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Endoscopic treatment of bronchopleural fistula using ethyl-2-cyanoacrylate: A report of two cases

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ABSTRACT

Bronchopleural fistula (BPF) is a serious complication after lung resection or chronic empyema. BPF often causes severe pneumonia or fatal airway bleeding due to bronchoarterial fistula. Although BPF often requires surgical treatment, another, more conservative treatment option is endoscopic bronchial occlusion for non-operable patients. Many endoscopic treatments have been reported. We report here two patients with BPF who underwent endoscopic bronchial occlusion. Patient 1 had postoperative BPF with empyema and Patient 2 had BPF due to chronic empyema. Because the BPF in Patient 1 was small, it could be successfully treated by endobronchial occlusion using only ethyl-2-cyanoacrylate. In contrast, because the BPF in Patient 2 was large, it could not be treated by endobronchial occlusion using ethyl-2-cyanoacrylate alone; it was successfully treated by endobronchial occlusion using the combination of ethyl-2-cyanoacrylate and a silicone spigot (endobronchial Watanabe spigot, EWS). When we attempt endoscopic bronchial occlusion with BPF for non-operable patients, ethyl-2-cyanoacrylate may be an option for small fistulas, while the combination of EWS and ethyl-2-cyanoacrylate may be suitable for large fistulas.

1. Introduction

Bronchopleural fistula (BPF) is a serious complication after lung resection that can often cause severe pneumonia and fatal airway bleeding due to bronchoarterial fistula. Another major cause of BPF is chronic empyema [1]. BPF with chronic empyema is an intractable complication in which chronic infection develops, destroying the lung. Purulent sputum from the empyema cavity and destroyed lung can cause recurrent pneumonia. In these situations, persistent air leaks require surgical treatment. However, because the general status of the patient is usually poor, endoscopic bronchial occlusion, as a less-invasive approach, is another treatment option. Recently, some endobronchial-occluding approaches have been reported.

We report here two patients with intractable BPF. Patient 1 had postoperative BPF treated with medical-grade ethyl-2-cyanoacrylate (alkyl-alpha-cyanoacrylate monomer, Aron alpha A®, Sankyo Co., Ltd., Tokyo), and Patient 2 had BPF with chronic empyema treated by the combination of a silicone spigot (endobronchial Watanabe spigot, EWS® (size range: 5–7 mm), Novatech, LaCiotat, France) and ethyl-2-cyanoacrylate.

2. Case report 1

A 77-year-old man with chronic obstructive pulmonary disease was diagnosed as having a T1cN0M0 lung adenocarcinoma and underwent left basal segmentectomy because of low lung function. Although he left our hospital at five postoperative days without any acute complications, he was readmitted with severe cough and dyspnea at approximately a month after surgery. He was diagnosed as BPF and treated with tube thoracostomy and antibiotics. At first, he refused open-window thoracostomy, and thus we performed completion left lower lobectomy. However, two weeks after completion lobectomy, the left lower lobe bronchial stump was broken down due to bronchial ischemia, and an air leak developed again. Chest computed tomography (CT) revealed the destroyed left lower lobe bronchial stump (Fig. 1). Finally, we performed an open-window thoracostomy followed by endoscopic bronchial occlusion.

He received intravenous pethidine hydrochloride (35 mg) as premedication. He underwent insertion of a bronchoscope through an endotracheal tube that was placed using the bronchoscope as a guide under local anesthesia and mild sedation. Endoscopic bronchial evaluation revealed a 2–3 mm defect in the back of the slit-like left lower lobe

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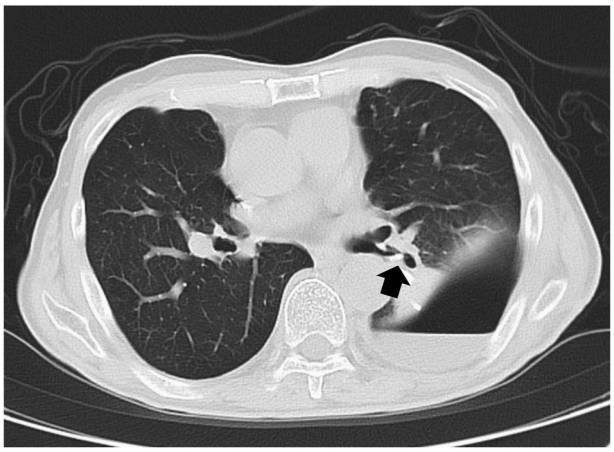

