34 Endoscopic Management of Pancreatic Pseudocysts

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Introduction

A pseudocyst is a persisting localized pancreatic or peripancreatic fluid collection that is generally rich in pancreatic enzymes. It is an encapsulated collection of fluid that lacks a true wall and is surrounded by a fibrous tissue wall without true epithelialization [10]. Pseudocysts are thought to form as a result of a leak from a disrupted pancreatic duct, or more commonly a side branch, and are frequently asymptomatic. They can be sequelae of severe acute pancreatitis or of chronic pancreatitis. Symptomatic pseudocysts can be managed endoscopically, radiologically, or surgically [9]. Pancreatic necrosis and cystic neoplasms can cause diagnostic dilemmas. This chapter focuses on the endoscopic management of pancreatic pseudocysts.

Incidence and Etiology of Pseudocysts

Pseudocysts occur after an acute attack of pancreatitis in approximately 10% of cases. The incidence of pseudocysts in the general population has been reported to be 0.5–1 per 100,000 adults per year [50]. In a study of 926 patients with non-alcoholic acute pancreatitis, 5% were noted to have pseudocyst formation 6 weeks after an acute attack of pancreatitis [32]. In their study, Kourtesis et al. [27] followed 128 consecutive patients with acute pancreatitis by computed tomography (CT) imaging, and 37% developed some type of acute fluid collection in the vicinity of pancreas. The majority of these acute fluid collections resolved spontaneously, and only 15 (12%) patients progressed to the development of symptomatic pseudocysts. Another study has reported a 7% overall incidence of pseudocysts as a complication of acute pancreatitis [22]. Although often radiologists and physicians loosely use the term, "pseudocyst," for anything remotely cystic associated with pancreatitis, the revised Atlanta classification system [6] categorizes fluid collections under 4 weeks old, without solid material, as "acute pancreatic fluid collections" (PFC); these have no necrosis and are without a well-defined wall. After 4 weeks, if PFCs have not resolved, and when these generally develop a wall, assuming they demonstrate no/minimal necrotic material (i.e., generally under 30% solid), they are then referred to as "pseudocysts." In contrast, collections more than 4 weeks old that contain a significant amount of solid or semisolid necrotic material, with or without liquid, are termed, "walled-off necrosis (WON)."

Although there is a lack of precise long-term data on the incidence of pseudocyst development in patients with chronic pancreatitis, it has been reported that around 30–40% patients with chronic pancreatitis develop pseudocysts in their lifetime [9].

Pseudocysts have been reported more commonly after alcohol-induced than after non-alcohol-related pancreatitis [39]. In a study of 357 patients with pancreatic pseudocysts, alcohol was reported to be a causative factor in 251 cases (70%), biliary tract disease in 28 (8%), blunt or penetrating abdominal trauma in 21 (6%), operative trauma in one case (0.3%), and idiopathic in 56 (16%) [51].

Practical Considerations

- Majority of the acute fluid collections resolve spontaneously, and only 7–12% patients progress to symptomatic pseudocysts.

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S. Sridhar, G.Y. Wu (eds.), *Diagnostic and Therapeutic Procedures in Gastroenterology*, Clinical Gastroenterology,
https://doi.org/10.1007/978-3-319-62993-3_34

Pathogenesis and Classification

Pseudocysts are generally formed due to rupture of the pancreatic duct or one of its side branches either by trauma or pancreatitis. This leads to extravasation of pancreatic juice that results in an acute fluid collection. Peripancreatic fluid can also sometimes form from edema, but usually does not result in an actual pseudocyst. Most patients with pseudocysts have demonstrable connections between the cyst and the main pancreatic duct or the side branch, but some lose their connection as the fibrosis walls off the area. Although necrosis is sometimes associated with these severe cases of pancreatitis, pseudocysts can occur without pancreatic necrosis; again, the pseudocysts themselves should have no substantial necrosis within the collection.

Liquified necrosis (postnecrotic pancreatic fluid collection, PNPFC) can mimic a pseudocyst, but generally is associated with a different natural history, different risk of infection, and different approach to management. They are usually not truly fluid-filled, but often have solid components and a semisolid gelatinous makeup that sometimes mimics fluid on imaging, especially CT (computed tomography) (Figs. 34.1 and 34.2). PNPFCs can persist beyond a month and evolve into "walled-off necrosis" (WON), which can be confused with a pseudocyst. T2-weighted MRI (magnetic resonance imaging) and ultrasound (US) are modalities that are better at differentiating solid from liquid contents.

In a patient with chronic pancreatitis, most often due to alcohol abuse, pseudocyst formation can occur by acute exacerbation of underlying disease (with the same mechanism as above) or by progressive ductal obstruction due to either downstream ductal stricturing or intraductal stone or protein plug formation. This prevents drainage of pancreatic juices into the small bowel. Elevation in upstream intraductal pressure predisposes to ductal leakage, with accumulation of peripancreatic fluid.

As mentioned above, many patients develop some type of acute pancreatic fluid collection (PFC) after acute pancreatitis, but this fluid collection is termed a pseudocyst only if it persists beyond 4–6 weeks and is surrounded by a fibrous tissue without true epithelialization [10, 39] and has no significant solid component. Pseudocysts can be sterile or infected; spontaneous infection of pseudocysts is rare and, when it occurs, is generally either due to contamination by an intervention or seeding from bacterial translocation or other causes of bacteremia. Spontaneous infection is even more rare for acute fluid collections not contaminated by intervention.

Pseudocysts were initially classified by D'Egidio and Schein [16] in 1991. They described three types of pseudocysts based on pancreatic duct anatomy, presence of communication between the cyst and the pancreatic duct, and underlying etiology of pancreatitis (acute or chronic). Type 1 was described as one that follows an acute attack of

Fig. 34.1 CT images after endoscopic cystogastrostomy appearing to demonstrate a new or persisting collection (*arrow*) near a drained cyst. This hypodense lesion appeared to be fluid-filled on CT, surrounded by a brighter hyperdense capsule, and was reported as a "pseudocyst." It was subsequently shown by MRI to be solid/semisolid walled-off necrosis (*WON*). (**a**) Axial image. (**b**) Coronal image

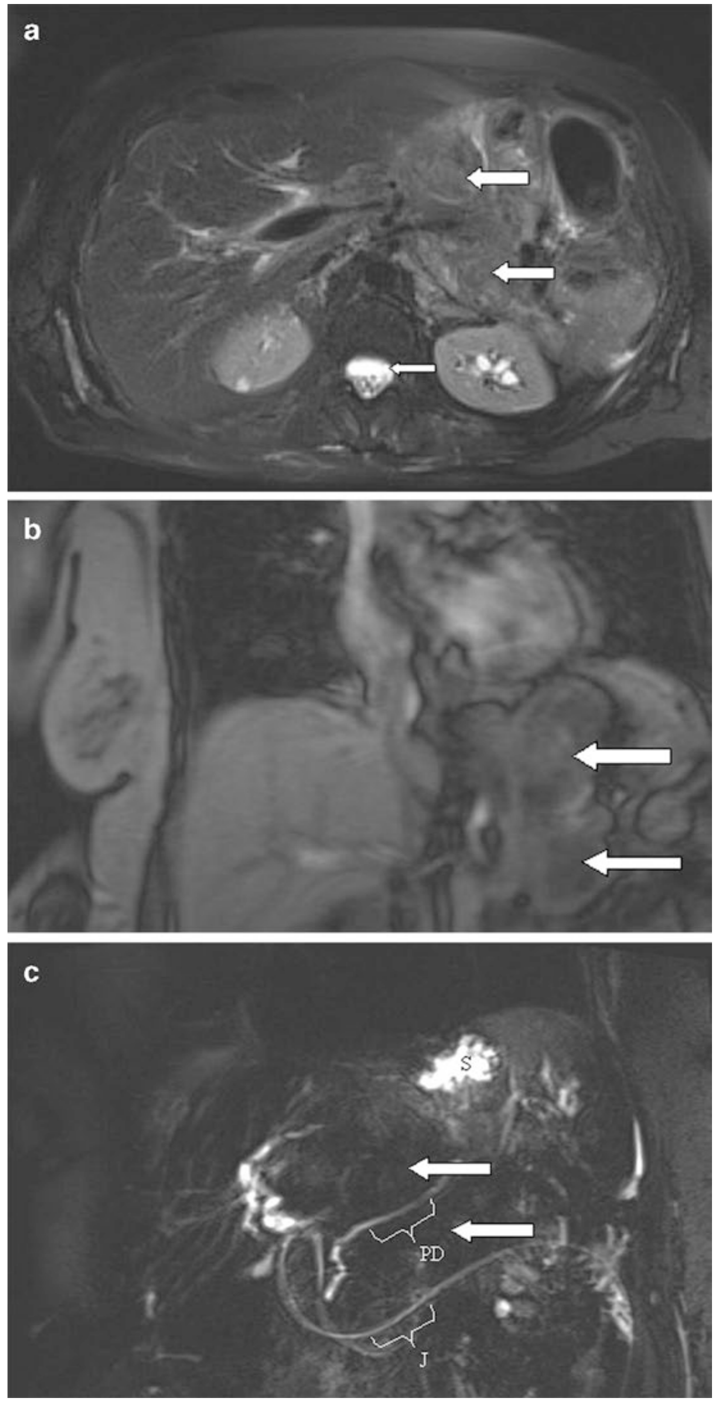

Fig. 34.2 T2-weighted MRI images in which stagnant fluids such as ductal or luminal fluid and cerebral spinal fluid (*small arrow*) appear white (high signal) showing that the "cyst" in Fig. 34.1 was not fluid-filled, but rather solid/semisolid pancreatic necrosis (mildly low signal) (*large arrows*). The heavily T2-weighted MRCP shows bright fluid in the stomach (*S*), and in the pancreatic duct (*PD*), but no bright fluid at all around the pancreas. A jejunal tube is also seen (*J*). (**a**) Axial image. (**b**) Coronal image. (**c**) MRCP image

