INTERNAL PANCREATIC FISTULAE – MANAGEMENT REVIEW

STANISŁAW HAĆ, ZBIGNIEW ŚLEDZIŃSKI

Department of General Endocrine and Transplant Surgery, Medical University in Gdańsk
Kierownik: prof. dr hab. Z. Śledziński

The pancreas is a component of the digestive system with a relatively complicated embryogenesis. The pancreas is formed during embryonic weeks 6–7 from two buds. It is a digestive system gland with a typical configuration of excretory ducts. Pancreatic juice is secreted into the ducts through two orifices in the duodenal wall. The two pancreatic ducts are the consequence of two embryonic buds.

Duct obstruction, abnormalities, and injuries result in fistula formation. Acute and chronic pancreatitis are the two most frequent reasons for pancreatic internal fistulae. Acute pancreatitis may result in partial pancreatic duct necrosis. During chronic pancreatitis, we observe the formation of pancreatic duct concrements and interstitial fibrosis. Chronic inflammation results in multiple strictures along the pancreatic duct. Microinjuries and segmental pancreatic juice hypertension also result in fistula development (fig. 1).

Less frequent causes of internal pancreatic fistulae are blunt pancreatic injuries.

HISTORY

Pancreatic juice extravasation into the peritoneal cavity was described by Smith in 1953 (1, 2). Pancreatic ascites was first named by Cameron in 1967 (3, 4). It was thought that pancreatic ascites was the consequence of post-inflammatory lymphatic stasis (5). The true pathogenesis of the event was recognized with the use of endoscopy in the 80s and 90s (1, 6, 7). The treatment of pancreatic ascites was repeated paracentesis and effusion evacuation (3, 5). Atropine and “nothing by mouth” was used to decrease pancreatic juice secretion.

Antibiotic prophylaxis and general supportive therapy was also used. In several cases, front and dorsal 250–550 R teletherapy was also used to provoke fibrosis of pancreatic fistulae (4, 8, 9). The success of the treatment strategy described was from 20 to 60% of patients (mean 48% in review papers) (3, 5, 10). Patients not improving after 8 weeks of medical treatment were operated upon. Some authors advised surgical treatment in pancreatic ascites with the presence pseudocysts (7).

![Fig. 1. Possible causes of internal pancreatic fistula](image)
DEFINITIONS

Pancreatic ascites

Pancreatic juice extravasation into the free peritoneal cavity is called pancreatic ascites (3). This event is usually easy to recognize when taken into consideration. Chronic pancreatitis coinciding with alcohol abuse is the most frequent cause of pancreatic ascites (PA) (4). Of patients with CP, 3.5% will develop pancreatic ascites (3, 6). PA is twice as prevalent in men, usually occurring between the ages of 20 and 50 (10). Because of similar etiology and symptoms, PA is often misdiagnosed as hepatic failure ascites (3, 4, 5). Pancreatic juice in ascitic fluid is not activated. Thus, PA doesn’t produce typical peritoneal irritation nor enzymatic necrosis, although it is potentially a proteolytic and lipolytic agent (7, 10, 11).

The most frequent symptoms of pancreatic ascites are free peritoneal fluid, cachexia and paralytic ileus (5, 10, 12). Confirmation of the disease can be made based on high diastase (>1000 IU/L) and protein (>3 g/L) concentration in the ascetic fluid (3, 5, 13). Taking into consideration medical history, there are no pancreatitis symptoms in 10% of patients with documented pancreatic ascites (3, 4, 10). Visualization of a fistula tract is the definitive confirmation of pancreatic ascites.

Pancreaticopleural fistula

A connection between the pancreatic duct and pleural cavity is called a pancreatic pleural effusion or pancreaticopleural fistula (8, 11, 14). A pancreatic fistula in this situation is usually situated on the posterior part of pancreatic gland and penetrates the chest cavity via the natural diaphragmatic openings. Pancreaticopleural fistula resulted in mild dyspnea with a cough in 50% of patients (3, 15). Pancreatic pleural effusion is recognized on the basis of the same laboratory tests as in pancreatic ascites (12, 13, 14). Similarly, this event is usually resistant to medical therapy and causes severe cachexia. In rare cases, pancreatic ascites accompanies pancreatic pleural effusion (5, 10, 16).

