

## REVIEW ARTICLE

# Recurrent Right-sided Massive Pleural Effusion of Pancreatic Etiology

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## ABSTRACT

Pleural effusion secondary to chronic pancreatitis is an uncommon condition accounting for less than 1% of patients. Patients are alcoholic but only 50% of patients have clinical symptoms and signs of previous pancreatitis. Symptoms are predominantly respiratory than abdominal. Raised pleural fluid amylase level in hemorrhagic fluid is diagnostic of pancreatic pleural effusion. Presence of pancreaticopleural fistula (PPF) can be demonstrated by computed tomography (CT) imaging or magnetic resonance cholangiopancreatography (MRCP), but these imaging methods sometimes fail to demonstrate fistulous tract. Herewith, we are presenting a rare case of recurrent right-sided massive pleural effusion secondary to chronic pancreatitis.

**Keywords:** Alcoholic, Amylase, Endoscopic retrograde cholangiopancreatography, Magnetic resonance cholangiopancreatography, Pancreatic pleural effusion.

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## INTRODUCTION

Pancreaticopleural fistulae and pancreatic ascites have been termed as internal pancreatic fistulae, which share common pathogenesis that includes the disruption of main pancreatic duct, resulting in leakage of pancreatic fluid.<sup>1</sup> This rare entity may be seen in patients with acute and chronic pancreatitis or may follow traumatic and surgical disruption of the pancreatic duct.<sup>1</sup> It is characterized by massive pleural fluid and has a tendency to recur following treatment. While conservative management with pancreatic duct stenting and inhibition of pancreatic secretion with octreotide may achieve closure of fistula in 31 to 45% of cases, surgery leads to healing in 80 to 90% of cases but carries a mortality up to 10%.<sup>1</sup>

## CASE REPORT

A 55-year-old man who was a chronic smoker and alcoholic for 20 years presented with complaints of diffuse upper abdomen pain, sudden onset, moderate aching type, more in the upper abdomen radiating to back, flanks and chest, aggravated on supine position relieves on medication. He gave history of dyspnea that was gradual onset, progressive over a period of 1 month, with no history of orthopnea or paroxysmal nocturnal dyspnea. It was associated with right lower chest pain suggestive of pleuritic type of pain increases on deep inspiration while relieves on medication with history of weight loss more than 5 kg within 1 month, with decreased appetite since 1 month. Past history is suggestive of pancreatitis 4 months ago. No significant past history of any other illness was present. Review of other systems was unremarkable.

At the time of admission, patient was afebrile, pulse was 90/minute and blood pressure in supine position was 100/70 mm Hg. Respiratory rate was 20/minute and SpO<sub>2</sub> on pulse oximetry was 90% at ambient room air, and BMI was 20 kg/m<sup>2</sup>. Respiratory system examination was consistent with massive right side pleural effusion with tracheal shift to left. Abdomen was soft, tenderness over epigastrium, right and left hypochondrium, hepatomegaly 2 cm below the right costal margin. Examination of other systems was normal. On investigation, hemoglobin was 11.6 gm/dL, total leukocyte count was 12,800/mm<sup>3</sup>, erythrocyte sedimentation rate was 22 at the end of 1 hour. Peripheral blood smear revealed normocytic hypochromic anemia with neutrophilic leukocytosis and eosinophilia. Biochemical investigations were: Random blood glucose—92 mg/dL, creatinine—0.8 mg/dL, blood urea nitrogen—26 mg/dL, serum calcium—8.7 mg%, triglyceride—91 mg/dL, total protein—5.7 gm/dL, albumin—2.4 gm/dL, total bilirubin—0.5 mg/dL, aspartate transferase—55 U/L, alanine transferase—71 U/L, alkaline phosphatase—340 IU/L, serum amylase—2424 U/L, serum lipase—810 U/L, HbsAg—positive. Sputum positive for *Klebsiella pneumoniae* sensitive to piperacillin-tazobactam and negative for acid fast bacilli and malignant cells. Chest X-ray was suggestive of massive pleural effusion on right side, with mediastinal shift to left. Ultrasonography of abdomen and thorax revealed: Bilateral pleural effusion: R>L, Minimal Ascites, normal-sized pancreas with mild peripancreatic fat