pancreatitis and has normal duct anatomy and only rarely communicates with the pancreatic duct. Type 2 pseudocysts follow an episode of acute-on-chronic pancreatitis and often have duct-pseudocyst communication with a diseased pancreatic duct, but the duct is not strictured. Type 3 cysts, referred to as "retention" pseudocysts, occur as a result of chronic pancreatitis and are uniformly associated with duct stricture/obstruction and pseudocyst to duct communication. This classification has variable use in current practice.

To help guide decisions regarding surgical vs. nonsurgical therapy, Nealon and Walser [36] classified pseudocysts based entirely on pancreatic duct anatomy. They described seven types of pseudocysts: type 1 has normal main duct with no communication with the cyst. Type 2 also has a normal main duct, but with duct-cyst communication. Type 3 has an otherwise normal main duct, but with stricture(s) and no duct-cyst communication. Type 4 has an otherwise normal main duct, with stricture(s) and duct-cyst communication. Type 5 has a complete cutoff duct, with a duct that is otherwise normal, with no communication with the cyst. Type 6 occurs in chronic pancreatitis (abnormal pancreatic duct), but has no duct-cyst communication. Type 7 occurs in the presence of chronic pancreatitis (abnormal pancreatic duct) and has duct-cyst communication. Ductal communication, a critical part of this classification, may be difficult to discern with noninvasive imaging, but dynamic secretin-stimulated MRCP (magnetic resonance cholangiopancreatography) and EUS (endoscopic ultrasound) are promising. It is seldom necessary to use invasive and high-risk studies such as endoscopic retrograde cholangiopancreatography (ERCP) for this purpose.

Clinical Presentation and Diagnosis

A careful history regarding the duration of the cyst, whether pancreatitis was present and whether an etiology of the pancreatitis is known, and whether other suspicious symptoms are present (that might suggest this could be a cystic neoplasm) are very important factors to decide the best management.

History, Physical Examination, and Laboratory Evaluations: Narrowing the Differential

Pseudocysts can present with a wide range of clinical problems depending upon the location and size of the fluid collection and the presence of infection. Patients with pseudocysts may be completely asymptomatic; or they can present with abdominal pain, anorexia and/or nausea and/or weight loss, abdominal mass effect from a large cyst pressing on the gastric outlet leading to persistent nausea/vomiting and gastric outlet obstruction, compression of the splenic vein with splenomegaly and left upper quadrant pain, or jaundice due to compression of the bile duct. The weight loss that can result from nausea and pain can be confusing regarding the differential diagnosis of a cystic tumor. Patients also can present with other complications of pseudocysts, such as infection, bleeding into the cyst or splenic artery pseudoaneurysm, rupture of the cyst, or thrombosis of the splenic or portal vein with bleeding or non-bleeding gastric varices [19]. Serum laboratory tests have limited utility, and results depend on the clinical presentation and etiology of underlying pancreatitis. By the time a pseudocyst is found, serum pancreatic enzymes from the acute pancreatitis have usually returned to normal or near-normal. A white blood count may alert one to the possibility of infection, although persistent minor elevations in the white count are common and can be due to coexisting smoldering pancreatitis.

Pseudocysts are usually identified by cross-sectional imaging studies, such as CT done for an evaluation of the severity of an attack of pancreatitis or for persistent symptoms like fever, vomiting, or abdominal pain, after an attack. Once a pancreatic cyst is identified by an imaging modality, the most important point is to differentiate pseudocysts from necrosis and from cystic neoplasms of the pancreas not related to pancreatitis (the most common cyst in patients without pancreatitis), and this could pose a difficult diagnostic and therapeutic dilemma for clinicians.

Unlike in other abdominal organs, most incidental cysts in the pancreas that are not pseudocysts are in fact cystic neoplasms, some of which have malignant potential (Fig. 34.3).

Practical Considerations

- Postnecrotic pancreatic fluid collection (PNPFC) is generally associated with a different natural history, different risk of infection, and different approach to management.
- Pseudocysts can be sterile or infected; spontaneous infection of pseudocysts is rare, and when it occurs, is generally either due to contamination by an intervention or seeding from bacterial translocation or other causes of bacteremia.

True "simple cysts" or congenital cysts of the pancreas are thought to be rare. It is crucial to differentiate pseudocysts from necrosis and other cystic lesions as management varies by the type of cystic lesion. History is often the most helpful element to help differentiate these lesions. Pancreatic fluid collections, pseudocysts (and PNPFCs or WON), usually follow an acute attack of pancreatitis, can present at any age, and can be located anywhere in the pancreas or its vicinity (although the tail and the neck are common areas of duct disruption). When they occur in the setting of chronic pancreatitis, there is often a history of heavy alcohol and smoking intake in the present or past, since alcohol and smoking are the etiology of the majority of non-genetic chronic pancreatitis cases. Abdominal trauma and family history can be other clues. If the pancreatitis appears otherwise idiopathic, one must consider the possibility that the cyst was present prior to the pancreatitis and that the pancreatitis occurred secondary to the cyst, rather than the cyst being due to pancreatitis; cystic tumors, especially ones that produce mucin which may obstruct the duct, can cause pancreatitis.

Practical Considerations

- Pseudocysts can present with a wide range of clinical problems depending upon the location and size of the fluid collection and the presence of infection.

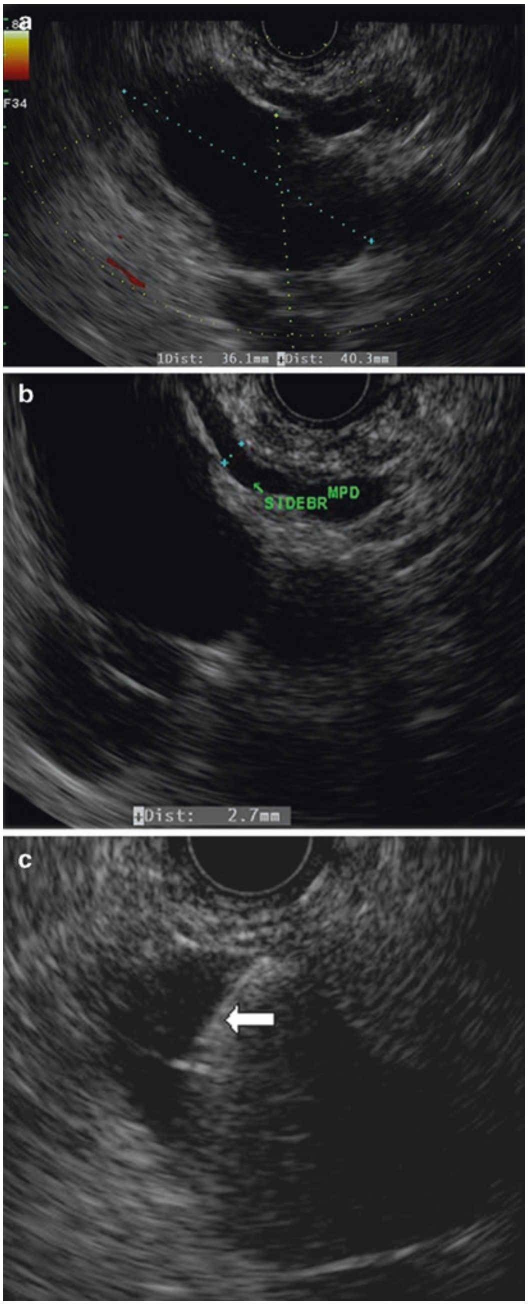

Fig. 34.3 Linear EUS of a slowly enlarging 3–4 cm Doppler-negative anechoic (cystic) lesion in the head of the pancreas in a middle-aged man without a history of pancreatitis. (**a**) A thin-walled cyst is seen with a dilated side branch (*SIDEBR*) from the main pancreatic duct (*MPD*) filling the cyst. (**b**) The lobular/tubular cyst morphology is consistent with a cluster of dilated side branches. (**c**) FNA with a 19 G needle (*arrow*) removed thick mucin consistent with a side branch variant IPMN. An intracystic brushing was obtained through the needle, but both fluid and brushing were acellular