Pancreatic pseudocysts

Pancreatic pseudocysts communicating with pancreatic duct or small interstitial ducts is the internal pancreatic fistula into restricted space – usually the retroperitoneum or the omental sac (3, 4, 15). A pancreatic pseudocyst is usually the consequence of pancreatic destruction during acute, chronic pancreatitis or pancreatic blunt trauma (17, 18, 26). There is an important difference between pancreatic pseudocysts and postinflammatory fluid collection. The former contains pancreatic juice. Pancreatic pseudocysts sometimes promote the occurrence of pancreatic ascites or pleural effusion (19, 20). Pancreatic ascites or pleural effusion is the consequence of pseudocyst disruption in 43% to 80% of cases (10). In 10% of patients, internal pancreatic fistulae resulted in direct pancreatic duct disruption, and in 10%, the cause of pancreatic internal fistulae is unclear. Among all patients with pancreatic pseudocysts, 6% to 14% will develop pancreatic ascites or pleural effusion (10). Pancreatic pseudocysts might be thought of as temporary stadium to pancreatic ascites or pancreatic pleural effusion (11).

Pancreatic injury

Pancreatic injury occurs in 2% to 50% of all abdominal injuries (21). Pancreatic injury is usually diagnosed at day “zero” in cases of abdominal exploration, or in the days following injury. Pancreatic duct injury might be complete or partial. Partial pancreatic duct injury is recognized when contrast given during endoscopic retrograde cholangiopancreatography (ERCP) appears proximal to the injured part of the duct (22).

INTERNAL PANCREATIC FISTULA CLASSIFICATION

Broe and Cameron defined 4 types of internal pancreatic fistulae with pancreatic ascites or pleural effusion (23):

Type 1 – direct leakage from the pancreatic duct without a pseudocyst.

Type 2 – leakage from a pseudocyst located in the pancreatic tail.

Type 3 – leakage from an obstructed proximal duct.

Type 4 – leakage from a pseudocyst located in the proximal portion.

Pancreatic pseudocysts are categorized according to localization, size and origin. D’Egidio and Scheina (1991) divide pseudocysts into three categories (24):

Type I – acute „post-necrotic” pseudocysts, usually occurring after AP and associated with...
normal ductal anatomy. Communication with the pancreatic duct is rare.

Type II – acute „post-necrotic” pseudocysts that occur after an episode of acute-on-chronic pancreatitis. There often is duct communication.

Type III – “Retention” pseudocysts that occur in CP and typically are associated with ductal strictures and duct communication.

In 2002, Nealon and Walser proposed a classification based solely on PD anatomy (25):

Type I – normal duct, no communication.

Type II – normal duct with duct-cyst communication.

Type III – otherwise normal duct with stricture, no duct-cyst communication.

Type IV – otherwise normal duct with stricture and duct-cyst communication.

Type V – otherwise normal duct with complete cut-off.

Type VI – chronic pancreatitis, no duct-cyst communication.

Type VII – chronic pancreatitis with duct-cyst communication.

Pancreatic injury is classified into 5 categories (21):

Stage 1 – pancreatic contusion without duct tear

Stage 2 – severe pancreatic contusion without pancreatic duct injury and without tissue defect.

Stage 3 – left side pancreatic transection or pancreatic injury with duct involvement.

Stage 4 – pancreatic head tear or pancreatic injury with biliary-pancreatic confluence involvement.

Stage 5 – multifragmental pancreatic head and duodenum disruption.

VISUALIZING TECHNIQUES

Visualization of the fistulous tract is an indication of an internal pancreatic fistula (26). Both ERCP and magnetic resonance cholangiopancreatography (MRCP) are standard procedures to diagnose a pancreatic fistula (11, 16, 27). Pseudocysts treated with percutaneous drainage might also be visualized directly by contrast injection (27).

The diagnostic power of ERCP and MRCP for internal pancreatic fistulae is between 59% and 100%, (8, 27). Pancreatic duct “cut offs” with strictures or concrement make it impossible to show the fistulous tract via ERCP. In this situation, the visualization of the fistula is only possible by MRCP or fistulography (16). In the operating theatre, a pancreatic fistula might be identified with intraoperative ERCP, transduodenal pancreatography, or proximal pancreatography after pancreatic tail resection or duct puncture.

About 10% of internal pancreatic fistulas are impossible to see with any visualizing technique and the diagnosis is based on laboratory and clinical criteria (28).

INTERNAL PANCREATIC FISTULA TREATMENT

Pancreatitis might cause several changes within the pancreas that are detrimental to the treatment strategy (10, 11).

