Management of Ductal Leaks

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Introduction

The development of acute pancreatitis is primarily caused by local enzyme activation and acute cytokine release in response to some form of insult to the pancreas. Early signs and symptoms of this inflammatory process include abdominal pain, ileus, and potentially a systemic inflammatory response syndrome (SIRS), and acute respiratory distress syndrome (ARDS). Depending on the severity of the insult, pancreatic tissue apoptosis or necrosis ensues. Perpetuation of the disease process may be the result of infection of necrotic tissue or an ongoing leak secondary to disrupted ductal epithelium from the inflammatory process [1–4]. Pancreatic trauma can also lead to an acute leak and traumatic pancreatitis. In the instance of penetrating trauma, this can lead to an acutely ill patient as compared with a clinically well patient after surgical trauma with a percutaneous drain left in place [5].

The potential manifestations of pancreatic leaks are multiple. Pancreatic leaks or fistulas are traditionally classified as internal or external [3, 6]. External leaks represent pancreaticocutaneous fistulas and are most typically iatrogenic in etiology. Internal leaks present in a myriad of different forms and include pancreatic ascites, pleural effusions, pseudocysts among others [4, 7]. The prognosis and management of pancreatic leaks varies based on the clinical manifestations of the leak.

Epidemiology

The incidence and prevalence of pancreatic duct leaks has not been thoroughly studied and remains unclear. However, up to 40 % of patients with acute pancreatitis will develop some type of acute fluid collection [8]. Only a small percentage of these patients will go on to develop a true pseudocyst or fistula. It appears that the etiology of pancreatitis is not important in determining whether a leak will ensue, but it is the severity of the insult that matters. Gallstone pancreatitis is, however, the most common cause of severe acute pancreatitis. One clinical entity that is known to involve high rates of pancreatic duct leaks is walled-off pancreatic necrosis (WOPN). In numerous studies WOPN patients have been shown to have disconnected duct syndrome (DDS) in 35–70 % of cases. It is unclear whether this ductal disruption is the cause of or a result of the WOPN [6, 9, 10].

Clinical Features

The symptoms and clinical manifestations of ductal leaks depend on multiple factors. The main determinants include the leak's location

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C.E. Forsmark and T.B. Gardner (eds.), *Prediction and Management of Severe Acute Pancreatitis*,
DOI 10.1007/978-1-4939-0971-1_12,

Table 12.1 Manifestations of pancreatic duct leaks

Internal fistula
– Peripancreatic fluid collection
– Pseudocyst
– Pancreatic ascites
– High amylase pleural fluid
– Pancreaticoenteric/biliary/bronchial fistula
– Walled-off pancreatic necrosis (WOPN)
– Smoldering pancreatitis
External fistula
– Pancreaticocutaneous fistula

within the gland, the size of the leak, and the body's ability to contain the leak's output (Table 12.1). Other factors include bacterial translocation, endotoxin release, extraluminal enzyme activation, and superinfection. Patients range from being completely asymptomatic to experiencing debilitating pain and potentially severe sepsis and other serious complications from resultant fluid collections. Signs and symptoms can include pain, nausea, vomiting, tachycardia, ileus, and hypotension [11, 12]. Certainly the severity of the pancreatitis that causes or results from the leak has the most bearing on the patient's initial symptoms and clinical course; later on the characteristics of the leak and the associated complications play the biggest role. The classic manifestation of a pancreatic duct leak is the formation of a pseudocyst, but other possibilities include walled-off pancreatic necrosis, pancreatic ascites, pleural effusions, and even pericardial effusions (Fig. 12.1).

The size of pancreatic duct leaks is highly variable and can range from a small trickle to high-grade output. The size of the leak does not necessarily correlate with the severity of the resulting symptoms and complications. Low-grade leaks typically result in intrapancreatic fluid collections, which can be asymptomatic or lead to a smoldering pancreatitis. This can be associated with variable degrees of pancreatic necrosis, which can in turn lead to multisystem organ failure or local and systemic infections [6, 13–15]. High-output leaks can similarly lead to pancreatic necrosis, but can also result in large peripancreatic or remote abdominal fluid collections, pancreatic ascites, high amylase pleural effusions, or have mediastinal involvement.

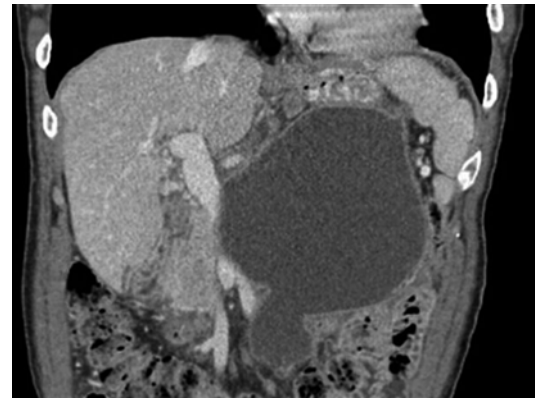

Fig. 12.1 Patient with severe acute pancreatitis with large pancreatic fluid collection

Leaks originating from the duct in the head of the pancreas can have a variety of manifestations. The leaking pancreatic fluid can be walled-off by the body and localized to the right upper quadrant. Collections in this location can impinge upon or fistulize to multiple different organs in this area. These collections can press on the common bile duct leading to biliary obstruction, jaundice, elevated liver function tests, or even cholangitis. Collections that impinge upon the duodenum or gastric outlet can lead to post-prandial pain, post-prandial nausea and vomiting, early satiety, and potentially gastric outlet obstruction. Leaks from the pancreatic head can also result in fluid tracking along the psoas and develop pelvic fluid collections. This fluid can even track into the scrotum and buttocks [16]. Often, pancreatic head leaks result in right pararenal fluid collections as well.