Imaging Studies and Possible Fluid Sampling

Different imaging modalities can be used to evaluate pseudocysts of the pancreas. The imaging studies could include US, CT, MRI, ERCP, and EUS. Ultrasound (transabdominal conventional US or EUS) and T2-weighted MRI (with or without T2-weighted MRCP sequences) are the best modalities for confirming or refuting solid components and necrosis mimicking a pseudocyst (Fig. 34.2). Both modalities are superior to CT in distinguishing solid material from fluid. CT can often misclassify necrosis, or sometimes even a solid mass, as a pseudocyst, because the Hounsfield units of murky fluid and solid material can overlap (Fig. 34.1). CT is generally insufficient, on its own, to proceed with management. Lastly, fine needle aspiration (FNA) by CT or EUS is available for equivocal lesions, but should be avoided in classical pseudocysts to avoid the risk of infection, unless therapeutic drainage is also planned; most classic pseudocysts do not need diagnostic aspiration.

Conventional Abdominal Ultrasound

On US, pseudocysts appear as an anechoic (black), round or oval, relatively smooth-walled, and well-defined structure (although some internal irregularity of the wall is common). Conventional US has certain limitations, especially when examining a relatively small lesion in the retroperitoneum, behind the stomach, especially in the presence of overlying bowel gas (ileus and gastric obstruction or distension often accompanies the acute pancreatitis), and is operator dependent [39]. The patient is often in significant pain, and because of this, the ability to press with the probe deeply on the abdomen, or roll the patient to get different views, may be limited. Generally, the sensitivity of US for the detection of moderate-sized pancreatic pseudocysts ranges from 75% to 90%, which is generally inferior to CT (sensitivity >90%). Again, US is one of the best modalities for distinguishing solid from liquid, and so significant solid debris within the cystic lesion generally implies necrosis (or more rarely, neoplasia). At the same time, US can also reliably detect cholelithiasis (arguably the best test for this) and biliary dilation. Again, this exam can be limited when the patient is in considerable pain or is distended.

CT, MRI, and ERCP

CT and MRI are very sensitive diagnostic modalities for pancreatic pseudocysts. In a patient with recent history suggestive of pancreatitis, finding a round, thick-walled, fluid-filled structure in the vicinity of pancreas is very suggestive of a pseudocyst. The major limitations of CT are its poor ability to distinguish fluid from necrosis, its inability to differentiate pseudocysts from cystic neoplasm of the pancreas, and the risks of intravenous contrast [44]. It is also poor at assessing ductal communication and pancreatic strictures or irregularity that may point to a diagnosis of chronic pancreatitis and help with treatment planning. Although not as good as EUS, it has reasonable sensitivity for pancreatic calcifications.

MRI/MRCP is superior to CT in depicting debris within pseudocysts and differentiating cysts from solid lesions (Figs. 34.1 and 34.2). Also, it can give detailed imaging of the pancreatic duct and bile duct. MRCP has some other advantages over CT including its superiority to detect choledocholithiasis [41], strictures, bleeding within the pseudocyst, and assessing duct to cyst communication (especially when secretin is given to stimulate pancreatic juice flow).

ERCP is not required to diagnose the pseudocyst, but it definitely has a role in the endoscopic therapy of the pseudocysts as described in the treatment section. Because of its risk of post-procedural pancreatitis, or worsening of existing pancreatitis, and the risk of contaminating the cyst with dye, which can lead to infection, ERCP is best avoided unless pancreatic ductal therapy is planned, temporary stenting of an externally compressed and obstructed biliary tree is needed, or removal of bile duct stones (that may have led to the attack of pancreatitis) is needed.

EUS and Possible Fine Needle Aspiration with Fluid Analysis

EUS is generally not the initial test used to diagnose pancreatic pseudocysts, but has a great role in further evaluation of cystic lesions diagnosed by other imaging modalities. It is arguably the imaging modality of choice to distinguish pseudocyst from other pancreatic cystic lesions in the equivocal scenarios described above. Again, EUS is one of the best imaging modalities to distinguish solid from liquid, to rule out significant debris/necrosis. It is also excellent at excluding an adjacent mass if there are suspicious symptoms such as weight loss. With EUS, very high-resolution images of the pancreas can be obtained due to the proximity of the pancreas to the stomach and duodenum; this proximity avoids intervening air and allows the use of higher-frequency high-resolution probes as compared with conventional US (because shallower depths of penetration are needed). This results in superior and probably unmatched ductal and parenchymal imaging.

EUS can be especially helpful when the cystic lesion is thought to possibly represent a cystic neoplasm, for example, cases wherein the cyst may have preceded the pancreatitis, cases involving elderly patients or unexplained pancreatitis, cases with constitutional symptoms such as weight loss, and cases without a clear history of pancreatitis. EUS can look at cyst morphology and duct communication and is very sensitive for picking up underlying chronic pancreatitis in those without a clear pancreatitis history.

A principal advantage of EUS as compared to MRI or CT is its capability of adding real-time EUS-guided FNA. In cases with an atypical imaging appearance, cases involving a cyst without a clear attack of pancreatitis, or cysts associated with a solid mass, EUS-guided fine needle aspiration (of the cyst or mass) may be needed. In contrast, if the cystic lesion has a pseudocyst-like morphology on EUS and is in the setting of explained (e.g., alcoholic) pancreatitis, FNA is not generally needed and should be avoided to reduce the risk of infection.

Cyst morphology and fluid analysis (amylase/lipase, mucin, carcinoembryonic antigen [CEA], and cytology) are used to further clarify cystic lesions that are equivocal. Fluid analysis of pseudocysts classically shows low CEA levels (although there is marked overlap with neoplasia) [13, 46], high amylase (signifying ductal communication) and inflammatory cells on cytology, and little to no mucin. Serous cystadenomas are most commonly seen in elderly women and make up 32–39% of all pancreatic cystic neoplasms [12]. On EUS, these cysts appear to have a cluster of microcysts, sometimes adjacent to a larger cyst, and often have central hyperechoic scar. Fluid analysis from these type of cysts classically shows no mucin, low amylase (no duct communication), very low CEA levels, and classically, monomorphic cuboidal cells on cytology (although the fluid is unfortunately often acellular). Cysts with malignant potential include intraductal papillary mucinous neoplasms (IPMN) and mucinous cyst neoplasms. The accuracy of EUS and MRCP for identifying small side branch IPMNs solely on morphology is improving. EUS-guided FNA and fluid analysis, when needed, show high CEA (>192 ng/mL), mucin, and high amylase/lipase levels (as they generally communicate with the main duct); cytological analysis is usually acellular or negative, but may be positive if malignant [13]. Mucinous cystadenomas are most commonly seen in middle-aged women and typically have macrocysts (>2 cm), are often unilocular, and generally have no communication with the pancreatic duct. Features suggestive of malignant transformation are thickened septations, thickened or irregular cyst walls, and the presence of mural nodules or mass; size and/or growth are associated with malignant potential. Fluid analysis shows high CEA, mucin, and low amylase levels; cytologic analysis may have atypical or neoplastic cells, but, again, is often negative or acellular.

The safety of EUS-guided FNA of cysts is well-established when the cyst is accessed with a single puncture and is drained dry. The risk of pancreatitis after EUS-guided FNA is only 2–3%, with the risk of infection less than 1% and intracystic hemorrhage less than 1% [23, 31]. To decrease the risk of infection, intra-procedural antibiotics are administered before or during the procedure and then often followed by antibiotics by mouth for 3–5 days post-procedure. The risk is likely higher if drainage is incomplete (more common in large cysts with thick fluid) or if debris or necrosis is present. Therefore, very large cysts, especially ones with debris, should generally not be aspirated for diagnosis unless the need for diagnostic sampling is justified, and ideally, a drain can also be placed simultaneously.

Practical Considerations

- Conventional ultrasound is one of the best modalities for distinguishing solid from liquid, and so significant solid debris within the cystic lesion generally implies necrosis (or more rarely, neoplasia).
- The major limitations of CT are its poor ability to distinguish fluid from necrosis, its inability to differentiate pseudocysts from cystic neoplasm of the pancreas, and the risks of intravenous contrast.
- MRI/MRCP is superior to CT in depicting debris within pseudocysts and differentiating cysts from solid lesions.
- EUS is generally not the initial test used to diagnose pancreatic pseudocysts.
- EUS is one of the best imaging modalities to distinguish solid from liquid, to rule out significant debris/necrosis and at excluding an adjacent mass, and to obtain FNA.

