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Case report

An atypical complicated left-sided bronchopleural fistula presenting more than seven months after lobectomy

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ABSTRACT

Background: Bronchopleural fistulas (BPF) are abnormal sinus tracts connecting the bronchi and pleural cavity and form after surgical resection of a lung lobe. It is a complication with potentially disastrous sequelae including, failure of the bronchial stump to heal, ischemia of the affected area, and/or infection of the stump. Bronchopleural fistulas caused by surgical intervention most commonly present on the right side and within 7–12 days post-operatively, i.e., subacutely. While the fistula may initially be asymptomatic, they carry a mortality rate of 25–71% in the absence of other comorbidities.

Case presentation: A 60-year-old female developed a BPF more than seven months after a left lower lobe lung lobectomy for non-small cell adenocarcinoma is presented. She was seen at our hospital on multiple occasions after her lobectomy with no evidence of a developing fistula on chest computer tomography (CT) during those visits. During her most recent presentation, roughly 7 months postoperatively, she was noted on imaging to have a new left-sided bronchopleural fistula. Bronchoscopy with lavage and culture of the fistula grew Pseudomonas Aeruginosa, for which she received appropriate treatment. Further surgical interventions were deferred due to poor prognosis. Her presentation differed from the typical BPF presentation in that it was left-sided and occurred out of the window of its usual occurrence.

Conclusion: Late-onset BPF is an important diagnosis to consider in patients who have undergone lung resection, regardless of the type of surgery or postoperative duration, especially when patients are known to have multiple predisposing factors.

1. Background

The overall incidence of BPFs is between 4 and 20% post-pneumonectomy, with an even lower incidence of less than 1% post-lobectomy [1]. Unfortunately, BPFs carry a mortality rate of 25%–71% with the most common cause of mortality stemming from aspiration pneumonia and subsequent acute respiratory distress syndrome (ARDS) or tension pneumothorax [2]. Many factors increase the risk of developing BPFs, including superimposed lung infections, postoperative mechanical ventilation, chemotherapy, mediastinal lymph node resection, high-dose pre-operative radiation therapy, poor nutritional status, and the use of corticosteroids [3,4]. Specifically, regarding nutritional status, if not optimized, it can increase the chances of developing a BPF and increase closure duration once formed. Also, studies have demonstrated faster closure times of BPFs after a simple drainage when nutritional status is optimal as opposed to longer times seen when nutrition is suboptimal [4].

Particularly, any right-sided pneumonectomy carries an increased risk for BPF formation when compared to left-sided procedures [3]. In addition to this location preference, the duration of onset of BPFs has been well documented. For instance, the majority of BPFs are known to occur as early as 1–7 days (acute BPF), between 8 and 30 days (subacute BPF), and >30 days (chronic BPF) [5], with almost all BPFs occurring within 3 months post-lobectomy. The acute form is almost always caused by surgical dehiscence and is the most lethal presentation, generally presenting with either tension pneumothorax or ARDS

Abbreviations: CT, computed tomography; CXR, chest x-ray; BPF, Bronchopleural fistula; RVR, rapid ventricular rate; ED, emergency department; BAL, bronchoalveolar lavage; LAMP, loop-mediated isothermal DNA amplification; ARDS, acute respiratory distress syndrome.

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secondary to pulmonary flooding. The subacute and chronic forms are primarily related to infections and are more commonly seen in patients with multiple comorbidities [2]. Here, we report a case of a patient with a previous diagnosis of stage 4 non-small cell adenocarcinoma of the lung who developed a left-sided BPF more than seven months post lobectomy. We have highlighted the importance of considering BPF as one of the differentials, irrespective of the side of lobectomy or duration post lobectomy. Prompt diagnosis is important for expedited treatment, as such fistulas usually harbor disease-causing bacteria.

2. Case presentation

A 60-year-old female with a medical history significant for T3 N2 M1b left lung non-small cell adenocarcinoma was brought to our facility because of confusion, new-onset weakness, slurred speech, and disorientation. The patient was initially diagnosed with left lung non-small cell adenocarcinoma stage T3 N2 M0 following endobronchial ultrasound with fine-needle aspiration two years prior to her current presentation. She was immunohistochemistry positive for cytokeratin 7, cytokeratin 5/6, and TTF, and negative for p63, consistent with metastatic adenocarcinoma of the lung at the time of her initial diagnosis. She was started on Carboplatin and Paclitaxel as per loop-mediated isothermal DNA amplification protocol, however, she only received one dose before declining further treatment due to worsening side effects. The patient was lost to follow up for one year inbetween hospitalizations. When she re-presented to our hospital one year after her initial diagnosis, CT scan of her chest (Fig. 1A), showed an increasing left lower lobe spiculated lung mass. The patient then underwent an elective video-assisted thoracoscopic surgery for left lower lung lobectomy with an intercostal muscle flap and mediastinal lymph node dissection. Her postoperative course was complicated by the development of an empyema, secondary to Haemophilus influenza, that was subsequently treated with oral amoxicillin-clavulanic acid.

