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Case report

Extracellular matrix fistula plug for repair of bronchopleural fistula

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ABSTRACT

Introduction: Bronchopleural fistula (BPF) is a feared complication of pulmonary resection. Fistula plugs (FP) have been described as an adequate treatment in anorectal disease. We describe our early experience placing an FP in the treatment of BPF.

Materials and methods: We retrospectively reviewed 5 patients for whom a FP was placed for BPF at our institution. Demographic data, initial perioperative information, method and technique of FP placement, and success is reported.

Results: Five patients (4 male, 1 female) with a median age of 63 years (range, 57–76 years) underwent 6 FP placements for BPF. Two patients were post-pneumonectomy and 3 patients post-lobectomy. The median time to presentation following surgery was 118 days (range 22–218). Upon bronchoscopic or operative re-evaluation, 3 patients had successful cessation of their air leak at 0, 1 and 4 days. Two of three patients subsequently underwent a thoracic muscle flap placement to augment healing. One patient had a persistent air leak despite 2 separate FP placements. The air leak stopped with endobronchial valves (EBV) which were deployed proximal to the FP, 9 days after placement of the FP. Another patient had a successful muscle flap placed 80 days after FP placement. There were no complications associated with the FP. Three of five patients were deemed successfully treated with FP placement alone.

Conclusion: In patients with a postoperative BPF and pleural window, placement of a FP had a modest success rate and can be considered as a treatment modality option for BPF.

1. Introduction

A dreaded complication of pulmonary resection is the development of a bronchopleural fistula (BPF), a communication between the bronchus and pleura. The reported incidence is between 1.5 and 28% for a pneumonectomy and about 0.5% for a lobectomy [1]. The mortality rate associated with BPFs ranges from 16–72% [1,2]. Complications associated with BPF are due to loss of sterility of the pleural space via direct communication with the non-sterile airway. BPF is associated with a higher morbidity and mortality, prolonged hospital stay, and higher resource utilization [3]. For these reasons, the swift diagnosis and treatment of BPF is important for patient outcomes.

Pulmonary physicians and thoracic surgeons are tasked with the challenge of treating BPF. Treatment has historically involved re-operation aimed at revisions and reinforcing the bronchial stump. The success rate of surgical closure of BPF has been reported between 80 and 95% [4]. Multiple various bronchoscopic approaches have been attempted as an alternative to surgery [3]. Success rates vary widely, and the lack of consensus suggests that no optimal therapy is currently available. Rather, the current interventions seem to be complementary and indicate that treatment should be individualized [3].

The placement of fistula plugs (FP) is well described in the treatment of anorectal disease [5–8]. For patients with a BPF and a pleural window, the placement of a FP can be used to treat the BPF. A combined bronchoscopic and surgical approach using a FP may serve as a viable alternative to surgery alone. We report our early experience looking at the role of FP placement in the treatment of BPF.

2. Methods

We reviewed the medical records of 5 patients with FP placement for BPF at our institution between March 2016 and March 2017. The Biodesign® Anal Fistula Plug Set (Cook Medical Inc., Bloomington, Indiana, USA) was used. Demographic information, initial perioperative information, method of FP placement, and success was reported. Success of a FP placement for the treatment of BPF was defined as

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Abbreviations

BPF	bronchopleural fistula
FP	fistula plug
ETT	endotracheal tube
EBV	endobronchial valve

complete cessation of the air leak with associated clinical improvement.

2.1. Technique

The placement of the FP was performed via flexible bronchoscopy in the airway with direct visualization from the operative field. A guidewire was advanced through the BPF either antegrade (advanced through the working channel of the bronchoscope, directed through the BPF into the surgical field, and grasped by the surgeon) or retrograde (advanced into the BPF and airway from the surgical field, grasped with forceps through the working channel of the bronchoscope and, pulled out through the lumen of the endotracheal tube (ETT)). Once accomplished, one end of the guidewire exits the BPF through the operative field and the other end exits through the ETT (Fig. 1A). As previously published in another report [9], one end of a suture was tied to the guidewire exiting the ETT. The opposite end of the suture was tied to the FP creating one continuous unit composed of the FP, suture, and guidewire. From the operative field, the continuous unit was pulled through the BPF while being watched simultaneously within the airway lumen bronchoscopically and followed as it is pulled and positioned snug into the BPF (Fig. 1B and C). Within < 24 hours, the plug swells with hydration and enhances its sealing effect.

