Respiratory Medicine Case Reports 34 (2021) 101554

Contents lists available at ScienceDirect

Respiratory Medicine Case Reports

journal homepage: www.elsevier.com/locate/rmcr

Endobronchial valve placement in secondary pneumothorax related to allergic bronchopulmonary aspergillosis

Deepa Ramadurai [a,*], David M. DiBardino [b], Gina Hong [a]

[a] Division of Pulmonary, Allergy, and Critical Care Medicine, University of Pennsylvania, Philadelphia, PA, USA
[b] Section of Interventional Pulmonology and Thoracic Oncology, Division of Pulmonary, Allergy, and Critical Care Medicine, University of Pennsylvania, Philadelphia, PA, USA

ARTICLE INFO

Keywords:
Allergic bronchopulmonary aspergillosis
Bronchopleural fistula management
Sendobronchial valve placement
Persistent air leak management
Secondary pneumothorax management

ABSTRACT

Secondary pneumothorax is a rare but serious complication of allergic bronchopulmonary aspergillosis (ABPA) and bronchiectasis [1,2]. Persistent air leak (PAL) after secondary pneumothorax is an ongoing abnormal communication between bronchi or alveoli and the pleural space, despite drainage. Ongoing PAL for 5 days after initial chest tube insertion necessitates prolonged ambulatory drainage or aggressive management with video-assisted thoracoscopic surgery (VATS) or pleurodesis [3,4]. There are no randomized trials examining the efficacy of endobronchial valves (EBVs) for PAL with underlying inflammatory pulmonary disease. We describe the successful use of an EBV for PAL in a man with ABPA on high dose steroids, with a large bronchopleural fistula (BPF).

1. Introduction

ABPA is a disorder characterized by a hypersensitivity reaction to *Aspergillus fumigatus* almost exclusively in patients with underlying asthma or cystic fibrosis [1,2,5]. Patients typically experience mucoid impaction of the bronchi with or without eosinophilic pneumonia, and serologic evidence of hypersensitivity (elevated immunoglobulin E [IgE] or positive skin allergen testing) to *Aspergillus*. Rarely, erosion from infected parenchyma to visceral pleura occurs in ABPA when complicated by pneumothorax, and can result in a BPF. EBV have demonstrated efficacy in PAL management post-pneumonectomy, lobectomy, and after lung volume reduction surgery, by occluding airflow into the pleural space through a BPF [6,7], however data is limited in infectious and inflammatory PAL. We report the case of a young man with ABPA complicated by bronchiectasis and copious mucopurulent secretions on prednisone in whom EBV was successfully utilized for management of PAL.

2. Case presentation

A 31-year-old man with a history of asthma presented after two months of progressive cough, fevers, and night sweats. Computed tomography of the chest revealed tubular branching opacities in the left lung. Based upon the presence of peripheral eosinophilia (absolute eosinophil count 740), serum IgE >5000 kU/L, and elevated *Aspergillus* specific IgE (13.9 kU/L), a diagnosis of ABPA was made. The patient underwent bronchoscopy revealing severe airway casting. Bronchoalveolar lavage (BAL) was positive for *Aspergillus* galactomannan antigen (optical density index [ODI] 4.85), and cultures grew *Aspergillus fumigatus* group and *Aspergillus flavus*. Serum galactomannan antigen was negative with an ODI of 0.06 (normal <0.5). Prednisone 60 mg daily and oral itraconazole were initiated. Two weeks later, at routine follow-up, decreased breath sounds in the left hemithorax were noted. Chest x-ray revealed a large pneumothorax with rightward mediastinal shift, and he was admitted to the hospital (Fig. 1A). A 16 French small-bore chest tube was successfully placed with partial lung re-expansion and discovery of a large PAL throughout the respiratory cycle. A repeat computed tomography of the chest revealed evidence of a substantial pleural defect representative of the site of a BPF in the left lower lobe (Fig. 1B). Despite reduction of prednisone, the BPF persisted. The patient could not tolerate less than −20 cm H_2O suction without worsening lung collapse, chest pain and dyspnea. Given the concerns for underlying wound healing on high doses of prednisone and possible fungal infection, VATS was deferred. The patient underwent bronchoscopy on hospital day 8. Using a 5 French Fogarty balloon, occlusion of the superior segment of the left lower lobe resulted in abrupt cessation of the PAL that was sustained during breath holds of 30 cmH_20 pressure. A