Treatment of Pancreatic Pseudocysts

Preprocedural Assessment

Most acute PFCs and pseudocysts resolve with supportive medical care that includes intravenous fluids as needed, analgesics and antiemetics. For patients who can tolerate oral intake, a low-fat diet is suggested at least in the short-term. Pancreatic non-enteric coated enzyme capsules (30–50,000 lipase units per meal) that release enzymes in the proximal small bowel and stimulant negative feedback to the pancreas are likely helpful in some patients, although the literature to support this is admittedly weak [11]. Octreotide is used very rarely to decrease pancreatic secretions in refractory ongoing leaks. For patients who cannot tolerate oral intake, nutrition can be provided via nasojejunal feeding or a percutaneous (direct or via a percutaneous gastrostomy) J-tube, for 4–8 weeks; total parenteral nutrition (TPN) is an option, but is a far inferior way of feeding due to higher rates of adverse metabolic and infectious events seen in randomized trials [1, 20, 25, 34, 53].

It is important to make sure that the cyst has “matured” from a PFC to a pseudocyst, with a well-developed wall, which generally takes at least 4 weeks. Interventional therapies, especially endoscopic ones, have better results, and fewer complications, when this is the case. In addition, it is important to allow sufficient time for the cyst to have a chance to spontaneously resolve, as most do. Before contemplating therapy, the pseudocyst should be associated with persisting symptoms. Although size does not matter, generally cysts under 4 cm in size do not cause significant symptoms (i.e., one should consider the possibility that any ongoing pain may be more likely due to ongoing/smoldering pancreatitis). An exception to this includes cysts in the head, where biliary or duodenal compression can occur with smaller diameter cysts. Nevertheless, placing a pigtail drain, by any means, into a cyst that is under 3–4 cm in size is technically difficult and often not feasible.

For cysts that do not resolve spontaneously with supportive medical management and become symptomatic or lead to development of a complication (gastric outlet obstruction, infection of the cyst, biliary obstruction), some type of drainage procedure will be required. The options for drainage include surgical, percutaneous, or endoscopic techniques. Before attempting any type of drainage, there are a few critical issues that need to be addressed.

First of all, it is important to consider alternative diagnoses (especially if there is no history of pancreatitis, idiopathic pancreatitis, etc.), especially a cystic neoplasm, as discussed above. Placing a transcutaneous or transluminal drain into a cystic neoplasm needs to be avoided, as it delays the neoplastic diagnosis and may seed the peritoneum with neoplastic fluid.

It is also important to distinguish pseudocyst from WON. In the latter, although treatment is similar to pseudocysts when asymptomatic or resolving, and not infected, conservative treatment is generally preferred given that treating WON with debridement or necrosectomy is more difficult than simply draining a pseudocyst. If complications occur, such as infection, then intervention is needed. Surgical treatment has been generally preferred for WON over transcutaneous or endoscopic drainage and debridement/lavage. However, in experienced hands, endoscopic drainage with endoscopic intracystic debridement (endoscopic necrosectomy) can be considered, selectively, especially in patients who are poor surgical candidates. The response rate is expected to be lower than in patients with sterile pseudocysts, and the adverse event rates are higher [8, 21]. However, recent data on endoscopic necrosectomy is encouraging, and the endoscopic approach may be comparable to minimally invasive surgical necrosectomy in terms of outcomes and cost [26].

It is important to exclude a pseudoaneurysm (usually of the splenic artery running near the cyst or in the cyst wall) which occurs in approximately 10% of patients with a pseudocyst [17, 40]. The presence of a pseudoaneurysm is suggested by unexplained gastrointestinal bleeding, sudden expansion of a pseudocyst, or an obscure drop in hematocrit. Severe and even fatal hemorrhage can occur following endoscopic drainage in patients with an unsuspected pseudoaneurysm. CT or MRI before drainage should help rule out a pseudoaneurysm, and if a suspicion is raised, angiography should be undertaken first. Without preprocedural arterial embolization, a pseudoaneurysm is a contraindication to transluminal drainage. In a study of 57 patients considered for endoscopic drainage of pancreatic pseudocysts, pseudoaneurysms were detected in five patients prior to the drainage procedure. These patients were treated with a multidisciplinary approach, including embolization or resection [33].

Surgical Drainage

Surgery is usually definitive, but is not generally first-line treatment. It could be done either open or in selected experienced centers, laparoscopically; open surgery carries a significant risk of morbidity and mortality (25% and 5%, respectively). Surgical treatment of pseudocysts can be accomplished by providing a communication between the pseudocyst cavity and the stomach or small bowel; or surgical treatment can involve resecting it entirely, often including the part of the pancreas that is leaking into it. In centers with the appropriate expertise, endoscopic management of pancreatic pseudocysts is often considered first, and surgical drainage is reserved for those patients not meeting criteria for endoscopic drainage, those who fail endoscopic management or have recurrence following successful endoscopic drainage, those that have a disconnected duct or tight downstream stricture that cannot be traversed with a stent, or those that have equivocal lesions (i.e., resection of a possible cystic tumor). In a retrospective study [2] of 94 patients in which 42 patients underwent internal surgical drainage and 52 patients underwent percutaneous pseudocyst drainage, seven were surgically managed patients, and four percutaneously treated patients had complications (16.7% vs 7.7%). A significantly higher mortality rate was associated with surgical therapy (7.1%) than with percutaneous therapy (0%) ($P < 0.05$). However, subsequent operation was required in 19.2% of the percutaneous drainage group compared with only 9.5% of the surgical group ($P > 0.05$).

Percutaneous Drainage

In this procedure, an external drainage is obtained by placement of drainage catheter percutaneously into the fluid cavity; this is not always feasible anatomically, especially in the head of pancreas. US or CT is used to guide the catheter placement; symptomatic pseudocysts that may not be accessible endoscopically can be handled this way in many cases. Catheter drainage is continued until the flow rate falls to 5–10 mL/day. The mean duration of drainage can be up to 6 weeks; longer durations of indwelling catheters can lead to pancreaticocutaneous fistula. This technique, though usually successful, carries a high risk of infection; in one series, it was reported to occur in 48% of the patients [2]. It can also be associated with significant patient discomfort, and the catheter can clog and may require repositioning and exchange. Percutaneous drainage is more likely to be successful in patients with normal pancreatic ducts without downstream stricture and no communication between the duct and the cyst. It should not generally be performed in patients with cysts containing bloody or solid material, unless dilation of the tract and insertion of larger bore catheters, with or without continuous irrigation, are planned. It is sometimes used preoperatively in some patients who are clearly going to need surgical resection for some reason, to make surgery technically easier.

Practical Considerations

- It is important to make sure that the cyst has "matured" from a PFC to a pseudocyst, which generally takes at least 4 weeks.
- For cysts that do not resolve spontaneously with supportive medical management and become symptomatic require some type of drainage procedure.

Although clearly second line for mature pseudocysts, percutaneous drainage is a helpful option for less well-defined early acute pancreatic fluid collections (PFCs) that are very symptomatic and cannot wait until they resolve or mature. Because they are not mature enough to be called pseudocysts, they may not be appropriate for endoscopic transluminal drainage, and large ones may not be anticipated to resolve with transpapillary drainage alone (>3–4 cm). In these cases, the drain is usually placed, and often, an ERCP is then performed to rule out downstream ductal pathology, bridge any disruption, and place a transpapillary pancreatic stent if ductal communication with the PFC is present. If the stent encourages transpapillary drainage, the drainage through the percutaneous catheter should quickly slow down, allowing the percutaneous catheter to be removed within days or weeks. Again, complete disruptions, or percutaneous drains that persistently drain over the coming weeks despite the above, should be referred for surgery, to avoid a long-term drain that may lead to a fistula.

Endoscopic Drainage

Pseudocysts can be managed endoscopically with transluminal drainage (cystogastrostomy, cystoduodenostomy) or by facilitating transpapillary drainage with a stent and/or pancreatic sphincterotomy. Endoscopic transluminal drainage is considered to be a preferred therapeutic approach for qualifying mature pseudocysts as it is less invasive, avoids the need to care for an external drain, and also has a high long-term success rate.

In patients with relatively small pseudocysts (less than 4–6 cm) communicating with the main pancreatic duct, transpapillary drainage with a temporary pancreatic stent may be tried as initial therapy, with or without a pancreatic sphincterotomy. A transluminal (transgastric or transduodenal) drainage approach is used in larger, well-circumscribed, mature, and symptomatic pseudocysts directly adjacent to the gastroduodenal wall (usually less than 1 cm separation between gastric and cyst lumens), without contraindications. Cross-sectional imaging helps assess the pseudocyst relationship to the gastrointestinal luminal wall. An immature pseudocyst wall is usually thin and poorly adherent to the gastrointestinal lumen; this may increase the risk of free perforation with endoscopic intervention. Endoscopic drainage should be delayed in such cases when possible.

