Staged Interventional and Surgical Treatment of Patient with Chronic Pancreatitis Complicated by Pancreaticopleural Fistula with Lung Abscesses

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Conflict of interest:
None declared

Patient:
Male, 37-year-old

Final Diagnosis:
Chronic alcoholic pancreatitis • pancreaticopleural fistula • left lung abscesses

Symptoms:
Fever with a body temperature of 39.1°C • left thoracic pain • severe cough with purulent sputum • shortness of breath • upper abdominal pain

Medication:
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Clinical Procedure:
Repeated thoracenteses • chest tube • drainage of lung abscesses • ultrasound-guided drainage of pancreatic pseudocyst • ultrasound-guided transparietal external-internal pancreatic duct stenting • Bern modification of Beger procedure

Specialty:
Surgery

Objective:
Unusual clinical course

Background:
Pancreaticopleural fistula is a rare complication of chronic pancreatitis. Its formation is associated with local disruption of the pancreatic duct or pseudocyst communicating with the ductal system. Rarely, other intrathoracic complications may develop such as mediastinitis, pericarditis, hemothorax, and pleural empyema. The combination of pancreaticopleural fistula with lung abscesses is extremely rare.

Case Report:
A 37-year-old male patient, a long-term alcohol abuser, was admitted with complaints on left thoracic and upper abdominal pain, fever with a body temperature of 39.1°C, and a severe cough with purulent sputum. Left-sided pneumonia with pleural effusion was diagnosed. Thoracentesis and then a pleural drainage were performed. However, the symptoms persisted. Pleural effusion amylase was very high – more than 60 000 IU/L. Computed tomography and magnetic resonance imaging revealed cystic changes in the pancreatic head, pseudocyst in the pancreatic body, dilation of the Wirsung duct, and pancreaticopleural fistula with several left lung abscesses. Step by step, the patient underwent drainage of lung abscesses, external drainage of the pancreatic pseudocyst, and external-internal stenting of the pancreatic duct under ultrasound guidance. After fistula resolution, the patient was readmitted and successfully underwent the Bern variant of the Beger procedure.

Six months later, he had no complaints and returned to work. In a follow-up examination, there was no fistula, no ductal hypertension, and only small pulmonary residual changes.

Conclusions:
A very rare case of chronic pancreatitis complicated by pancreaticopleural fistula with lung abscesses is presented. The clinical outcome was good due to the staged character of treatment and participation of a multidisciplinary specialist team.

MeSH Keywords:
Lung Abscess • Pancreatic Fistula • Pancreatitis, Chronic

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Background

Pancreaticopleural fistula (PPF) is a rare complication of chronic pancreatitis (CP) that develops in 0.4% of patients with pancreatitis and 4.5% of patients with pancreatic pseudocysts [1]. PPF formation is related to local disruption of the pancreatic duct or pseudocyst connected with the ductal system [1–3]. If the pancreatic duct disruption is posterior into the retroperitoneum, it will track along the path of least resistance, namely up into the mediastinum along the aorta or esophagus. The pancreatic juice enters the chest and breaks through one or both pleura(e) and forms – on the background of negative intrathoracic pressure – chronic pancreatic pleural effusion [1,2]. In very rare cases, due to enzymatic injury of fixed lung tissue, a pancreaticobronchial fistula (PBF) can occur [4,5]. However, the intrathoracic complications of PPF are not limited to enzymatic pleural effusions and PBF. Pathologic conditions such as hemoptysis [6–8], hemorhorax [9–11], pleural empyema [8,12–18], mediastinitis [19,20], pericarditis, and pericardial tamponade [21–24] are described in the literature. The pathogenesis of most of these complications probably involves a synergetic effect of 2 aggressive factors: enzymatic tissue damage and infection.

PPF itself is a rare condition, and the complications aforementioned are even more rare (each of them is described in only a few publications). Therefore, the management of these intrathoracic complications of PPF is not well developed.

We have treated 17 patients with CP complicated by PPF, which represents one of the largest institutional series. Here, we present for the first time a case report of PPF complicated by (or combined with) lung abscesses.

