Keywords
Pancreaticopleural fistula · Pleural effusion · Trapped lung

Abstract
A pancreaticopleural fistula (PPF) is a rare complication of chronic pancreatitis secondary to a pancreatic pseudocyst or any disruption of the main pancreatic duct. It commonly presents as a recurrent left-sided pleural effusion after multiple thoracentesis. We present a rare case of a 41-year-old woman with numerous flares of chronic pancreatitis presenting with large bilateral serosanguinous pleural effusions and trapped lung secondary to a PPF. To our knowledge, this is the first documented case of a PPF leading to bilateral pleural effusions resulting in a trapped lung.

Introduction
Pleural effusions secondary to pancreaticopleural fistulas (PPFs) are extremely rare, occurring in approximately 0.4% of chronic pancreatitis patients and accounting for approximately 1% of pleural effusion cases [1, 2]. PPFs occur in acute or chronic pancreatitis and typically arise from a pancreatic pseudocyst or disruption of the main pancreatic duct. Less commonly, they may also result from trauma. Demographically, these are commonly seen in patients with chronic alcohol use, more often in males [3, 4]. Inflammation from exposure to pancreatic digestive enzymes results in the formation of an anterior tract from the pancreas...
into the anterior retroperitoneum, resulting in fluid accumulation and subsequent communication with the pleural cavity [5]. Thus, diagnosis is often complicated by the typical patient presentation of dyspnea and other respiratory complaints [1].

Pleural effusions secondary to PPFs characteristically recur and are diagnostically positive for amylase and lipase [4]. Thoracentesis typically reveals exudative pleural fluid with appearance ranging from straw-colored to serosanguinous [6, 7]. They most often occur on the left side, with less than 1/3 occurring on the right side [3]. Even more rarely, pleural effusions resulting from PPFs may present bilaterally [8]. If these pleural effusions are not drained for an extensive period of time, retention of the fluid may lead to the extremely rare development of a trapped lung [9]. Once clinical suspicion points highly toward a PPF, diagnostics such as magnetic resonance cholangiopancreatography (MRCP) or endoscopic retrograde cholangiopancreatography (ERCP) are utilized for anatomic mapping with the possibility of ERCP also being used therapeutically for stent placement at the site of duct disruption [4, 9]. The stent functions as a mechanical obstruction of the fistula to prevent further pleural effusion recurrence and may further serve to dilate the strictures of the pancreatic duct [2, 4]. Here, we present a rare case of large bilateral pleural effusions arising from a PPF with a complicated course of a trapped lung and loculated pneumothorax, ultimately diagnosed and stented through the utilization of ERCP.

**Case Presentation**

Our patient is a 41-year-old woman with a history of chronic pancreatitis for 21 years due to EtOH abuse, dyspepsia, chronic hepatitis C, and hypertension. Her chronic pancreatitis and dyspepsia were managed with pancrelipase and famotidine. Of note, the patient had a 30-pack-year smoking history and denied current alcohol use. Upon arrival at the emergency department, our patient reported a 3-day history of dyspnea on exertion and orthopnea. She endorsed nonradiating right-sided chest pain and denied hemoptysis, productive cough, chest trauma, or vomiting. The patient presented with tachycardia to 100 s and tachypnea to 30 s and with a pulse oximetry reading of 95%. The patient was trialed on BiPAP for improvement of acute hypoxic respiratory failure and ultimately required placement of a high-flow nasal cannula. She was then weaned to room air within less than 24 h after admission.

The physical exam was remarkable for diffuse crackles in lung fields bilaterally, decreased breath sounds at the lung bases bilaterally, and tachycardia. Abdominal exam was benign. Chest X-ray demonstrated large left pleural effusion and moderate to large right pleural effusion, with predominantly perihilar alveolar opacities (Fig. 1). Therapeutic thoracentesis on the left side revealed 1.550 L of markedly bloody, serosanguinous pleural fluid with the following values: amylase 630 U/L, lipase 805 U/L, LDH 681 U/L, adenosine deaminase 29.3 U/L, cholesterol 58 mg/dL, glucose 114 mg/dL, protein 5.0 g/dL, and triglycerides 25 mg/dL. ANA screen was negative. Cytology demonstrated histiocytes and benign mesothelial cells, with no malignant cells identified.

