Application of Fibrin Sealant (Tisseel) Via Bronchoscopy in the Management of a Postlobectomy Bronchopleural Fistula

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Abstract

Bronchopleural fistula (BPF) is the most serious postoperative complication of thoracic surgery. We report a patient with non-small-cell lung cancer (NSCLC) who developed BPF after undergoing lobectomy. To close the fistula, we instilled fibrin sealant (Tisseel) in the bronchial stump via a fiberoptic bronchoscope using a balloon catheter. We discuss the technique and our results obtained with this method.
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Key words: *Bronchopleural fistula, fibrin sealant.*
Abbreviations: *BPF = bronchopleural fistula, RUL = right upper lobe, NSCLC = non-small-cell lung cancer, CT = computed tomography, PROBAL = protected bronchoalveolar lavage.*

Introduction

Currently, pulmonary resection remains as the preferred treatment for localized non-small-cell lung cancer (NSCLC) (1). Bronchial resection and anastomosis carry a significant risk of fistula formation, a rate of 2-5%, and are associated with high mortality, of 18-50%. Surgical repair of BPF is contraindicated when a patient's condition is life-threatening (1-4). Endoscopic fistula closure has been reported as a favorable alternative to surgical intervention and its associated complications. In this case study, we report our experience with closing a BPF using bronchoscopic instillation of fibrin sealant material (Tisseel).

Case Report

A 56-year-old man with a medical history of myocardial infarction was admitted to our hospital with a 1-month history of progressively worsening dyspnea, coughing, and weakness. He had a 50-pack-year smoking history. His family history was unremarkable. His chest examination was consistent with emphysema, and physical examination findings for other systems were normal. A chest x-ray obtained at admission showed nonhomogeneous diffuse

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infiltration with well defined margins in the middle zones of the right lung, and enlargement of the right hilus. The results of pulmonary function tests were consistent with mild obstructive airway disease. Thoracic computed tomography (CT) revealed a 5 x 7 cm tumoral mass in the anterior segment of the right upper lobe (RUL) and lymphadenopathy in the region of the right hilus, with nodes larger than 2 x 2 cm. Abdominal CT showed multiple benign cysts in the liver and kidneys. Whole-body bone scintigraphy and cerebral CT were normal. The patient's bronchoscopic evaluation revealed narrowing of the right main bronchus with no evidence of an endobronchial tumor. Examination of a CT-guided transthoracic needle biopsy specimen led to the diagnosis of squamous cell carcinoma.

Our patient had a $T_2N_2M_0$ tumor of stage IIIA NSCLC, and was scheduled for thoracotomy. Surgery involved resection of the RUL, and of the peribronchial/hilar and mediastinal lymph nodes. The patient suffered from bronchospasm and ischemic ECG changes. Postoperatively, there was persistent air leakage from his thoracostomy tube without evidence of a technical problem with the pleural drainage apparatus. A chest x-ray revealed 40% pneumothorax and subcutaneous emphysema on the right side. On the 7th day after the operation, the patient's condition did not improve. The presumptive diagnosis was persistent BPF at the bronchial stump of the RUL.