Leaks that develop in the pancreatic tail often result in left upper quadrant or perisplenic fluid collections [3, 17]. Collections that develop in this area can fistulize to the ligament of Treitz or the transverse colon [18–20]. Fluid from the tail can also track into the retroperitoneum and lead to acute pararenal or pelvic fluid collections. Alternatively, this fluid can track up into the thorax and develop high amylase pleural effusion [21–24]. Symptoms vary based on the location of the fluid collection but can include left upper quadrant pain, nausea, post-prandial pain, shortness of breath, or sepsis in the event of a colonic fistula.

Leaks originating in the genu or body of the pancreas often create fluid collections in the lesser sac. Necrotizing pancreatitis with walled-off pancreatic necrosis frequently results in leaks in this area in the form of DDS [3, 25–29]. Unfortunately, CT and other imaging studies are poor at differentiating WOPN from a pseudocyst and therefore most collections occurring in this area should be regarded as possible WOPN [4, 30–32]. Similar to patients with pancreatic tail leaks, body leaks can also create pleural effusions, pericardial effusions, and even pancreaticobronchial fistulas [3, 33]. Patients with pancreatic body leaks can also develop pancreatic ascites [6, 21, 23, 34]. Patients with pancreatic ascites will experience abdominal pain and increased abdominal girth, potentially with shortness of breath from pressure on the diaphragm and occasionally spontaneous bacterial peritonitis.

Diagnosis

In order to manage pancreatic duct leaks one must first successfully make the diagnosis. In the past this was commonly done with ERCP, which can also be therapeutic. However, the advent of excellent cross-sectional imaging and the risk of pancreatitis associated with ERCP have moved the use of ERCP to primarily therapeutic purposes. In the right clinical setting the uses of abdominal ultrasound, pancreatic protocol CT, secretin-MRCP (S-MRCP), and aspiration of fluid collections are often successful at making the diagnosis [3, 8, 35–39] (Table 12.2).

Table 12.2 Diagnosis of pancreatic leaks

External fistula
– Pancreatogram through JP or IR drain
– Persistent high amylase output through JP or IR drain
Internal fistula
Pleural effusion
– CXR, abdominal, and thoracic CT
– High amylase with aspiration
Pancreatic ascites
– Ultrasound, CT, or MR of abdomen
– High amylase with paracentesis
Pseudocyst
– CT, MRI, EUS, ERCP
WOPN
– CT, MRI, EUS
Duct disruption
– ERCP or S-MRCP

The diagnosis of an external pancreatic fistula is typically straightforward as long as the diagnosis is considered. A patient with persistent output from a JP drain after pancreatic surgery or peripancreatic surgery should have the fluid checked for amylase levels, which will be elevated in the setting of a pancreatic leak [40]. Inadvertent damage to the pancreas during peripancreatic surgery is far more common than damage to the stomach or colon. Also, in patients with variable output of clear pancreatic juice following percutaneous drainage of a pseudocyst or peripancreatic fluid collection, one can consider contrast injection through the drain to assess for a pancreatogram, which confirms the diagnosis. These tests should also be considered in patients with percutaneous output of clear fluids after a penetrating injury.

For making the diagnosis of an internal fistula, a pancreatic protocol CT is typically the best initial diagnostic test for patients with smoldering or severe pancreatitis [41]. If a fluid collection is seen in this type of clinical picture, it can generally be diagnosed as a leak. However, leaks are implied rather than defined by CT and sequential scans with evidence of enlarging collections may be needed for diagnosis. CT is also an imperfect test because it often overestimates the fluid component of a cyst and therefore can misdiagnose WOPN as a pseudocyst [9]. Historically, ERCP has been used to diagnose leaks; however, the S-MRCP may now frequently be used in its place as it has been shown to be able to characterize an active leak and minimizes the potential complications associated with ERCP, such as worsening pancreatitis [37–39, 42]. S-MRCP is also able to diagnose DDS, which is a situation where ERCP alone will not be able to control the problem.

The diagnosis of a pancreatic leak is most commonly considered when a patient presents with typical clinical picture of pancreatitis followed by persistent or recurrent symptoms. However, it is far more difficult when a patient

without a known history of pancreatitis is found to have a pancreatic or peripancreatic cyst. In this situation chronic pancreatitis changes such as parenchymal or ductal calcifications can suggest the diagnosis. Also, a uniform appearance, lack of cyst calcifications, and a thick outer rind can suggest a pseudocyst. Endoscopic ultrasound can often provide better characterization of the cyst and can allow for fine-needle aspiration to sample cyst fluid for amylase, CEA, and cytology, which can help differentiate pseudocysts from cystic neoplasms [43].

Management

Historically, the management of pancreatic duct leaks was typically surgical. Medical or conservative management with gut rest, TPN, and octreotide has been shown to be beneficial in some patients, although refractory cases are quite common, particularly in the setting of a high-volume leak. The advent of ERCP has allowed endoscopists to place transpapillary stents to facilitate leak closure [44] (Fig. 12.2).