Approximately six months after her video-assisted thoracoscopic surgery (i.e., two weeks before her current presentation), the patient presented to our facility again with complaints of not feeling well and a syncopal episode. A CT scan of the chest at that time (Fig. 1B) did not show any developing BPF per the radiology report. A brain MRI was also performed, which revealed multiple enhancing intracranial masses with significant edema. The patient underwent left occipital tumor resection because of the large size of the lesion with associated edema as seen on CT imaging. This resection was followed by adjuvant external beam radiation therapy. The pathology from the occipital lobe resection confirmed metastatic adenocarcinoma of pulmonary origin. She was started on Levetiracetam and a tapered dose of Dexamethasone post-resection and discharged home after stabilization of her condition. Two weeks later (i.e., during the current presentation), she presented with mental status changes and complaints of severe headaches and neck pain. The patient met the systemic inflammatory response syndrome criteria (i.e., pulse of 104 beats per minute and respiratory rate of 26 per minute) on admission for which she received appropriate antibiotics and fluid resuscitation. Initial work up in the emergency department (ED), including chest x-ray (CXR) and CT scan of the head, showed no evidence of acute disease; however, CT scan of the chest showed interval development of a bronchopleural fistula in the left lower lobe with minimal airspace disease and small amount of pleural fluid (Fig. 1C). Subsequent bronchoscopy with bronchoalveolar lavage (BAL) was performed with fluid cultures that subsequently grew *Pseudomonas Aeruginosa*, for which she received Pipercillin-Tazobactam that adequately controlled her infection resulting in only partial improvements in mentation. Thus, her altered mental status and lethargy were likely secondary to mass effect caused by cancer metastases and associated edema as seen on brain imaging. Given the patients poor prognosis, cardiothoracic surgery was deemed inappropriate, as the risks for complications were higher than the presumed benefits of surgery. Other forms of intervention to close the fistula were not considered because, as earlier mentioned, only mild improvements in mentation was noted upon treatment of her lung infection and, therefore, any further intervention to close the fistula was unlikely to improve her mental status. Even though the risk for fistula reinfection was high, management of her other comorbidities (such as brain metastasis) took precedence. The patient's respiratory status, as well as her functional status, continued to decline (laboratory values are visual in Table 1) throughout her hospitalization. During the remainder of her hospitalization, she also

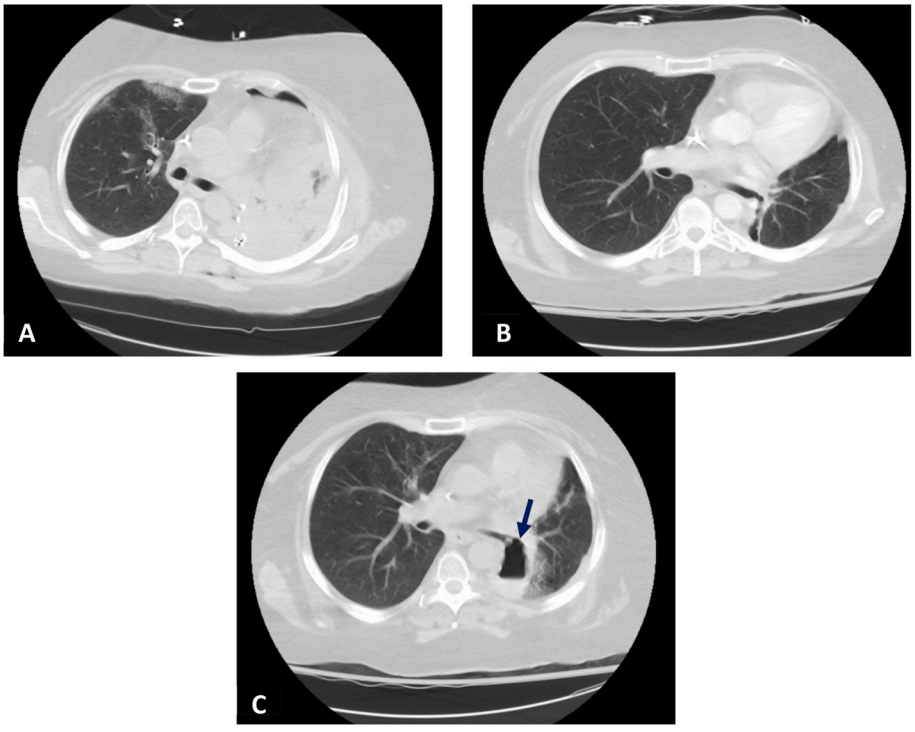

Fig. 1. (A) Non-contrast CT scan of the chest two weeks after left lower lobe pneumonectomy. A representative image showing absence of a BPF. **(B)** Non-contrast CT of the chest 6 months after the first chest CT was obtained. Only post-surgical changes in the left lower lung field were noted. No visible BPF noted per the radiology report. **(C)** Non-contrast CT of the chest 7 months after the first chest CT scan. A notable development of a BPF in the left lower lung field (blue arrow). An air-filled thick-walled cavity in the lower left hemidiaphragm (not shown) was also seen.

experienced atrial fibrillation with a rapid ventricular response for which she was treated with Amiodarone. She continued to decline and was later noted to have an acute change in mental status. New imaging of her brain showed a brain stem hemorrhage secondary to rupture of a berry aneurysm. The patient subsequently expired.