Efficacy and Cost-Effectiveness of Endoscopic Management

The landmark success of endoscopic transmural pseudocyst drainage in the setting of chronic pancreatitis was reported in 1989 [15]. The technical success rate of the drainage procedure has since been reported to be up to 97%, with definitive resolution in more than 80% [14]. In cases of pancreatic necrosis and solid debris (what we now call WON), the success rate is significantly lower and is close to 60%. However, as mentioned above, in patients who are not good surgical candidates, endoscopic drainage and debridement can be considered [8, 21, 29]. One must be aware that for this WON indication, several procedures are often needed, usually as an inpatient, and often with an endoscopically placed nasocystic irrigation catheter (or with combined technique of endoscopic and percutaneous drainage catheter), to allow flushing out of the cyst contents between procedures.

Single stents through a small cystogastrostomy often result in inadequate drainage, leading to infection and a poor outcome. Failure can also occur due to untreated underlying downstream pancreatic ductal obstruction, unexpected necrotic debris that may otherwise have needed extensive endoscopic necrosectomy and lavage, and/or due to unexpected septations that do not allow drainage of some parts of the cyst.

Vilmann et al. [49] and Giovannini et al. [18] first described the single step EUS-guided cystogastrostomy in 1998. However, the routine use of EUS to guide endoscopic transmural drainage for bulging (Fig. 34.4) pseudocysts remains controversial. Although a randomized trial did not show a difference in success rates or complication rates [24], a meta-analysis [37] has concluded that EUS-guidance, on average, results in higher procedural technical success. In particular, it is required in cases of non-bulging pseudocysts; as such, EUS is often required for the cysts that are located in the tail, which

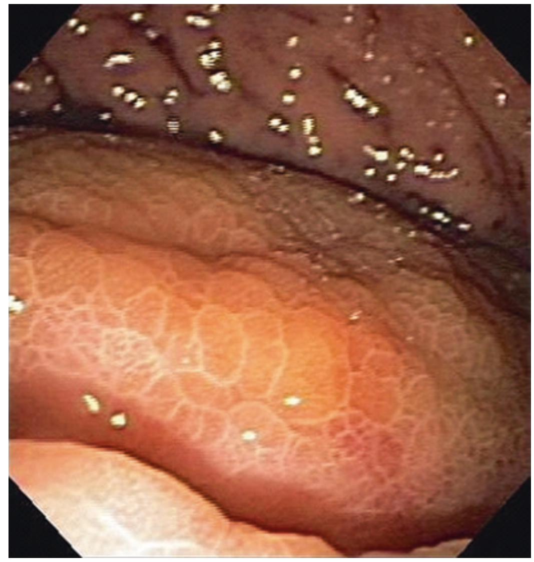

Fig. 34.4 An endoscopic view demonstrating a bulge in the body of the stomach from a compressing pseudocyst, with overlying congested mucosa

often do not cause endoscopically visible luminal compression [43, 48]. These tail cysts are usually drained through the proximal stomach, and EUS guidance helps in this location in the avoidance of the nearby spleen, splenic vessels and collaterals or varices, and diaphragm. In addition, as mentioned previously, EUS is also helpful as a second opinion prior to drainage in detecting unexpected solid debris, assessing the distance between the gastrointestinal lumen and the pseudocyst lumen in determining the maturity of the pseudocyst wall. MR can perform most of these functions very well, however, except perhaps the ruling out of small intramural vessels, and is more widely available. When the cyst is very large (>6–8 cm), MR is also arguably more likely to be effective at assessing cyst contents and its relationship to other structures, as the back wall of the cyst will usually be too far away to be seen well with EUS. In large cysts, cross-sectional imaging and EUS are often complementary.

Practical Considerations

- Surgical drainage is usually definitive, but is not generally the first-line treatment. It carries a significant risk of morbidity and mortality.
- Percutaneous drainage is usually successful, carries a high risk of infection.
- Endoscopic transluminal drainage is considered to be a preferred therapeutic approach for qualifying mature pseudocysts as it is less invasive, avoids the need to care for an external drain, and also has a high long-term success rate.

A retrospective study compared EUS-guided cystogastrostomy with surgery in patients with uncomplicated pancreatic pseudocysts [47]. No significant differences were found in rates of treatment success (100% vs 95%, $p = 0.36$), procedural complications (none in either cohort), or reinterventions (10% vs 0%, $p = 0.13$) between surgery and EUS-guided cystogastrostomy. The post-procedure hospital stay for EUS-guided cystogastrostomy was significantly shorter than for surgical cystogastrostomy (mean of 2.65 vs 6.5 days, $p = 0.008$). The average direct cost per case for EUS-guided cystogastrostomy was significantly less than surgical cystogastrostomy ($9077 vs $14,815, $P = 0.01$; cost savings of $5738 per patient). In another more recent study of 122 patients who underwent EUS-guided drainage by using plastic stents, the overall treatment success was 94.3%. Most patients (83.6%) required only one intervention, while 10.7% required more than one intervention, and 5.7% failed treatment [5].

Technique of Cystogastrostomy/Duodenostomy

The endoscope (by visual bulge – Fig. 34.4) or EUS scope (by ultrasound image) is used to detect an optimal site of puncture of pseudocyst via the gastric or duodenal wall. EUS and color Doppler can be used to identify a vessel-free site for the puncture; alternatively, a miniprobe can be used to confirm that a borderline endoscopic bulge actually corresponds to an underlying cyst. The puncture is then made with either a large-caliber EUS needle (which ideally can accommodate a guide wire) or a fine sclerotherapy needle; a cystogram is performed under fluoroscopy. In the case of EUS guidance, a cystogram may not be necessary, but practically, even a faint cystogram can help anticipate the size and location of the wire loop on fluoroscopy (to make sure the wire is staying within cyst lumen). If a 19 G needle has been used, a wire (0.025- or 0.035-in. by 450-cm) can be passed through the needle and into the cyst. A 22G needle can also be used; however, it only accommodates a 0.017 or 0.021 in. wire. Wires can shear on the needle's sharp bevel while it is withdrawn, so they should be withdrawn with great care. This risk can also be lowered through the use of a blunt-ended trocar-style needle which has a sharp stylet that is removed after the puncture and before the wire insertion (EchoTip Access needle; Cook Medical Bloomington, IN). Lastly, a needle-knife sphincterotome or a 10F cystotome (6F cystotome not available in USA) (Fig. 34.5) can be used to burn a hole through the gastric wall and into the cyst cavity using the same site through which the transgastric cystography was performed, followed by a wire through the catheter. A large gauge (0.035″ or a 0.025″) guide wire is generally chosen as it provides more stability for accessories exchanges, and a generous amount of wire is generally curled up a few times in the cyst cavity under fluoroscopic guidance.

After wire access is achieved (Fig. 34.6), an ERCP cannula or a dilating balloon is used to dilate the entry site (blunt dissection) (Fig. 34.7), or cautery can be used to enlarge the hole (regular or needle-knife sphincterotome, or a cystotome); the former "cautery-free" technique may be associated with a lower bleeding risk, especially delayed bleeding [35]. A randomized trial comparing mechanical and electrocautery initial tract dilation in 47 patients with pseudocysts showed more adverse events with electrocautery ($n = 4$) than with mechanical dilation ($n = 1$) [30]. All patients who had adverse events had no luminal bulge and had vessels in the gastric-pseudocyst wall. The size of the balloon used for dilation of the tract is based on the size of the cyst, presence of necrotic material, proximity of vessels and viscosity of the aspirated pseudocyst fluid, but is generally 6–10 mm. After dilation of the tract, a large amount of fluid can rapidly drain into the lumen, which requires aggressive prompt suctioning via the endoscope to prevent pulmonary aspiration. Then, a double pigtail catheter (generally 7–10 F) is placed over the guide wire (Fig. 34.8), followed by recannulation alongside the first stent, replacing a wire in the cyst, and placing a second (or third) stent. Double lumen catheters, such as a balloon stone extraction catheter or a Howell biliary introducer, can be used to place two wires into the cyst to begin with, without having to recannulate to place the second wire. The disadvantage of this approach is that only a 7F stent will fit down a therapeutic channel when a second wire is beside the stent. If the cyst fluid appears very thick or particulate in consistency, then a nasocystic catheter to provide prolonged lavage of the cyst, for inpatients, can be considered to decrease the risk of stent/tract occlusion and infection.

