Complications of Acute Pancreatitis

INTRODUCTION

Acute pancreatitis is an acute inflammatory process of the pancreas, which has variable involvement of other regional tissues and/or remote organ systems. The disease can be classified as mild or severe depending on the extent of inflammation and organ involvement. Mild pancreatitis consists of interstitial (edematous) pancreatitis on imaging with minimal or no extrapancreatic organ dysfunction or involvement. Severe pancreatitis manifests with organ failure in addition to local complications such as pseudocysts, necrosis, abscess formation, fistulization, or vascular complications. This review focuses on the local complications of acute pancreatitis and their management thereof.

Pseudocysts

Pseudocysts can develop after an episode of acute pancreatitis in approximately 10% of cases. A pancreatic pseudocyst is a maturing circumscribed collection of pancreatic secretions encased in granulation tissue occurring in or around the pancreas as a result of inflammatory pancreatitis with or without ductal disruption (Figure 1). Pseudocysts account for about 80% of cystic lesions of the pancreas. They may be single or multiple, within or outside of the pancreas, and can vary in size. Most pseudocysts communicate with the pancreatic ductal system and contain high concentrations of digestive enzymes. The walls of a pseudocyst are formed by the adjacent structures, which may include the stomach, transverse mesocolon, gastrocolic omentum, and the pancreas itself. The key feature of a pseudocyst is the lining, which contains fibrous material and granulation tissue and has no true epithelial lining. This distinguishes pseudocysts from a true cystic lesion of the pancreas.

There have been two suggested hypotheses for pseudocyst formation as a result of acute pancreatitis. The first is that pancreatic inflammation may result in necrosis of pancreatic and peripancreatic tissue, which can then progress into liquefaction of the parenchyma and surrounding tissue with subsequent organization and eventual evolvement into a pseudocyst. The second hypothesis suggests that pancreatic parenchymal necrosis leads to ductal disruption and gross leakage of pancreatic fluid, which subsequently undergoes organization and evolvement into a pseudocyst.

The classification of these pancreatic fluid collections as pseudocysts versus pancreatic necrosis, pancreatic abscesses, or peripancreatic fluid collections can be difficult. The nomenclature of pancreatic pseudocyst was agreed upon by a consensus of experts at the Atlanta Symposium who defined a pseudocyst as a fluid collection that was >4 weeks old and surrounded by a well-defined wall; however, in clinical practice,
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fluid collections found on imaging during and after an episode of acute pancreatitis may not be so easily classified.\(^1,6\) If the diagnosis is questionable, further testing may be performed including aspiration of fluid under computed tomography (CT) or endoscopic ultrasound (EUS) guidance. Compared to the other types of acute pancreatic fluid collections, pancreatic pseudocysts tend to have higher concentrations of pancreatic enzymes and minimal to no tissue debris and are for the most part sterile.\(^6\) The diagnosis of pseudocyst may also be supported by the presence of pancreatic ascites or pancreatic pleural effusion that have high amylase concentrations >1000 IU/L.\(^7\)

**Management**

The traditional treatment of pseudocysts was based on a classic study that suggested that a pseudocyst persisting for >6 weeks rarely resolved and had a complication rate nearing 50% during continued observation.\(^10\) However, this study was comprised primarily of inner-city alcoholics who had a high incidence of acute alcoholic pancreatitis, and as such, these observations may not apply to other populations. In fact, recent data suggest that an asymptomatic pseudocyst does not require treatment regardless of size.\(^8,9\) A retrospective review of 68 patients with a pseudocyst followed conservatively showed that there was only a 9% incidence of major complications including perforation, pseudoaneurysm, and abscess formation. Twenty-seven percent of patients underwent elective surgery due mostly to pseudocyst enlargement with associated pain. Sixty-three percent of patients remained well without symptoms or complications for a mean of 51 months.\(^8\) These findings suggest that it may be satisfactory to monitor asymptomatic pseudocysts with serial imaging.