* Corresponding author. Pulmonary and Critical Care Medicine Harron Lung Center 3400 Civic Center Blvd, Perelman Center, 1st Floor West Philadelphia, PA, 19104.
E-mail address: Deepa.Ramadurai@pennmedicine.upenn.edu (D. Ramadurai).

https://doi.org/10.1016/j.rmcr.2021.101554
Received 8 September 2021; Received in revised form 5 October 2021; Accepted 8 November 2021
Available online 10 November 2021

Abbreviations

ABPA	Allergic bronchopulmonary aspergillosis
PAL	Persistent air leak
VATS	Video-assisted thorascopic surgery
EBV	Endobronchial valve
BPF	Bronchopleural fistula
IgE	Immunoglobulin E
LOS	Length of stay

Spiration size 5 EBV was deployed into the superior segment. A small pneumothorax remained on chest imaging post-bronchoscopy (Fig. 1C). Although there was significant clinical improvement, a small residual PAL remained resulting in the inability to remove the chest tube. Therefore, a Heimlich valve was placed on hospital day 9 prior to discharge.

The patient was seen weekly in outpatient clinic after discharge. After seventeen days, the pneumothorax had resolved, and the chest tube was clamped. The following day, the pneumothorax remained absent on chest x-ray and the chest tube was pulled. One month after chest tube removal, his EBV was removed (Fig. 2). Bronchoalveolar lavage of left lower lobe at the time of EBV removal was negative for fungus. He had complete resolution of his left pneumothorax (Fig. 1D). Prednisone was weaned slowly while azole therapy was maintained, His symptoms remain well-controlled six months later. Spirometry shows forced expiratory volume in 1 second is 3.54 L (75% of predicted) and forced vital capacity 4.79 L (83% predicted). He is now off prednisone and antifungals, maintained on an inhaled corticosteroid and dupilumab.

3. Discussion

Although rare, secondary pneumothorax is a serious complication of ABPA with varying clinical severity and significant morbidity. To our knowledge, there are three case reports of secondary pneumothorax in ABPA, with limited discussion of mechanism and general management strategies, and therefore the epidemiologic considerations are limited [1,2,8]. Pneumothorax is, however, recognized as a complication of cystic fibrosis, where *Aspergillus* infection and ABPA are known risk factors for this specific complication [9]. One large, retrospective observational cohort study of 28,858 patients with cystic fibrosis found *Aspergillus* and ABPA was associated with increased risk of pneumothorax, with odds ratios of 1.3 and 1.5 respectively [10]. Ours is the first case report to explore a unique, minimally invasive approach utilizing EBV placement to promote healing of a BPF in ABPA.

The efficacy of EBVs in infectious or inflammatory PAL is uncertain. EBVs were approved for use in post-operative PAL through a Humanitarian Device Exemption (HDE) from the Food and Drug Administration after case report data demonstrated a reduction in hospital length of stay (LOS) and associated complications [3,4,11,12]. Notably, the HDE is intended for temporary valve use (roughly 6 weeks) in conditions where the visceral pleura will in fact heal. However, the resistance to mucous drainage presents a concern when extrapolating this post-surgical experience to other conditions. This case report is limited in that it is applicable primarily to patients with underlying inflammatory lung