Case Report

A 37-year-old Russian male patient was urgently admitted to Nikolayevsky Hospital on July 03, 2018. He complained of pain in left hemithorax and left upper abdomen, fever with a body temperature of 39.1°C, and severe cough with purulent greenish sputum. He became ill 7 days before admission to the hospital. Mild pain appeared in the left hypochondrium, and after 3 to 4 days a cough and shortness of breath added to his symptoms and increased with time. For more than 15 years, he was an alcohol abuser and tobacco smoker. During the last 2 years, he complained of periodic upper abdominal pain. He had shortness of breath and was unable to remain in a prone position due to increased dyspnea and cough with increased sputum volume. Vital signs at the time of admission were as follows: blood pressure of 140/90 mmHg, heart rate of 98 beats per minute, temperature of 38.2°C, and respiratory rate of 23 breaths per minute.

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Auscultation revealed absent breath sound in the lower half and reduced breath sounds with wheezing under the upper half of the left hemithorax. Laboratory tests showed hemoglobin, 12.5 g/dL, white blood cells, 16 800/mm³, and platelets, 590 000/mm³. Blood chemistry showed elevated serum amylase (3684 IU/L), lipase (1754 IU/L) and C-reactive protein (150.1 g/L). Immunological tests were found to be positive for hepatitis C and negative for human immunodeficiency virus (HIV). The remaining laboratory parameters were unremarkable.

Chest radiograph showed left pleural effusion that reached the level of the third rib (Figure 1). Abdominal ultrasound revealed structural changes of the pancreas (diffuse parenchymal heterogeneity, small calcifications, irregular contours) without its enlargement. Upper gastrointestinal endoscopy showed chronic gastric and duodenal inflammation. The patient was diagnosed with left-sided pneumonia complicated by pleural effusion, combining with the acute onset of chronic alcoholic pancreatitis. At thoracentesis, approximately 4.5 L of a brownish, turbid fluid was evacuated. Antibiotic treatment (cefotaxime 1 g twice daily and metronidazole 400 mg 3 times daily) with analgesics and intravenous hydration was commenced. Antibiotic treatment (cefotaxime 1 g twice daily and metronidazole 400 mg 3 times daily) with analgesics and intravenous hydration was commenced. Pleural fluid and sputum cultures showed no bacterial growth. Subsequently, we examined the sputum one more time, and the result of the sputum culture was again negative. In addition, sputum analysis for mycobacterium tuberculosis was also negative. Thus, the choice of antibiotic therapy in this case was purely empirical but took into account the recommendations of the clinical pharmacologist. Repeated chest radiographs showed infiltration in the left lower lobe and persisting pleural effusion. On abdominal computed tomography (CT) scans, cystic changes of the pancreatic head and body and fluid in the subhepatic space were present.

Figure 1. Chest radiography at admission that demonstrates massive left-sided pleural effusion.
Despite treatment, including repeated thoracenteses, the patient did not substantially improve. Antibiotic treatment scheme was changed to pefloxacin (400 mg twice daily). On repeated x-rays, there were 2 left lung abscesses with gas-fluid levels (Figure 2A, 2B). Due to fluid reaccumulation, the left pleural cavity was drained. At this stage, a measurement of the pleural fluid enzymes was undertaken, showing very high concentrations (amylase was approximately 60 200 IU/L, lipase could not be precisely measured due to a very high concentration), and PPF was suspected. Abdominal magnetic resonance imaging (MRI) revealed a slightly dilated (5 to 6 mm) pancreatic duct, cystic transformation of the pancreatic head, and a pseudocyst (53×71 mm) in the body of the gland. Considering the complicated CP and rarity of a clinical situation (combination of PPF and lung abscesses), the patient was transferred to Mariinsky Hospital (the main clinical location of our academic departments) on August 05, 2018. As earlier, he had dyspnea, cough with purulent sputum, fever, and was able to sleep only in a sitting position.

Chest CT showed multiple left lung abscesses; the largest one was 10×8 cm (Figure 2C).

After multidisciplinary discussion, it was decided that the patient’s treatment should be staged and as minimally invasive as possible.

During the first stage, 2 lung abscesses were drained under radiologic guidance on August 08, 2018. Additional abscess cavity was drained 2 days later. To decrease pancreatic ductal hypertension, the pancreatic body pseudocyst was externally drained under ultrasound navigation on August 08, 2018. The amylase level in pseudocyst fluid was 13 200 IU/L.

Later, the patient’s condition slowly improved. However, the fluid outflow from pseudocyst drain (approximately 100 mL daily) as well as from pleural drains remained stable.

