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CASE REPORT

Two cases of air leak syndrome after bone marrow transplantation successfully treated by the pleural covering technique

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Abstract
Air leak syndrome (ALS) is a rare complication after bone marrow transplantation (BMT) and usually has a fatal outcome because of the high recurrence rate and treatment-refractory nature. A 32-year-old man with a history of BMT for acute lymphoblastic leukemia suffered from metachronous bilateral ALS. Bullectomy and the pleural covering procedure (PLC) were successfully performed for each side of the thorax. After surgery, no relapse of pneumothorax was seen for 2 years on the right side and for 1 year on the left side. A 38-year-old man with a history of BMT for acute myelogenous leukemia (AML) suffered from ALS at the thorax on the left side. Bullectomy and the PLC were successfully performed. After that no recurrence of left pneumothorax for 7 years. We experienced two cases of ALS after BMT successfully treated by the PLC. This technique may be a viable treatment option for future lung transplantation.

Keywords Air leak syndrome · Bone marrow transplantation · Pleural covering procedure

Introduction

Air leak syndrome (ALS), also called as air-leakage syndrome or thoracic air-leakage syndrome, is a rare complication related to late-onset non-infectious pulmonary complications (LONPICS), such as bronchiolitis obliterans, after bone marrow transplantation (BMT) and usually has a fatal outcome. Because lung transplantation is often the only radical treatment option for end-stage LONPICS, pleural adhesion should be avoided if possible for these patients. A new surgical technique known as total pleural covering was recently established. It has been reported that, with this procedure, the pleura is covered, and adhesion of the chest cavity can be prevented [1]. We herein report two cases of ALS after BMT that were successfully treated with the pleural covering technique.

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Case report

Case 1

A 32-year-old man with a history of acute lymphoblastic leukemia (ALL) underwent allogeneic bone marrow transplantation from an unrelated and human leukocyte antigen (HLA)-identical donor in 2011. He subsequently developed chronic graft-versus-host disease (cGVHD) affecting the lung. In 2012, he presented with dyspnea, and high-resolution computed tomography (CT) suggested characteristic findings of bronchial obliterans (BO). Three years after transplantation (in 2014), the first episode of pneumothorax occurred in the right lung. Because the degree of collapse of the lung was mild, the disease improved without drainage at that time. Right-sided pneumothorax recurred in 2015, and surgery was indicated.

We performed resection of the bulla located in the apex of his right lung via the thoracoscopic approach at that time. Pneumothorax recurred, however, 1 month after surgery. Chemical pleurodesis was attempted twice with minocycline to prevent air leakage but was not successful. Re-operation was then indicated. At surgery, the pleura was quite fragile, and severe adhesion was observed around the apex due to the previous surgery. After the adhesion was dissected, the

bullae were observed at the top of segment 6 of the right lung. After ligating the bullae, the pleural covering procedure was performed to reinforce the affected visceral pleura and prevent recurrence of pneumothorax. In detail, almost all of the visceral pleura of the right upper lobe was covered with three oxidized regenerative cellulose (ORC) mesh sheets, and fibrin glue was sprayed to fix the sheets (Fig. 1).

In 2016, the patient suffered from dyspnea, and chest CT revealed left-sided pneumothorax. In this CT, there were no remarkable changes around the pleural covering area at right upper lobe such as pleural thickness as a postoperative change of the previous surgery (Fig. 2). Although a chest tube was inserted, the air leakage was massive. Surgery was then indicated. Based on the experience of the previous surgery, bulla resection and pleural covering was planned via a thoracoscopic approach this time. At surgery, severe bullous changes in the visceral pleura at the left upper division were observed. After bullectomy, the majority of the visceral pleura of his left upper lobe and segment 6 were covered with five ORC mesh sheets and fibrin glue (Fig. 3). The postoperative course was uneventful, and the air leakage was successfully controlled. To date, at 12 months after the surgery, no relapse of the pneumothorax has been seen.

Case 2

A 38-year-old man with a history of acute myelogenous leukemia (AML) underwent allogenic BMT from an unrelated and HLA-identical donor in 2005. In 2006, he developed dyspnea. Chest high-resolution CT revealed the presence of interstitial lung disease with mosaic attenuation and bronchial dilatation, which were characteristic findings of BO. In 2010, he suffered from cough and severe dyspnea. Chest

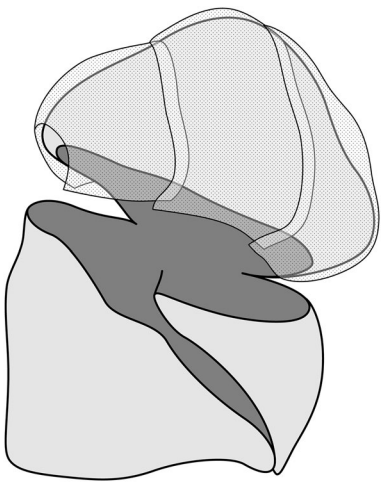

Fig. 1 Schema of operative findings. **a** The right upper lobes were covered with three oxidized regenerative cellulose (ORC) mesh sheets in case 1

