ABSTRACT - Introduction: Pancreaticopleural fistula is a rare complication of chronic pancreatitis. Objective: To describe pancreaticopleural fistula due to chronic pancreatitis and perform an extensive review of literature on this topic. Methods: Comprehensive narrative review through online research on the databases Medline and Lilacs for articles published over the last 20 years. There were 22 case reports and four case series selected. Results: The main indication for surgical treatment is the failure of clinical and/or endoscopic treatments. Surgery is based on internal pancreatic drainage, especially by means of pancreaticojejunostomy, and/or pancreatic resections. Conclusion: Pancreaticopleural fistula is a rare complication of chronic pancreatitis and the Frey procedure may be an appropriate therapeutic option in selected cases when clinical and endoscopic treatments are unsuccessful.

INTRODUCTION

Chronic pancreatitis is a progressive and irreversible inflammatory process characterized by the replacement of the pancreatic parenchyma by fibrotic tissue. This disease has as main clinical manifestations chronic and incapacitating abdominal pain, and loss of the exocrine and endocrine functions of the pancreas. Patients frequently require endoscopic and/or surgical procedures for the treatment of disease-related complications, being pancreaticopleural fistula very rare. It is estimated to occur in 0.4% of patients with pancreatitis, mostly resulting from chronic alcoholic pancreatitis. It corresponds to a condition in which pancreatic secretions drain directly into the pleural cavity, resulting from a chronic inflammatory process, acute inflammation or traumatic or iatrogenic rupture of the pancreatic duct. Usually it presents as massive and relapsing pleural effusions, often on the left side and with high content of pancreatic amylase.

A review of the literature published over the last 20 years was conducted through an online search for the MeSH terms “pancreatitis, chronic” AND “pleural effusion” AND “fistula” in Medline (via PubMed) and “pancreatite crônica OR pancreatite crônica OR pancreatitis crônica” AND “pleural effusion OR derrame pleural” AND/OR “fistula” in Lilacs (via BVS). Original studies that reported single cases or case series of this disease or correlated conditions were included. Articles that consisted of in vitro or animal studies, articles in which the participants’ characteristics did not match those mentioned...
above, poster session abstracts, review articles and other types of publications were excluded. Other papers were used for contextualization and discussion. At the end, cases from the involved institution were presented.

RESULTS

After extensive online research, 26 studies were included, being 22 case reports and four case series. Table 1 summarizes the main articles found and their reported outcomes. A flow diagram of the review is presented in Figure 1.

![Flow diagram of the review of literature](image)

**FIGURE 1** - Flow diagram of the review of literature

Here are added, to the total amount of cases related in the literature over 20 years period, two cases of pancreaticopleural fistula attended in authors institutions, based on retrospective analysis of data collected on medical records. With this addition to total of patients in the literature with this two is 40.

The first case from the authors was related to a 46-year-old man with a history of alcoholism and long-term smoking, admitted to the emergency department due to mild dyspnea, with a diagnosis of right-sided pleural effusion. After a thoracocentesis, an amylase level of 61,000 IU/l was found in the pleural fluid. Abdominal tomography showed pancreatic changes compatible with chronic pancreatitis. Treatment with oral fasting, total parenteral nutrition, symptomatic medications and thoracocentesis was warranted. Due to the maintenance of pleural effusion, the patient underwent a pleural drainage and pleuroscopy. He evolved with high output drainage, and octreotide infusion was indicated. After three weeks of treatment and maintenance of pleural effusion, the patient was referred for an endoscopic retrograde cholangiopancreatography, which showed a dilated and winding main pancreatic duct, with a cranial fistulous pathway, and bleeding externalized by the duodenal papilla, which precluded the placement of a pancreatic stent. He underwent a selective arteriography of celiac trunk and a scintigraphy with marked red cells, both negative for active bleeding. It was opted for the Roux-en-Y pancreaticojejunostomy associated with partial resection of the pancreatic head (Frey procedure). He presented a satisfactory postoperative evolution, with regression of the pleural effusion and a Frey procedure was carried out. He presented a satisfactory postoperative evolution, with regression of the pleural effusion and thoracocentesis was warranted. Surgical treatment was warranted, and a Frey procedure was carried out. He presented a satisfactory postoperative evolution, with regression of the pleural effusion after eight days and hospital discharge the following day. He is currently in the ninth postoperative year of follow-up, using pancreatic enzymes due to exocrine insufficiency, with no pain and no signs of endocrine insufficiency.