At this stage, the surgical intervention would have been extremely hazardous due to the patient's poor clinical condition. The alternative was to attempt palliative bronchoscopic obliteration of the BPF using a fibrin sealant (Tisseel KIT 1.0, Immuno AG, Vienna, Austria). The patient was brought to the operating room, where standard anesthetic monitoring, including an arterial line, was initiated. Anesthesia was induced using midazolam and propofol. Both drugs were titrated to maintain spontaneous ventilation and minimize coughing reflex and hemodynamic responses. Once the patient was anesthesized, flexible bronchoscopy showed that the RUL stump had not healed well, and that air was leaking from one side of the stump. The fistula was approximately 6 mm in diameter, and granulation tissue was observed at one edge of the stump (Figure 1). Using a fiberoptic bronchoscope, we placed a two-lumen protected bronchoalveolar lavage (PROBAL) catheter over the RUL bronchial stump. Next, we inflated the catheter balloon with 1.5 ml of air so as to occlude the stump lumen. Absence of bubbling in the chest tube water seal confirmed that the bronchial stump was completely occluded. Keeping the inflated PROBAL catheter in this position, we injected the first component of the sealant, a combination of lyophilized Tisseel and aprotinin solution (1 ml) that was reconstituted in a Fibrinotherm combined warming and stirring device, through the catheter's second lumen (Figure 2). Next, we injected 1 ml of reconstituted thrombin solution (lyophilized thrombin and calcium chloride solution) through the same tube. Finally, we injected 10 ml of air to achieve rapid solidification of the fibrin glue. The inflated PROBAL catheter was held in position for 5 minutes to allow effective sealing. During this period, we noted a small amount of air leakage from the chest tube. As the leakage was significantly reduced, we decided to terminate the procedure, and removed the catheter and bronchoscope.

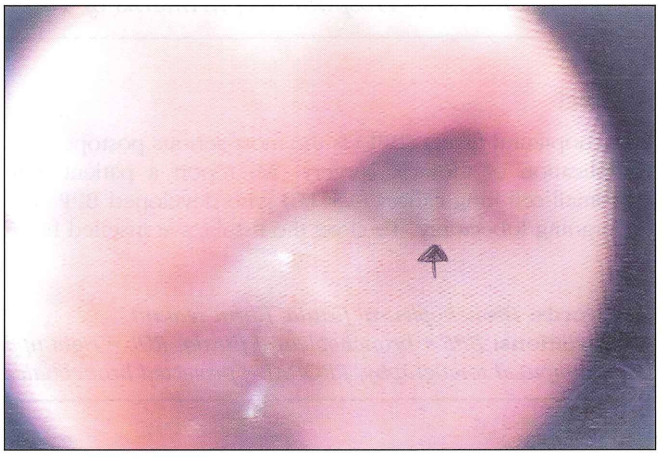

Fig. 1. *Endobronchial view of the bronchopleural fistula at the RUL bronchial stump.*

Fig. 2. *Occlusion of the RUL bronchial stump by PROBAL catheter.*

A postbronchoscopic chest x-ray showed that the patient's pneumothorax persisted. The amount of bubbling in the water seal drainage system was significantly

reduced, but did not disappear completely. Six hours later, the patient underwent a second bronchoscopy session in order to apply more Tisseel to the fistula. During this repeated session, when the tip of the scope reached the site of interest, we observed that one side of the fistula had been closed nicely by the first fibrin-sealing attempt, but that there was still some leakage. We applied more Tisseel solution, repeating the steps described above. A few minutes after the second session, the patient began to cough, and white plug of solidified Tisseel was detected in the trachea. Once we aspirated the plug from the airway, the patient's condition improved immediately. There was markedly less air leakage after the second application of sealant, and an x-ray showed that the area of pneumothorax had decreased from 40% to 10%. When the chest tube was clamped, the right lung did not collapse, suggesting effective repair of the BPF.

The patient was discharged after his chest tube was removed, and we have monitored his condition regularly for 6 months. We were unable to close the BPF completely using Tisseel sealing, but were successful in healing a significant portion of the defect (estimated closure 70-80%) with this method. The patient's radiographical findings have not changed since his discharge from hospital.

Discussion

BPF remains as a very serious complication of pulmonary resection, and is associated with the life-threatening sequelae such as sudden dyspnea, tension pneumothorax, subcutaneous emphysema, respiratory insufficiency, aspiration pneumonia, or any combination of these conditions (1-4). The severity of the clinical features and prognosis differs with each patient. BPF can occur as an acute and life-threatening condition with pulmonary oedema and tension pneumothorax, or can be subacute, reflecting an insidious clinical course (4). Compared with postlobectomy BPF, fistulae that occur postpneumonectomy are more serious and associated with mortality of up to 50%. Le Brigand classified BPF as early (1-7 days), intermediate (8-20 days), and late (more than 30 days), according to the time of appearance after surgery (3). He reported that early BPF was associated with perioperative technical error, whereas intermediate and late BPF were linked to impaired healing of the bronchial stump. We suspected BPF in our case on the basis of air leakage persisted more than 5 days after surgery. We considered our patient's defect an "early fistula" and attributed it to perioperative technical problems.