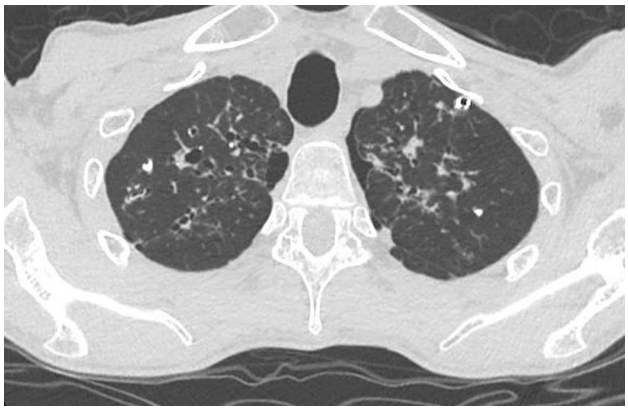

Fig. 2 A preoperative computed tomographic image of the chest showed left pneumothorax and a mosaic attenuation pattern

X-ray and CT showed pneumothorax and the acute progression of BO. He received steroid pulse therapy (methylprednisolone at 1 g/day for 3 days) under the diagnosis of BO exacerbation, and it improved his symptoms. However, the left-sided pneumothorax was exacerbated, and chest tube drainage was performed. Because the air leakage was prolonged, surgery was indicated. Plication of the bullae and the pleural covering procedure was performed via the thoracoscopic approach. Visceral pleura thickening and a pleural defect at the upper division were observed. The pleural defect was initially covered with the subcutaneous free fat pad harvested from the utility port to fix the fistula. The majority of the visceral pleura of his left upper lobe was subsequently covered with two ORC mesh and fibrin glue (Fig. 4). The postoperative course was uneventful. Chest CT showed no recurrence of left pneumothorax at 7 years after the operation.

Discussion

LONPICs, such as BO, BO organizing pneumoniae, interstitial pneumoniae and pulmonary fibrosis, occur in 20% of patients undergoing BMT as chronic-GVHD (cGVHD) [2]. LONPICs is recognized as a life-threatening disease because of the higher rate of morbidity and mortality. Immunosuppressive therapy is considered to be the standard treatment for LONPICs; however, the efficacy of such therapy is not sufficient. In particular, the mortality rate of BO following BMT is high, and lung transplantation is indicated in some patients with BO following BMT [3]. ALS, including pneumothorax, mediastinal emphysema, and subcutaneous emphysema, is a rare complication after BMT, occurring in 1.2–2.3% of cases [4]. ALS usually occurs in patients with BO due to the obstruction of terminal bronchioles [5]. The survival rate of patients

