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Acute Pancreatitis with an Ongoing Pancreatic Duct Leak Complicated by Refractory Pleural Effusion: A Case Report

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Study Design A
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Conflict of interest: None declared

Patient: Female, 52-year-old
Final Diagnosis: Pancreatic duct leak
Symptoms: Epigastric pain
Medication: —
Clinical Procedure: —
Specialty: Gastroenterology and Hepatology

Objective: Rare disease

Background: Acute pancreatitis causes a significant systemic inflammatory response that affects multiple organs. Pulmonary complications include pleural effusions, hypoxia, atelectasis, and acute respiratory distress syndrome. Pleural effusion is an indicator of poor prognosis in pancreatitis. This case report supports the few existing reports about best practice for the diagnosis and treatment of a pancreatic duct leak causing refractory right pleural effusion.

Case Report: In this case report, a woman with long-term rheumatoid arthritis and recent severe gallstone pancreatitis required hospital readmission for progressive shortness of breath from recurrent massive right pleural effusion from the pancreatitis with an ongoing pancreatic leak and a pseudocyst. She had diagnostic thoracentesis and magnetic resonance cholangiopancreatography (MRCP) that was followed by endoscopic retrograde cholangiopancreatography (ERCP) and stent placement as a therapeutic procedure, with complete resolution of her symptoms.

Conclusions: This case report demonstrates an atypical presentation of complications from severe pancreatitis. MRCP is the criterion standard and best initial test for diagnosing a fistula. When possible, ERCP is preferred for the initial evaluation and treatment of pancreatic leaks and fistulas. In the present case report, treatment with endoscopic cystogastrotomies was effective for the internal drainage of the pseudocyst, pancreatic duct leak, and eventual resolution of the pleural effusion.

Keywords: Digestive System Fistula • Pancreatitis • Pericardial Effusion

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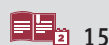
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Background

Severe acute pancreatitis has been associated with a high in-hospital mortality rate [1,2]. Pancreatic ascites and pleural effusion have been reported as complications of severe pancreatitis. In these cases, the pathophysiology is related to the disruption of the pancreatic duct, which causes fistula formation in the abdomen or pleural space [1]. A pancreatic fistula is a well-recognized complication of pancreatitis in acute or chronic pancreatitis; it is mostly due to gallstone formation or excessive alcohol consumption [1]. The diagnosis of pancreatitis-induced right-sided pleural effusion requires high clinical suspicion combined with laboratory findings and confirmation by magnetic resonance cholangiopancreatography (MRCP) [3]. The management of this condition is multidisciplinary, involving a pulmonologist, gastroenterologist, radiologist, and a thoracic surgeon [2,4]. If patients with recent severe pancreatitis present with shortness of breath and refractory pleural effusion, clinicians should have high suspicion of a severe pancreatitis complication causing a pancreatic leak. After confirming elevated amylase levels from analysis of the thoracentesis fluid, MRCP is recommended as an initial diagnostic work-up if available, or endoscopic retrograde cholangiopancreatography (ERCP) is recommended as a diagnostic and therapeutic procedure.

Case Report

A 52-year-old woman had severe deforming rheumatoid arthritis since she was in her 20s and was on long-term treatment with prednisone. Initially, she presented with epigastric abdominal pain and diarrhea for 4 days. The sharp pain was severe (10/10 in the epigastric region) and radiated to her back. She had an elevated lipase level of 311 IU/L. MRCP revealed gallstone pancreatitis with no common bile duct dilation, although there was extensive fat stranding of the pancreas that extended into the root of the mesenteries with a small amount of free fluid. This episode of pain was considered to be severe pancreatitis. Due to the extensive fat stranding, it could represent early necrosis; there was evidence of peripancreatic fluid collection near the head and tail of the pancreas. She met the criteria for severe pancreatitis using the Modified Glasgow Imrie Severity Criteria for Acute Pancreatitis (patient score 3, albumin <2 g/dL, calcium <8 mg/dL, and white blood cells >154000/uL). A gastroenterologic evaluation resulted in the recommendation for a surgical consultation. The cholecystectomy was postponed due to the severe pancreatitis and she had tested positive for SARS-CoV-2, indicating a high perioperative mortality and complication rate. However, as she was asymptomatic with an unknown onset of the SARS-CoV-2 infection, she was not treated for it. The pancreatitis was managed with standard treatment and care. Subsequently, she