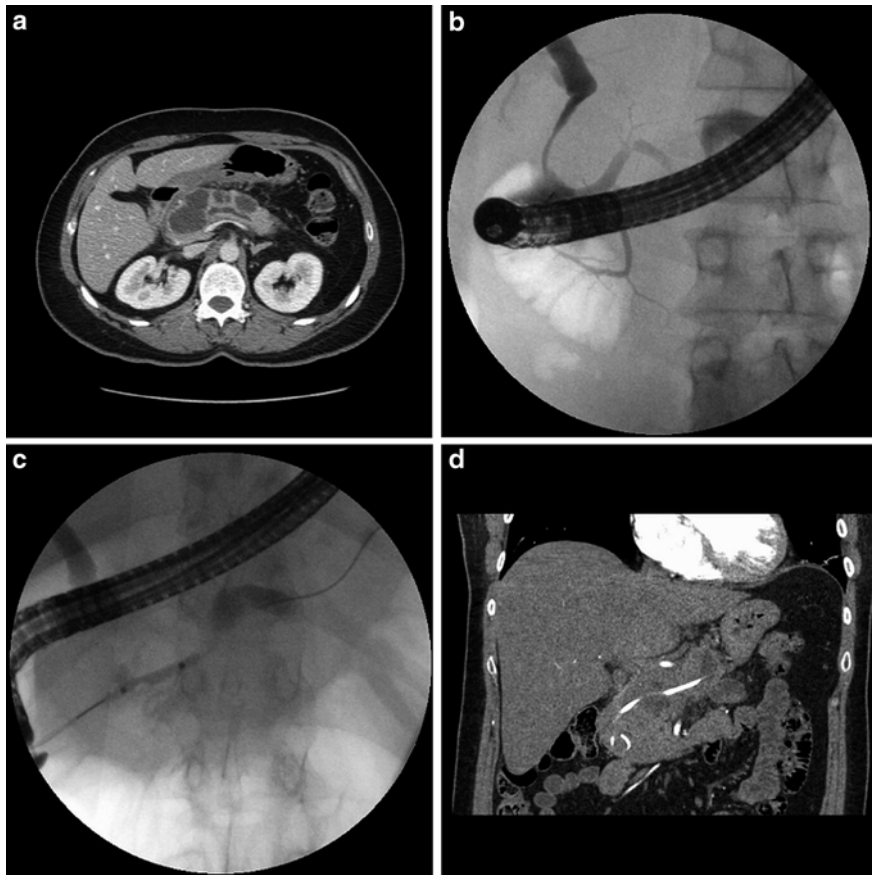

Fig. 12.2 Patient with acute biliary pancreatitis with subsequent development of multiple intrapancreatic fluid collections and symptoms of smoldering pancreatitis. Ductal disruption and downstream ductal stenosis treated with balloon dilation and stent placement. (**a**) CT with intrapancreatic fluid collections. (**b**) Pancreatogram demonstrating ductal leak. (**c**) Balloon dilation of stricture. (**d**) CT with stent post-ERCP

This intervention combined with other therapeutic endoscopy techniques has allowed many patients to avoid surgery.

Having the ability to place a pancreatic duct stent does not mean that one must provide endotherapy whenever the possibility of a pancreatic leak is entertained. Patients with pancreatic leaks are best served by a team including interventional radiologists, pancreaticobiliary surgeons, and endoscopists [1, 3, 45]. Ideally, the interventional plan should be developed in a collaborative way and involve high-quality cross-sectional imaging in the form of CT and/or MRI to map the leak and its complications. The main contraindication to ERCP in the setting of a leak is the inability to provide endotherapy as in that situation the unsuccessful intervention may lead to infection of the previously sterile fluid collection and subsequently result in the need for drainage or possibly surgery [32]. One example of such a situation is DDS, where the role of ERCP to treat this condition is limited while injection of the pancreatic duct can result in infection of preexisting sterile fluid collections. Furthermore, many patients with pancreatic leaks will experience resolution of their leaks without any intervention. For instance, the majority of low-volume leaks after pancreatic surgery are easily controlled with a JP drain and will spontaneously close over days to weeks [23, 46].

While not all patients with a pancreatic duct leak require intervention, a large number will benefit from endotherapy, percutaneous drainage, or surgical interventions. Indications for interventions include enlarging fluid collections despite conservative management, symptomatic or infected fluid collections, external fistulas, and recurrent pain or pancreatitis during recurrent attempts at refeeding [41].

Pancreatic Ascites

Patients with pancreatic ascites typically present with abdominal distention and abdominal pain. The diagnosis can be made by measuring the levels of amylase and lipase in paracentesis fluid; very high levels confirm the diagnosis. This manifestation typically occurs in the setting of a large volume pancreatic leak which the body has failed to contain. Pancreatic ascites have been historically managed primarily by making the patient NPO with TPN and octreotide with the addition of paracentesis and thoracentesis if a pleural effusion is also found. If the patient did not respond to this conservative management a salvage operation was performed. In this setting pancreatic resections carry an 8–11 % mortality and the leaks have a 15 % recurrence rate [41].

Given the high mortality and recurrence rates with surgical interventions for pancreatic ascites endotherapy is an attractive alternative. Our group was the first to demonstrate that the placement of a transpapillary pancreatic duct stent via ERCP was an effective treatment in this setting [34]. These results have been confirmed in several other studies [47–50]. It has also been shown that placing the stent across the ductal disruption optimizes the likelihood of a therapeutic response.

The mechanism by which pancreatic stenting is effective in the setting of pancreatic ascites is by returning flow of pancreatic juices into the duodenum rather than through the leak, therefore allowing the leak to heal. The stent bypasses upstream barriers to ductal flow such as the sphincter, or inflammatory strictures in the duct. This approach will not be effective if the pancreatic ascites are the result of DDS. In DDS a section of the pancreas has been completely separated from the head of the pancreas, making a stent across the ampulla ineffective and surgery has historically been recommended [41, 50].