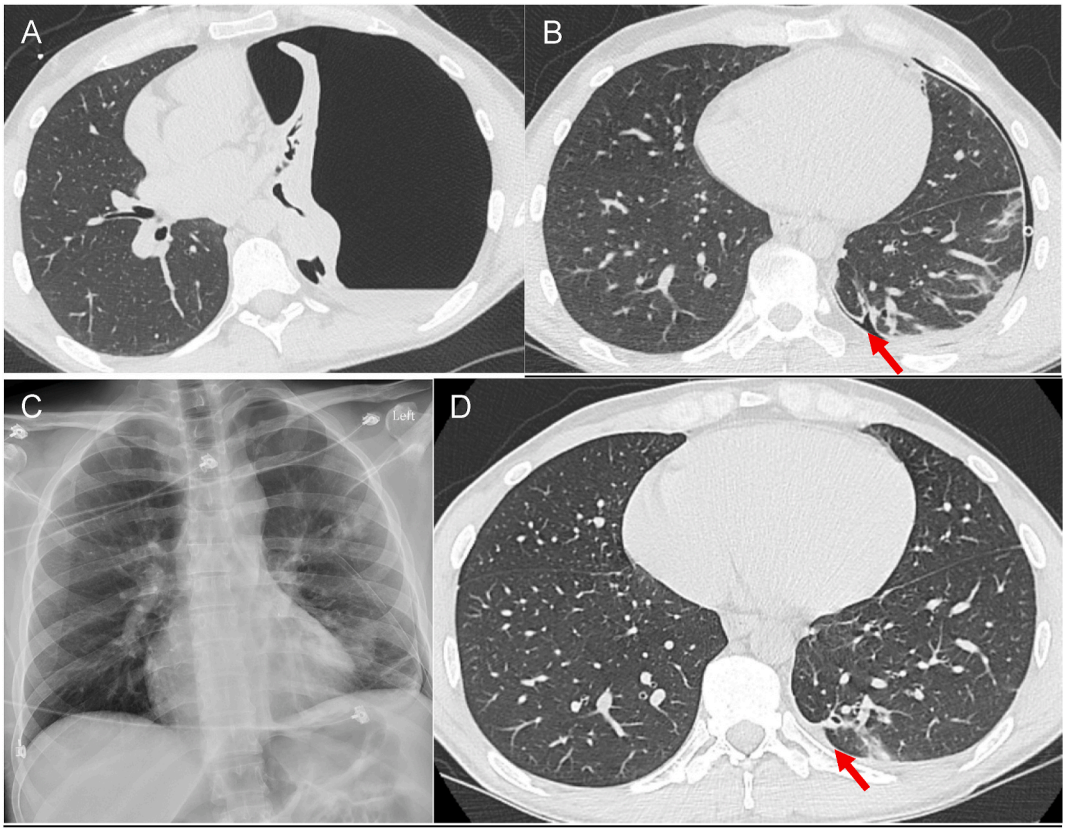

Fig. 1. A) Computed tomography of the chest demonstrating a large left pneumothorax with rightward mediastinal shift and a small left pleural effusion. B) Axial computed tomography of the chest demonstrating a bronchopleural fistula (BPF) in the left lower lobe (red arrow). A chest tube remains in place with a small residual pneumothorax. C) Chest x-ray following endobronchial valve placement on hospital day 8. D) Computed tomography of the chest obtained three months following hospital discharge and six weeks following endobronchial valve removal, demonstrating cystic bronchiectasis in the left lung with significantly improved bronchial impaction of the left lower lobe and BPF resolution (red arrow). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