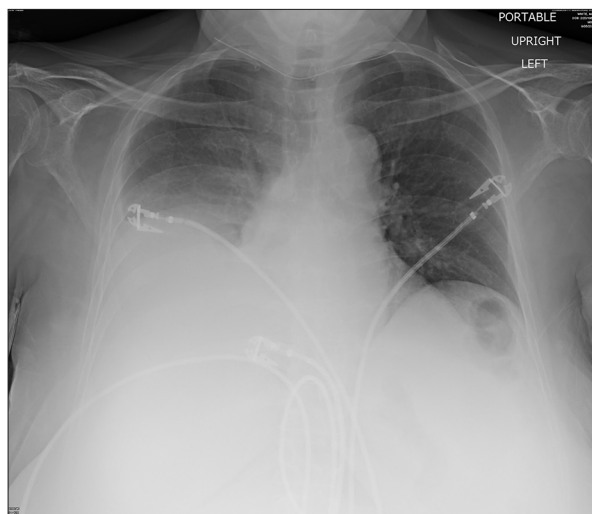


Figure 1. Chest X-ray showed an elevation of the right hemidiaphragm with right base atelectasis and moderate right pleural effusion.

developed a large, symptomatic right pleural effusion. This was suspected to be related to an inflammatory response from the pancreatitis. Given the size of the effusion and the background of rheumatoid arthritis, a diagnostic and therapeutic thoracentesis was performed. Ultrasound-guided thoracentesis drained 1 L of clear amber fluid from the right posterior chest wall, which was analyzed using Light's criteria [5] and it was consistent with an exudative effusion. Pleural fluid studies revealed a pH of 7.53, pleural fluid lactate dehydrogenase (LDH) of 390 U/L with a corresponding serum LDH of 178 U/L, total protein was 4.2 g/dL, and total serum protein was 6.2 g/dL. The pleural fluid showed 8074 cells/uL of red blood cells and 7030 cells/uL of white blood cells with 80% neutrophils. The amylase content of this sample was not tested as this was considered a pleural effusion related to the pancreatitis. She continued to have significant leukocytosis and pain preventing oral nutrition and needed total parenteral nutrition (TPN). A repeat computed tomography (CT) demonstrated worsened small bowel wall thickening; it was thickest at the center. There was suspicion of severe infectious vs inflammatory enteritis with associated ascites. There was significant omental fat stranding, and concern about infection and/or malignancy. Some non-enhancing fluid collection near the pancreatic tail was noted. The outcome of the surgical consultation was a diagnostic laparoscopic evaluation with an omental biopsy (given the immunocompromised state) to exclude any atypical infection or malignancy. There were no significant abnormalities identified during the 4-quadrant laparoscopic exploration. The peritoneal fluid was aspirated and a partial omentectomy was performed; both these samples were sent to the pathology laboratory. Pathologic inspection identified benign fatty tissue with small focal patches of reactive mesothelial cells and chronic inflammatory and

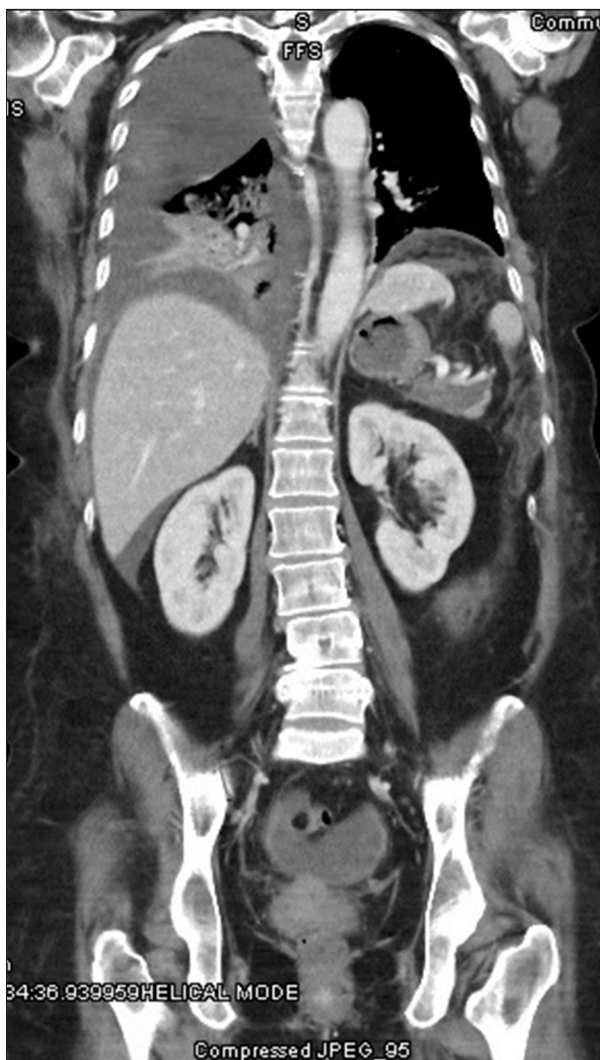


Figure 2. Coronal computed tomography scan of the chest and abdomen showed loculated moderate right pleural effusion and a small left pleural effusion with an associated right middle-lobe and right lower-lobe atelectasis and consolidation.

histiocytic cells with small fat-necrotic nodules. Her condition improved in response to the standard treatment for pancreatitis; she was stable and discharged home after 33 days. Given the severity of the pancreatitis, it was anticipated that an interval cholecystectomy would be completed as an outpatient procedure in 1 to 2 weeks.