Surgical repair of BPF is indicated in the presence of the life-threatening complications, as listed above. The options include open-window drainage, thoracoplasty, omentopexy, and intrathoracic muscle transposition. However, when the condition of the mediastinum is good enough to allow sufficient respiratory function, conservative therapy involving chest tube drainage with continuous suction and endoscopic closure of the fistula is recommended (2, 4, 6, 7). Based on the stability of our patient's mediastinal structures, in accord with the literature we opted for conservative management. When the patient's clinical and radiographical condition did not improve with drainage, we decided to close the fistula using minimally invasive endoscopic treatment.

A few reports of promising results of the endoscopic closure of postoperative BPF began to appear in the medical literature in the 1980s. These publications all agreed that the technique is of high therapeutic value, since it is minimally invasive and tolerated well by all patients. Today, several nonsurgical techniques are available for attempting endobronchial closure of BPF, including the use of methacrylate, tissue glue, fibrin glue, gelfoam, tetracycline and autologous blood patch, lead plugs, and balloon catheters (4, 6, 10). The suggested mechanism for all of them is acute mechanical occlusion of airway leakage, which allows the tissue of the fistula to heal over (1, 4). Performing these methods via fiberoptic bronchoscopy allows the physician to treat small peripheral fistulae (1, 4). The fibrin glue is used to seal both proximal and peripheral BPF (1, 2, 10). For peripheral BPF, balloon catheter occlusion is used to identify and block the leaking bronchus (10). In our case, inflating the PROBAL catheter at the end of the bronchial stump allowed the fibrin glue to solidify in the airway proximal to the balloon.

Onotera et al. reported on the use of Tisseel, and recommended that the reagents be applied through a four-lumen catheter to avoid premature mixing of the fibrin compound with its thrombin activator (10). Hollaus and associates reported one of the largest series of the patients treated with these same reagents (2). They injected the two components of the fibrin glue in proper sequence through a rigid bronchoscope, and recorded no complications with undesired solidification of the reagents (2). We treated our patient through a fiberoptic bronchoscope and used a two-lumen catheter, one lumen being used to inflate the balloon. The reagents were injected one after the other through the second lumen. In support of the findings of Hollaus et al., we did not encounter any problems with premature glue solidification. Its reason might be that we

rapidly injected the two consecutive reagents under high pressure, which may have limited the chance of any reaction causing quick polymerization of these reagents.

Hollaus and associates stated that smaller fistulae of less than 3 mm diameter can be treated successfully using a fibrin glue. They noted that larger fistulae require more complex therapy, such as placement of a bony matrix, and that defects of more than 8 mm diameter are not suited to endoscopic therapy (2). They also stated that repeated sessions of the endoscopic fibrin sealing are necessary when initial closure is incomplete (2). We applied Tisseel twice in one day, and the air leakage was markedly reduced after the second application. Although the air leakage did not resolve completely with the second treatment, since the patient tolerated clamping of the chest tube well, we decided to allow time for the remaining portion of the fistula to heal spontaneously, a process reported to take 2 to 8 weeks (2). Extended follow-up of this patient will be very important in terms of verifying the efficacy of this method.

In conclusion, our observations are in accord with those of the other authors who have used endoscopic application of a fibrin glue to treat BPF. This technique offers several advantages. It is easy to perform, minimally invasive intervention, that can lead to complete resolution of a high-risk complication. As well, multiple treatments can be applied, making it possible to treat larger fistulae.

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