Medical treatment of internal pancreatic fistula is focused on pancreatic exocrine output reduction and morbidity prevention. Internal pancreatic fistulae coincide with malnutrition or cachexia. Patients require total or partial parenteral nutrition with enteral nutrition by naso-enteral tube or microjejunostomy (10, 11). Standard medical treatment involves administration of somatostatin (octreotide 0,05-1,5 mg/d SC, somatostatin 180 µg/d – 250 g/h, and sandostatin LAR 20 mg/4 weeks) (10, 11, 29). All coagulation system abnormalities should be treated before endoscopic or surgical intervention (10). The authors of this study recommend antibiotic prophylaxis with carbapenem or fluoroquinolon and general supportive therapy (10). There are some reports of successful medical treatment of pancreatic fistulae (29). However, the analysis of a large series does not suggest medical treatment of internal pancreatic fistulae is the only option (10).

Endotherapy is the gold standard in internal pancreatic fistula treatment today (10, 26, 30, 31). Pancreatic duct concrements should be removed endoscopically (32). Occasionally extracorporal shock wave lithotripsy (ESWL) is used to facilitate endoscopic pancreatic duct decompression (32, 33). ESWL is used during pancreatic concrement treatment in 36% to 68% of all patients. The efficacy of this procedure is high in the case of thee or fewer concrements, up to 10 mm in diameter, not encrusted into the pancreatic duct wall, and situated close to the duodenum (32).

The optimum treatment in internal pancreatic fistula is to endoscopically “bridge” the leakage point with a pancreatic prosthesis (22,
This procedure is possible more often in pancreatic fistula located in the distal (close to duodenum) section. However, some authors have described several successful cases of pancreatic duct decompression without fistula “bridging” (10, 26). Pancreatic pseudocysts resulting from critical obstruction of the pancreatic duct or connecting the second or third degree ducts require internal drainage (19, 34). Antibiotic prophylaxis is routinely used before endotherapy and after for 5 to 7 days (unasy or imipenem) (35). However, the infection risk after endotherapy for a pseudocyst is associated with drainage insufficiency. Pseudocysts containing hyperechogenic material pose the highest risk of infection (35). Pseudocysts should be located up to 10 mm from the digestive tract lumen. The pseudocyst wall should be “mature” i.e. well defined and enhanced in CT, usually after 4 weeks post disease. The selected location for endoscopic internal drainage should not contain vessels and especially collateral circulation (32). To decrease the risk of hemorrhage, the endoscopic transmural procedure should be followed by endoultrasound or the technique of injection and retraction though this requires additional cutting (14). Endoscopic internal drainage is sufficient in pseudocyst therapy in 70% to 90% of cases (35). Transduodenal pseudocyst drainage is successful in 58% to 93% of cases (6, 26, 35). Endotherapy and endoscopic stenting and naso-pancreatic drainage is effective as a definitive treatment of internal pancreatic fistulae in 80% to 91% of cases (15, 31, 32).

Some data suggest that pseudocysts larger than 10 cm in diameter should be an indication for surgical treatment because of high risk of recurrence and morbidity (36). Early internal pancreatic fistula relapse reaches anywhere from 10 to 20% and does not exclude another endotherapy attempt (32, 37).

A stable or improving clinical status after endotherapy should indicate medical treatment for 3 to 8 weeks (10, 11 32). Internal pancreatic fistulae resistant to endotherapy should be treated surgically (10, 11, 38). The surgical treatment strategy depends on the fistula localization and pancreatic duct patency between the fistula and duodenal papilla (fig. 2).

The goals of surgical treatment for internal pancreatic fistulae are to minimize the degree of pancreatic resection and achieve effective control of pancreatic juice drainage (1, 10, 11, 17, 39). An anterior surface pancreatic fistula, without the presence of a pseudocyst is usually managed with Roux-en-Y fistulo-jejuno anastomosis (11). Pseudocysts communicating with the pancreatic duct require internal drainage (11). A proximal fistula (left from mesenteric vessels) or a fistula on the posterior pancreatic surface might be resected with primary pancreatic stump anastomosis or stump closure (10). Transduodenal sphincterotomy and sphincteroplasty are now reasonable because of endoscopy availability. Pancreatic pseudocyst drainage should follow causative treatment as the results and relapse rate of simple internal drainage confirm (17, 24). Ohge et al., reported a small series of patients with pancreatic pleural effusion treated by “upstream” internal drainage after pancreatic tail resection, just for fistula decompression (1, 10). This method might be an alternative surgical method, especially in fistulas located on the posterior surface, as it allows for omission of subtotal pancreatic resection in pancreatic duct strictures in the head of the gland (10).