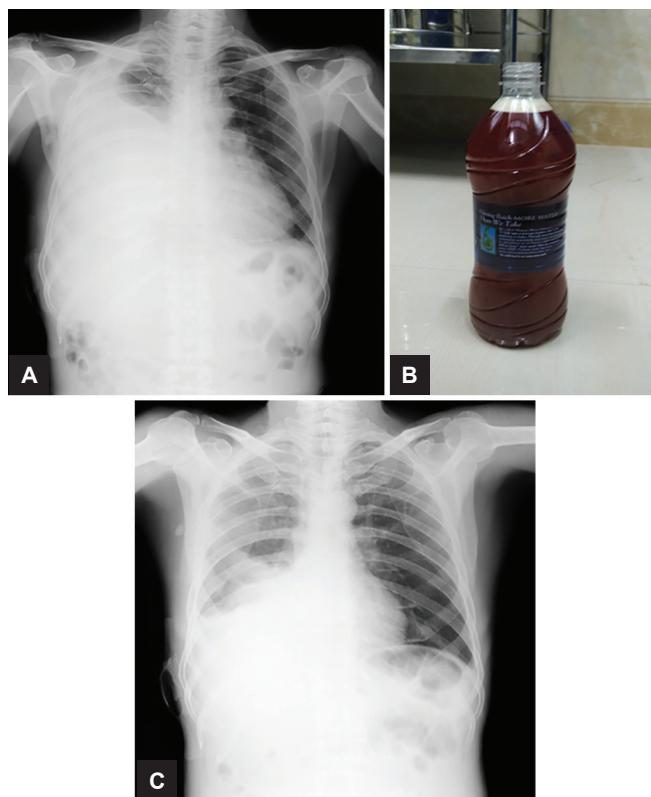
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stranding, prominent main pancreatic duct measure—3 mm. Diagnostic and therapeutic thoracocentesis was done which revealed hemorrhagic fluid. His pleural fluid biochemistry was: Protein—2.8 g/dL, lactate dehydrogenase—473 U/L, glucose—92 mg/dL. The pleural fluid adenosine deaminase (ADA) was normal, amylase—40,000 U/L, suggestive of pancreatic pleural effusion. The pleural fluid cytology on microscopic examination showed a cell count of  $1250/\text{mm}^3$  (neutrophils 60%, lymphocytes 30%) along with few macrophages in a hemorrhagic background. Pleural fluid was negative for malignant cells on three occasions. Gram stain did not reveal presence of any organism, and fluid was also sent for bacterial culture. Thoracocentesis repeated five times over a period of 13 days relieved symptoms, but pleural fluid accumulated over next 10 days (Figs 1A to C).

Ascitic fluid analysis: Low SAAG, high protein—2.8g/dL, normal sugar levels—114 mg/dL, high LDH—385 U/L, high amylase—553 IU/L, normal ADA—10 U/L, suggestive of pancreatic ascites. Suspecting a pancreaticopleural fistula (PPF) causing ascites and effusion, subjected him to contrast-enhanced computed tomography (CECT) of thorax and abdomen revealed acute necrotizing pancreatitis with modified CT severity score 6 and minimal ascites; massive right-sided pleural effusion with underlying collapse of the right lung with minimal left-sided pleural effusion. Magnetic resonance retrograde cholangiopancreatography (MRCP) revealed common bile duct dilatation with no intrahepatic biliary radical dilatation which neither showed any evidence of fistulous tract. Hence, proceeded with endoscopic retrograde cholangiopancreatography (ERCP) and stenting of main pancreatic duct which either failed due to cicatrization of duodenal

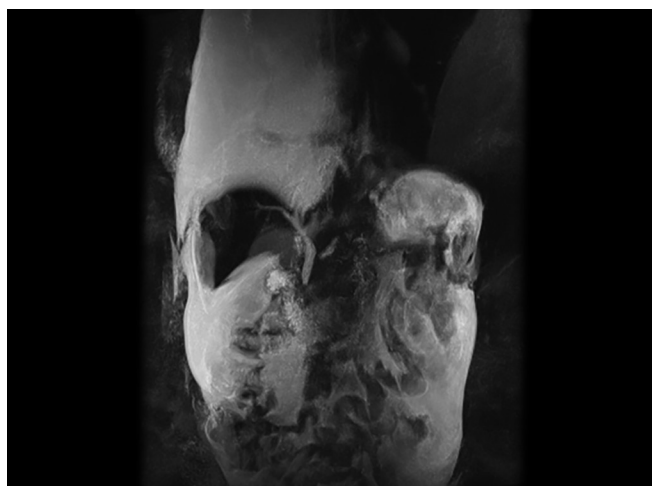


**Figs 1A to C:** (A) Chest X-ray PA view showing massive right pleural effusion with mediastinal shift toward left; (B) hemorrhagic pleural fluid; and (C) after four thoracocentesis chest X-ray PA view showing resolution of pleural fluid, but reaccumulated 10 days later

papilla. Treatment—conservative line of management—Inj. octreotide 100  $\mu\text{g}$  iv tid for 10 days followed by ICD insertion and drainage of pleural fluid which relieved his symptoms. A repeat chest X-ray showed no accumulation of pleural fluid with serum amylase and lipase being normal over a period of 45 days (Figs 2 and 3).