A soft bristle brush included in the FP kit can be used to intentionally cause mild bronchial mucosa irritation along the BPF tract immediately prior to placement of the FP to promote native tissue ingrowth, healing, and augment BPF closure. We applied this in one patient using an extended sheath through the working channel of the bronchoscope.

3. Results

Five patients (4 male, 1 female) with a median age of 63 years (range, 57–76 years) underwent 6 FP placements for BPF. Two patients were post-pneumonectomy and 3 patients post-lobectomy. The median time to presentation following surgery was 118 days (range, 22–218 days). After placement of the FP alone, 3 patients had complete cessation of their air leak at 0, 1 and 4 days.

One patient had a persistent air leak despite 2 separate FP placements. The air leak stopped with endobronchial valves (EBV) which were deployed proximal to the FP, 9 days after FP placement. Another patient had a successful muscle flap BPF closure 80 days after FP placement.

Two of three patients with complete cessation of their air leak subsequently underwent a thoracic muscle flap placement to augment healing. The third successfully treated patient was able to be weaned off of mechanical ventilation and transferred out of the intensive care unit shortly after FP placement. However, at 27 days post FP placement, he

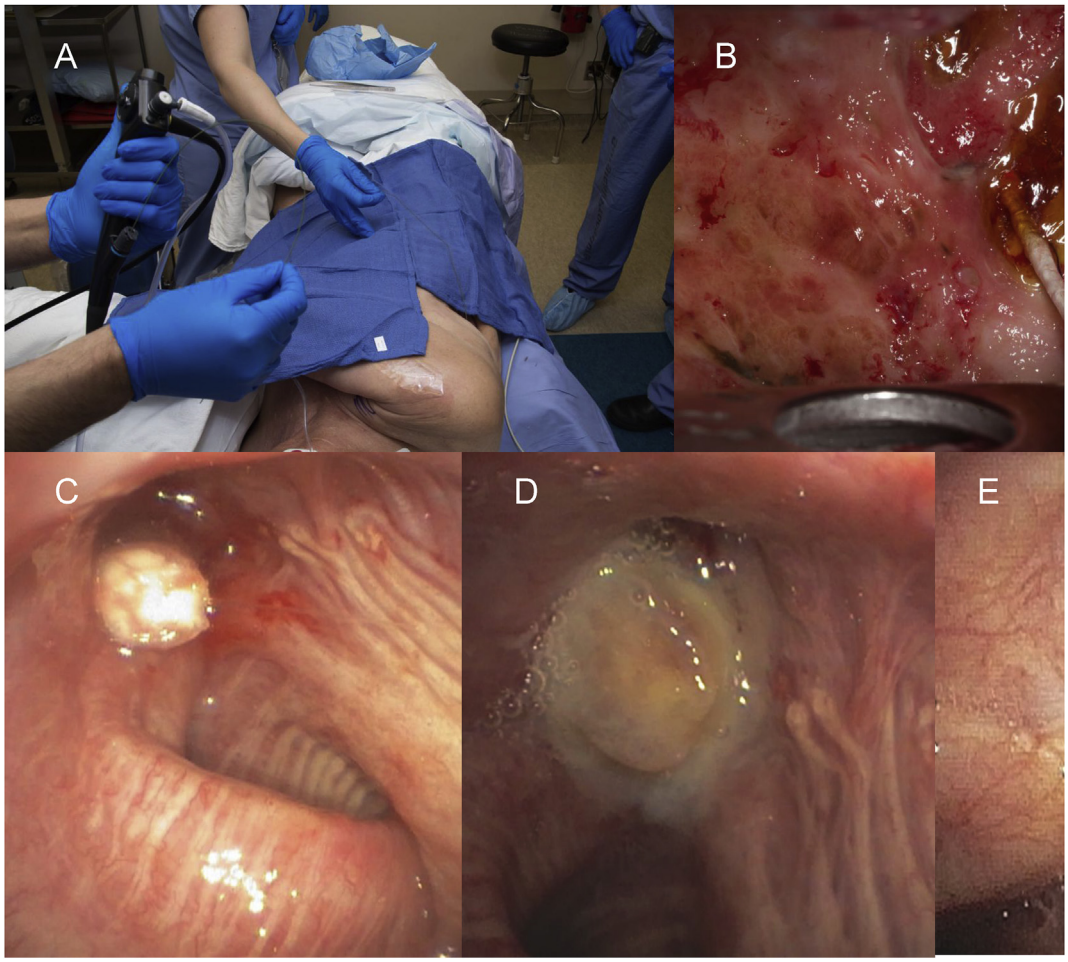

Fig. 1. (A) FP placement via bronchoscopy with direct visual guidance from the operative field. (B) FP placement secured into the BPF with BioGlue. (C–D) Bronchoscopic image of the FP on postoperative days 0, 1, and 28 days, respectively.

suffered from dislodgement of his FP during a chest wound dressing change. He subsequently had multiple unsuccessful EBVs placed and removed, and was eventually discharged with an Amplatzer device (St. Jude Medical, St. Paul, MN, USA) in the fistula.

4. Discussion

The success rate of surgical closure of BPF has been reported to be has high as 95% [3]. Surgical closure includes chronic open drainage, direct stump closure with intercostal muscle reinforcement, omental flap, transsternal bronchial closure, and thoracoplasty with or without extrathoracic chest wall muscle transposition [3].

Alternatively, many reports of successful bronchoscopic techniques and options of BPF closure using different devices have been attempted. These include antibiotics [10], cellulose [11], ethanol [12], cyanoacrylate compounds [13,14], vascular devices and plugs [15–17], fibrin or tissue glue [18–20], Watanabe spigots [21], EBVs [22–24], and autologous blood patches [25]. All have reported variable success rates and their own inherent limitations. The use of a collagen screw plug for treatment of BPF has been described in an animal study [26] and a collagen matrix fistula plug in one published human case report [27].