Fig. 1. Chest CT of Patient 1: Chest CT revealed the destroyed left lower lobe bronchial stump (arrow), suggesting postoperative BPF.

bronchial stump only on inspiration. The bronchoscope was deployed into the left main bronchus just above the stump. Ethyl-2-cyanoacrylate (1.0 ml) was injected into the left lower lobe bronchial stump through the guide sheath (Fig. 2A). The mucosa around the bronchial stump changed to a whitish color about 50 seconds after injection (Fig. 2B). At present, during two months follow up after this procedure, the defect was sealed and air leakage was not noted.

3. Case report 2

A 65-year-old man was admitted to our hospital because of hemoptysis. He presented with chronic empyema caused by *Aspergillus* spp. in the residual thoracic cavity after treatment for tuberculosis. We performed tube thoracostomy, however it failed because the content of the pyothorax developed a very hard. Because he had low lung function and a decreased performance status, completion pneumonectomy was not indicated. Therefore, we performed surgical debridement and open-window thoracotomy. Intraoperative observation revealed that multiple bronchopleural fistulas were located on the surface of the destroyed right lung, while air leakage and purulent sputum flowed out from the fistulas.

Five days after the operation, we attempted endoscopic bronchial occlusion using EWS. He received intubation under local anesthesia and mild sedation with midazolam, and then underwent insertion of a bronchoscope through an endotracheal tube. EWS (7 mm) was placed into the bronchus (right posterior segmental bronchus (B2)) using grasping forceps. Chest CT showed an occluded EWS in the right B2 of the destroyed right lung (Fig. 3A). Although air leakage was not observed just after endoscopic bronchial occlusion using EWS, EWS occluding B2 had fallen into the thoracic cavity because the BPF was larger than 7 mm, and air leakage recurred on postoperative day 8 (Fig. 3B).

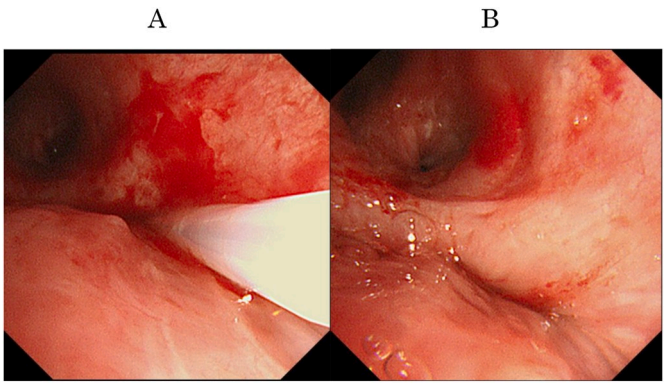

Fig. 2. Bronchoscopic findings in Patient 1:(A) Ethyl-2-cyanoacrylate was injected into the left lower lobe bronchial stump through the guide sheath. (B) The mucosa around the bronchial stump changed to a whitish color after injection. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

We again attempted endoscopic bronchial occlusion under local anesthesia and mild sedation. The bronchoscope was deployed into the right upper lobe bronchus through an endotracheal tube (Fig. 4A). After confirming that the air leakage was localized to the right B2, EWS (7 mm) was again placed in the target bronchus (Fig. 4B). Next, ethyl-2-cyanoacrylate (1.0 ml) was injected through the guide sheath into the space between the bronchial wall and EWS (Fig. 4C). Ethyl-2-cyanoacrylate rapidly hardened and changed to a white color about 60 seconds after injection (Fig. 4D). Air leakage was not observed after this procedure and the postoperative course was uneventful, but the patient died of pneumonia in the left lung three months after the procedure.