To accelerate the PPF healing, it was decided to perform stenting of the pancreatic duct. Transcutaneous external-internal stenting with 14 Fr pancreatic stent (Boston Scientific, USA) was successfully performed by an interventional surgeon (RGA), who has significant experience in pancreatic duct procedures, on August 30, 2018. Puncture of slightly dilated duct was done through gastrocolic ligament and firm pancreatic tail tissue. Puncture pancreatography showed a fistula track from the pancreatic body pseudocyst (Figure 3). A 10-mm-long ductal stricture was found in the head of the gland, and guidewire and then stent were pushed through it into the duodenum with some difficulty.

The postoperative period was uneventful. After 3 days of octreotide injections (100 µg 3 times daily), the serum amylase
level was dropped to 150 IU/L, and this medication was dis-
continued. Five days post-surgery, pseudocyst drain outflow
was stopped, and a drain was removed. Pleural drains were
also removed on day 14 after pancreatic stenting.

The patient’s symptoms quickly improved, with normalization of
body temperature, decrease of dyspnea, and disappearance of
cough and sputum. Follow-up CT scan revealed small localized
hydropneumothorax that did not require additional drainage.
Abdominal MRI showed diffuse parenchymal changes typical
for CP, small pancreatic head pseudocysts with a decrease in
their size (Figure 4A), and ductal hypertension. The PPF track
was still visible (Figure 4B).

The patient was discharged in satisfactory condition on
September 10, 2018 and readmitted 5 weeks later for pan-
creatic surgery. All the previous procedures in this case were
lifesaving in fact, and indications for them were absolute.
Indications for major pancreatic surgery, however, were rela-
tive. These indications were established together with the pa-
tient, because he wanted to get rid of external drainage. For
our part, we wanted to remove the pathologically changed pan-
creatic head tissue and reliably eliminate ductal hypertension.

Chest CT (September 20, 2018) revealed a residual air-containing
cavity (4×5 cm), without a fluid component, in the lower lobe of
the left lung (Figure 5). The consulting thoracic surgeon stated
that this finding is a normal outcome of the lung abscess and
did not require any intervention. Pancreatography via stent-
ing tube showed good contrast passage into the duodenum
without visualization of pseudocyst and fistula track (Figure 6).

Abdominal MRI (September 21, 2018) showed a further de-
crease in the size of pancreatic head pseudocysts and pan-
creatic duct.

Pancreatic surgery was performed on September 26, 2018.
We performed the Bern modification of duodenum-preserving
pancreatic head resection (Beger procedure) – see Figure 7,
with formation of pancreatowirsungojejunal anastomosis with
Roux-en-Y retrocolic jejunal loop. The postoperative period

Figure 4. Abdominal MRI 8 days after pancreatic duct stenting: (A) cystic changes in the pancreatic head; (B) residual fistulous track
(all marked by arrows).

Figure 5. Chest CT scan after second admission. Residual post-
abscess changes of lung tissue (marked by oval).
was uncomplicated. The patient was discharged on day 14 post-surgery.

Outpatient ultrasound examination 6 months post-operation showed signs of CP (heterogeneous echo-structure of the gland with small parenchymal calcification) but without pseudocysts and ductal dilatation (Figure 8).

The patient was invited for follow-up examination at the hospital 1 year after surgery, but he refused it. Nevertheless, he agreed to answer our questions by telephone. He had no complaints (including no thoracic or abdominal pain). He works as a builder; the volume of physical work performed was comparable to what he was performing before the present illness. The patient smokes 5 to 8 cigarettes per day and does not deny the intake of strong alcoholic beverages “in small doses”, but he did not clarify the frequency and volumes of their use. There were no clinical signs of exocrine and endocrine pancreatic insufficiency in the patient, and he did not use pancreatic enzyme supplementation, even occasionally.

**Discussion**

PPF is a rare complication of CP, and diagnostics and treatment of this condition remains challenging and often requires a multidisciplinary approach.