Recently a few reports have evaluated the use of transluminal fully covered self-expandable metal stents (FCSEMS) for pseudocyst drainage. However, there are no comparison studies to suggest clinical necessity and cost effectiveness of plastic versus metal stents. A prospective study of 20 patients with pseudocysts treated by FCSEMS (Wallflex, Boston Scientific Corp, Natick, MA) had complete resolution of the pseudocyst in 70%, with 15% adverse events and 15% stent migration rate [38]. A new lumen-apposing metal stent (Axios, Xlumina Inc., Mountain View, CA) has also been used for cystogastrostomy drainage with varying success. A multicenter prospective cohort study of 15 patients with pseudocysts and 46 patients with WON used a lumen-apposing metal stent. Pseudocysts resolved in 93% of the patients (81% resolution in WON) with overall adverse events in 9% and stent migration rate in 10.5% cases [52]. A lumen-apposing, self-expanding metal stent incorporated in an electro cautery enhanced delivery system (Hot Axios) for EUS-guided drainage of PFCs has recently become available. In a retrospective study of 93 patients with PFCs (80% with complex collections with necrosis), penetration of the

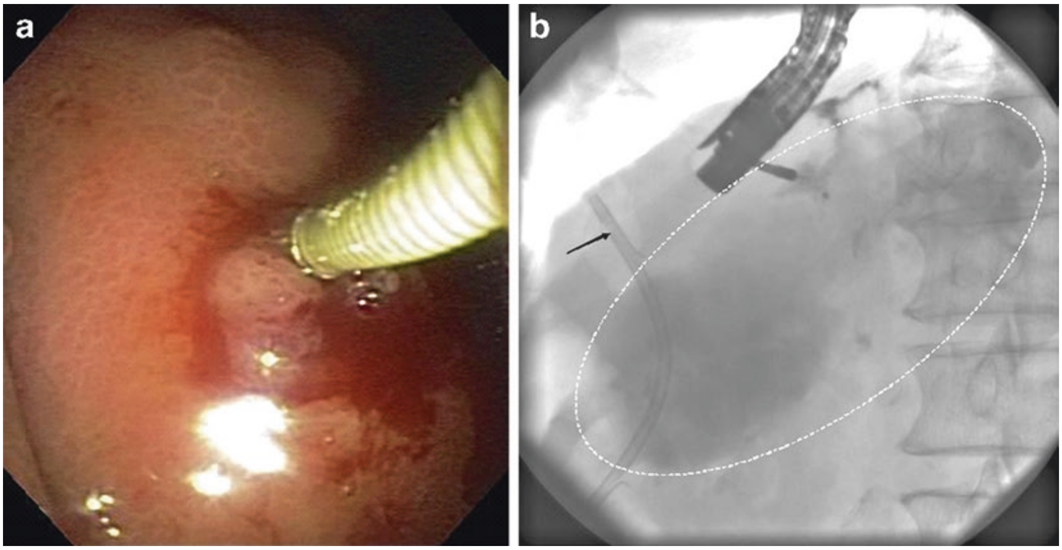

Fig. 34.5 A cystotome entering a pseudocyst through the gastric wall (**a**) after performing a partial transgastric cystogram (*dotted line*) using a fluoroscopically guided sclerotherapy needle inserted into the endoscopic bulge. (**b**) A biliary stent (*arrow*) had already been placed to relieve compression of the biliary tree by the cyst

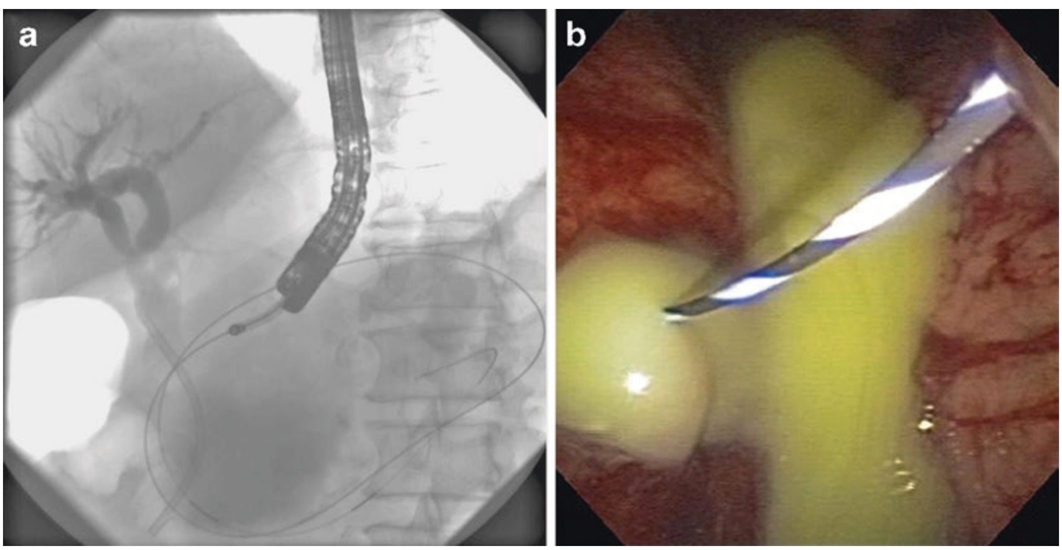

Fig. 34.6 Wire access to the cyst through the gastric wall. Wire coiled in the pseudocyst seen by fluoroscopy (**a**), with drainage of pseudocyst contents into the stomach around the wire seen endoscopically (**b**)

PFC was accomplished directly with this device in 74.2% of patients, and successful stent placement was accomplished in all but 1 patient, mostly without fluoroscopic assistance. Complete resolution of the PFC was achieved in 86 cases (92.5%), with no recurrence during follow-up. Treatment failure occurred in 6 patients with major adverse events reported in 5 patients [42]. With advancement in technology endoscopic drainage of pancreatic fluid, collection may become technically easier; however, placement of plastic stents provides effective drainage of pseudocysts, at significantly less expense than FCSEMS (Figs. 34.9 and 34.10).

All patients receive a short course of antibiotics. If patients have concomitant biliary obstruction due to pseudocyst compression, they are usually treated with temporary biliary stent placement, with a subsequent repeat cholangiogram and removal of the biliary stent at a second ERCP a few months later. Although not mandatory, a pancreatogram is often helpful to exclude downstream ductal obstruction, exclude main duct disruption, and assess for a significant active duct leak in order to determine if a temporary pancreatic stent would be helpful. Transmural drainage allows the disconnected pancreatic segment to drain via an enteral bypass into the GI lumen while stents are left in place.

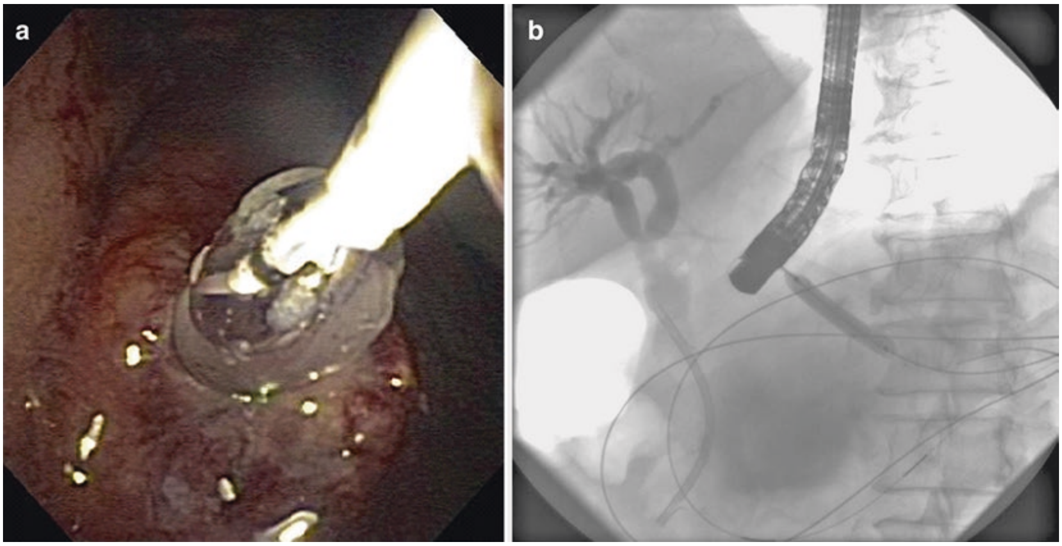

Fig. 34.7 An endoscopic (**a**) and fluoroscopic (**b**) view of a hydrostatic 6 mm balloon used to dilate the cystogastrostomy tract over a wire