Pseudocyst

Pseudocysts are the most common presentation of a pancreatic duct leak and can typically be diagnosed by high-quality cross-sectional imaging. Characteristics of pseudocysts include a well-formed, thick capsule and a homogenous internal fluid component. Pseudocysts either

represent an ongoing ductal leak or the after effect of a healed leak. Unfortunately, it has become clear that cross-sectional imaging is ineffective at differentiating between a true pseudocyst and evolving necrosis or WOPN [32]. CT imaging tends to overemphasize the fluid component of these cystic lesions and can miss areas of necrotic tissue and debris. Therefore, the treatment of peripancreatic collections should not be taken lightly and is best handled by a team including gastroenterologists, interventional radiologists, and surgeons [1, 3, 45]. A clinical history of severe acute pancreatitis should suggest that resultant fluid collections have a high likelihood of representing WOPN. The management of pseudocysts and WOPN differs significantly and patients with WOPN treated as pseudocysts can have severe complications [32]. The management of WOPN is covered in other chapters in this book.

Historically, symptomatic or non-resolving pseudocysts were treated with open surgery with cyst-enteric or cyst-gastric anastomoses and complex cysts were further treated with drainage [52–55]. However, surgery had a 25–30 % rate of morbidity and a 2–5 % 30-day mortality as well as a 10–20 % recurrence rate [40, 55–57]. Because of these high rates of complications most centers have moved to laparoscopic surgical procedures if surgery is performed, and an insistence on preoperative ERCP or MRCP [56, 58–60]. Furthermore, many centers have moved to nonsurgical management of pseudocysts either with endoscopic or interventional radiology drainage.

The first description of endoscopic drainage of pancreatic pseudocysts was in 1975 by Rogers who used a transgastric needle to drain a pseudocyst, although this collection did recur rapidly [61]. Not long thereafter our group published the first description of using electrocautery to fistulize pseudocysts into the stomach, demonstrating a permanent cure in three out of four patients [62]. While the procedure has been enriched to some degree since then, the basics remain the same. The endoscopist must first establish access to the cyst cavity with a needle-knife sphincterotome or a 19-gauge EUS needle. Patients should receive pre-procedural antibiotics. Previously the initial access incision was enlarged with electrocautery, but now most endoscopists use hydrostatic balloons of varying diameters for this purpose. Once the cystogastrostomy or cystenterotomy has been dilated, most endoscopists will place two or more double pigtail stents or varying sizes across the defect to maintain the patency of the fistula to allow for complete resolution of the pseudocyst [63–70]. Double pigtail stents are typically used for this situation in order to reduce the risk of migration [71]. After drainage the patient is followed with imaging such as CT until complete resolution of the cyst, at which point the stents are removed. Alternatively, stents can be left indefinitely, particularly in the setting of DDS [72, 73]. ERCP can be done at the same time as pseudocyst drainage to characterize ductal anatomy and place a stent if a persistent leak is identified [1, 5].

With the advent of EUS, many have advocated for EUS as the preferred choice to initiate pseudocyst drainage. For patients who have concomitant gastric varices it is generally preferred to utilize EUS so that intervening blood vessels can be identified and avoided. EUS also allows for endoscopic drainage, even in cases where a bulge within the gastrointestinal lumen cannot be identified on endoscopy [68, 70, 74–76]. With the first generation of linear echoendoscopes, the working channel diameter was only 2.8 mm, which limited the size of stents that could be inserted; therefore, initially, most endoscopists would exchange the echoendoscope for a duodenoscope after a wire was advanced into the cyst cavity. New therapeutic linear scopes have a larger 3.7-mm diameter channel, which allows for placement of up to 10-Fr stents. Antillon et al. were the first to publish a series demonstrating that single-step EUS pseudocyst drainage was safe and had good efficacy [77]. Kahelah et al. evaluated EUS-guided drainage by following 99 patients undergoing pseudocyst drainage, 46 with EUS and 53 without. Patients who had a visible bulge in the GI tract had drainage without EUS, while those with no bulge had EUS-guided drainage. They demonstrated no difference in efficacy or safety between the groups suggesting that non-EUS-guided drainage remains a reasonable choice for the right patient [78].

Another technique that can be used instead of, or in addition to, transmural drainage of pseudocysts is transpapillary drainage of pseudocysts. Multiple published series have demonstrated the effectiveness of placing stents into the pseudocyst cavity through the major or minor papilla [45, 79–81]. Stents can either be placed into the cavity itself or across the leak within the pancreatic duct. Trevino et al. demonstrated that this method of stenting can also be used to improve the success of transmural drainage as a combination approach [82].

An alternative to endoscopic or surgical treatment of pseudocysts is percutaneous drainage. This method has been shown to be up to 90 % effective for the treatment of pseudocysts [83]. The administration of subcutaneous octreotide to patients who underwent percutaneous drainage has been demonstrated to reduce the amount of time to pseudocyst resolution [84]. The main downside to percutaneous drainage is the high rates of development of percutaneous fistulas. One way to reduce this risk is with concomitant transmural drainage, as has been demonstrated for the treatment of WOPN [85]. In the event of a percutaneous fistula, salvage transmural drainage through a combined interventional radiology and endoscopic procedure has been shown to be effective [86]. The main situations where percutaneous drainage is preferred include patients who are symptomatic but have immature fluid collections and patients who are not surgical candidates and have fluid collections that are not adjacent to the gastrointestinal tract.

