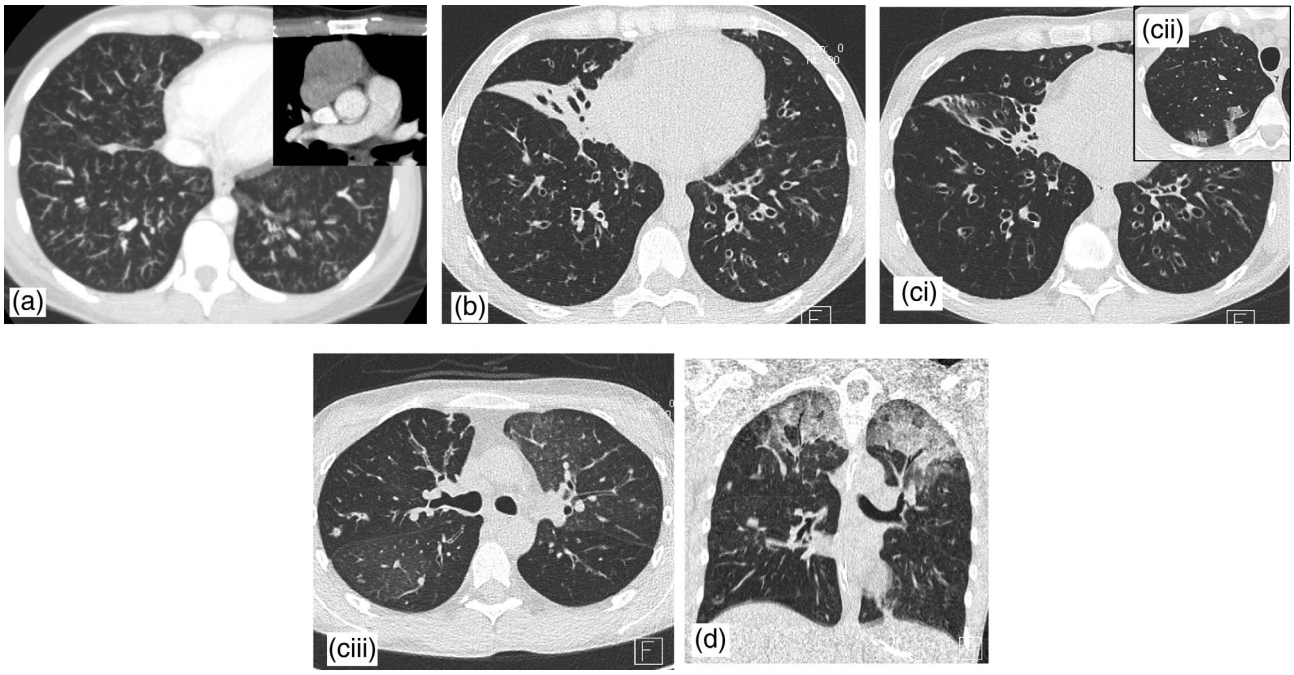

FIGURE 1 (a) Baseline computed tomography (CT) scan; diffuse tree-in-bud pattern, 3 mm maximum intensity projection (MIP) reconstruction. Thymoma in the anterior mediastinum. (b) CT scan three months after RT (five months after thymectomy); bronchiectasis, same tree-in-bud pattern, and right middle lobe atelectasis. (c) CT scan 17 months after radiotherapy (RT); progression of bronchiectasis (ci), small areas of ground-glass opacity (GGO) (cii), and large areas of air trapping in expiratory scans (ciii). (d) CT scan at respiratory failure, 20 months after RT (8 days before lung transplantation (LTx); areas of GGO in previously normal aerated lung

A microscopic complete resection of a Masaoka stage IIB B2 thymoma was followed with postoperative radiotherapy (RT). A total dose of 50 Gy was delivered to the mediastinum in 25 fractions using Active Breathing Coordinator technology and volumetric-modulated arc therapy to reduce toxicity. During her last few RT sessions, she developed a productive cough, fever and some shortness of breath that improved with antibiotic therapy. Her FEV1 was 73%.

Three months after RT, she developed additional respiratory symptoms. CT revealed the progression of bronchiectasis and bronchiolitis (Figure 1(b)). Good's syndrome, alpha-1-antitrypsin deficiency, cystic fibrosis, primary ciliary dyskinesia, HIV, allergic bronchopulmonary aspergillosis, mycobacterial infections, systemic connective tissue disorders, immunodeficiencies, and gastroesophageal reflux disease were ruled out during extensive additional clinical evaluation. Histopathology revision of the resected specimen reclassified the thymoma from B2 to AB subtype. She was treated with antibiotics, a short course of methylprednisolone, bronchodilators, and respiratory physiotherapy. Her FEV1 was 45%.

