Internal Medicine
The Japanese Society of Internal Medicine
doi: 10.2169/internalmedicine.8965-17
Intern Med 57: 75-79, 2018
http://internmed.jp

【 CASE REPORT 】

Usefulness of Bronchial Thermoplasty for Patients with a Deteriorating Lung Function

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Abstract:
Bronchial thermoplasty is a novel procedure for patients with severe asthma showing a stable lung function. We herein report two cases with a deteriorating lung function. The lung function tended to improve in one case, while the other case discontinued mepolizumab medication after the procedure. Treatment was performed safely under general anesthesia in both cases. The use of bronchial thermoplasty may therefore be useful for the treatment of patients with a deteriorating lung function.

Key words: bronchial thermoplasty (BT), deterioration of lung function, severe asthma

(Intern Med 57: 75-79, 2018)
(DOI: 10.2169/internalmedicine.8965-17)

Introduction

Bronchial thermoplasty (BT) is a technique in which radiofrequency ablation is applied sequentially to the peripheral sub-segmental airways (1, 2). BT reduces this airway smooth muscle mass by applying radiofrequency energy to large airways (3). Three major trials have supported the utility of BT as a safe modality to reduce exacerbation and improve the quality of life in patients with uncontrolled asthma (4-6). Although BT is generally performed under topical anesthesia and sedation in patients with a stable lung function, general anesthesia is needed in patients unable to cooperate or when unstable vital signs are expected (3). We herein present the effectiveness of BT under general anesthesia in two cases with a deteriorating lung function. The lung function tended to improve after BT in one case, while mepolizumab medication was discontinued in the other case following the procedure.

Case Reports

Case 1

A 70-year-old woman presented with a history of refractory asthma for 5 years. She was treated with inhaled corticosteroids (ICS), long-acting beta-agonist (LABA), long-acting muscarinic antagonist (LAMA), and antiallergic drug therapy. She had sometimes been treated with oral or systemic corticosteroids for exertional dyspnea. However, these treatments were all found to be insufficient, and BT was therefore indicated.

On physical examination, her peripheral arterial blood oxygen saturation (SpO_2) was 96% in room air, but chest auscultation revealed diffuse expiratory wheezing. Computed tomography (CT) scans showed diffuse bronchial wall thickening and postinflammatory changes (Fig. 1A). Laboratory findings showed moderate leukocytosis with a left shift and an increase in the number of neutrophilic granulocytes. The levels of lymphocytes, monocytes, and eosinophilic granulocytes were relatively normal (Table 1). The patient's post-bronchodilator forced expiratory volume in 1.0 s (FEV_1) was 910 mL (%FEV_1; 49.4%) and vital capacity (VC) was 1,980 mL (%VC; 79.7%) in a pulmonary function test (Table 2).

BT was performed under general anesthesia because of a deteriorating lung function and patient anxiety. She received prednisone at 50 mg/day for the three days prior to the procedure, the day of the procedure, and the day after the procedure (Fig. 2). The airways were treated in three separate sessions, each 3 weeks apart: the right lower lobe was treated in the first session (32 activations), the left lower lobe in the second session (40 activations), and both upper