It remains unclear whether one method of pseudocyst drainage is superior as no large randomized trials have compared the different options. Recently, Varadarajulu et al. published the results of a randomized controlled trial comparing surgical and endoscopic pseudocyst drainage techniques. In this study 20 patients underwent surgical drainage and 20 underwent endoscopic drainage. Both methods demonstrated excellent success at initial resolution of the pseudocyst in all patients, and only one patient had recurrence in the surgical group and none in the endoscopic group. Patients in the endoscopic group had decreased hospital stay, decreased healthcare costs, and improved physical and mental health [87]. The same group previously published a retrospective study also comparing surgical and endoscopic methods and again showed no difference in efficacy, but decreased costs and hospital stay in the endoscopic group [69]. Several studies have compared EUS and non-EUS-guided transmural drainage and have generally demonstrated that patients with a bulge in the gastrointestinal tract seen can be drained by EUS or non-EUS methods without significant differences [78]. However, if no bulge is seen then EUS drainage will generally be successful, while non-EUS drainage should not be attempted without good cross-sectional imaging to direct therapy. Varadarajulu et al. randomized patients to EUS or EGD drainage and found that all 14 EUS drainages were successful, while only 5 of 15 patients randomized to EGD drainage were done successfully; all 10 EGD failures were crossed-over to EUS drainage with a successful outcome [88]. Park et al. published the results of another randomized trial that showed similar results with eight patients with no bulge crossing over to successful EUS drainage, with all patients in the study having eventual successful drainage [89]. In a study published by Fockens et al., the use of EUS changed management in 37.5 % of pseudocyst drainages because of a multitude of unexpected findings [90].

In summary, endoscopic treatment of pancreatic pseudocysts appears to be effective, with a 94 % initial success rate, 90 % cyst resolution rate, and a 16 % recurrence rate with a 20 % complication rate and mortality rate less than 1 % [91]. Outcomes are different based on the etiology of fluid collections [32]. EUS drainage is preferred and is required if no bulge is seen within the gastrointestinal tract. Because of the risk of adverse events, endoscopic drainage is best done in settings with significant experience and a multidisciplinary team. Alternative drainage options include surgery or percutaneous drainage.

Pancreatic Fistula and Trauma

Pancreaticoenteric fistulas occur in a variety of situations, including erosion of pseudocysts, WOPN, or percutaneous drains into neighboring structures. These fistulas can occur in the setting of acute or chronic pancreatitis. Often, these fistulas can present as spontaneous, rapid resolution of fluid collections and require no treatment. However, a stenosis can develop at the site of ductal disruptions, which may result in relapsing attacks of pancreatitis. Fistulization into the bile duct may result in cholestasis or cholangitis, while fistulas into the colon may result in recurrent sepsis.

Our group has now treated more than 30 patients with pancreaticoenteric fistulas. In our initial series of eight patients with pancreaticoenteric fistulas, three healed after transpapillary stenting, three healed after downsizing or removal of an external drain that had eroded into a loop of bowel, and two required surgical intervention [92]. Biliary fistulas will generally heal with simultaneous biliary and pancreatic duct stents if DDS is not present [93]. An alternative treatment for pancreaticocolonic fistulas is diverting ileostomy. This intervention reduces bacterial translocation and resultant sepsis [94].

Acute abdominal trauma can also result in pancreatitis and pancreatic duct leaks and fistulas. This can result in a wide variety of manifestations and symptoms may be masked by other injuries. Pancreatic injury occurs in 55 % of blunt trauma and 8 % of penetrating abdominal injuries. Pancreatic injury is associated with up to 30 % mortality and 45 % morbidity [95]. Therefore, pancreatic injury should be considered in all cases of severe abdominal trauma. In pancreatic trauma the integrity of the main pancreatic duct is the most important determinant of prognosis. Unfortunately, CT imaging is very poor at diagnosing pancreatic injuries, with a sensitivity of roughly 50 %. However, ERCP has been shown to be very accurate at diagnosing pancreatic trauma [96].

The high mortality associated with pancreatic injury and worse prognosis with later diagnosis have led some to propose early ERCP if there is any suspicion of pancreatic injury. Kim et al. diagnosed abnormal pancreatograms in 14 of 23 patients with acute abdominal trauma. Eight of these patients had complete transections, which were treated with surgery, three had main pancreatic duct leaks that were confined to the parenchyma and treated with stenting, and three branch leaks were successfully treated conservatively. The authors concluded that early ERCP was beneficial in patients with possible pancreatic duct injury [97]. Bhasin et al. reported the successful endoscopic treatment of 9 of 11 patients with pancreatic trauma with transpapillary stenting, nasopancreatic drain, or cystogastrostomy, with the other two patients requiring surgery for complete transections [98]. Other small series have also demonstrated that minor ductal trauma can be treated with pancreatic stenting [5, 51]. However, higher-grade trauma still generally requires emergent surgical intervention.

While ERCP does provide the benefit of potentially intervening in some pancreatic injuries, it does expose patients to the risk of procedural pancreatitis and can be limited by the endoscopists' ability to cannulate the pancreatic duct. MRCP and S-MRCP may be an improved modality to define which patients will have the greatest benefit from therapeutic ERCP while avoiding the potential complications of ERCP for those who will not require endotherapy. MRCP has the additional benefit of being able to image the parts of the pancreas that are proximal to any ductal disruption and are therefore not visible on ERCP [37–39]. It remains unclear which modality is superior for evaluating potential pancreatic injury and further research is necessary.

External Fistula

External pancreatic fistulas are typically iatrogenic in etiology. The most common situations in which they arise are percutaneous drainage of pancreatic fluid collections such as WOPN or after pancreatic surgery. The likelihood of developing an external fistula increases greatly if percutaneous drainage is performed in the setting of DDS [85].

Patients undergoing surgery for non-pancreatic indications may develop pancreaticocutaneous fistulas if unintended trauma to the pancreas occurs [1, 3, 6, 45]. Penetrating abdominal trauma is a non-iatrogenic cause of external fistulas.