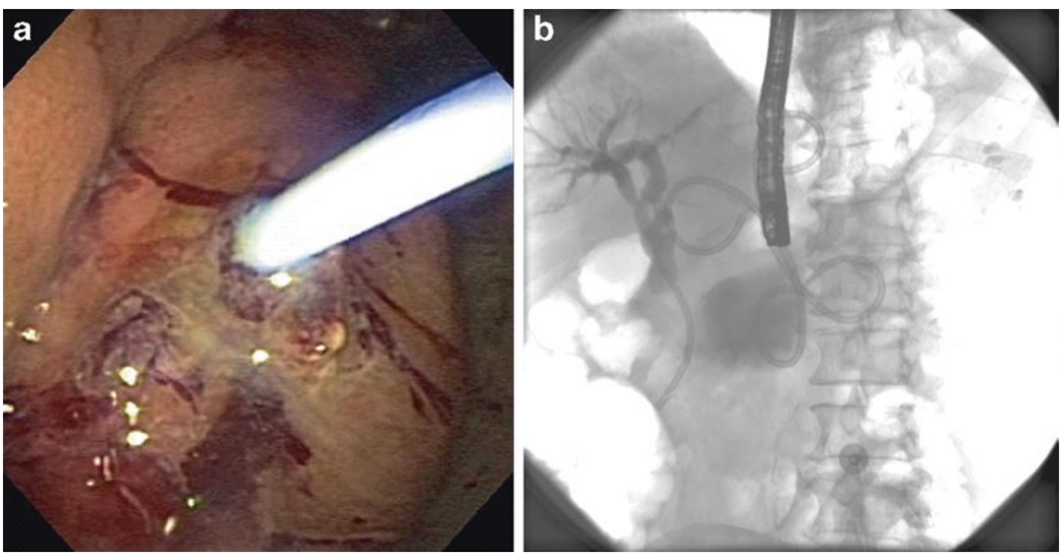

Fig. 34.8 A cystogastrostomy stent (**a**) was placed over the guide wire after balloon dilation, followed by placement of a double pigtail stent connecting the gastric lumen and the cyst lumen (**b**)

Recurrence is high after the transluminal stents are removed if an active leak is still present and downstream obstruction or disruption was not treated; in such cases, leaving stents may decrease the risk of recurrence [4]. Alternatively, instead of a direct pancreatogram, some prefer an MRCP in follow-up, after resolution of the cyst by transluminal drainage, to assess for pancreatic duct integrity, before removing transluminal stents; the large amount of fluid compressing the pancreas usually makes an MRCP pre-drainage inaccurate for this purpose. Periampullary edema can sometimes be so severe (due to active pancreatitis or due to venous congestion from compression) that the ampulla is obscured and ERCP with selective cannulation may be difficult or impossible.

A follow-up CT scan (or EUS or MRCP) in 1–2 months is then obtained. Assuming there is no significant residual collection, the stents can be removed at upper endoscopy with a snare. In patients whose pseudocysts have not resolved in 4–6 weeks, there are several options. First, one can wait. Second, one can assess the pancreatic duct for obstruction or disruption by pancreatography (ERCP or MRCP), with transpapillary stenting as needed. Third, one can dilate the transluminal tract and empirically replace the stents, remove solid material with endoscopic necrosectomy, or attempt additional transmural puncture of loculated areas. Multiple endoscopic sessions may be required in cases of persistent necrosis, with snare, forceps or extraction basket removal of

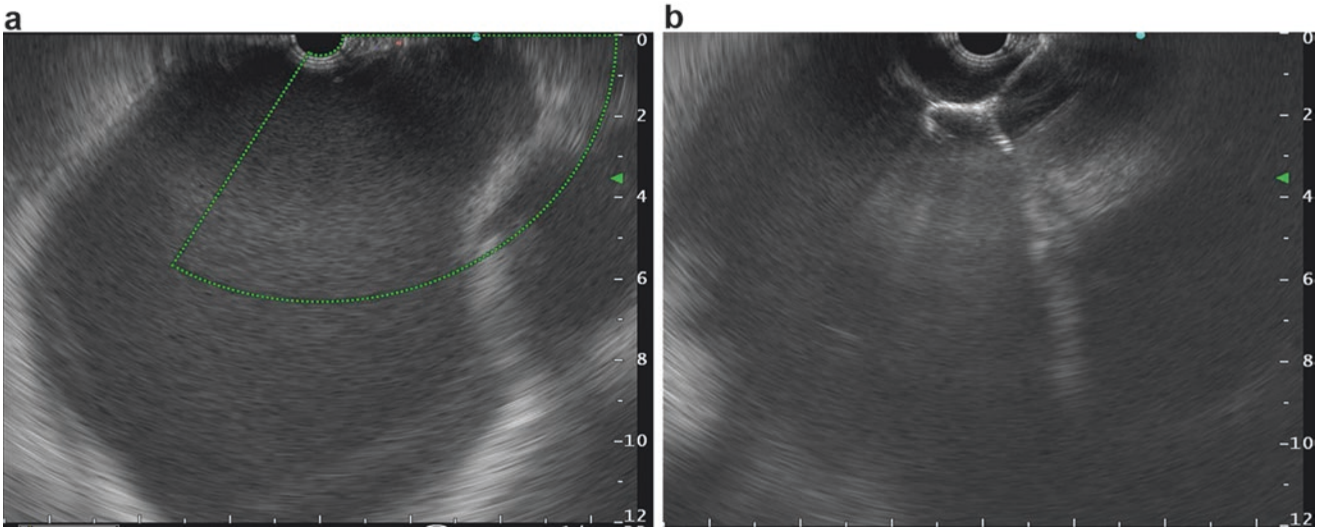

Fig. 34.9 EUS-guided cystogastrostomy image of the deploying lumen-apposing metal stent

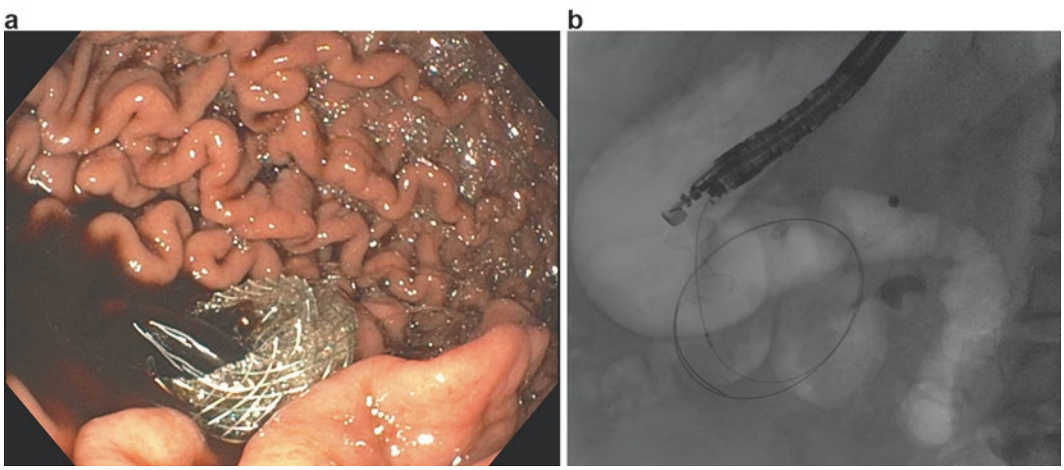

Fig. 34.10 An endoscopic (**a**) and fluoroscopic (**b**) view of the fully deployed lumen-apposing metal stent

necrotic debris under direct vision via the transluminal tract. Surgery should be considered for non-resolution of symptomatic pseudocysts, symptomatic recurrence without reversible factors, or in the presence of persistent symptomatic or infected walled off necrosis (WON).

Transpapillary Drainage

When a transpapillary pancreatic stent placement is needed, a pancreatic sphincterotomy is usually also performed, but is not mandatory, especially if chronic pancreatitis or intraductal stones are also present. Stones are removed when possible, and strictures are dilated and stented. If there is no obstruction, but a leak is demonstrated into the cyst from the duct, a small caliber stent is reasonable as a trial. It is controversial whether the stent inner tip should be placed in the duct (as it would be for a bile duct leak) or in the cyst itself; the latter provides more effective direct drainage, but stenting a blown out side branch into a larger caliber duct may prevent the side branch blowout from sealing over and, as such, may not be good in the long term. If the duct is partially disrupted, rejoining the duct with a stent over a wire, if the wire can bridge the disruption, is attempted [28, 45] (Fig. 34.11). Prophylactic and post-procedural antibiotics are provided for a few days given the unavoidable contamination of a sterile collection. The stent is generally pulled after satisfactory resolution of duct pathology on follow-up ERCP 1–2 months later.

