

Pancreaticopleural Fistula in the Setting of Pancreatic Divisum with Complete Resolution after Conservative Treatment

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Pancreaticopleural fistula (PPF) is a rare complication of pancreatitis and usually constitutes a diagnostic challenge. There are many causes for recurrent and chronic pancreatitis, with the main etiology being alcohol and choledocholithiasis [1]. However, the association between pancreatic divisum (PD), a common congenital anomaly of the pancreas that is rarely symptomatic, and complications of pancreatitis is still not firmly established [2]. Furthermore, the optimal management of PPF is still uncertain due to its rarity [3]. We describe a rare case of a 45-year-old woman with recurrent pancreatitis that presented with a PPF on the background of PD, successfully managed with conservative treatment. The purpose of this report is to highlight the rare association between PPF and PD together with the excellent response to conservative therapy.

PATIENT DESCRIPTION

A 45-year-old woman with a history of asthma and smoking presented to our hospital with shortness of breath, chest pain, and a large left pleural effusion on chest X-ray. In the previous year,

she was admitted three times with acute pancreatitis. All three episodes were amenable to conservative treatment. An abdominal computed tomography (CT) scan performed a year prior to her latest admission showed features of acute necrotizing pancreatitis. A following CT scan performed showed two organized peripancreatic collections at the area of the body and tail of the pancreas compatible with pseudocysts. No obvious cause for pancreatitis was found. The patient denied any regular consumption of alcohol, non-prescription medication, or relevant family history. No biliary stones were seen on ultrasound or CT studies.

On arrival, the patient was hemodynamically stable with dull respiratory sounds over her left lung. Her laboratory work was significant for leukocytosis of 20,000 cells/ μ l and D-dimer of 1900 ng/ml. Liver function tests were normal, and her blood gases revealed respiratory acidosis. A chest X-ray revealed a large left-sided pleural effusion. A chest CT angiogram was performed, which ruled out a pulmonary embolism.

Due to the patient's respiratory distress and respiratory acidosis, the left pleural effusion was drained via a chest tube with significant improvement in her symptoms. A sample of the pleural effusion showed an elevated amylase level of 2244 U/l. The patient was admitted to the surgical ward for further treatment and was started on 1 gram of

intravenous (IV) ceftriaxone.

On further investigation, a magnetic resonance cholangiopancreatography (MRCP) was conducted, which showed a fistula tract between the peripancreatic pseudocyst and the left pleural space in addition to a PD. The main pancreatic duct was obscured by the large pseudocyst, and therefore disconnected pancreatic duct syndrome could not be ruled out.

Due to the patient's stable condition, we decided to pursue a conservative approach and the patient started a course of IV somatostatin analogue in conjunction with total parenteral nutrition. All involved in the patient's care tracked her progress and revisited the issue of treatment based on the success of the conservative approach. Somatostatin analogue therapy was started on the fourth day of the patient's admission. In addition, a culture from the pleural fluid was positive for *Haemophilus parainfluenza*. Metronidazole was added to the antibiotic regimen of ceftriaxone. Over the next days, our patient's clinical condition and laboratory results steadily improved. After one week of treatment, there was no fluid accumulation in her chest tube, and it was removed. Shortly after, she was discharged home. Four months later, a follow-up out-patient MRCP revealed near complete absorption of the pancreatic pseudocysts. In the 5 months

after the patient's last hospitalization, she experienced one mild episode of pancreatitis.

COMMENT

PPF is an uncommon complication of recurrent and chronic pancreatitis. It is estimated to occur in 0.4% of cases of pancreatitis [1]. The clinical presentation may be evasive and therefore require a high index of suspicion. The initial presentation is typically a large pleural effusion refractory to therapeutic thoracentesis, in contrast to reactive pleural effusion, which is more common in acute pancreatitis. The presence of high amylase in the pleural effusion is very suggestive [1]. However, the diagnostic confirmation usually relies on imaging.

The common initial imaging studies are a CT scan, MRCP, or endoscopic retrograde cholangiopancreatography (ERCP). CT is a non-invasive test but does not demonstrate the fistula between the pancreas and the pleural space in most cases [1]. The accuracy of ERCP is variable and operator dependent. It encompasses a 3–7% risk for pancreatitis [1]. According to the current data, MRCP has the highest sensitivity for the diagnosis of PPF and therefore is the preferred choice for visualizing the fistula [3].

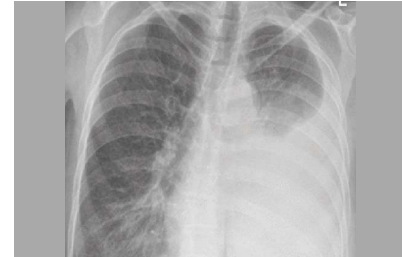
Middle-aged men between 40 and 50 years, who have a history of chronic alcoholism and develop pancreatitis, form the common group of patients who develop PPF [1]. Our patient had no history of chronic or excessive intake of alcohol. A significant finding in our patient was the presence of PD, which seemed to be the only apparent etiology for her recurrent pancreatitis. PD is a common congenital anomaly of the pancreas, which results from an abnormal fusion of the ventral and dorsal pancreatic ducts during fetal development. As a result, pancreatic fluid flow to the minor pancreatic duct leading to an obstruction in outflow,

predisposes patients to pancreatitis. There is a higher frequency of PD in patients with recurrent idiopathic pancreatitis ranging from 8–26%, thereby implying that it may be a possible causative factor [2]. However, larger series were not able to confirm this association with a similar prevalence of PD in patients with or without pancreatitis [4]. Accumulating data showing an association of PD with several genetic mutations such as SPINK1 and CFTR suggest that PD does not cause pancreatitis by itself but serves more as a co-factor [4]. There are few reports on PPF in patients with pancreatitis and PD. PD as a cause for PPF remains questionable as does the effectiveness of minor papilla intervention during ERCP.