Fig. 2. Possible surgical methods of treatment
a – endotherapy, b – pancreatogastroanastomosis, c – pancreatojejunoanastomosis, d – pancreatic fistula anastomosis with intestine loop, e – pancreaticojejunoanastomosis following distal pancreatic resection
Some clinicians have reported the successful use of extraordinary surgical procedures in pancreatic internal fistula treatment, like the pedunculated muscular flap technique or distal pancreatico-gastrostomy after distal pancreatic resection (40, 41, 42).

Several authors prefer bilateral subcostal abdominal access (17, 43). In this technique, the hepatic or splenic colon flexure is mobilized and gently swept inferiorly. The left portion of the pancreatic gland might be explored from the spleen attachments to the pancreatic tail and elevation on the pedicle of splenic vessels (21). Internal pancreatic fistula as a complication of chronic pancreatitis has resulted in pancreatic fibrosis and attachment to splenic vessels. Spleen preservation in pancreatic tail resection is not possible in about 30% of cases (17).

Some authors prefer pancreatic tissue transection using a surgical blade and utilizing electrocautery or nonabsorbable monofilament stitches 4/5-0 (17, 43) to control bleeding. The preferred method to control pancreatic tissue bleeding is stitching without clamping with forceps (43, 44). The pancreatic stump is anastomosed with two layers of single stitches with 3-0 coated silk or, more often, 3/4/5-0 nonabsorbable monofilament (17, 43). The pancreatic stump is then invaginated into jejunal lumen during placement of the stitches (43). A 60 cm long section of the jejunal limb is usually brought through the base of the right transverse mesocolon (17). Pancreatic proximal resection and internal pseudocyst drainage are performed in both open and laparoscopic procedures in selected centers (10, 36, 45). The results of these two techniques are similar, but it should be noted that patients undergoing laparoscopy are preselected and the presented series are relatively small.

Surgical treatments of the internal pancreatic fistula have a general failure risk ranging from 12% to 18% with 12% morbidity and about 8% mortality (10, 18). Relapse frequency increases up to 50% if the fistulous tract was not visualized preoperatively (10, 18, 26).

Pancreatic injury treatment depends on the degree of pancreatic damage, time, and the presence of associated injuries (21). First and 2nd degree injuries represent 60% and 20% of all pancreatic injuries, with 3rd degree compri-

sing 15% and more serious injuries only accounting for 5%. In pancreatic penetrating injuries, in the first 48 h survivors, pancreatic fistulae develop in only 12% to 33% of cases (21, 46, 47). Pancreatic blunt trauma results in pseudocysts in 30% of cases (21). Pancreatic injuries that are operated upon require drainage or stitching (21). It is not recommended to use two channel drains with suction because of the high rate of intraabdominal infection (21). Complex injuries of the epigastrium require an individual approach and extend beyond the range of this review (21).

Surgical efficacy in pancreatic injury treatment depends on the surgical skill. The main goals of surgical treatment are complete debridement of the operating field, the use of not absorbable stitching material, and the controlled repair of injured pancreatic ducts (21). A traumatic tear of the pancreas requires resection and anastomosis of the stump or stumps into the digestive tract (21). However, there are reports of successful endoscopic treatment of complete pancreatic duct injury (10).

Regarding where patients with internal pancreatic fistulae should be treated, the answer is only the high volume center with experienced endoscopy, radiology and surgery, based on the reported data.

**SUMMARY**

- Pancreatic ascites or pancreatic pleural effusion should be taken into consideration in every patient resistant to standard therapy.
- Every patient with an internal pancreatic fistula should be referred to the center experienced in pancreatic endotherapy and pancreatic surgery.
- It seems that the successful endoscopic treatment of an internal pancreatic fistula depends much more on the center experience than on the kind of fistula.
- Before internal pancreatic fistula treatment is begun, the fistulous tract should be visualized at any cost.
- Internal pancreatic fistulae should be treated using the least invasive method.
- The minimal degree of pancreatic resection and controlled, effective pancreatic juice drainage are the classical goals of internal pancreatic fistula surgical treatment.
REFERENCES


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Adress correspondence: 80-952 Gdańsk, ul. Dębinki 7