4. Discussion

If BPF is suspected, emergent thoracic drainage followed by surgical therapy is standard in daily practice. Although several studies have reported the success of endoscopic treatment using glues to repair smaller BPF, a higher failure rate has been documented in the presence of large BPF [1–3]. Cardillo et al. reported that the cure rate with endobronchial treatment was 88% in BPF 3 mm or less, but only 60% in BPF larger than 3 mm [2]. Hollaus et al. reported that patients with fistulas smaller than 3 mm and no life-threatening sepsis due to empyema were suitable for endobronchial treatment, whereas BPFs larger than 8 mm were not suitable for endobronchial treatment [3]. They reported that 6 of 29 (20.6%) patients who only underwent endobronchial treatment died, while none of the patients (0 of 5) who underwent open window drainage died. They concluded that endobronchial treatment of BPF is an efficient alternative, especially when surgical intervention is not possible because of the poor physical condition of the patient [3].

Hartmann and Rausch [4] and Ratliff et al. [5] first reported successful endobronchial treatment of BPF using glue and a lead shot, respectively. Since then, many successful techniques and devices for the endoscopic bronchial occlusion of BPF have been reported, including ethanol [6], polyethylene glycol [7], cyanoacrylate [4,8–14], fibrin or tissue glue [3,15–18], EWS [14,19–24], antibiotics [25,26], albumin-glutaraldehyde tissue adhesion [27], cellulose [28], gel foams [29], coils [12,30,31], and vascular-occluding devices [32,33]. Although there is no evidence to support which is the best sealant for BPF, the choice of occluding material depends on the size of the fistula and whether it is acute or chronic. Regarding the choice of the occluding material, previous reports have recommended glues or sealants for small and acute BPF, while solid devices were recommended for large and chronic BPF [1–3]. In our report, BPF in Patient 1 was successfully treated by ethyl-2-cyanoacrylate alone, while BPF in Patient 2 was not; however, the combination of ethyl-2-cyanoacrylate and EWS was successful. We suspected that this difference was due to the size of the fistulas. The failure of sealing compounds for large fistula can be due to insufficient stability in the target lesion.

Generally, solid plugs such as an EWS are more stable than liquid plugs such as glue. However, solid plugs can sometimes be difficult to deliver to the target site, which depends on the site of the bronchus. Several techniques to deliver an EWS to a target fistula have been reported [19–24]. Furthermore, after a fistula is filled using EWS, it has to be stabilized in place until granulation tissues form and the fistula resolves. However, the introduction of foreign matter into the body might result in persistent cough. One of the potential problems with endobronchial occlusion using an EWS in daily practice is dislodgement of the EWS due to coughing. Moreover, in some cases, the EWS can fall into

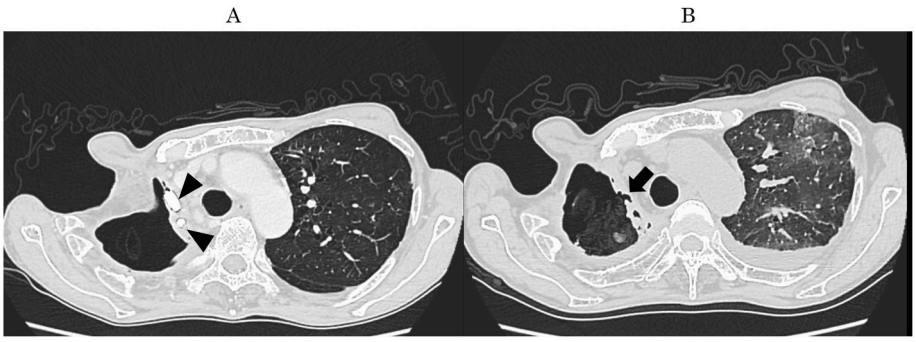

Fig. 3. Chest CT of Patient 2: (A) Chest CT showed occluded EWS in the right B2 of the destroyed shrunken right lung (arrow heads). (B) Chest CT showed that the EWS that had occluded the right B2 had fallen into the thoracic cavity (arrow).