Approximately 1 month after discharge from the hospital, she presented with 1 week of significant progressively worsening dyspnea with tachypnea leading to lightheadedness, which had prompted her to return to the hospital. Although she had a longstanding history of rheumatoid arthritis, she denied any history of pleural or pulmonary complications. She had no history of asthma, pneumonia, or tuberculosis.



Figure 3. Magnetic resonance cholangiopancreatography: 3.9×1.8 cm fluid collection seen near the pancreatic tail.

Her physical exam was remarkable for dullness to percussion over the right thorax and absent breath sounds on the right side. Her vital signs were within the normal limits. Significant pleural effusion on the right side was noted on a chest X-ray (**Figure 1**), and there were no increases in the inflammatory markers (C-reactive protein 9.4 mg/dL and erythrocyte sedimentation rate 72 mm/h) and no elevation of the white blood cell count. Her laboratory results were significant for hypokalemia (potassium 2.8 mEq/L), low albumin (1.9 gm/dL), and elevated globulin (3.5 gm/dL). Her liver enzymes and lipase were normal. A CT scan with contrast (**Figure 2**) showed moderate right pleural effusion with persistent loculated fluid collection near the tail of the pancreas and cholelithiasis. An ultrasound-guided thoracentesis was performed and drained approximately 1.3 L of serous fluid, which yielded negative results for cytology and gram stains, and was exudative in nature, with an amylase level of >12 000 units.

On the second day of hospitalization, an MRCP was recommended (**Figure 3**) due to high suspicion of a pancreatic leak or fistula. The MRCP with secretin stimulation did not show a clear fistulous tract; however, the concern for a pleural pancreatic fistula or pancreatic duct leak with ascites remained. A laparoscopic cholecystectomy was performed without complications. The intraoperative evaluation demonstrated minimal ascites fluid, which was sampled and showed a marked elevation in the fluid amylase.

ERCP was performed and showed a pancreatic leak at the pancreatic tail (**Figure 4**) and a pancreatic duct stent was inserted. She tolerated all the procedures without any complications. The pleural fluids reaccumulated over the next 48 hours, this was confirmed by a chest X-ray, and the shortness of breath recurred. Another CT confirmed the diagnosis of pleural effusion

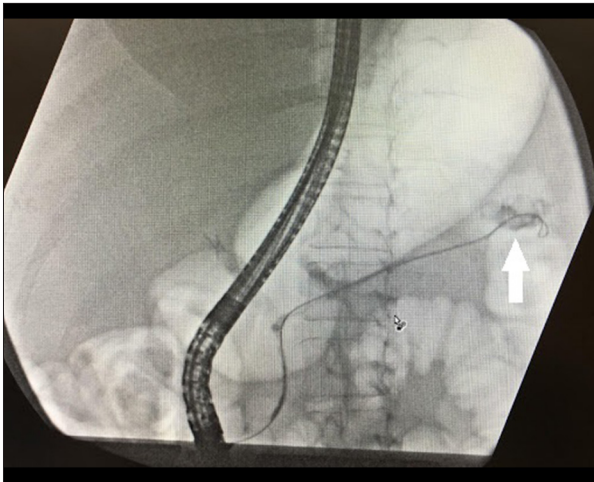


Figure 4. Endoscopic retrograde cholangiopancreatography with contrast extravasation at the distal tail of the pancreas and into the peritoneal cavity.

and the decision to perform endoscopic cystogastrostomies was made. The patient was referred to a tertiary center, where she underwent a repeat ERCP and stent replacement. She underwent endoscopic cystogastrostomies with internal pseudocyst drainage and tolerated it well. At the 2-week and 6-week follow-up appointments, she was symptom free. The patient gave informed consent for the publication of this case report.