**Fig. 2:** Contrast-enhanced computed tomography of thorax and abdomen was done. Diagnosed to have acute necrotizing pancreatitis with modified CT severity score 6 and minimal ascites, massive right-sided pleural effusion with underlying collapse of the right lung with minimal left-sided pleural effusion



**Fig. 3:** Magnetic resonance cholangiopancreatography: Common bile duct dilatation with no intrahepatic biliary radical dilatation and showed no evidence of fistulous tract

## DISCUSSION

Most of the patients with pancreatic pleural effusion are alcoholics; only 50% of them have a clinical history and signs of previous pancreatitis. PPF is an unusual complication of chronic pancreatitis and estimated to occur in only 0.4% of patients with chronic pancreatitis and 4.5% of patients with pancreatic pseudocysts.<sup>3</sup> Respiratory complications of acute pancreatitis are clinically or radiologically detectable in 33% of patients and include pulmonary infiltrates or atelectasis (15%), pleural effusions (4–17%), and pulmonary edema (8–50%). Presence of pleural effusion is currently considered as an indication of severe pancreatitis and not just a marker of the disease. Pleural effusions in acute pancreatitis are usually small, occasionally bloody, and are characterized by high amylase (up to 30 times greater than corresponding serum value), protein (>30 gm/L), and lactic acid dehydrogenase ratio more than 0.6 serum value levels. The pleural fluid glucose level is comparable to that of the serum. The pleural fluid differential white blood cell (WBC) count usually reveals predominantly polymorphonuclear leukocytes, and the pleural fluid WBC can vary from 1000 to 50,000 cells/mm<sup>3</sup>.<sup>4,6</sup> The majority of pleural effusions (68%) are left-sided, 22% are bilateral, and 10% are right-sided only. Two main causes of pleural effusion are transdiaphragmatic lymphatic blockage or pancreaticopleural fistulae secondary to leak and disruption of the pancreatic duct or pseudocyst caused by an episode of acute pancreatitis. The leak or disruption is more likely to lead to a pleural effusion if the duct disruption is posteriorly into the retroperitoneum. The pancreatic enzymes can track up into the mediastinum and then rupture into the pleural cavity either left side or bilaterally and so create a connection between the pancreatic duct and the pleural cavity.<sup>5</sup> Direct demonstration of the fistula may be difficult in a number of cases; CT imaging was able to diagnose fistula only in 33 to 47% of cases. MRCP has 80% sensitivity to demonstrate PPF while ERCP can demonstrate PPF in 46 to 78% of cases.<sup>3</sup> In our patient clinically, the massive pleural effusion with strongly increased activities of amylase and increased protein concentration with pancreatitis suggests a diagnosis of PPF.

Pleural effusion due to pancreatitis is recurrent and requires repeated thoracentesis or intercostal drainage; however, pancreatic pseudocysts have been found in 69 to 77% of patients with PPF.<sup>3</sup>

Available treatment modalities include: (1) Conservative/medical management; (2) ERCP—with or without endoscopic pancreatic stent placement; and (3) surgery.<sup>5</sup>

The aim of medical treatment is to reduce stimulation of pancreatic exocrine secretions.<sup>2-4</sup> Medical treatment constitutes thoracentesis and/or tube thoracostomy and administration of somatostatin analogs. Thoracentesis

or tube thoracostomy gives symptomatic relief to the patient. Duration of conservative management varies from 2 to 4 weeks. However, octreotide can be given for 2 to 5 months, chest tube drainage can be done from 6 to 24 days. Octreotide is given as an initial dose of 50 mg three times a day up to maximum dose of 250 mg three times daily. Octreotide significantly reduces fistula output and decreases the time of fistula closure. Measures like prohibition of oral intake, nasogastric tube insertion, and parenteral nutrition used in the past are no longer necessary. ERCP with endoscopic pancreatic stenting is an effective therapeutic option for fistulas present in the head and body of the pancreas.

Surgical treatment is safe, effective, and appropriate either when medical management fails or where the underlying condition requires surgical intervention. Surgical treatment options include either pancreatic resection or enteropancreatic anastomosis to the site of pancreatic duct leakage or to the pseudocyst. Conservative treatment of PPF has a success rate of 30 to 60%, recurrence rate of 15%, and mortality rate of 12%. In contrast, operative therapy has a success rate of 90% and recurrence rate up to 18%.

## CONCLUSION

Pancreaticopleural fistula is difficult to diagnose and at times difficult to treat. They require a high index of clinical suspicion to diagnose, particularly in the setting of recurrent pleural effusions with coexisting history of pancreatitis or alcohol abuse. The predominant symptoms are related to chest rather than abdomen. Early pleural fluid amylase testing will avoid delayed diagnosis.

Patients with pancreatitis without abdominal pain and with pleural effusion should be considered as one of the differential diagnoses in patients presenting with sudden onset breathlessness and massive pleural effusion.

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