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Received: January 31, 2017; Accepted: May 8, 2017; Advance Publication by J-STAGE: October 16, 2017
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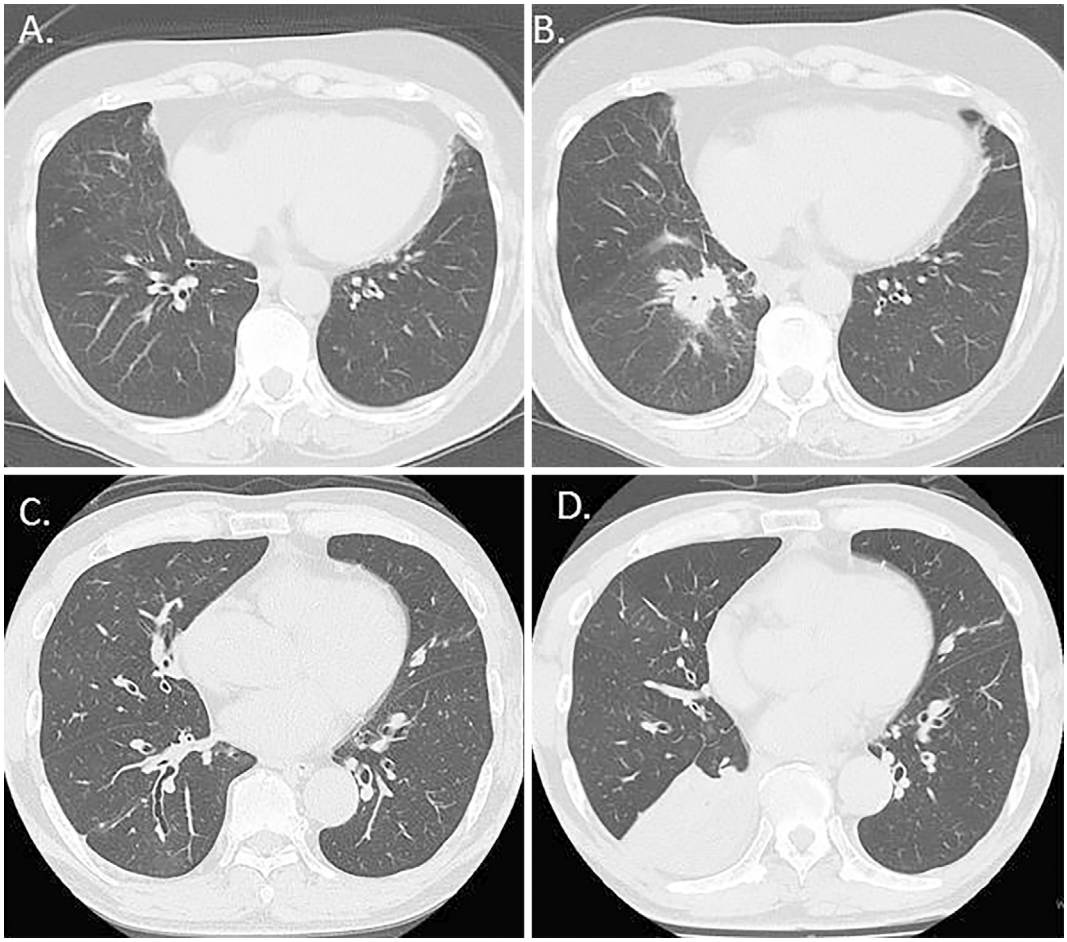

Figure 1. **A, B, C, and D: Lung window. A: Computed tomography scans showed diffuse bronchial wall thickening and postinflammatory changes. B: Pulmonary infiltration was observed after bronchial thermoplasty. C: Computed tomography scans revealed diffuse bronchial wall thickening. D: Pulmonary atelectasis was observed after bronchial thermoplasty.**

Table 1. **Laboratory Findings of the Two Cases.**

	Case 1	Case 2
Laboratory findings		
WBC (10^3/μL)	11.0	9.1
Neut (%)	77.5	75.5
Eosi (%)	1.0	0.2
Baso (%)	0.1	0.7
Mono (%)	7.8	6.2
Lymph (%)	13.6	17.4
C-reactive protein (mg/dL)	0.30	0.22
IgE (IU/mL)	155	455

WBC: white blood cells, Neut: neutrophilic granulocytes, Eosi: eosinophilic granulocytes, Baso: basophilic granulocytes, Mono: monophilic granulocytes, Lymph: lymphocytes, IgE: Immunoglobulin E

Table 2. **Pulmonary Function Test and AQLQ Score Findings in Case 1.**

Post-bronchodilator	Before BT	After BT
FEV_1(mL)	910	1,130
Expected FEV_1(mL)	1,840	1,800
%FEV_1(%)	49.4	62.8
VC (mL)	1,980	2,120
%VC (%)	79.7	86.4
AQLQ score	3.04	5.09

BT: Bronchial thermoplasty, FEV_1: Forced expiratory volume in 1.0 s, VC: Vital capacity, AQLQ: Asthma Quality of Life Questionnaire

Symptoms or pulmonary function was tended to improve 1 month after the procedure.

lobes in the final session (59 activations). The procedure was performed using flexible bronchoscopy (BF-260; Olympus, Tokyo, Japan) immediately and uneventfully under general anesthesia. Focal wheezing and pulmonary infiltration were observed (Fig. 1B), but the adverse effects disappeared within 1 week. The patient was treated with systemic corticosteroids (125 mg of methylprednisolone sodium succinate) for wheezing on the same day after the final procedure. Both the symptoms and pulmonary function tended to improve at 1 month after the procedure (Table 2). Exacerbations requiring corticosteroids were also significantly reduced. The pulmonary function also tended to improve after