The main criterion for the diagnosis of PPF is a highly increased concentration of amylase and lipase in pleural fluid [2,19,25,26]. This test is very simple. However, the correct diagnosis of PPF is often made relatively late. The main cause for this phenomenon is that the majority of PPF patients have “pulmonary” complaints: shortness of breath, cough, chest pain, and abdominal symptoms are minimal or even completely absent [3,26,27]. Therefore, the idea of the likelihood of complicated pancreatitis in a patient with pleural effusion usually appears after a more or less long period of time and treatment (usually ineffective). The data from English clinicians are very demonstrative: in a group of 4 patients, the time frames for establishing the correct diagnosis for PPF were very long: 12, 28, 33, and 49 (!) days [26]. The case report from the USA is even more impressive [28]: over a period of 4 months, the patient underwent 4 large-volume thoracenteses, 2 chest tube placements, and 2 thoracotomies (!) for recurrent pleural effusions. The etiology remained obscure until the fourth thoracentesis, when fluid amylase was measured and found to be markedly elevated. Importantly, these results were obtained...
in countries with a highly developed economy and medicine! Obviously, the awareness of the medical community regarding PPF remains insufficient worldwide.

In our case, the delay in correct diagnosis was explained by the fact that the patient had typical symptoms of pneumonia with pleural effusion, and only after the treatment was performed – it would seem quite adequate, but did not have the desired effect – was the pleural fluid amylase examined.

More than 30 years ago, Cooper et al. recommended measuring the pleural fluid amylase content in any case of exudative pleural effusion of unknown etiology [29]. As it seems now, post factum, this test could have been performed earlier in our case; the “typical portraits” of patients with severe pneumonia/lung abscess and CP are very similar. In both cases, these patients are thin, young or middle-aged men, usually heavy smokers and alcohol drinkers, with a low level of social protection and financial well-being.

By the time the correct diagnosis of PPF with lung abscesses was established, the question arose as to the optimal patient treatment. The first step was drainage of the lung abscess to prevent sepsis, which is the main cause of death in patients with PPF [30]. As the second step, we performed external pseudocyst drainage. We expected that the decrease (not even the complete elimination) of pancreatic ductal hypertension, achieved by this intervention, would allow for PPF resolution. External drainage of an abdominomediastinal fluid collection [31] or a formed pseudocyst [32] enabled healing the PPF without additional endoscopic and surgical interventions.

As an alternative treatment at this stage, endoscopic stenting of the pancreatic duct after sphincterotomy or nasopancreatic drainage can be considered. However, the patient definitively refused intervention under sedation, and we already refused endotracheal anesthesia, believing that it to be extremely undesirable in a patient with lung abscesses and persistent respiratory distress. Furthermore, external drainage of the pancreatic pseudocyst, in comparison with the endoscopic stenting procedure, is a less technically difficult and much less traumatic intervention. It should be emphasized that at that time we were dealing with a patient in severe condition, sharply weakened, and exhausted. His severe dyspnea persisted, even after drainage of lung abscesses, and he was unable to lie on his back at all. Ultrasound-guided pseudocyst drainage was performed under local anesthesia with the patient in a semisitting position.

After this procedure, the patient’s condition began to improve gradually. Shortly thereafter, it became substantially easier for the patient to breathe, and his sleep and appetite improved. However, the fluid output via pleural drainage continues, a phenomenon that indicated the persistence of PPF. Eventually, we decided to stent the pancreatic duct. In our case, we performed percutaneous external-internal stenting under ultrasound control. In principle, it is often very difficult to insert the thinnest guidewire into the almost non-dilated Wirsung duct through the gland tissue of the stony density and then to push in the stent. However, the procedure was performed by a very experienced interventional surgeon with an extensive background of pancreatic operations and was completely successful.

Currently, endoscopic procedures – stenting and nasopancreatic drainage – are widely used in the management of PPF [30,33]. Hastier et al. suggest that endoscopic intervention is the first-line treatment for this condition and that surgical intervention should be reserved as a second-line treatment [34]. Unfortunately, some publications [14,35] show the very small percentage of successful endoscopic procedures in PPF, due to severe pathological changes in the pancreas (compression of the pancreatic duct with stony gland tissue, duct deformity, lithiasis) and to some extent insufficient experience in endoscopic surgery on the pancreatic duct.

In our opinion, in the presented case, percutaneous intervention was preferable to endoscopic stenting: first, it required only local anesthesia; second, it was free from the specific complications of sphincterotomy (bleeding and duodenal perforation). For the worldwide practice of treating PPF, the procedure performed in our case is unique. We found in the literature only one observation of PPF in which the pancreatic stent was inserted under ultrasound guidance [36]. However, in that case the authors used endoscopic ultrasound with the rendezvous technique, rather than the conventional ultrasound, as in our case.