A chest CT was done after the left thoracentesis that demonstrated the expansion of the moderate to large right pleural effusion and new development of left hydropneumothorax, along with a large posteroinferior mediastinal fluid/mass that could represent pleural and pericardial or pancreatic fluid (Fig. 2). CT of the abdomen was notable for enlargement of the pancreatic duct and a stable pancreatic pseudocyst. Given the positive adenosine deaminase in the pleural fluid, a QuantiFERON Gold was ordered and returned positive. Active TB was subsequently ruled out with negative AFB culture and MTB PCR. A pigtail catheter was placed on the left side for definitive management of hydropneumothorax with a collapsed lung. Subsequent chest X-ray demonstrated slightly worsened hydropneumothorax, concerning
for a persistent trapped lung with ex vacuo findings (Fig. 3). A subsequent chest CT demonstrated large left-sided pneumothorax ex vacuo with small persistent right-sided pleural effusion. Thoracic surgery was consulted, and a left lung video-assisted thoracoscopic surgery decortication for the treatment of the trapped lung was performed. Several pleural biopsies were taken to evaluate for malignancy, TB, or fungal etiology, which revealed an abscess with fibrosis and pleura with inflammation and focal mesothelial hyperplasia. Due to recurrent expansion of right-sided exudative loculated effusion, a right chest tube was placed and a few days later, a left chest tube was placed for reaccumulating intrapleural fluid.

Gastroenterology was consulted for ERCP with endoscopic ultrasound to further evaluate for a pancreatic source of elevated amylase in the pleural fluid. Endoscopic ultrasound was negative for masses, lymphadenopathy, or other signs of malignancy. ERCP demonstrated a dilated pancreatic duct and leakage at the tail or upstream body, likely representing a fistula to the pleura. Sphincterotomy was performed, and a plastic stent was placed to promote flow of pancreatic secretions internally, thus decreasing flow through the fistula and facilitating closure of the fistula. Bilateral pleural effusions subsequently improved and did not reaccumulate, and the chest tubes were removed.
Discussion

A PPF is a rare complication of acute or chronic pancreatitis or is rarely caused iatrogenically [10]. Chronic pancreatitis secondary to alcohol abuse is the most common cause of PPFs [1]. The fistula typically occurs in the setting of a pseudocyst that communicates with the pleural cavity or through a channel between the pancreatic duct and pleura. In either case, the pancreatic fluid flows through the retroperitoneum and into the pleura [10]. The most common presenting clinical symptoms are shortness of breath, cough, and chest pain. As these clinical manifestations more commonly point toward a pulmonary or cardiac etiology, diagnosis of a PPF is often delayed and allows for the development of complications such as lung entrapment. The diagnostic workup typically includes chest X-ray revealing the pleural effusion(s) and subsequent thoracentesis, yielding elevated levels of amylase and lipase in the pleural fluid [1]. Diagnosis may be able to be confirmed via MRCP (80% sensitivity), ERCP (78% sensitivity), or CT (47% sensitivity) [10].

In the case of our patient, the pleural fluid amylase level of 630 U/L was significantly lower than typically found in PPFs which are usually greater than 1,000 U/L and can reach greater than 6,000 U/L. Further, our patient presented with bilateral pleural effusions which only occurs in approximately 14–16% of PPF cases [11]. Although these findings lowered the likelihood of a PPF, a CT scan of the abdomen did reveal a pseudocyst which is present in approximately 69–77% of patients with a PPF [12]. Together, these raised our clinical suspicion toward the PPF, and we sought to determine a pancreatic etiology of our patient’s bilateral pleural effusions. However, before we could perform a diagnostic ERCP, the clinical course of our patient became complicated by the development of trapped lung. Trapped lung typically arises from pleural disease or endobronchial obstruction, causing an inability of the lung to fully expand. It usually presents as a pleural effusion that is unable to be completely drained or a post-thoracentesis hydropneumothorax as in the case of our patient [13]. Treatment usually consists of supportive therapy or more aggressive measures such as thoracostomy in refractory cases [14]. A trapped lung occurring in the setting of a PPF is extremely rare with only a few reported cases resulting from a unilateral pleural effusion [1, 3, 15]. Surgical treatment with decortication was successfully utilized in one of these cases, as in our patient who presented with bilateral pleural effusions [15].

Fig. 3. Chest X-ray demonstrating loculated left pneumothorax with concern for trapped lung (arrows).
Management of PPFs can be divided into three categories – surgical, endoscopic, or medical. Medical management includes octreotide to decrease pancreatic secretions. Endoscopic management with balloon dilation and intraductal stenting is another option. Surgical management may be indicated if medical and/or endoscopic treatments fail and can include pancreaticojejunostomy or partial pancreatic resections [8]. In one reported case of a PPF causing bilateral pleural effusions, surgical management was required as the effusions were refractory to medical therapy, and the placement of a stent via ERCP was too technically difficult [11]. Medical and endoscopic treatments have been successful in approximately 31–45% of reported PPFs in contrast to surgical treatment which is successful in approximately 80–90% of PPFs [3]. In our case, we were able to manage the fistula endoscopically without postoperative complications.