Discussion

The inflammatory process in acute pancreatitis is a severe form of inflammation, which is often complicated by multi-organ dysfunction syndrome and has a mortality rate of 15% to 20%. Once this inflammatory process is initiated within the acinar cells, it leads to a generalized systemic inflammatory response syndrome [6]. On the other hand, chronic pancreatitis is an ongoing pathologic response to pancreatic injury that leads to permanent structural changes in the pancreas, resulting in the impairment of exocrine and endocrine functions [7]. Pancreatic duct disruption is a well-recognized complication of these processes, leading to the formation of a pseudocyst or a fistula. Pancreatic duct leaks occur as a result of acute and chronic pancreatitis or in the setting of pancreatic trauma. The manifestations of these leaks include pseudocysts, pancreatic ascites, high amylase pleural effusions, disconnected duct syndrome, and internal and external pancreatic fistulas. Pancreatic leaks or fistulas are traditionally classified into internal or external leaks or fistulas [7,8]. External leaks represent pancreatico-cutaneous fistulas and are typically iatrogenic in etiology. Internal leaks present in multiple forms, including pancreatic ascites, pleural effusions, and pseudocysts [8,9]. The prognosis and management of pancreatic leaks varies based on the clinical manifestations of the leak.

Leaks can occur in the setting of pancreatic trauma or as sequelae from surgical interventions. Pancreatic ascites and pleural effusion are rare complications of chronic and acute pancreatitis and have a mortality rate of 20% to 30% [8]. These pleural effusions are characterized by high amylase levels up to 30 times greater than the corresponding serum levels, protein >30 gm/L, and an LDH ratio of >0.6. Sixty-eight percent of the pleural effusions are left-sided, while 22% are bilateral and <10% are right-sided [9]. The mechanism of pleural effusion is related to a trans-diaphragmatic lymphatic blockage, a pancreatic pleural fistula connecting the peritoneal and pleural spaces together, or to diaphragmatic defects like blebs and fenestration defects [10,11].

The diagnosis of pancreatic pleural effusion depends on high clinical suspicion, detailed history-taking, massive pleural effusion with high amylase levels, and a confirmatory imaging test [12]; this can be an ultrasound with low sensitivity or a CT scan with contrast (low sensitivity) due to the low fistula-wall enhancement and narrow and tortuous pathways [12,13]. ERCP is an invasive method that has a sensitivity rate of 78%. MRCP, on the other hand, is the criterion standard and best initial test for diagnosing the fistula and visualizing the pathway; it has a sensitivity rate of 80% [14]. Zhang et al reported in a meta-analysis that as yet there is no consensus regarding the treatment of choice. However, the clinicians' preferred option is conservative therapy as an initial step, despite its low success rate. Due to the ongoing sympathetic pleural effusion, patients often require surgery and/or ERCP with stent placement. When possible, ERCP alone is preferred for the initial treatment of pancreatic leaks and fistulas [15]. Zhang et al recommended ERCP as the first choice of treatment after an initial short conservative treatment, due to a shorter hospital stay and an improved outcome.

In the present case, the patient had rheumatoid arthritis and complicated pancreatitis with a first hospital admission for severe inflammatory pancreatitis from gallstones. Given the severe nature of the pancreatitis, her treatment was conservative and cholecystectomy was deferred. Her hospitalization was prolonged and she required TPN. She had right-sided pleural effusion that was suspected to be related to the inflammatory process from the pancreatitis. She was discharged, and nearly 1 month later she required readmission for a large recurrent pleural effusion.

Her evaluation was restarted after the thoracentesis, as that was able to exclude effusion related to her known history of rheumatoid arthritis and was consistent with effusion related to the ongoing pancreatitis with significantly elevated amylase in the pleural fluid. Despite the laparoscopic cholecystectomy, the effusion continued to redevelop and she required further evaluation. The repeat CT and magnetic resonance imaging

demonstrated evidence of a pseudocyst and there was additional concern for a pancreatic leak. ERCP was performed and showed contrast extravasation into the peritoneal cavity from the pancreatic tail. This was probably a sequela of her severe pancreatitis and is consistent with a pancreatic duct leak or disconnected pancreatic duct syndrome. Retrospectively, this was possibly the cause of the inflamed appearance of the omentum and recurring effusions. Perhaps performing ERCP earlier would have been beneficial for diagnostic purposes. In the event that ERCP stenting was ineffective, a laparoscopic distal pancreatectomy and cholecystectomy could have been performed simultaneously. Despite imaging and ERCP, there was no evidence to confirm the pancreatico-pleural fistula and her recurrent effusions were attributed to the ongoing pancreatic leakage from the distal pancreas. During ERCP, a pancreatic stent was inserted; however, she required additional treatment with endoscopic cystogastrotomies for internal drainage of the pancreatic pseudocysts.

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Conclusions

This case report demonstrates the atypical presentation of complications from severe pancreatitis. For patients with recent severe pancreatitis who present with shortness of breath and refractory pleural effusion, clinicians should have high suspicion for severe pancreatitis complications causing a pancreatic leak. After confirming elevated amylase levels from analysis of the thoracentesis fluid, MRCP is recommended as an initial diagnostic work-up if available, or ERCP as a diagnostic and therapeutic procedure.

Institution Where Work Was Done

Community Memorial Hospital, Ventura CA, U.S.A.

Conflicts of Interest

None.