There is paucity of literature on the optimal management of PPF, and practice is based mostly on case reports and case series. No selective criteria exist as to which patient would respond to medical therapy or would benefit from early endoscopic or surgical intervention. In most studies, medical therapy, especially somatostatin, is only successful in up to one-third of cases [3]. Failed conservative management is associated with increased rates of complications and reduction in fistula resolution [2]. Therefore, conservative management is usually attempted for up to 2–3 weeks before starting endoscopic or surgical interventions. Recent reports have shown high fistula closure rates with endoscopic intervention, including ERCP with sphincterotomy and placement of a pancreatic [5]. However, ERCP is an invasive procedure and is associated with complications like post-ERCP pancreatitis and infection, bleeding, and infection of pancreatic fluid collections [5]. Our patient responded well to conservative therapy with resolution of the PPF in one week and subsequent removal of the pleural drainage. This result underscores the effectiveness and safety of conservative management as an initial

Figure 1. Radiological findings

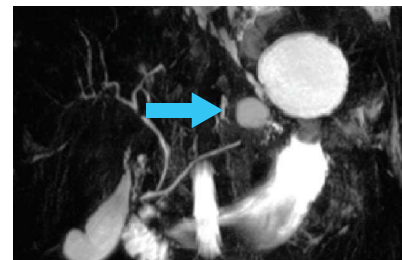
[A] Chest X-ray showing a large left pleural effusion at initial presentation



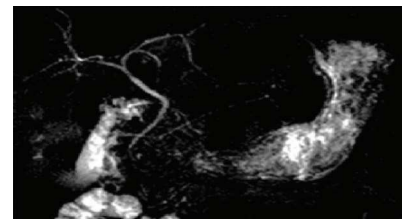
[B] Axial abdominal computed tomography with intravenous contrast enhancement demonstrating two peripancreatic pseudocyst



[C] Abdominal magnetic resonance cholangiopancreatography demonstrating complete pancreatic divisum with concurrent pancreaticopleural fistula (blue arrowhead)



[D] Abdominal magnetic resonance cholangiopancreatography a year after presentation revealing resolution of pancreaticopleural effusion and peripancreatic pseudocysts



strategy in PPF resolution while avoiding potential risks associated with interventional procedures.

CONCLUSIONS

Due to the rarity of PPF, especially in conjunction with PD, determining the most suitable therapy is still unclear. Our case demonstrates that medical treatment with somatostatin analogues can still be very effective in fistula closure. Furthermore, the benefit of endoscopy in the rare setting of PPF and PD is still uncertain,

given the unproven association between PD and pancreatitis.

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References

1. Ali T, Srinivasan N, Le V, Chimpiri AR, Tierney WM. Pancreaticopleural fistula. *Pancreas* 2009; 38: e26–e31
2. Wronski M, Słodkowski M, Cebulski W, Moronczyk D, Krasnodebski IW. Optimizing management of pancreaticopleural fistulas. *World J Gastroenterol* 2011; 17: 4696–703.
3. Akahane T, Kuriyama S, Matsumoto M, et al. Pancreatic pleural effusion with a pancreaticopleural fistula diagnosed by magnetic resonance cholangiopancreatography and cured by somatostatin analogue treatment. *Abdom Imaging* 2003; 28: 92–5.
4. DiMagno EP. Pancreas divisum does not cause pancreatitis but associates with CFTR mutations. *Am J Gastroenterol* 2012; 107: 318–20.
5. Chan S, Petersile M, Churrango G, Zivny J. Endoscopic management as a viable therapy for pancreaticopleural and pancreaticopericardial fistulas. *ACG Case Rep J* 2021; 8: e00533.

The more original a discovery, the more obvious it seems afterward.

Arthur Koestler (1905–1983), Hungarian-born author and journalist

Capsule

Engineered bacteria as melanoma vaccine

The skin microbiome usually lives in harmony with our tissues without inducing inflammation or mounting an infection. However, certain bacterial colonists, including the skin bacterium *Staphylococcus epidermidis*, can induce a highly specific adaptive immune response, the function of which is unclear. **Chen** et al. engineered an *S. epidermidis* strain to express melanoma tumor antigens and then tested their ability to drive antitumor immune system. Engineered *S. epidermidis* generated tumor-

specific T cells that infiltrated and reduced the growth of localized and metastatic melanoma. In combination with immune checkpoint inhibitors. These engineered skin bacteria caused mice to reject established tumors. These findings suggest that immune responses from engineered commensals may have therapeutic potential against other tumor antigens of interest.

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Capsule

Evolution of synchronous female bilateral breast cancers and response to treatment

Synchronous bilateral breast cancer (sBBC) occurs after both breasts have been affected by the same germline genetics and environmental exposures. Little evidence exists regarding immune infiltration and response to treatment in sBBCs. **Hamy** and co-authors showed that the impact of the subtype of breast cancer on levels of tumor infiltrating lymphocytes (TILs, n = 277) and on pathologic complete response (pCR) rates (n = 140) differed according to the concordant or discordant subtype of breast cancer of the contralateral tumor: luminal breast tumors with a discordant contralateral tumor had higher TIL levels and higher pCR rates than those with a concordant

contralateral tumor. Tumor sequencing revealed that left and right tumors (n = 20) were independent regarding somatic mutations, copy number alterations and clonal phylogeny, whereas primary tumor and residual disease were closely related both from the somatic mutation and from the transcriptomic point of view. This study indicates that tumor-intrinsic characteristics may have a role in the association of tumor immunity and pCR and demonstrates that the characteristics of the contralateral tumor are also associated with immune infiltration and response to treatment.

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