

TREATMENT

Bronchial Thermoplasty: Therapeutic Success in Severe Asthma Associated with Persistent Airflow Obstruction

AMIT K. MAHAJAN, M.D. AND D. KYLE HOGARTH, M.D., F.C.C.P.*

Department of Pulmonary and Critical Care Medicine, University of Chicago Medical Center, Chicago, IL, USA.

Introduction. Severe persistent asthma is a disabling condition associated with significant morbidity and rising mortality worldwide. The recent advent of bronchial thermoplasty (BT) has offered a revolutionary therapeutic option for the treatment of severe persistent asthma. This minimally invasive bronchoscopic procedure focuses on anatomical manipulation of bronchial smooth muscle to attenuate airway hyperresponsiveness. **Case report.** This case report describes treatment of a 42-year-old female with BT for her debilitating asthma. Following a complicated treatment course of BT, she attained significant relief from her symptoms and had noticeably improved functionality. **Conclusion.** This case represents BT success and a change to the traditional paradigm governing the treatment of refractory asthma.

Keywords asthma, bronchial thermoplasty

INTRODUCTION

Severe persistent asthma is a disabling condition involving a constellation of airway inflammation and smooth muscle bronchoconstriction. Asthma is associated with significant morbidity and rising mortality worldwide. The recent advent of bronchial thermoplasty (BT) offers a new treatment option for individuals suffering from severe persistent asthma. During BT, radiofrequency ablation is directed toward airways distal to the mainstem bronchi. This therapy serves to reduce bronchial smooth muscle mass by thinning airway muscle fibers without actually burning tissue (1). Following BT, airway smooth muscle hyperresponsiveness and bronchoconstriction are attenuated resulting in reduced exacerbation frequency and severity. This case report describes a 42-year-old female with debilitating asthma despite appropriate medical therapy and demonstrates that the use of BT is a safe and effective therapeutic option for the treatment of severe persistent asthma.

CASE REPORT

The patient is a 42-year-old South Asian female with a history of severe persistent asthma diagnosed at 2 years of age. She endorsed a number of asthma triggers, including respiratory infections and exposure to irritants such as cigarette smoke, polluted air, dust, mold, and pollen. She described shortness of breath on mild exertion and found it difficult to perform regular activities of daily living, including childcare. The patient's Asthma Control Questionnaire (ACQ) score was 14. The patient was never a smoker and had a history of eczema in addition to recurrent sinus infections. She also endorsed allergies to sulfa drugs, toradol, and reglan. Formal pulmonary

function tests prior to presentation revealed a forced expiratory volume in 1 second (FEV1) of 0.95 liters and a forced vital capacity (FVC) of 1.72 liters. She exhibited persistent airway obstruction with an FEV1 to FVC ratio of 55%. The patient was compliant with asthma therapy which entailed 500 mg of inhaled fluticasone twice daily in conjunction with a long-acting beta-agonist and montelukast. She was also receiving tiotropium, antihistamines, and a rescue short-acting beta-agonist. The patient was unable to tolerate oral corticosteroids due to the dysphoria and suicidal ideations she experienced when taking this medication. Additionally, she was treated with the monoclonal antibody omalizumab and off-label use of a statin for her asthma. Despite these treatments, she suffered from asthma exacerbations requiring either visitation to a physician's office or hospital admission approximately every 2.5 months.

The patient's first treatment with BT was performed on the right lower lobe and involved 23 tissue actuations. The procedure was performed without immediate complication. Her outpatient spirometry obtained in clinic 1 month prior to BT showed an FEV1 of 1.06 liters or 36% of predicted. Two days following the first session of BT she experienced worsening shortness of breath refractory to hourly nebulized albuterol. The patient was admitted to the medical intensive care unit (MICU) for observation and was discharged home shortly after treatment with inhaled bronchodilators with a course of azithromycin. The patient again required hospitalization following her second treatment of BT targeting the left lower lobe 3 weeks later. This treatment involved 40 tissue actuations and was complicated by partial atelectasis of the treated left lower lobe on a post-procedural chest radiograph. The partial collapse was thought to be secondary to mucus plugging. She was observed on the general medicine service for 2 days and discharged home on nebulized budesonide. The patient's final BT treatment was performed 4 weeks later. This time,

*Corresponding author: D. Kyle Hogarth, M.D., F.C.C.P., Department of Pulmonary and Critical Care Medicine, University of Chicago Medical Center, 5841 South Maryland, MC 6076, Chicago, IL 60637, USA; Tel: 773-702-4773; Fax: 773-702-6500; E-mail: dhogarth@uchicago.edu

both the right upper lobe and the left upper lobe were treated, requiring a combined total of 41 tissue actuations. Following this treatment she again complained of dyspnea with associated wheezing following the procedure. She was admitted to the MICU and treated with continuous nebulized albuterol in addition to 80 mg of oral prednisone, understanding her history of psychiatric complications with oral corticosteroids use. She improved significantly over 2 days and was discharged home.