Our experience in the treatment of PPF is substantial. In a 2014 monograph, 12 cases were analyzed [37]. Currently, our series comprises 17 cases. For some patients – exhausted, cachectic, and having additional complications of pancreatitis – staged surgical treatment was unavoidable. Before the practical implementation of less-invasive endoscopic and interventional methods of pancreatic duct drainage, we used open pancreatic sphincterotomy with subsequent external drainage of the pancreatic duct [37]. We direct our colleagues’ focus to this surgical intervention because in the international literature, including the largest review articles on the topic [1,3,25,30,33,38,39], the operation of external drainage of the pancreatic duct is not mentioned at all.

An alternative to external drainage may be the operation of open stenting of the pancreatic duct, proposed and initially tested in our country [40]. So far, there have been no cases of its use in PPF, but we believe that such cases will be registered in the near future.
In this case, the Bern modification of Beger procedure was chosen as the definitive treatment. We have a good impression on a series of these operations in CP, including the presented case. The experience of using resection-draining surgeries in present or recently resolved PPF and PBF is very limited. Four cases of Frey procedure have been published, 3 of which were performed for PPF and 1 for PBF, with good results [33,41,42]. In one case, after long-term unsuccessful conservative treatment, Beger procedure was performed [43]. Finally, in one PBF case, the authors used a duodenum-preserving resection of the pancreatic head with a V-shaped excision of the pancreatic tissue along the duct of the body and tail of the gland [44].

It should be emphasized that enzymatic pleural effusion in PPF is not always the “final” complication of the fistula. In some cases, especially with late diagnosis and treatment, other more severe and life-threatening intrathoracic complications, such as hemotherox, pleural empyema, mediastinitis, pericarditis, and PBF, may develop [8–24]. Management of these complications is not well studied (usually being empirical).

We were able to find in the literature only 1 case of lung abscess in PPF [5]. The abscess developed as a complication of PBF, so its pathogenesis was different from our case. The patient was treated by pulmonary resection and distal pancreatic resection with splenectomy, which led to the recovery.

It remains unclear to us how to define lung abscesses in our case: as a complication of PPF or as a concomitant disease that developed independently of PPF? However, knowing the exact answer to this question would not be a key factor in determining the patient’s treatment.

Unfortunately, we were unable to examine the patient 1 year after the surgery, as we planned. The reason for this was the patient’s categorical refusal for hospitalization and examination. In general, many CP patients are undisciplined, with low compliance with examination and treatment. There are similar cases in the literature when, after successful treatment of PPF, patients either refused a control examination [45] or were completely lost to follow-up [9,46]. We had to be satisfied with the result of a telephone survey, which showed that the patient had no complaints (neither abdominal nor thoracic); he works and feels good.

The satisfactory treatment outcome in our case was the result of the coordinated work of a multidisciplinary team of specialists: internists, pulmonologists, intensive care specialists, general surgeons, a pancreatic surgeon, an interventional surgeon, a thoracic surgeon, medical radiologists, and a clinical pharmacologist. The importance of a multidisciplinary approach in the treatment of PPF tailored to the individual patient is also noted in recent publications [15,28,47].

**Conclusions**

We presented a very rare case of CP complicated by PPF and enzymatic pleural effusion with the formation of lung abscesses. Initially, the clinical situation was interpreted as a combination of exacerbation of CP with left-sided pneumonia complicated by pleural effusion. The correct diagnosis was made with a delay, which is a fairly characteristic phenomenon for PPF. The severity of the patient’s condition and respiratory failure allow the use of only minor interventions.

Step by step, the patient underwent drainage of lung abscesses, external drainage of the pancreatic pseudocyst, and external-internal stenting of the pancreatic duct under ultrasound guidance. After PPF resolution, the patient was re-hospitalized and underwent the Bern modification of the Beger procedure. The individual approach to and staged character of the surgical treatment as part of a multidisciplinary collaboration allowed us to achieve a satisfactory clinical outcome.

**Conflict of interests**

None.

**Abbreviations**

PPF – pancreaticopleural fistula; CP – chronic pancreatitis; PBF – pancreaticobronchial fistula; CT – computed tomography; MRI – magnetic resonance imaging.
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