The patient's next hospital admission followed 17 months post-RT due to respiratory insufficiency. Her lung function showed severe air trapping without increase in the total lung volume (RV 178%, TLC 85%, FEV1 30%). The progression of bronchiectasis, signs of severe air trapping compatible with advanced constrictive bronchiolitis, and some small nonspecific opacities in the upper lung fields suggesting organizing pneumonia were found on HRCT (Figure 1(c)). Broad-spectrum antibiotics and a short course of methylprednisolone treatment brought only minimal clinical improvement. She was discharged with long-term oxygen therapy and referred for lung transplantation evaluation.

However, only a week after hospital discharge, she developed acute respiratory failure demanding intubation and mechanical ventilatory support. A CT scan showed progression of mainly ground-glass opacities (GGOs) in all parts of the upper lung fields not affected by air trapping (Figure 1 (d)). No trigger was confirmed, and the lung was progressively more difficult to ventilate. She was listed for urgent LTx receiving a very high Eurotransplant lung allocation score (LAS) of 85.2.

Bilateral sequential LTx via hemiclamshell thoracotomy with intraoperative use of extra-corporeal membranous oxygenation (ECMO) was performed within 24 h of listing. No significant adhesions/fibrosis were found in the RT field. The areas of pericardial fat overlying the heart, the aortopulmonary window, and the area behind the innominate vein were cleared during LTx. The postoperative course was uneventful; the patient was extubated on postoperative day (POD) 4 and discharged home on POD 35. Six months after lung transplantation, the patient is in very good clinical condition and has normal lung function.

The pathology report of the explanted lung revealed acute and chronic bronchitis and constrictive bronchiolitis,

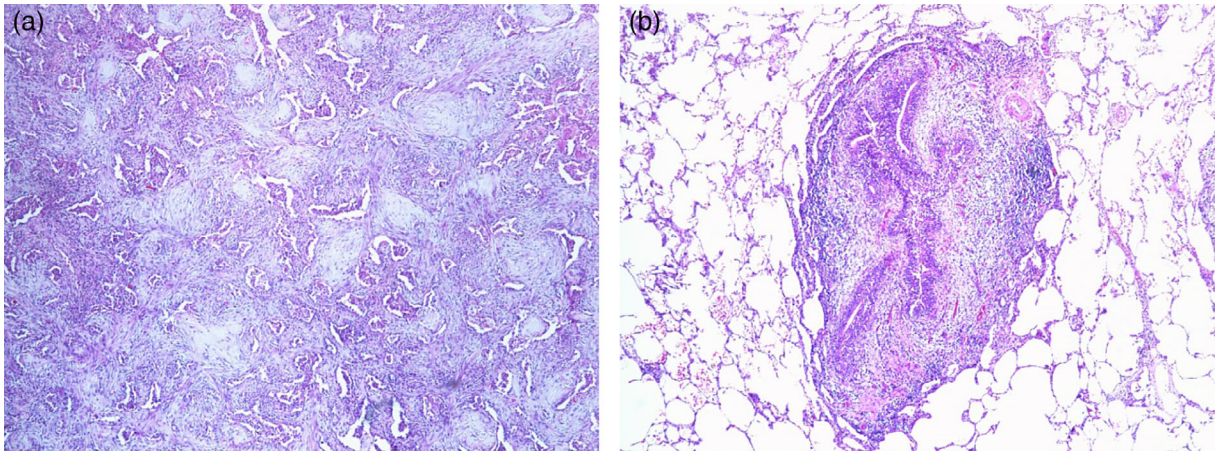

FIGURE 2 (a) Characteristic onion skin fibrosis of bronchiolitis obliterans/organizing pneumonia with obliteration of the lung parenchyma. Hematoxylin & eosin (H&E), 40x. (b) Constrictive bronchiolitis with mixed chronic inflammatory infiltrate and submucosal fibrosis with constriction of the bronchiolar lumen. H&E, 40x

bronchiectasis and bronchiololectasis. There were signs of organizing pneumonia with obliterative bronchiolitis of the upper lobes, consistent with RIOP (Figure 2).

DISCUSSION

Here, we report a unique case of a patient with thymic neoplasm-associated severe constrictive bronchiolitis with bronchiectasis treated with lung transplantation.

Although LTx is an established treatment option in severe bronchiectasis, we were faced with several dilemmas in this case. A recent history of malignancy is an absolute contraindication for LTx. According to guidelines, a five-year disease-free interval must be demonstrated in most cases, while a two-year disease-free interval is reasonable if combined with a low predicted risk of recurrence after lung transplantation.[5] Our patient had a stage II AB thymoma, which has a very favorable outcome[6] with a 22-month disease-free interval (from thymectomy to respiratory failure), thus justifying LTx.

The major pathology in our case was thymoma-induced constrictive bronchiolitis and bronchiectasis as a parathymic immunological complication. A diffuse panbronchiolitis-like manifestation and bronchiectasis are the clinical parathymic phenomena of an abnormal immune attack caused by direct or indirect damage of the target cells, driven by lymphocytes or autoantibodies.[7,8] The largest retrospective study of bronchiectasis in patients with thymic neoplasms found that some patients may develop bronchiectasis even after thymectomy, suggesting that abnormal immune status caused by thymic neoplasms might not stop after thymectomy.[9] This may be related to incompleteness of the thymectomy, as it is well known that microscopic foci of thymic tissue can sometimes be found in the pericardial fat overlying the heart, in the aortopulmonary window, and behind the innominate vein;[10] that is areas that are often not included in the thymectomy.