The management of external pancreatic fistulas varies based on their etiology and clinical presentation. Many patients, particularly those with fistulas after pancreatic surgery, will respond to conservative management. Conservative therapy consists of nasojejunal feeding, systemic antibiotics to prevent or treat infectious complications, correction of fluid and electrolyte imbalances, and skin care. In particular, nasojejunal feeding has been shown to improve closure rates and decrease time to closure of pancreaticocutaneous fistulas as compared with TPN [99]. The use of somatostatin analogues such as octreotide in this setting has been studied extensively. Based on currently available data it appears that these agents can reduce the output of external pancreatic fistulas but do not affect the likelihood of or time to fistula closure [100]. Therefore, the use of octreotide should be limited to patients with high-output fistulas that are causing extensive electrolyte imbalance or significant skin complications.

Unfortunately, not all patients with cutaneous fistulas will respond to conservative therapy. Patients with fistulas after pancreatic surgery are likely to respond over weeks to months while patients with percutaneous drainage for DDS are highly unlikely to respond. For unresponsive patients, endoscopic therapy is usually the next option. Our group first described the use of multiple length stents for bridging ductal disruptions and short stents for tail leaks in this setting. Nine patients with cutaneous fistulas were included in the study with various etiologies for their fistulas. Three patients had stents placed that bridged the site of disruption, while the other six had stents that did not bridge the disruption. Successful closure of the fistula was achieved in eight of nine patients, including 5 within 48 h of stent placement [101].

Since our description, several other series have been published on the effectiveness of pancreatic stents for external fistulas. Costamagna et al. described the endoscopic management of 16 patients who developed fistulas after open abdominal surgery and failed conservative management. In this study patients were primarily treated with nasopancreatic drains, which were subsequently removed when the fistula closed. Drains were successfully placed in 11 of 15 patients and all patients were successfully treated except for one who was subsequently successfully treated with a pancreatic stent. Mean time to fistula closure was only 8.8 days and there was no fistula recurrence after a mean 24.7 months of follow-up [102]. Halttunen et al. also described 18 patients with cutaneous pancreatic fistulas treated endoscopically. In this series 13 patients had effective closure of the fistula. Overall published results have shown an 85 % rate of successful stent placement in the setting of cutaneous fistulas, with 92 % of those successfully stented achieving closure of the fistula [103].

DDS is commonly complicated by external pancreatic leaks but is generally not amenable to transpapillary pancreatic stenting. Fistulas from DDS are secondary to persistent fluid output from a tail segment of the pancreas that has been completely separated from the head of the pancreas by pancreatic necrosis. In this setting, placement of a transpapillary stent has no impact on the flow of pancreatic juice from this tail segment. Our group has recently described a combined endoscopic and interventional radiology technique for treatment of pancreaticocutaneous fistulas in the setting of DDS [86]. In this technique, initially a radiologist will pass a TIPS needle into the fistula tract. Using fluoroscopic and endoscopic guidance this needle is then passed through the gastric wall into the stomach lumen. The tract into the stomach is then dilated with an 8-Fr microcatheter after which two guide wires are passed into the stomach and grasped by the endoscopist using a snare and pulled up through the endoscope. Over the guidewire the transgastric tract is then further dilated with an 8-mm balloon. Subsequently, two double pigtail stents are passed over the wires to bridge the gastric wall. This technique has been used successfully in 15 patients. Three patients had recurrent fluid collections in a 25-month follow-up period secondary to stent migration, but all three