In conclusion, we present a case of large, bilateral pleural effusions and a trapped lung secondary to a PPF in the setting of chronic pancreatitis. Although a rare occurrence, it is essential that PPFs be included in the differential diagnoses when presented with a case of persistent bilateral pleural effusions even in the absence of abdominal symptoms if the patient has a history of pancreatitis. Detection of amylase in the pleural fluid along with diagnostic imaging via ERCP or MRCP is imperative to confirming the diagnosis. Intervention with pancreatic sphincterotomy and stent placement may be of benefit to prevent further pleural damage. While this presentation is rare, more research needs to be done to identify the true prevalence of this pathologic process.

**Statement of Ethics**

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. Ethics approval was not required in accordance with local and national guidelines.

**Conflict of Interest Statement**

The authors declare that they have no conflicts of interest to disclose.

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**Author Contributions**

All authors certify that he or she has participated sufficiently in the intellectual content and the analysis of data. Myra Ali wrote portions of the abstract, introduction, case report, discussion, conclusion, and references. Madeline MacDonald wrote portions of the abstract and discussion. Aileen Bui wrote portions of the case report and discussion. Kevin Zhang, Jin Sun Kim, and Amanda Cruz wrote portions of the case report and discussion along with editing the rough draft. José Luis González and Arnold Tsai wrote portions of the discussion and edited the final draft. Each author has reviewed the final version of the manuscript and approves it for publication.
Data Availability Statement

All data generated or analyzed are included in this article. Further inquiries can be directed to the corresponding author.

References

1. Tay CM, Chang SK. Diagnosis and management of pancreaticopleural fistula. *Singapore Med J*. 2013;54(4):190–4.
2. Dhebri AR, Ferran N. Nonsurgical management of pancreaticopleural fistula. *JOP*. 2005;6(2):152–61.
3. Bediwy AS. Pancreatico-pleural fistula: a rare cause of massive right-sided pleural effusion. *Egypt J Chest Dis Tuberculosis*. 2015;64(1):149–51.
4. Aswani Y, Hira P. Pancreaticopleural fistula: a review. *JOP*. 2015;16(1):90–4.
5. Sut M, Gray R, Ramachandran M, Diamond T. Pancreaticopleural fistula: a rare complication of ERCP-induced pancreatitis. *Ulster Med J*. 2009;78(3):185–6.
6. Chan EE, Shielat VG. Pancreaticopleural fistula causing massive right hydrothorax and respiratory failure. *Case Rep Surg*. 2016;2016:8294056.
7. El-Beialy H, Fernandez I. Unusual case of persistent unilateral pleural effusion secondary to pancreaticopleural fistula. *Int J Surg Case Rep*. 2012;3(9):435–6.
8. Ramahi A, Aburayyan K, Said Ahmed TS, Rohit V, Taleb M. Pancreaticopleural fistula: a rare presentation and a rare complication. *Cureus*. 2019;11(6):e4984.
9. Wronska M, Slodkowski M, Cebulski W, Moronczyk D, Krasnodebski IW. Optimizing management of pancreaticopleural fistulas. *World J Gastroenterol*. 2011;17(42):4696–703.
10. Cazzo E, Apodaca-Rueda M, Gestic MA, Chaim FHM, Saito HPA, Utrini MP, et al. Management of pancreaticopleural fistulas secondary to chronic pancreatitis. *Arq Bras Cir Dig*. 2017;30(3):225–8.
11. Sonoda S, Taniguchi M, Sato T, Yamasaki M, Enjoji M, Mae S, et al. Bilateral pleural fluid caused by a pancreaticopleural fistula requiring surgical treatment. *Intern Med*. 2012;51(18):2655–61.
12. Machado NO. Pancreaticopleural fistula: revisited. *Diagn Ther Endosc*. 2012;2012:815476.
13. Huggins JT, Doelken P, Sahn SA. The unexpandable lung. *F1000 Med Rep*. 2010;2:77.
14. Doelken P, Sahn SA. Trapped lung. *Semin Respir Crit Care Med*. 2001;22(6):631–6.
15. Blayney MJ, Nguyen A, Aboulafia DM. Diagnosis and management of a pancreaticopleural fistula in a patient with aids and a large pleural effusion. *J Int Assoc Provid AIDS Care*. 2016;15(6):459–62.