The most commonly reported symptom of a pseudocyst is upper abdominal pain, but other less common symptoms include early satiety, nausea, vomiting, jaundice, pruritus, edema, or gastrointestinal bleeding. These symptoms correlate to local obstruction of structures such as the gastric outlet, IVC, common bile duct, small bowel, colon, splenic, or portal veins and are usually related to the pseudocyst size and its location. Occasionally, a pseudocyst can rupture into the stomach in the small bowel (Figure 2). Other reported complications attributed to pseudocysts include infection, intracystic hemorrhage, or rupture, leading to pancreatic ascites. Pseudocysts have also been reported to migrate into chest as well as other unusual locations.\(^9\)

In the clinical setting of a pseudocyst related to acute pancreatitis, new symptoms of abdominal pain, fever, or chills should be recognized as possible emergence of an infection or abscess formation, and appropriate surgical, endoscopic, or radiologic management should be undertaken depending on the presenting symptoms and findings.

**Drainage**

Surgical drainage was at one time the only form of therapy available for symptomatic pseudocysts or pseudocysts that required drainage due to infection. However, over the last 10 years, imaging-guided percutaneous catheter drainage and endoscopic drainage have become increasingly popular. However, to date, there are no randomized, comparative studies that evaluate the efficacy or morbidity associated with these drainage modalities. Local expertise has driven the use of one method over another in determining which approach is most appropriate.\(^8,9,11,12\)

Surgical drainage remains the most accepted modality for pancreatic pseudocyst management. The surgical literature describes newer laparoscopic methods for drainage, though most data have come from open surgical drainage procedures. Open surgical drainage may be accomplished via cystgastrostomy, cystenterostomy (with or without creation of a Roux Limb), or surgical resection. First described in 1994, several different approaches of laparoscopic drainage have been used. Laparoscopic cystgastrostomy can be performed using an anterior transgastric approach requiring an anterior gastrostomy for access with cystgastrostomy creation via the posterior gastric wall.\(^13,14\) A posterior approach has also been described with creation of a single gastrostomy in continuity with the pseudocyst via the lesser sac.\(^15\) The latter is considered technically easier and is associated with less intraoperative bleeding.\(^14,16,17\)

In general, morbidity and mortality associated with surgical drainage has been shown to be substantial with rates of 25% and 5%, respectively.\(^18-20\) Some series have reported pseudocyst recurrence rates after surgical drainage to be as high 15%, and can be more frequent if the main pancreatic duct is obstructed downstream from the surgical anastomosis.\(^20\) Preoperative endoscopic retrograde cholangiopancreatography (ERCP) is usually performed to determine if ductal obstruction exists, and

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in such cases, pseudocyst resections can be offered.

Imaging-guided percutaneous catheter drainage has been reported to be as effective as surgical management of a pseudocyst whether the cyst is sterile or infected.\textsuperscript{21-23} However, there are several complications associated with this procedure, with the most common being drain-track infections, occurring in up to 50\% of cases.\textsuperscript{21} The more concerning complication, however, is the formation of an external fistula. This risk is associated with any percutaneous catheter intervention, but in the setting of pseudocyst drainage with high concentration of pancreatic enzymes, it is much higher. Ductal anatomy has been shown to correlate with both the success of percutaneous method as well as the development of complications after percutaneous drainage. Pseudocysts with normal pancreatic ducts and those associated with pancreatic duct strictures without duct disruption or cyst communication have higher rates of successful drainage. Strictures in association with pancreatic duct disruption and cyst communication and those associated with complete cut-off of the pancreatic duct have relatively poor outcomes. The latter features also predispose to long-term pancreatic external fistula formation. ERCP is usually performed to determine ductal anatomy prior to percutaneous drainage. Ill-defined anatomy is considered to be a relative contraindication to imaging-guided percutaneous drainage.\textsuperscript{24}

Pseudocyst decompression can be achieved by two endoscopic methods. Transpapillary drainage via stenting through the ampulla directly into the pseudocyst itself or by creating an endoscopically placed cystgastrostomy or cystduodenostomy.\textsuperscript{25,26} Studies have not shown a significant difference in outcomes for the respective approaches in pseudocyst drainage. Regardless of the technique used, the catheter is removed after three to four weeks if closure of the pseudocyst is seen on imaging.