DISCUSSION

Pancreaticopleural fistula is an infrequent complication that may be secondary to acute or chronic pancreatitis, as well as to external or iatrogenic pancreatic trauma. However, this complication is related to chronic pancreatitis of alcoholic origin in 99% of cases.

The pathophysiology of the pancreaticopleural fistula consists of the formation of a posterior pathway of the pancreatic duct to the pleura or, more frequently, after the formation of a pseudocyst and subsequent communication with the pleural cavity. In both cases, the fluid flows through the retroperitoneum through the plane of least resistance into the pleural cavity, usually through the esophageal hiatus. Communications with the pericardium, bronchial tree and esophagus have also been described. Transdiaphragmatic communication is the less common situation.

Regarding the clinical presentation, Uchiyama et al. observed that dyspnea, abdominal pain, cough and chest pain are present in 68% of cases. Many patients undergo extensive lung investigation before the pancreas is identified as the primary site of the disease. Abdominal symptoms are infrequent. Pancreatic ascites are associated with pancreaticopleural fistula in 20% of cases, and in 4% there is an association with pericarditis.

Diagnosis is usually performed by thoracocentesis after chest radiography, with laboratory findings of elevated levels of amylase and lipase in the pleural fluid. Serum amylase has no diagnostic validity, since it is low in some cases. The differential diagnosis of pleural effusions should be made with acute pancreatitis, gynecological, pulmonary, and metastatic tumors, pneumonia, esophageal perforation, lymphoma, leukemia and pulmonary tuberculosis. The diagnosis can be confirmed by endoscopic retrograde cholangiopancreatography in 80% of the cases, showing the fistulous pathway in 59%. In 70% of cases, computed tomography associated with it identifies the fistulous path. Magnetic resonance cholangiopancreatography may demonstrate pancreatic involvement and fistula without the need for contrast, constituting a non-invasive alternative.