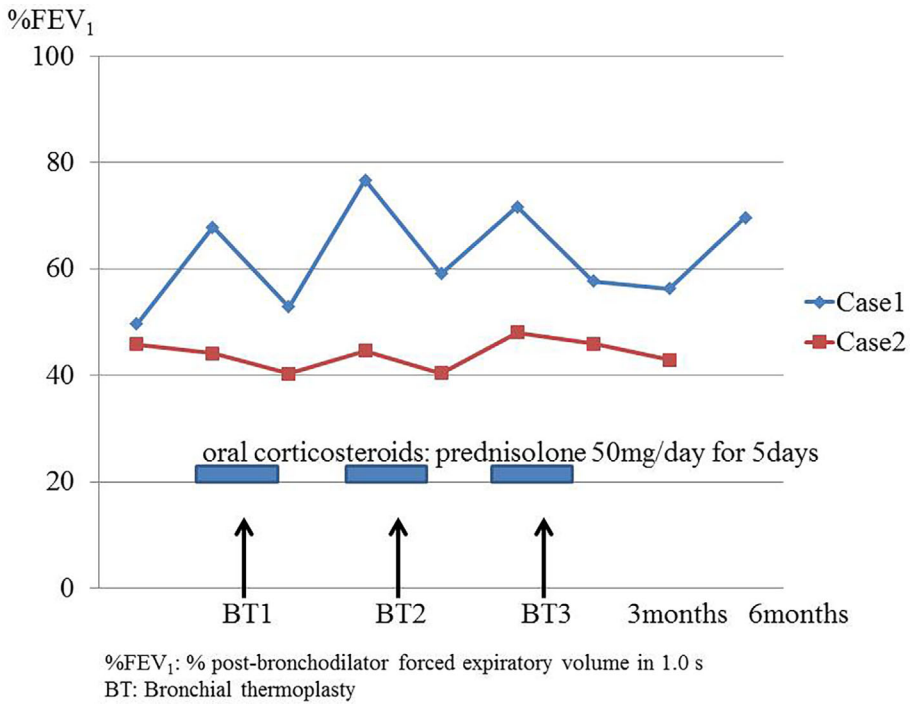

Figure 2. **Time course of %FEV$_1$ in two patients. The pulmonary function tended to improve after bronchial thermoplasty six months later in Case 1. A stable pulmonary function was observed after the procedure three months later in Case 2. The patients received prednisone at 50 mg/day for the three days prior to the procedure, the day of the procedure, and the day after the procedure.**

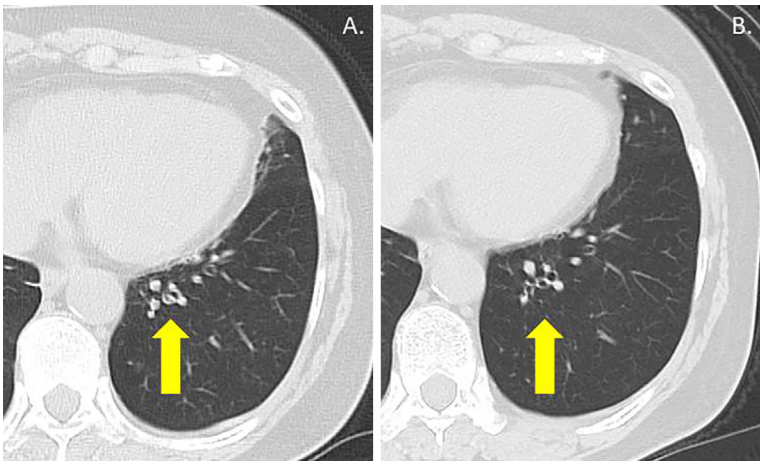

Figure 3. **A and B: Lung window. Computed tomography scans showing a regression of mucus secretion after bronchial thermoplasty six months after undergoing BT in Case 1.**

bronchial thermoplasty six months later. The patient's post-bronchodilator FEV$_1$ was 1,260 mL (%FEV$_1$; 69.6%) (Fig. 2). Clinical laboratory data such as the eosinophil counts and changes in the exhaled nitric oxide levels (FeNO) after the treatment did not improve six months later. FeNO was 125 ppb both before and after the treatment. The eosinophil counts changed from 110 to 115 after the treatment. Meanwhile, CT scans showed a regression of mucus secretion after bronchial thermoplasty six months later (Fig. 3).

Case 2

A 58-year-old man with refractory asthma had been treated with ICS, LABA, LAMA, and antiallergic drug therapy for 10 years. He had sometimes been treated with systemic or oral corticosteroids. Although omalizumab therapy was not effective, mepolizumab therapy was useful for his clinical symptoms, such as dry cough. He was regarded as being indicated for BT because of prolonged exertional dyspnea.

On physical examination, his vital signs were stable. His

Table 3. Pulmonary Function Test and AQLQ Score Findings in Case 2.