The progression of bronchiolitis and bronchiectasis to end-stage lung disease, although initiated by bronchiolitis, was significantly accelerated by RIOP. RIOP was first reported in 1995[2,3] in women receiving RT for breast cancer, but also in lung cancer patients[11] and even after stereotactic body RT.[12] It typically responds well to treatment with systemic corticosteroids and, so far, no mortality has been associated with RIOP.[4] Relapses of RIOP are most frequent (71%) during steroid tapering or withdrawal.[13] This also happened in our case: slight clinical and radiological regression after short-course steroid therapy was followed by a massive relapse within a week of steroid withdrawal.

In conclusion, thymoma-related constrictive bronchiolitis and bronchiectasis can progress and cause respiratory failure even in patients who have undergone a complete thymectomy. In patients with respiratory symptoms, a screening for bronchiolitis should be considered before deciding on RT, because it could induce RIOP and exacerbate the condition. Our case shows that thymoma-related constrictive bronchiolitis and bronchiectasis can be successfully treated by bilateral lung transplantation.

CONFLICT OF INTEREST

The authors have nothing to disclose.

ORCID

Tomaž Štupnik https://orcid.org/0000-0002-9019-806X
Karmen Stanič https://orcid.org/0000-0002-1239-0427

REFERENCES

1. Liu Y, Xu Y, Tian X, Huang H, Hou X, Chen M, et al. Thymic neoplasms patients complicated with bronchiectasis: case series in a Chinese hospital and literature review. Thorac Cancer. 2019;10:791–8.
2. Pasteur MC, Bilton D, Hill AT. British Thoracic Society guideline for non-CF bronchiectasis. Thorax. 2010;65(Suppl 1):i1–58.
3. Crestani B, Kambouchner M, Soler P, Crequit J, Brauner M, Battesti JP, et al. Migratory bronchiolitis obliterans organizing pneumonia after unilateral radiation therapy for breast carcinoma. Eur Respir J. 1995;8:318–21.

4. Bayle JY, Nesme P, Béjui-Thivolet F, Loire R, Guérin JC, Cordier JF. Migratory organizing pneumonitis "primed" by radiation therapy. Eur Respir J. 1995;8:322–6.
5. Otani K, Seo Y, Ogawa K. Radiation-induced organizing pneumonia: a characteristic disease that requires symptom-oriented management. Int J Mol Sci. 2017;18:281.
6. Weill D, Benden C, Corris PA, Dark JH, Davis RD, Keshavjee S, et al. A consensus document for the selection of lung transplant candidates: 2014–an update from the pulmonary transplantation Council of the International Society for heart and lung transplantation. J Heart Lung Transp. 2015;34:1–15.
7. Weis C-A, Yao X, Deng Y, Detterbeck FC, Marino M, Nicholson AG, et al. The impact of thymoma histotype on prognosis in a worldwide database. J Thorac Oncol. 2015;10:367–72.
8. Litwin SD, Zanjani ED. Lymphocytes suppressing both immunoglobulin production and erythroid differentiation in hypogammaglobulinaemia. Nature. 1977;266:57–8.
9. Charles RJ, Sabo KM, Kidd PG, Abkowitz JL. The pathophysiology of pure red cell aplasia: implications for therapy. Blood. 1996;87:4831–8.
10. Jaretzki A, Wolff M. "Maximal" thymectomy for myasthenia gravis. Surgical anatomy and operative technique. J Thorac Cardiovasc Surg. 1988;96:711–6.
11. Nogi S, Nakayama H, Tajima Y, Okubo M, Mikami R, Sugahara S, et al. Cryptogenic organizing pneumonia associated with radiation: a report of two cases. Oncol Lett. 2014;7:321–4.
12. Ochiai S, Nomoto Y, Yamashita Y, Murashima S, Hasegawa D, Kurobe Y, et al. Radiation-induced organizing pneumonia after stereotactic body radiotherapy for lung tumor. J Radiat Res. 2015;56:904–11.
13. Otani K, Nishiyama K, Ito Y, Kawaguchi Y, Inaji H. Steroid treatment increases the recurrence of radiation-induced organizing pneumonia after breast-conserving therapy. Cancer Med. 2014;3:947–53.

How to cite this article: Štupnik T, Dolenšek MI, Mlakar J, Stanič K, Harlander M, Škrgat S. Urgent lung transplantation for thymic neoplasm-associated severe constrictive bronchiolitis with bronchiectasis and radiotherapy-induced organizing pneumonia: A case report. *Thorac Cancer*. 2021;12:1757–1760. https://doi.org/10.1111/1759-7714.13936