There are no randomized studies that indicate the most appropriate treatment of pancreaticopleural fistulas. At first, clinical management with parenteral nutrition and infusion of somatostatin analogs are performed for two to three weeks, with or without pleural drainage. However, resolution of the anatomical continuity of the pancreatic duct is what defines the good evolution of the condition. The efficacy of conservative treatment varies from 30-60% in some series and from 0-33% in others. Recently, endoscopic treatment has been more widely.
| Author                          | Gender/ Age (years) | Pancreatitis' etiology | Presenting symptoms | Imaging diagnosis         | Treatment                                                                 | Outcome                        |
|--------------------------------|---------------------|------------------------|---------------------|--------------------------|---------------------------------------------------------------------------|--------------------------------|
| Molinuevo et al.1             | M/28                | Alcoholic              | Dyspnea             | CT, ERCP                 | Pleural drainage, Puestow procedure                                        | Asymptomatic after 12 months   |
|                               | M/37                | Alcoholic              | Dyspnea             | CT, ERCP                 | Thoracoctectomy, Puestow procedure                                        | Asymptomatic after 24 months   |
|                               | M/41                | Alcoholic              | Dyspnea             | CT, ERCP                 | Thoracoctectomy, Distal pancreatectomy with Roux-en-Y pancreaticojejunostomy | Asymptomatic after 20 months   |
| Mater et al.10                | M/50                | Alcoholic              | Dyspnea, chest pain | CT, ERCP, MRI            | Thoracoctectomy, total parenteral nutrition, somatostatin infusion, Distal pancreatectomy with longitudinal pancreaticojejunostomy | NR                             |
|                               | M/32                | Alcoholic              | Dyspnea             | CT, ERCP                 | Thoracoctectomy, somatostatin infusion, placement of an endoscopic stent  | Uneventful in the immediate post-procedure period |
| Neher et al.11                | M/53                | Alcoholic              | Dyspnea, chest pain | CT, ERCP                 | Thoracoctectomy, placement of an endoscopic stent                         | Without pleural effusion after five months |
| Takeo et al.12                | M/67                | Alcoholic              | NR                  | CT, ERCP                 | Thoracoctectomy, total parenteral nutrition, octreotide                    | Asymptomatic at discharge      |
| Ito et al.13                  | M/52                | Alcoholic              | Coughing, back pain | CT                       | Pleural drainage, octreotide                                              | NR                             |
|                               | F/39                | Alcoholic              | Coughing, sputum    | CT                       | Conservative                                                              | NR                             |
| Akahane et al.8               | M/69                | Alcoholic              | Dyspnea, dyspnea    | CT, MRI, ERCP            | Thoracoctectomy, total parenteral nutrition, octreotide                    | Asymptomatic after five years   |
| Lanternier et al.16           | M/64                | Alcoholic              | Dyspnea, coughing, cardiac tamponade | CT, MRI, ERCP | Pleural drainage, placement of endoscopic stent, distal pancreatectomy with pancreaticojejunostomy | Without recurrence after 12 months |
| Lamme et al.14                | F/44                | Alcoholic              | Dyspnea, coughing   | NR                       | Pleural drainage                                                          | Death by pneumonia             |
|                                | M/54                | Alcoholic              | Dyspnea, coughing   | NR                       | Pleural drainage, endoscopic sphincterotomy, octreotide                     | Lost to follow-up after discharge |
|                                | M/42                | Alcoholic              | Dyspnea, coughing   | CT, ERCP, MRI            | Pleural drainage, endoscopic placement of pancreatic stents, octreotide    | Doing well after two months    |
|                                | M/54                | Alcoholic              | Dyspnea, coughing   | CT, ERCP, MRI            | Pleural drainage, octreotide                                              | Doing well after six months    |
| Meybeck et al.17              | M/39                | Alcoholic              | Dyspnea, chest pain | CT                       | Pleural drainage, octreotide, antibiotics, pleural decortication, percutaneous drainage of pancreatic pseudocyst | Partial involution of the pseudocyst and regression of pulmonary images after six months |
| Neumann et al.18              | M/68                | NR                     | Dyspnea, chest pain | CT, ERCP                 | Placement of an endoscopic stent, antibiotics                              | Regression after three weeks   |
|                                | F/47                | Alcoholic              | Dyspnea, chest pain | CT, ERCP                 | Pleural drainage, endoscopic sphincterotomy, octreotide                     | Lost to follow-up after discharge |
|                                | M/46                | Alcoholic              | Dyspnea, chest pain | CT, ERCP                 | Pleural drainage, endoscopic placement of pancreatic stents, octreotide    | Doing well after two months    |
|                                | M/55                | Alcoholic              | Dyspnea, chest pain | CT, ERCP, MRI            | Pleural drainage, octreotide                                              | Doing well after six months    |
| Zubiaurre et al.18             | M/40                | Alcoholic              | Dyspnea, back pain  | CT, MRI                  | Pleural drainage, total parenteral nutrition                               | Remission after one month      |
| Koshitani et al.23            | M/45                | Alcoholic              | Fever, coughing     | CT, ERCP                 | Pleural drainage, placement of an endoscopic stent                         | No recurrence after 33 months  |
|                                | M/56                | Alcoholic              | Dyspnea             | CT, ERCP                 | Pleural drainage, placement of an endoscopic stent, percutaneous drainage of pancreatic pseudocyst, distal pancreatectomy | No recurrence after 20 months  |
|                                | M/65                | Alcoholic              | Dyspnea on exertion | CT, ERCP                 | Pleural drainage, endoscopic placement of stent                            | No recurrence after eight months|
| Cociere et al.24              | M/59                | Alcoholic              | Dyspnea             | CT, ERCP, MRI            | Thoracoctectomy, Frey procedure                                            | No recurrence after three years |
| Vyas et al.25                 | M/53                | NR                     | Dyspnea, fever, hemoptysis, chest pain | CT, MRI, ERCP | Pleural drainage, pancreaticojejunostomy                                  | NR                             |
| Cooper et al.23               | M/72                | Pancreas pseudodivisum | Dyspnea             | CT, MRI, ERCP            | Thoracoctectomy, EUS-guided placement of pancreatic stent                 | No recurrence after one year   |
| Thyagaraj et al.24             | M/49                | Alcoholic, incomplete pancreas divisum | Dyspnea, chest pain, weight loss | CT, MRI | Pleural drainage, distal pancreatectomy                                    | NR                             |
| Ferris et al.25               | F/51                | Alcoholic              | Dyspnea, epigastric pain | CT, MRI, ERCP | Thoracoctectomy, Endoscopic placement of stent, antibiotics            | Resolution in the immediate post-procedure period |
| Sonoda et al.26               | M/53                | Alcoholic              | Dry coughing, dyspnea, heart palpitations | CT, MRI, ERCP | Pleural drainage, total parenteral nutrition, octreotide, distal pancreatectomy | Doing well immediately after recovery from surgery |
| Shah et al.27                 | M/32                | Alcoholic              | Dyspnea, chest pain, coughing, abdominal pain | CT, MRI, ERCP | Endoscopic placement of stent                                             | No recurrence after one year   |
| Mota et al.28                 | F/52                | Alcoholic              | Dyspnea             | CT                       | Thoracoctectomy, Partingon-Rochelle procedure                              | Doing well immediately after recovery from surgery |
| Gomes et al.29                | M/44                | Alcoholic              | Dyspnea at exertion, dry coughing, chest pain | CT, ERCP | Thoracoctectomy, total parenteral nutrition                              | Regression of pleural effusion on discharge |
| Hirosawa et al.30             | M/58                | Alcoholic              | Chest pain          | CT, ERCP                 | Pleural drainage, endoscopic placement of stent, antibiotics              | Regression of pleural effusion on discharge; patient lost to follow-up and died after two years of an unknown cause |
| Ok et al.31                   | M/32                | Alcoholic              | Epigastric pain     | ERCP                     | Pleural drainage, total parenteral nutrition, endoscopic placement of stent | Regression after 4 weeks        |
| Sánchez et al.32              | M/51                | Alcoholic              | Dyspnea, chest pain | CT, MRI, ERCP            | Thoracoctectomy, distal enteral nutrition, octreotide, endoscopic placement of stent | Asymptomatic after two years   |
| Soares et al.33               | M/43                | NR (HIV-positive under anti-retroviral therapy) | Dyspnea             | CT, MRI, ERCP            | Pleural drainage, total parenteral nutrition, somatostatin analogs, endoscopic sphincterotomy, distal pancreatectomy with Roux-en-Y pancreaticojejunostomy | Regression of pleural effusion 10 days after surgery |