Post-bronchodilator	Before BT	After BT
FEV_1(mL)	1,500	1,480
Expected FEV_1(mL)	3,290	3,220
%FEV_1(%)	45.6	45.9
VC (mL)	3,450	3,540
%VC (%)	85.9	89.9
AQLQ score	5.06	5.71

BT: Bronchial thermoplasty, FEV_1: Forced expiratory volume in 1.0 s, VC: Vital capacity, AQLQ: Asthma Quality of Life Questionnaire

Improvement of symptoms was observed without mepolizumab medication 1 month after the procedure.

peripheral SpO_2 was 95% in room air. Chest auscultation revealed diffuse expiratory wheezing, but other systemic examinations did not reveal any significant abnormalities. Chest CT scans revealed diffuse bronchial wall thickening (Fig. 1C). Laboratory data showed moderate leukocytosis with a left shift, an increase in the number of neutrophilic granulocytes, and an abnormal C-reactive protein level. His immunoglobulin E level was 445.0 IU/mL (Table 1). All other data were mostly normal. The post-bronchodilator FEV_1 was 1,500 mL (%FEV_1; 45.6%) and VC was 3,450 mL (%VC; 85.9%) in a pulmonary function test. The post-bronchodilator FEV_1 before mepolizumab therapy (100 mg; subcutaneous injection) had been 1,150 mL (%FEV_1; 35.0%) 2 months previously.

Owing to a deteriorating lung function, suspicion of unstable vital signs during the procedure, and patient anxiety, BT was performed under general anesthesia. He received prednisone at 50 mg/day for the three days prior to the procedure, the day of the procedure, and the day after the procedure (Fig. 2). The right lower lobe was treated in the first session (30 activations), the left lower lobe in the second session (33 activations), and both upper lobes in the final session (52 activations). The procedure was performed using flexible bronchoscopy (BF-260) uneventfully. Focal wheezing in all sessions and pulmonary atelectasis in the first session were observed (Fig. 1D), but the adverse effects disappeared within 1 week. He was treated with antibiotics (2 g of ceftriaxone per day in the first session and 100 mg of sitafloxacin hydrate per day in the other sessions for 4 days) for bronchopneumonia. Improvements of symptoms and stable pulmonary function were observed 1 and 3 month after the procedure (Table 3, Fig. 2). The eosinophil counts changed from 18 to 561 after the treatment three months later. Meanwhile, FeNO changed from 35 to 30 after the treatment three months later. Mepolizumab was successfully discontinued following the procedure for three months.

Discussion

BT is usually recommended in patients with baseline FEV_1 ≥65% predicted to be able to cooperate or when stable vital signs are expected during the procedure (3-6). However, Langton reported that some patients with a predicted baseline FEV_1 of <60% showed a significantly improved FEV_1 (7). In Case 1, FEV_1 tended to improve from 910 mL (%FEV_1 49.4%) to 1,130 mL (%FEV_1 62.8%) after the procedure. In both cases described herein, the procedure was performed immediately and uneventfully under general anesthesia. General anesthesia during the procedure may be useful in patients with a deteriorating lung function. In addition, the adequate and effective administration of sedatives and analgesics to achieve and maintain moderate or conscious sedation is generally important to successfully perform BT procedures according to a previous report. Midazolam and fentanyl are currently recommended and are excellent choices because of their familiarity, ability to be carefully titrated, and if necessary, to be rapidly reversed (8). In this report, pulmonary atelectasis in the first session was observed under general anesthesia in Case 2. It is unclear whether general anesthesia is preferable to topical (venous) anesthesia in patients with a low lung function owing to an increased risk of CO_2 narcosis and complications including severe atelectasis. Therefore, a further large scale study is needed to clarify this point.

Mepolizumab medication was successfully discontinued following the procedure for three months in Case 2. Mepolizumab blocks human IL-5 from binding to the IL-5 receptor and is effective for eosinophilic asthma (9, 10). This treatment was approved by the US Food and Drug Administration (FDA) in 2015 and has been widely used in Japan since 2016. In Case 2, FEV_1 improved from 1,150 mL (%FEV_1 35.0%) to 1,500 mL (%FEV_1 45.6%) after medication with mepolizumab, and the procedure was performed uneventfully under general anesthesia. As current therapies including monoclonal antibody treatments are too expensive for severe asthma patients (11), BT could thus become a cost-effective means of standard therapy in such cases.

BT was approved by the FDA in 2010 for the treatment of refractory asthma. Recently, many clinical trials have yielded new insights into the histopathological changes that occur in the airways following BT, as well as the feasibility of performing BT (12). However, there have been few reports outside of clinical trials regarding patient selection and the outcomes achieved (7). This case report presented the results of two patients with a deteriorating lung function who safely and effectively underwent BT under general anesthesia. Prospective studies are needed to improve the levels of safety and patient satisfaction associated with this procedure. The performance of BT may therefore be useful in patients with severe asthma.

The authors state that they have no Conflict of Interest (COI).

Acknowledgement

We thank Drs. Narumi Kariya and Azusa Hayashi for performing the bronchoscopic examinations and for their helpful discussions.

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