3. Discussion and conclusion

BPFs commonly occur after a right-sided lobectomy and are typically early-onset postoperatively. Our patient was found to have a rare presentation with a BPF developing more than seven months after a left-sided lobectomy. The diagnosis of BPF is typically made by combining clinical, radiographic, and bronchoscopic findings. Typically, patients present with symptoms that include fever, chills, purulent cough, and shortness of breath that could be secondary to pneumothorax formation, or an infectious process [2]. Our patient's presentation was atypical in that she did not present with any of these symptoms, although it was highly suspected that she had an infectious etiology despite a negative CXR. Our suspicion for an infectious etiology was based on the patient's initial presentation of encephalopathy with no identifiable cause in the setting of recent intracranial surgery for metastatic lung cancer [6]. A CT scan of the chest was ordered primarily to rule out interval development of other pathologies, which resulted in the diagnosis of a newly developed left-sided BPF.

The management of BPFs is highly case-dependent and involves conservative and/or surgical interventions, focusing on chest drainage in cases complicated by effusions and/or empyema [7]. In some cases, obliteration of the residual pleural cavity is recommended [8]. For cases of BPF with empyema, a multimodal approach including tracheobronchial conical stent insertion, open pleural packing, and omentoplastic closure of bronchial stump is known to be effective [3,4,9]. However, consideration for any further surgical intervention in a patient with BPF should always be approached with caution since success is dependent on the patient's overall health and physiological status. And given our patient's current presentation and poor prognosis, further surgical interventions were deferred. Of note, emergent intervention was also not warranted as she did not present with a pneumothorax nor was found to be aspirating (as she passed a bedside swallow test). Per recommendations from the infectious disease team, intravenous Piperacillin-Tazobactam and inhaled Tobramycin were deemed to be the best care option available for her.

Several key points can be extracted from this case: (I) BPF should always be on the list of differential diagnoses in patients who have undergone pulmonary surgery (specifically pneumonectomy and lobectomy), irrespective of the lung side/lobe operated on and the time frame since surgery. (II) If a BPF is found on CT imaging, follow up bronchoscopy with BAL and culture should be performed since such fistulas are prone to infection, however, no clear-cut guidelines exist for treating this complex issue [10]. (III) Patients with poor clinical status presenting with late-onset BPFs, as highlighted in this case, generally carry poor prognoses. This should influence the choice of clinical decision and patient care. That is, such patients who are not fit to tolerate the stress of another surgical intervention are more likely to benefit from a more conservative management as opposed to aggressive surgical interventions. Minimally invasive procedures such as gluing (if the fistula size is within the appropriate recommendations), coiling, or stenting of the fistula can improve a patient's quality of life and should always be considered. Decisions on what treatment to pursue is highly case-dependent and must be clinically and ethically assessed. Lastly, physicians should note that the effectiveness of any treatment and the mortality associated with any intervention are strictly dependent on the size of the fistula, time of onset to time of diagnosis, and the baseline clinical condition of the patient.

In summary, late-onset BPF must be considered in patients who have undergone lung resection, irrespective of the lung region resected or postoperative duration. This should especially be considered in patients who have multiple predisposing factors, as highlighted in this case.

Table 1
Pertinent laboratory data at the time of presentation and care transition.

Complete Blood Count	Levels on admission	Levels at time of expiration	Normal range
White blood cells	7.8	11.5	(4.5–11.0 thou/mm3)
Neutrophils %	91.3	86.7	(50.0–75.0%)
Lymphocytes %	5.7	6.3	(17.0–42.0%)
Monocytes %	2.7	6.6	(4.0–11.0%)
Eosinophils %	0.1	0.1	(0.4–6.0%)
Basophils %	0.2	0.3	(0.0–2.0%)
Absolute Neut. Count	7.1	10	(thousands/mm^3)
Red blood cells	3.53	4.38	(3.80–5.20 million/uL)
Hemoglobin	11.2	13.6	(12.0–15.0 g/dL)
Hematocrit	33.4	40.3	(35.0–49.0%)
Mean corpuscular volume	94.4	92.1	(80.0–100.0 fL)
Platelet Count	157	136	(150–450 thousand/mm3)
BMP			
Sodium	133	130	(136–145 mmol/L)
Potassium	4.3	4.2	(3.5–5.1 mmol/L)
Chloride	103	99	(98–107 mmol/L)
Carbon Dioxide	22	24	(21–32 meq/L)
Anion Gap	12.3	11.2	(3.0–15.0 mEQ/L)
Blood urea nitrogen	21	14	(7–18 mg/dL)
Creatinine	0.76	0.61	(0.60–1.30 mg/dL)
eGFR	77	100	(=>90)
Glucose	112	89	(74–106 mg/dL)
Calcium	7.9	8.5	(8.5–10.1 mg/dL)

Disclaimer

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Declaration of competing interest

The authors of this paper have no conflicts of interest to diclose.

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