M=male; F=female; NR=not reported; CT=computed tomography; MRI=magnetic resonance imaging; ERCP=endoscopic retrograde cholangiopancreatography

TABLE 1 - Reported cases of pancreaticopleural fistulas secondary to chronic pancreatitis over the last 20 years.
performed, consisting of balloon dilatation and placement of intraductal prostheses, with success rates of up to 25% being reported with this treatment modality16,17,24,4,33,6,30,28,26,27.

The main indication for surgical treatment is the failure of clinical and/or endoscopic treatments16,18,15,29. Surgery is based on internal pancreatic drainage, especially by means of pancreaticojejunostomy, and/or pancreatic resections, depending on the degree of involvement of the main duct and the pancreatic portion involved. A review by King et al.14 observed that attempts at prolonged periods of medical therapy tend to delay the resolution of the fistula compared with patients who undergo definitive operative intervention early in the course of treatment.

There is no consensus regarding the optimal treatment. Conservative management should be the first option; despite its low rates of complete resolution, there are reports of success and this modality avoids the possibility of complications arising from invasive procedures; however, it is often associated with lengthy hospital stays9,12,13,16,22,11. Endoscopic treatment should be the second-line therapy, indicated for those individuals who did not respond to clinical measures, since it presents good results and lower morbidity and mortality than surgery.2,15,24,4,33,27. Hence, surgery should be warranted in the refractory cases11,13,15,33,30,8,29. There is no consensus in regard to the optimal technique to be adopted; it must depend on the individual characteristics of each case. Individuals with predominantly cephalic disease would benefit from Feger or Beger procedures3; those with diffuse dilatation of the duct without severe involvement of the pancreas head would be appropriately treated by means of a Puestow/Partington-Rochelle procedure9,15,22,28; those with disease restricted to the pancreas tail or distal body would benefit from distal pancreatectomies, with or without pancreaticojejunostomy, depending on the caliber of the pancreatic duct16,15,13,30. Since surgery is reportedly the best treatment approach to treat the abdominal symptoms, especially refractory pain2,3,25,24,4,28,26,27, it should also be considered a more definitive treatment for these individuals, since it may bring a more integrative relief of both thoracic and abdominal consequences of the disease.

CONCLUSION

Pancreaticopleural fistula is a rare complication of chronic pancreatitis and the Frey procedure may be an appropriate treatment option when clinical and endoscopic treatments are unsuccessful.

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