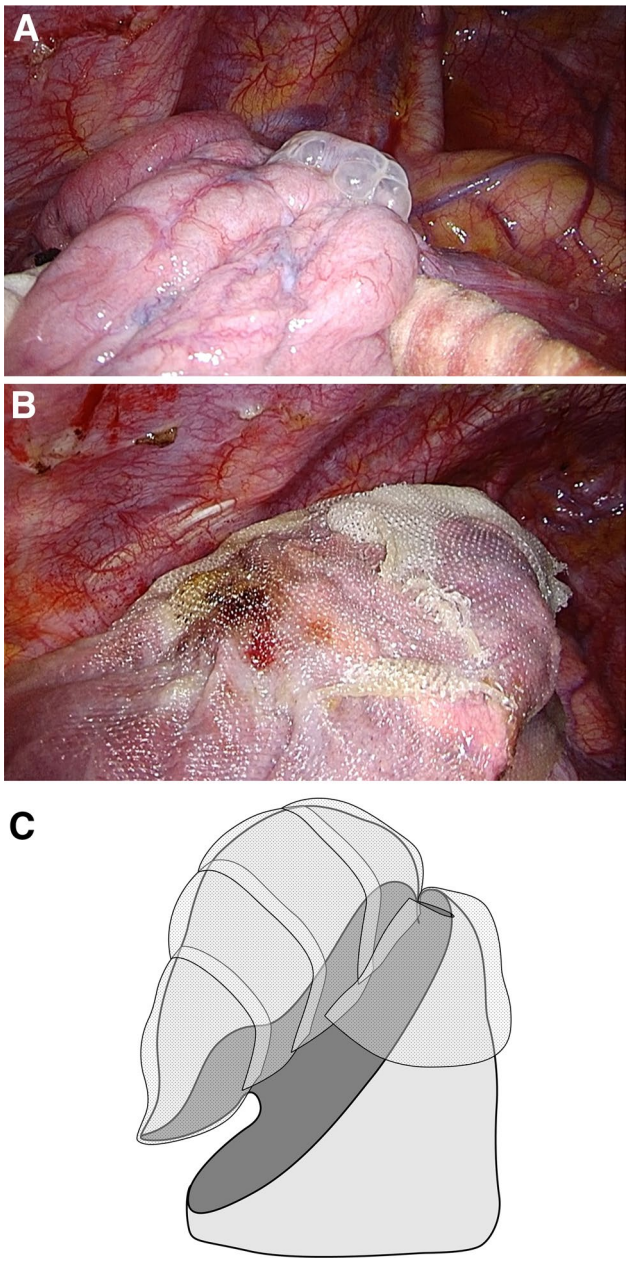

Fig. 3 Operative findings of the left lung via VATS. **a** A thin-walled bulla was present. Small bullae were also found at the interlobar and mediastinal surfaces of the left upper lobe and segment 6. **b** After the bullae were resected and the harvested fat pad was attached at the staple line with fibrin glue, most of the visceral pleura of the left upper lobe and segment 6 were covered with regenerated ORC mesh and fibrin glue. **c** Schema of operative findings. The left upper lobe and segment 6 were covered with five ORC mesh sheets and fibrin glue in case1

after the occurrence of ALS is extremely poor, with a 3-year survival rate of 18.2% [4].

The optimum method of treating ALS is controversial. Although bullectomy and pleurodesis are conventional treatment methods for pneumothorax, these procedures often fail.

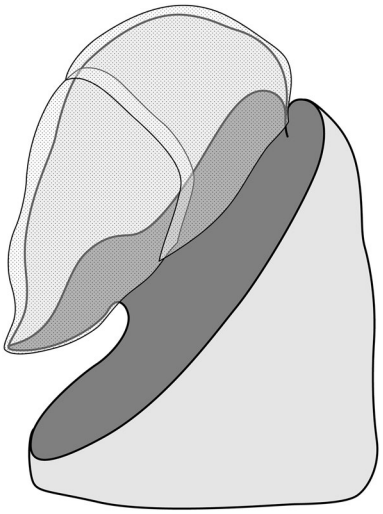

Fig. 4 Schema of operative findings. The left upper lobe was subsequently covered with two ORC mesh in case2

In fact, in the present case one, right-sided pneumothorax recurred after bullectomy. At the initial surgery, we performed apical bullae resection alone and did not protect the remaining visceral pleura because we did not find any other bullae. However, at the following surgery, fragile bullae that had not been detected at the previous surgery were present at the apex of segment 6. Given our experience, we believe that not only resection of the bullae but also the protection of fragile visceral pleura in ALS patient should be taken into account at surgery.

Besides surgery, chemical pleurodesis is frequently chosen for ALS because patients with ALS usually have a poor general condition. Chemical pleurodesis, however, has some disadvantages. First, the chemical agents used for pleurodesis carry serious risks, such as tissue injury and irreversible damage. Second, chemical pleurodesis causes severe adhesion of the pleural cavity. Such adhesion is particularly harmful for BO patients, who may eventually be indicated for lung transplantation. Severe adhesion in the pleural cavity increases the bleeding and prolongs the operation time in lung transplantation surgery, especially when extracorporeal circulation and anti-coagulant use is needed, and such a situation can become critical [6].

In this clinical context, a more suitable method with a low recurrence rate is required for treatment of ALS. The novel surgical procedure of total pleural covering (TPC) was recently established by Kurihara et al. [1] TPC is a surgical procedure used for pleural enforcement of the entire lung to prevent and control pneumothorax and pleural adhesion using an ORC mesh. In their animal experiments, they showed that covering tissue with ORC prevents long-term foreign body reactions and adhesion at the surgical site and also strengthens the visceral pleura by thickening [7]. Regarding the clinical data, 43 patients with lymphangiomyomatosis (LAM) were treated

with TPC, and this procedure successfully prevented the recurrence of pneumothorax in these patients, was minimally invasive, and rarely caused restrictive ventilatory impairment [7].

Our experiences suggest that the pleural covering technique is a suitable procedure for not only LAM but also ALS after BMT, as both diseases share common features, i.e., the potential need for lung transplantation and reinforcement of the visceral pleura.

Conclusion

We experienced two cases of ALS after BMT successfully treated by the pleural covering technique. This technique may be a viable treatment option for patients with ALS after BMT, as it provides reinforcement to the visceral pleura and helps prevent pleural adhesion, which is beneficial for future lung transplantation.

Compliance with ethical standards

Conflict of interest The authors have no conflicts of interest to declare.

Ethical approval The study protocol was approved by the Ethical Review Board for Clinical Studies at Osaka University (control number 10026-3).

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