In the animal study [26], 9 of 10 dogs with postpneumonectomy-induced BPFs were successfully treated with a collagen screw plug. Autologous platelet-rich plasma was used concurrently and applied over the plug to enhance the seal. The unsuccessful case was related to tension pneumothorax that developed after the FP was dislodged. In the single published case report [27], an empyema after a right middle and lower lobectomy was treated with a Clagett procedure. He subsequently developed a BPF which was treated successfully with a FP that was placed through the cavity directly into the BPF. Omentum was mobilized from the stomach and colon through a midline laparotomy and was placed into the Clagett cavity through a small defect created in the diaphragm. The thoracic cavity and laparotomy were closed in layers and the treatment was a success.

In 1962, a landmark article by Clagett and Geraci [28] described a 2-stage technique for the management of postpneumonectomy empyema. The procedure consisted of open pleural drainage, closure of the BPF, debridement of non-viable tissue, obliteration of the pleural cavity with antibiotic solution and finally, wound closure. The Clagett procedure, as it has since been called, has been reported to be effective in 88% of patients [29]. Failures were often the result of persistent or recurrent BPF [30]. Pairolero and Arnold [31] attempted to address this issue by modifying the Clagett procedure. They demonstrated that intrathoracic transposition of well-vascularized extrathoracic muscle to reinforce the bronchial stump closure protects it from further ischemia, necrosis, and subsequent dehiscence. It also serves to decrease the size of the pleural cavity and was shown to be a safe and effective treatment of BPF.

The Cook Medical FP used is a bioabsorbable xenograft made from lyophilized porcine small intestine. It is a complex collagen conical structure that is 9.5 cm long and at its widest diameter, 0.6 cm. It's tapered shape and length allows for easy modifications to fit in any fistula. Collagen, a basic component of connective tissue, is biodegradable, biocompatible, and is not known to cause any adverse immune reaction [5,26]. The collagen FP provides an acellular scaffold matrix that is similar to human extracellular matrix, which allows for native tissue in-growth, promotes cellular proliferation, and tissue healing [5,32]. Host integration into the implant begins within a few days through penetrating capillaries (Fig. 2) and eventually, the FP is repopulated by the host's cells [5]. Tissue remodeling is generally felt to be complete by the sixth month after implantation, though one of our cases showed complete mucosal closure can occur at 4 weeks (Fig. 1E) [5,6].