If the cyst is accompanied by a complete main pancreatic duct disruption, it is unlikely that endoscopic therapy will ultimately succeed. Although the cyst may resolve, if one cannot reconnect the pancreas, the disconnected upstream pancreas will likely continue to cause obstructive symptoms (leak downstream from disruption) or cause the cyst to recur (leak upstream from disruption). Surgery should be strongly

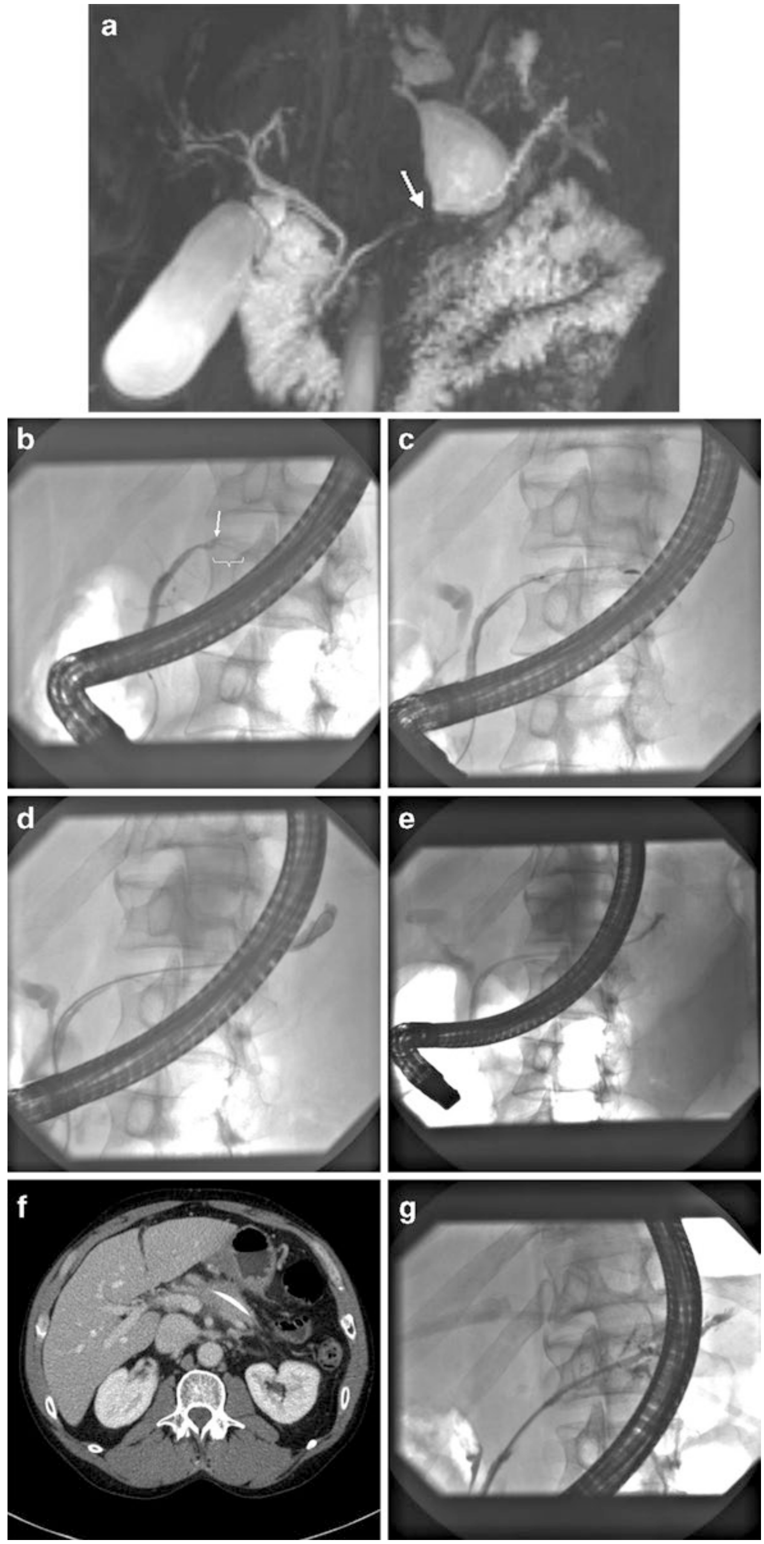

Fig. 34.11 A patient with alcoholic pancreatitis, persisting pseudocyst and pain. An image of a secretin-stimulated MRCP (**a**) and ERCP (**b**) leading to suspicion of a duct disruption (*small arrow*) as shown by a wisp of dye exiting from a partially cut-off pancreatogram in the body of the pancreas (*bracket*). The upstream duct (*PD*) appeared to be dilated on MRCP, and a wire was threaded across this area (**c**). Dye was injected to confirm that the wire was in the partially disconnected tail (**d**), and a stent was inserted (**e**). In follow-up, the cyst resolved on CT (**f**), and the pancreatic duct appeared to be reconnected (**g**)

considered in these cases. In selected cases, especially when the bulk of the disconnected tail is small, long-term transluminal stenting, perhaps with annual imaging thereafter, could be entertained as an alternative to surgery, hoping that the disconnected tail will atrophy over time. Long-term effectiveness and safety data on this approach are not available, so this should be a multidisciplinary decision, with the patient well-informed of the unknown outcomes.

Complications and Their Avoidance

Complications of endoscopic pseudocyst drainage include secondary infection, bleeding, perforation, and stent migration. The frequency of these has been reported around (11–37%) in literature [3, 8, 24]. Case selection is the key to reducing complications – not all apparent "cysts" reported on CT can or should be treated with endoscopic drainage.

Infection is the most common complication following endoscopic drainage of pseudocysts. The infection usually develops due to malfunction or obstruction of stents or due to significant unrecognized necrosis. Use of peri- and post-procedural antibiotics can help reduce this risk. Fortunately, the majority of infectious complications can be managed endoscopically, or with percutaneous drainage of loculated areas; cases of multiloculated infected necrosis often require surgery. Avoidance of this technique when there is significant necrosis, or early recognition of underlying pancreatic necrosis followed by extensive endoscopic debridement ("necrosectomy") and/or placement of nasal or percutaneous lavage drains in centers comfortable with these techniques, can reduce the need for surgical intervention for infection [7]. As stated above, inadequate drainage from small transluminal tracts and/or single stenting increases the risk of infection. FNAs that contaminate a cyst, without complete drainage, can also lead to infection.

Significant bleeding can occur due to inadvertent puncture of a submucosal vessel or varix; this can generally be prevented by use of an EUS-guided puncture. Although rare, the presence of a pseudoaneurysm can lead to fatal hemorrhage either by guide wire trauma as it coils along the inside of the cyst, erosion of a transluminal stent, or simply due to rapid changes in the cyst wall tension as the size of the cyst rapidly changes. Preprocedure imaging can usually detect this. One study suggested that blunt dissection with a dilating balloon over a wire that is placed through a needle after a needle puncture (i.e., a Seldinger technique), without cautery, has a lower risk than using cautery to enter the cyst and expand the cystogastrostomy lumen with a standard sphincterotome [35]. However, it is not clear if the higher risk of a cautery approach still applies when the diameter of the hole that is made with cautery is limited (such as a small entry with a needle-knife) or when the cutting is done with a circumferential cauterizing device such as a cystotome. The Seldinger technique can be difficult with a side-viewing scope as the tip of the 19 G needle can be damaged by the elevator, with cases of needle tip fragmentation into the cyst having been reported.

Perforation has been reported to occur in about 3% of cases [3, 21]. Perforation is more likely to occur when the pseudocyst wall is poorly defined by imaging studies or has a distance of greater than 1 cm from the intestinal lumen or if the cyst has not been present long enough to become adherent to the luminal structure into which it is being drained. Cystic tumors masquerading as pseudocysts are often not adherent to the GI lumen, because there is usually little or no inflammatory reaction around them, and as such, they are more likely to be associated with perforation or free-air. Usually, free-air can be managed conservatively, with antibiotics and fasting, but emergent percutaneous drainage or surgery may be required.

Conclusion

- Endoscopic drainage, with or without EUS guidance, can be considered a first-line cyst drainage modality for symptomatic pseudocysts (pancreatic fluid collections (PFCs) persisting more than 4 weeks) adjacent to the gastrointestinal wall without contraindications; EUS guidance is often needed for cysts located in the tail.
- Surgery is generally reserved for salvage therapy, for complicated cysts (e.g., with infection and/or significant necrosis), and for those cases associated with complete duct disruptions. In the latter, selected long-term transmural stents can be considered as an alternative to surgery, after a multidisciplinary discussion.
- Transpapillary drainage with a pancreatic stent and/or sphincterotomy is useful as monotherapy for small pseudocysts with ductal communication and is a useful adjunct to transluminal drainage when downstream ductal pathology exists.
- Acute PFCs, PNPFCs and WON, and cystic tumors can mimic pseudocysts, but require different interventions and have different considerations.
- Careful history-taking, waiting for cyst maturity, and US/MR/EUS imaging are key.
- Though recent data on endoscopic transluminal therapy for complicated pseudocysts (e.g., infected) or in symptomatic necrosis are very encouraging as being comparable to surgery in selected cases, the safety and superiority over surgery is not as clear as in uncomplicated pseudocysts.
- Expertise in the technique of transluminal endoscopic debridement of necrosis is limited to a small number of advanced endoscopists and centers, and often requires inpatient lavage and multiple procedures.

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