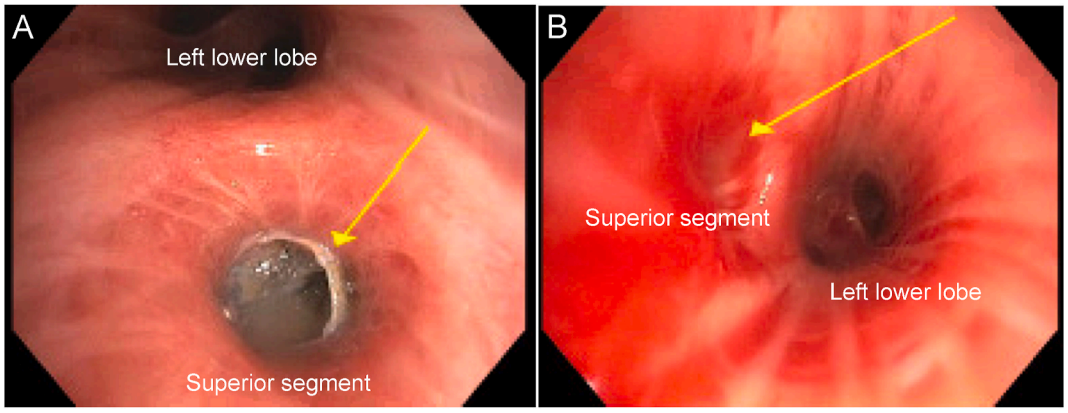

Fig. 2. Bronchoscopy images from endobronchial valve removal one month after chest tube removal. A) The yellow arrow identifies the endobronchial valve in place in the superior segment of the left lower lobe. B) The yellow arrow points to the superior segment of the left lower lobe after removal of the endobronchial valve. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

disease (such as bronchiectasis) with subsequent secondary pneumothorax. The young age and lack of comorbidities of the patient in this case also may limit the application to an older population with more comorbidities. When selecting a patient for possible EBV with an underlying suppurative or inflammatory condition, weighing risks and benefits closely and ensuring close outpatient follow-up are crucial.

Few case reports and prospective case series have examined EBVs for PAL outside of pulmonary surgery. A small prospective study by Reed et al. in the Annals of Thoracic Surgery discussed the use of EBVs for PAL in 21 medically complex patients, 11 of whom had primary or secondary pneumothoraces, including 3 with cavitary lung infections and 1 with rheumatoid lung disease. Of these 11 patients, 10 survived with a median LOS after valve placement of 5 days and successful chest tube removal at 15 days. Another case series by Gillespie et al. outlined the treatment of 7 patients with PAF, one of whom had a history of rheumatoid arthritis complicated by cavitary aspergillosis with pleural involvement with recent VATS. PAL improved immediately amongst all 7 patients. LOS was prolonged in the patient with cavitary aspergillosis. The largest case series by Arjan and colleagues describes the use of 101 EBVs in 19 patients with secondary pneumothoraces due to infection. Chest tubes were removed without additional intervention in 86.4% with only 15.8% mortality. These cases substantiate the claim that EBV use in suppurative lung disease should be considered in cases of prohibitive surgical risk.

The Spiration Valves Against Standard Therapy trial is currently underway, and expected to provide multicenter, randomized controlled data on the Spiration Valve System in PAL management, although this trial will exclude patients with sepsis, pneumonia, and acute respiratory distress syndrome. Future studies are needed to prospectively assess the efficacy of EBVs specifically in immunosuppressed patients with infectious BPFs.

Alternatives to EBV placement for PAL include stent jailing or metal coils. These options present a problem with infectious PAL given the concern for worsening post-obstructive inflammation and parenchymal destruction. With a one-way EBV, there is still capacity to empty the distal airways. Various sealants have also been described for use, but with variable success. Alcohol sclerosis and laser use are additional alternatives, for which literature on utility is limited [4].

From the patient perspective, the placement of an EBV reduced the length of hospital stay and allowed for resumption of daily activities and mobility sooner than ongoing chest tube management or VATS, as he was discharged the day after EBV placement. This improvement in quality of life with a minimally invasive procedure was especially important as a patient-centered outcome. Our case outlines the successful use of an EBV in PAL for a patient with underlying bronchiectatic lung disease, copious secretions from ABPA on concurrent high dose steroids, and a very large BPF.

4. Conclusion

- Despite plausible reasons for EBV failure including underlying inflammatory lung disease, significant secretion burden, and immunosuppression, visceral pleura healing can occur with the use of EBV in PAL without exacerbating mucoid impaction in lieu of surgery.
- The use of EBV may be able to decrease the hospital LOS for individuals with significant medical comorbidities and PAL with underlying inflammatory lung disease, which is an important metric to consider for future therapy assessment in complex PAL.
- When PAL is a complication of secondary pneumothorax with underlying inflammatory or infectious lung disease, multidisciplinary discussion should include the option of EBV placement.

Ethics approval and consent to participate

N/A.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

Availability of data and materials

N/A

Funding

None.