Our experience with FP placement for BPF is promising. Three of 5 patients had their BPF successfully treated with a FP and 2 of them went on to receive muscle flaps post FP placement. While one of our successfully treated patients suffered a dislodgement of his FP at 27 days, he was still considered a success as he demonstrated complete cessation of his air leak with water submersion intraoperatively. Furthermore, he was successfully weaned off mechanical ventilation, and transferred out of the intensive care unit. We suspect that placement of a muscle flap earlier in his hospital course may have diminished the likelihood of FP dislodgement.

Mechanical ventilation may be required in some patients with BPF and can be especially challenging to manage. The air escaping through the BPF not only delays healing of the fistulous tract, but because this is an area of low resistance, it accounts for a significant loss of volume, jeopardizing the minute ventilation and oxygenation. It can also lead to difficulty with lung re-expansion, ventilation/perfusion mismatch, and the inability to maintain positive end-expiratory pressure [33]. The goal in promoting healing of the BPF was to limit flow through the tract which we successfully achieved.

In the 2 unsuccessful FP placements, 1 had a FP attempted twice and ultimately went on to have EBVs placed with eventual cessation of his air leak. This was likely the result of failure of the surrounding tissue integrating into the FP implant. There was no detectable size mismatch and it was not dislodged. The second patient was discharged home 2 days after FP placement as her air leak had significantly decreased. However, a follow up outpatient bronchoscopy 4 weeks later showed a persistent tiny defect medial to where the FP was placed. Clinically, she did well as an outpatient and went on to receive a thoracic muscle flap 80 days after the FP was attempted. It is possible that a size mismatch between the BPF and FP was the cause of a persistent defect adjacent to the FP, which may not have been recognized immediately after placement.

Our sample size is small with a modest success rate. Further modifications in technique may enhance BPF closure and success rates. Specifically, when the FP protrudes from the fistulous tract into the open chest cavity, dressing changes may dislodge the FP. This can be mitigated by anchoring the FP in position utilizing a suture in the operative field, trimming the FP to the appropriate size and length, and being cautious not to displace the FP during dressing changes. Collaboration between interventional pulmonology and thoracic surgery is imperative to the success of BPF closure.

5. Conclusion

In patients with a postoperative BPF and a pleural window,

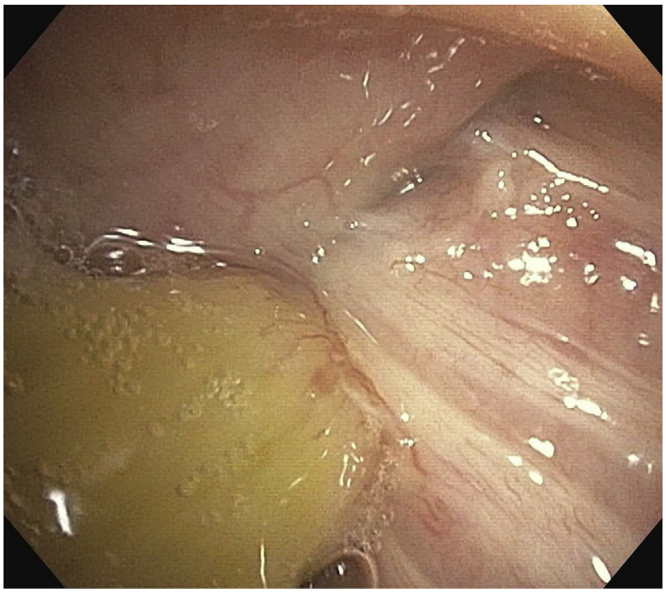

Fig. 2. Tissue in-growth and capillary penetration of a FP.

placement of a porcine-derived, extracellular matrix FP has a modest success rate and can be considered as a viable treatment modality for BPF. Further study is warranted to determine the optimal use of this approach to treat a BPF.

Conflicts of interest

Dr. Ryan Kern reports personal fees for consulting from Boston Scientific, Auris Surgical Robotics, and Olympus Corporation of Americas during the conduct of this study.

Source of funding

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Off-label disclosure

We describe the use of a fistula plug for the treatment of bronchopleural fistula. This is not approved by the FDA. This device is not labeled for the use under discussion.

Author contributions

All authors provided equal substantial contributions to the conception, acquisition, analysis, and interpretation of data for the manuscript. Drs. Sakata and Kern are responsible for the final version to be published.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.rmcr.2018.09.010.

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