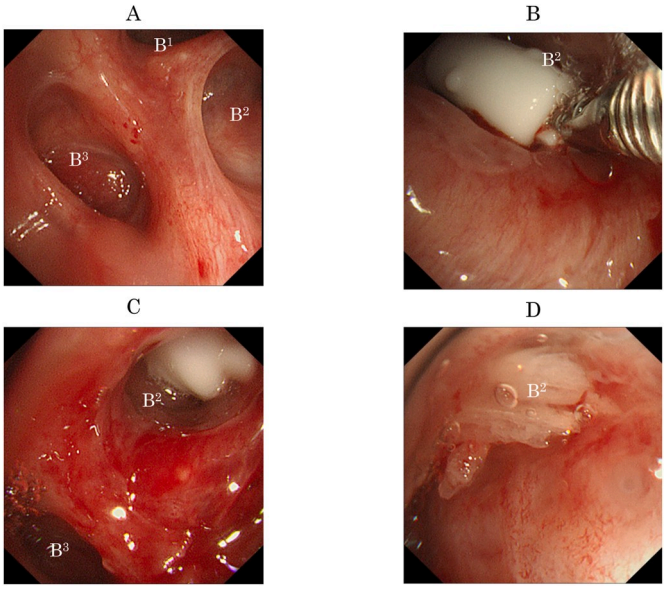

Fig. 4. Bronchoscopic findings in Patient 2: (A) The bronchoscope was deployed into the right upper lobe bronchus. (B) EWS was placed into the right B2 using grasping forceps. (C) Ethyl-2-cyanoacrylate was injected through the guide sheath into the space between the bronchial wall and EWS. (D) Ethyl-2-cyanoacrylate hardened and changed to a white color about 60 seconds after injection. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

the thoracic cavity when the fistula opens toward the thoracic space, as in our Patient 2.

On the other hand, with regard to liquid plugs, we selected ethyl-2-cyanoacrylate in the present cases because cyanoacrylate is more adhesive than fibrin glue. Cyanoacrylates are classified as synthetic glues that rapidly polymerize to form a solid on contact with body fluids or tissue. Initially, they act as a plug. Later, they seal by inducing an inflammatory response that leads to fibrosis and mucosal proliferation, which seals the defect more firmly [34]. Although there have been a few reports on the use of ethyl-2-cyanoacrylate for endoscopic bronchial occlusion, these cases had small fistulas and were in an early stage without empyema [35,36]. As another type of cyanoacrylate glue, n-butyl-2-cyanoacrylate (NBCA) has been reported [14]. Ethyl-2-cyanoacrylate and NBCA differ in that the former is more strongly adhesive and the cured glue is harder than that of the latter, while the latter is less toxic than the former [37]. Hence, NBCA can be injected into selected vessels, and thus is widely used for endoscopic control of bleeding from gastric varices [38]. However, because NBCA was not approved for use in organs except for the skin and vessels in Japan, we selected ethyl-2-cyanoacrylate glue in our cases.

Regarding the use of a combination of liquid and solid plugs for BPF, several options have been reported. These include NBCA and coils [39,40], fibrin glue and fibrin-coated collagen plugs [41], NBCA and polyvinyl alcohol [2,13,42], NBCA and vascular-occluding materials [12,43], NBCA and EWS [14], ethyl-2-cyanoacrylate and oxycell cotton [36], fibrin glue and sponge calf bone [3] and Fogarty catheter and cellulose [28]. In the present Patient 2, we placed an EWS into the large BPF, and then injected ethyl-2-cyanoacrylate into the space between the bronchial wall and the EWS. To the best of our knowledge, this is the first successful case in which a BPF was closed using the combination of EWS and ethyl-2-cyanoacrylate. Cardillo et al. recommended combination therapy with solid and liquid plugs for BPF larger than 8 mm if the patient was judged to be non-operable [2]. It seems as though ethyl-2-cyanoacrylate may help to affix an EWS at the target site. Thus, we consider the combination of EWS and ethyl-2-cyanoacrylate to be better than the use of ethyl-2-cyanoacrylate alone for the treatment of large BPF, as in our Patient 2.

5. Conclusion

When we attempt endoscopic bronchial occlusion for non-operable patients with BPF, ethyl-2-cyanoacrylate may be useful for small fistulas, while the combination of EWS and ethyl-2-cyanoacrylate may be useful for large fistulas. Endobronchial closure with the combination of EWS and ethyl-2-cyanoacrylate may be an option for the treatment of intractable large BPF in non-operable patients because of high operative risks.

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Declaration of competing interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

Abbreviations

BPF	Bronchopleural Fistula
B2	Posterior segmental bronchus
CT	Computed Tomography
EWS	Endobronchial Watanabe Spigot
NBCA	N-Butyl-2-Cyanoacrylate

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