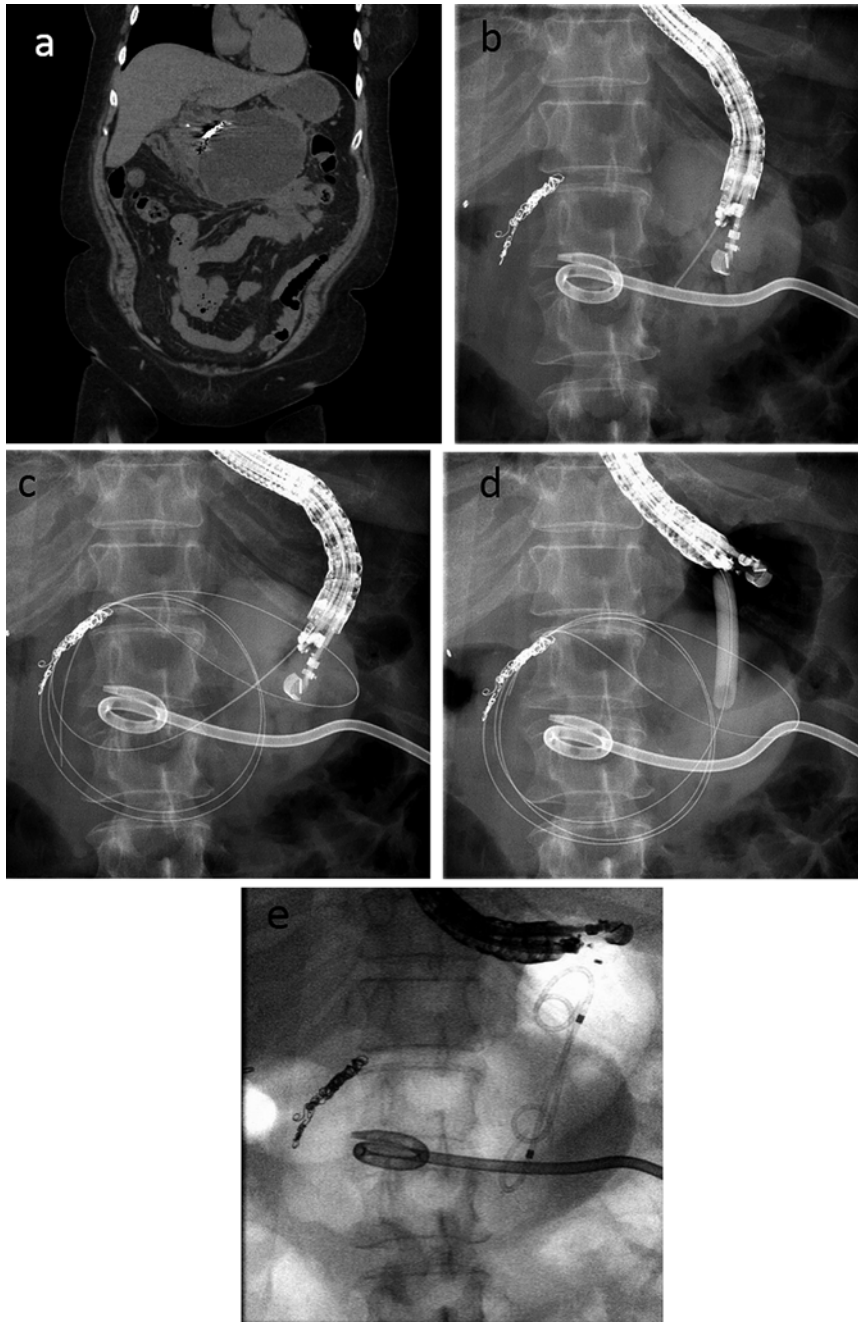

Fig. 12.3 Patient with severe acute pancreatitis with walled-off pancreatic necrosis and disconnected duct syndrome treated with percutaneous drain and transgastric stents. (**a**) CT demonstrating large WOPN. (**b**) EUS 19-gauge needle access and contrast injection of collection. (**c**) Guidewire placed within collection. (**d**) Balloon dilation of cystogastrostomy tract. (**e**) Two double pigtail transgastric stents placed across cystogastrostomy

were treated with endoscopic transmural drainage. Our current management strategy for WOPN attempts to prevent cutaneous fistulas in the setting of DDS by placing both percutaneous and transgastric drains at the onset of treatment [85] (Fig. 12.3).

In addition to their role in our combined technique described above, interventional radiologists

also have the ability to treat external pancreatic fistulas with techniques such as cyanoacrylate injection. Effective use of percutaneous drains has also been shown to be highly effective treatment for postsurgical pancreatic fistulas [104].

Disconnected Duct Syndrome

DDS represents the most severe form of a pancreatic leak as the pancreatic duct is effectively transected. This generally occurs as a result of severe acute pancreatitis with pancreatic necrosis. It occurs in up to 50 % of patients with necrotizing pancreatitis [105]. This occurs when any portion of the head, genu, or body of the pancreas is necrosed with autodigestion of the main pancreatic duct. This results in the entire upstream portion of the pancreas being isolated and not in communication with the papilla. Given that this isolated segment of the pancreas will continue to produce its exocrine pancreatic juices, they may be secreted into the abdominal cavity, resulting in a significant fistula. This type of fistula is not amenable to transpapillary stenting because the isolated portion of the pancreas cannot be reached from the papilla and, therefore, the leak cannot be bridged.

Historically DDS has required surgical excision of the isolated tail segment of the pancreas. However, endoscopic and interventional treatments have been introduced with varying success [106].

Endoscopic management of DDS has been described in several series [2, 73, 86, 105, 107] (Fig. 12.4). The treatment involves transmural drainage of fluid collections followed by leaving

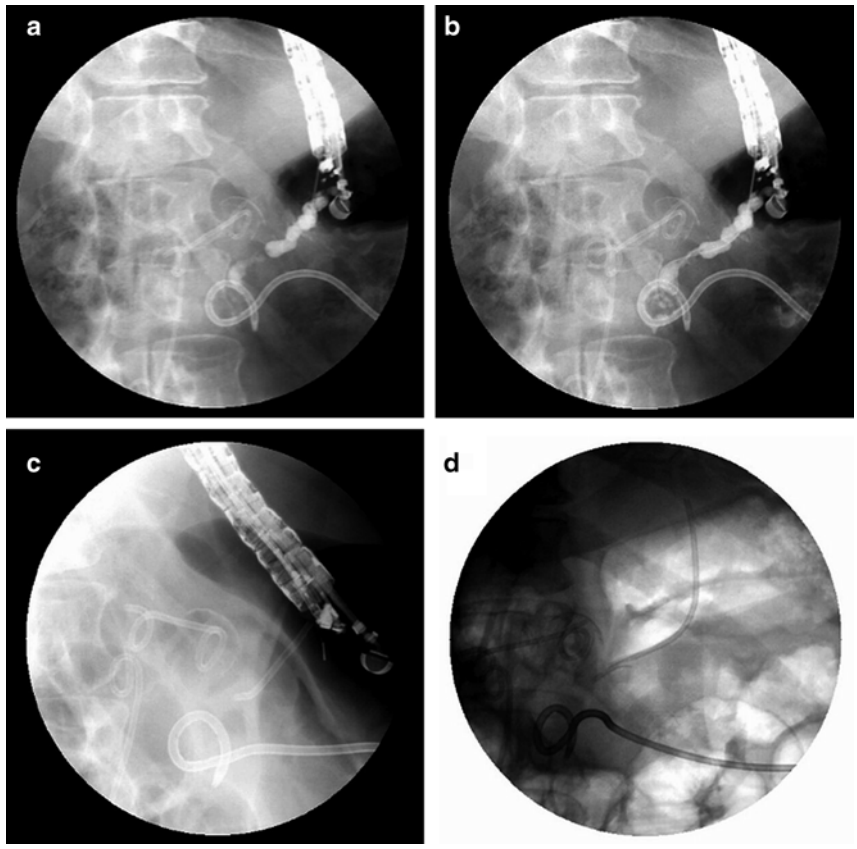

Fig. 12.4 Patient with disconnected duct syndrome with external pancreatic fistula. EUS-guided pancreatogram demonstrates disconnected tail segment's duct. Treated with transgastric stenting. (**a**) Initial transgastric EUS-guided pancreatogram demonstrates disconnected segment of dilated pancreatic duct. (**b**) Guidewire placed within the pancreatic duct. (**c**–**d**) Stent placed into disconnected duct

transmural stents in place indefinitely. Leaving transmural stents in place indefinitely creates an outlet for the pancreatic juice from the isolated tail, therefore preventing the development of fluid collections and symptoms.