Six months following completion of BT the patient was seen in clinic for follow-up. She was doing well from a respiratory perspective. She claimed to be more active, less fatigued, and capable of completing activities of daily living without shortness of breath. She considered her life to be much more fulfilling. She was able to begin pulmonary rehab as well, a treatment option she was incapable of attempting in the past due to shortness of breath on exertion. Her spirometry reflected a slight drop in pulmonary function compared to measurements made prior to BT, with an FEV1 of 0.96 liters or 32% predicted. Despite the drop in her pulmonary function she was less dyspneic and had a significant improvement in her quality of life.

DISCUSSION

BT is a novel and effective therapeutic option for patients with severe persistent asthma. While the triggers for asthma are a complex orchestra of environmental and physiologic factors, smooth muscle mass remains a central concern in all severe asthmatics. Individuals suffering from severe or fatal asthma often have increased airway smooth muscle mass (2). Higher deposition of smooth muscle within airway submucosa, increased expression of contractile proteins, and amplified activation of smooth muscle contractile units likely contribute to the extreme airway hyperresponsiveness and bronchoconstriction witnessed in severe and fatal asthma (2). Because of the prevailing evidence of increased airway smooth muscle mass-associated hyperresponsiveness in patients with severe persistent asthma, BT was the rational therapy for the featured patient.

While the conventional approach for assessing asthma therapeutic effectiveness has relied on changes in pulmonary function, namely FEV1, a number of alternative benchmarks have attracted attention for evaluating clinical success. Exacerbation frequency, morning peak flow, percentage of symptom-free days, and improvement in quality of life are becoming important markers for judging therapeutic success. Cox et al. described outcomes in 52 patients undergoing a full course of BT. While values for airway responsiveness and FEV1 did not differ significantly between the BT group and the control group, there was a significant reduction in the mean rates of mild exacerbations from baseline at 12-month follow-up. Additionally, there were significant improvements in morning peak expiratory flow, scores on the Asthma Quality of Life Questionnaire and ACQ, the percentage of symptom-free days, and fewer puffs of rescue medication requirements (3). Similarly, while our patient did not show improvement in her FEV1 6 months following BT,

she did experience an improved quality of life, increased functionality, and fewer exacerbations.

While improvement in FEV1 cannot always be used to judge therapeutic success, spirometry can be telling of disease severity. Our patient's significantly reduced pulmonary function represents severe disease and poor response to medical therapy. Our patient's FEV1 was severely reduced to 36% prior to BT and declined further following therapy despite an improvement in functionality. Her pulmonary function would have excluded her from many of the sentinel BT trials. The Effectiveness and Safety of Bronchial Thermoplasty in the Treatment of Severe Asthma Trial conducted by the Asthma Intervention Research 2 (AIR2) Trial study group included patients with a prebronchodilator response >60% of predicted (4). Life-threatening asthma was a key exclusion criterion in the trial. Our patient's symptomatic improvement despite her severely reduced FEV1 shows that treatment with BT is a realistic intervention in patients with life-threatening asthma, despite her inability to have been included in the AIR2 trial.

Although BT is considered a minimally invasive procedure, short- and intermediate-term complications are not surprising. Cox et al. also described 407 adverse respiratory events in 52 patients following a complete course of BT, with dyspnea being the most common complication. Of the 407 events recorded, 69% were considered mild, 28% were considered moderate, and 3% were considered severe. In the BT group, the majority of adverse events occurred within 1 day after the procedure and resolved an average of 7 days after the onset of the event. Additionally, hospitalizations for adverse respiratory events during the treatment period were more frequent in the BT group than in the control group (3).

CONCLUSION

BT is a procedure that has the potential to radically alter the traditional paradigm governing the treatment of severe asthma. Long-term outcomes have yet to be assessed due to the procedure's relative infancy. Although BT harbors a prolonged treatment course with possibility of temporary worsening of respiratory symptoms during therapy, the potential benefits are dramatic and unmistakable. While this is a minimally invasive procedure, it should be understood that post-procedural asthma exacerbations can occur and clinicians should have a low threshold for monitoring patients in a hospital setting following BT. Patients who understand the potential risks and benefits of BT for severe persistent asthma will undoubtedly recognize that this procedure has the capabilities of providing much needed control over an unrelenting disease.

DECLARATION OF INTEREST

Dr. Hogarth wishes to declare an honorarium for lectures on behalf of Boston Scientific. Additionally, he organized an unrestricted CME thermoplasty course at the University of Chicago Medical Center. He also participated in the

Asthma Intervention Research 2 (AIR2) Trial and Bronchial Thermoplasty in Severe Persistent Asthma (PAS2) trial.

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