Authors' contributions

DR, DD, and GH all equally contributed to the manuscript conceptualization and design. DR performed data collection. DR, DD, and GH all contributed to the interpretation of results, manuscript preparation, and approve of the final version of the manuscript. All authors are ultimately responsible for the content of the manuscript as presented.

Declaration of competing interest

The authors declare that they have no competing interests.

Acknowledgements

Dr. Gina Hong is an Assistant Professor in the Division of Pulmonary and Critical Care at the Hospital of the University of Pennsylvania, where her practice and research focuses on the treatment of patients with cystic fibrosis and bronchiectasis. Dr. David DiBardino is an Assistant Professor in the Division of Pulmonary and Critical Care and Section of Interventional Pulmonology at the Hospital of the University of Pennsylvania.

References

[1] M.A. Judson, C. Marshall, G. Beale, J.B. Holt, Pneumothorax and bronchopleural fistula during treatment of allergic bronchopulmonary aspergillosis, *South Med J*. Sep 86 (9) (1993) 1061–1063, https://doi.org/10.1097/00007611-199309000-00019.

[2] A.J. Ricketti, P.A. Greenberger, J. Glassroth, Spontaneous pneumothorax in allergic bronchopulmonary aspergillosis, *Arch Intern Med*. Jan 144 (1) (1984) 151–152.

[3] J.M. Travaline, R.J. McKenna Jr., T. De Giacomo, et al., Treatment of persistent pulmonary air leaks using endobronchial valves, *Chest*. Aug 136 (2) (2009) 355–360, https://doi.org/10.1378/chest.08-2389.

[4] K.C. Dugan, B. Laxmanan, S. Murgu, D.K. Hogarth, Management of persistent air leaks, *Chest*. Aug 152 (2) (2017) 417–423, https://doi.org/10.1016/j.chest.2017.02.020.

[5] R. Agarwal, Allergic Bronchopulmonary Aspergillosis. *Chest*. Mar 135 (3) (2009) 805–826, https://doi.org/10.1378/chest.08-2586.

[6] A.K. Mahajan, S.J. Khandhar, Bronchoscopic valves for prolonged air leak: current status and technique, *J Thorac Dis*. Mar 9 (Suppl 2) (2017) S110–S115, https://doi.org/10.21037/jtd.2016.12.63.

[7] D.R. Lazarus, R.F. Casal, Persistent air leaks: a review with an emphasis on bronchoscopic management, *J Thorac Dis*. Nov 9 (11) (2017) 4660–4670, https://doi.org/10.21037/jtd.2017.10.122.

[8] T. Suri, N. Makkar, A. Ray, R. Sood, A unique case of hydropneumothorax in allergic bronchopulmonary aspergillosis, *Med Mycol Case Rep*. Sep 25 (2019) 29–31, https://doi.org/10.1016/j.mmcr.2019.07.003.

[9] I.P. Kioumis, K. Zarogoulidis, H. Huang, et al., Pneumothorax in cystic fibrosis, J. Thorac. Dis. 6 (Suppl 4) (Oct 2014) S480–S487, https://doi.org/10.3978/j.issn.2072-1439.2014.09.27.

[10] P.A. Flume, C. Strange, X. Ye, M. Ebeling, T. Hulsey, L.L. Clark, Pneumothorax in cystic fibrosis, *Chest*. Aug 128 (2) (2005) 720–728, https://doi.org/10.1378/chest.128.2.720.

[11] C.R. Gilbert, R.F. Casal, H.J. Lee, et al., Use of one-way intrabronchial valves in air leak management after tube thoracostomy drainage, Ann. Thorac. Surg. 101 (5) (May 2016) 1891–1896, https://doi.org/10.1016/j.athoracsur.2015.10.113.

[12] M. Schweigert, D. Kraus, J.H. Ficker, H.J. Stein, Closure of persisting air leaks in patients with severe pleural empyema–use of endoscopic one-way endobronchial valve, *Eur J Cardiothorac Surg*. Mar 39 (3) (2011) 401–403, https://doi.org/10.1016/j.ejcts.2010.07.004.