Deviere et al. were the first to describe their experience with transmural drainage for DDS. They demonstrated successful endoscopic treatment in 12 of 13 patients with DDS [73]. Pelaez-Luna et al. published the Mayo clinic experience with DDS. Over a 7-year period they treated 31 patients with DDS, with 5 patients going straight to surgery and 26 undergoing endoscopic treatment. Of the patients undergoing endoscopic treatment, 19 had good long-term success while 7 eventually required surgery [2]. Varadarajulu et al. also described their experience with 33 patients with DDS. In their series 8 patients underwent surgery while 22 were successfully treated with transmural drainage with prolonged stenting. No patients experienced recurrent fluid collections despite three having spontaneous passage of stents after more than 100 days of follow-up [105]. Other small series have also demonstrated some success with endoscopic drainage.

Our group recently described a combined endoscopic and percutaneous treatment for WOPN and DDS with excellent results [85] (see Fig. 12.3). In our prior experience treating WOPN with percutaneous drains alone, many patients developed external fistulas secondary to DDS with the inability to subsequently remove the drains. Therefore, we now place transmural stents in addition to percutaneous drains for the treatment of WOPN. Transmural stents are left in place indefinitely for patients with DDS and pulled if the duct is intact once the fluid collections resolve. With this new technique we have avoided both cutaneous fistulas and greatly reduced the need for surgery for DDS. We have now treated more than 100 patients with WOPN with this technique with <1 % death related to pancreatitis and <5 % requiring surgery.

In addition to endoscopic treatments for DDS, interventional radiologists can offer other minimally invasive, surgery-sparing treatments. Our group has recently described a combined IR and endoscopic treatment for DDS and external pancreatic fistulas [86]. Further details regarding this technique are described in the section on external fistulas above. Interventional radiology administered cyanoacrylate or other glues has also been described as a treatment for DDS with an external pancreatic fistula [108, 109]. In this technique a guidewire is advanced into the main pancreatic duct within the isolated segment of the pancreas. Subsequently, a microcatheter is advanced over the wire and glue is then injected to completely fill the pancreatic duct and all of its side branches within this section of the pancreas. This works best with a small, 3- to 4-cm segment of pancreas and is associated with mild procedural pancreatitis in 50 % of patients.

Adverse Events

The most common adverse events when using endoscopy to treat pancreatic duct leaks are procedural-related pancreatitis and iatrogenic fistulas. However, other complications including drug reaction, aspiration, cardiopulmonary events, cholangitis, bleeding, and perforation can occur [110]. Pancreatitis flares approximate 10 % but may approach 50 % if pancreatic duct stenting is unsuccessful after multiple accessories are advanced into the pancreatic duct. The placement of a transpapillary stent does lower the risk of pancreatitis and attenuates the disease course if pancreatitis does occur [111]. Similarly, the administration of PR indomethacin has been shown to reduce the risk of post-ERCP pancreatitis in high-risk individuals [112]. Stent characteristics can also affect the risk of pancreatitis. Stent diameter should be adjusted to the size of the duct. For instance, a 7-Fr stent should not be used for a duct that is only 4 Fr in diameter. Similarly, a 1-cm long stent should not be used to bridge a ductal leak that is only 4 cm from the papilla.

Subacute adverse events can occur from introduction of bacteria into fluid collections or

necrotic debris at the time of ERCP. As such, all patients with internal fistula should get prophylactic antibiotics prior to ERCP, particularly in the case of WOPN. Contaminated collections should be considered for percutaneous or transmural drainage or a course of post-ERCP antibiotics.

Pancreatic stent occlusion can be associated with pancreatic sepsis and obstructive pancreatitis [113]. Also, long-term transpapillary stent placement can cause iatrogenic ductitis with focal strictures and side branch ectasis [114]. Therefore, stents should be removed or exchanged 4–6 weeks after placement. Stents placed for treatment of external fistulas should be removed 1 week after the fistula closes.

Conclusion

Over the past 30 years, the management of patients with pancreatic duct leaks and their multiple consequences and manifestations has evolved. Rather than surgeons managing all leak patients who do not respond to conservative therapy, patients are now best served by a multidisciplinary team including gastroenterologists, interventional radiologists, and pancreatic surgeons. Many leak patients can be managed by endoscopic or radiologic-guided interventions and therefore avoid surgery. ERCP with transpapillary stenting remains the cornerstone of therapy for leaks that do not have DDS. Stenting will likely result in resolution of the leak, particularly if the stent is able to bridge the disruption. Peripancreatic fluid collections such as pseudocysts and WOPN can be treated with endoscopic transmural drainage, percutaneous drainage, or a combination of the two techniques. DDS is no longer a condition treated only with surgery as many patients will respond to long-term transmural stenting and some may respond to IR-directed therapies. Pancreatic leaks remain a challenging and highly morbid complication of pancreatitis, but endoscopic techniques have evolved and likely will continue to evolve to improve outcomes for these patients.

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