Long-term resolution with successful endoscopic drainage of pseudocysts has been reported in most series, with rates ranging from 65\% to 89\%.\textsuperscript{27} The major complication with endoscopic pseudocyst drainage is bleeding, retroperitoneal perforation, and infection. Bleeding has been considered to be the most important, with about a 5\% risk of requiring surgical interventions. Some series have suggested that nasocystic drainage

Figure 1. Pancreatic pseudocyst
with irrigation may prevent occlusion and can be used in infected pseudocysts or possibly even in organized necrosis.\textsuperscript{28,29} Recurrence rates have been reported to range from 6\% to 18\%; however, rates may be reduced with long-term pancreatic duct stenting in patients with severe duct disruption.\textsuperscript{30}

**Necrotizing Pancreatitis and Abscess Formation**

Pancreatic necrosis is a local complication that can occur in up to 10\%-20\% of patients suffering from acute pancreatitis.\textsuperscript{31} The diagnosis can be made based on imaging and is defined by the presence of >30\% of nonenhancement of the pancreas on contrast-enhanced CT or magnetic resonance imaging (MRI). Infected necrosis refers to bacterial contamination of necrotic pancreatic tissue in the absence of abscess formation. It can progress to abscess formation and is defined as a collection of pus resulting from infected liquefaction of necrotic pancreatic tissue. Infected pseudocysts, as described previously, are an infected fluid collection with high concentrations of pancreatic enzymes within a defined fibrous wall lacking underlying epithelial lining. Although there is overlap in the characterization of localized infections of the pancreas, recognizing the nomenclature describing the complication has importance with regards to management. Figure 3 shows evidence of walled off pancreatic necrosis on CT scan.

**Sterile Necrosis**

Sterile pancreatic necrosis occurs early in the course of pancreatitis and is typically seen within the first 10–14 days of illness. Contrast-enhanced CT is the gold standard in the diagnosis of necrotizing pancreatitis. The development of necrosis is a continuous process that occurs within hours of symptom onset; however, contrast-enhanced CT in the first several days will miss the formation of necrotic parenchyma and can be misleading. The sensitivity of contrast-enhanced CT for pancreatic necrosis nears 100\% between 4 to 10 days after onset of pancreatitis.\textsuperscript{32} Often patients with necrosis present as necrotizing pancreatitis. This is the most severe presentation of pancreatic inflammation. The amount of necrotic tissue is the strongest predictor of mortality in necrotizing pancreatitis.
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After diagnosis, the treatment is maximal supportive care including nutrition and preventing infections from intravenous lines. The role for prophylactic antibiotics to prevent infection has been shown to be questionable and not recommended. Surgical debridement of sterile pancreatic necrosis has not proven to improve morbidity or mortality in majority of patients. However, surgical debridement is often needed when necrosis becomes infected.

**Infected Necrosis**

Infected pancreatic necrosis generally occurs after 10–14 days of illness. Bacterial infection is a major determinant of mortality. Severe systemic complications are common in patients with sterile necrosis, but mortality rates are relatively low, with a reported incidence of 5%–10%. With development of pancreatic infection, the mortality increases to 20%–30%, despite surgical debridement. Diagnosis of infection can be made via fine-needle aspiration (FNA). CT-guided FNA has been safe in the diagnosis of infected necrosis. The gram stain alone has a sensitivity of almost 95%. In the event of a negative FNA with a persistent suspicion for infection, repeat aspirations can be performed every 4 to 7 days.

In patients diagnosed with infected necrosis who have persistent sepsis or organ failure, surgical debridement should be strongly considered. However, in stable patients with infected necrosis, maximal supportive care and the use of antibiotics should be provided. Optimal timing for surgical debridement is at least 3 to 4 weeks after onset of illness. Delayed debridement allows for clinical stabilization of the patient, resolution of organ dysfunction, lowered inflammatory reaction in the retroperitoneum, and the delineation of live and dead tissue via organization and formation of a fibrous wall. This clinical entity is known as walled-off pancreatic necrosis (WOPN). The benefits of waiting for WOPN is the resolution of systemic inflammation and determination of live and dead tissue delineation which would result in less invasive methods of debridement. Early-phase debridement within the first 3 to 4 weeks requires an open surgical approach where as late-phase debridement of WOPN can be treated laparoscopically, percutaneously, or endoscopically.

**Pancreatic Abscess**

Pancreatic abscess is a late complication of acute necrotizing pancreatitis, which occurs more than 4 weeks after the initial illness. The management and complications are similar to that of infected pseudocysts. Abscess formation can cause pressure effects and obstruction by compression of surrounding structures, including the colon, stomach, duodenum, and the common bile duct. The mortality rate associated with pancreatic abscess is generally much lower than that of infected necrosis. Initiation of antibiotics followed by surgical, percutaneous, or endoscopic drainage should be performed. Abscesses that are drained percutaneously or endoscopically which do not show clinical improvement should undergo surgical drainage immediately.

Surgical debridement or drainage of the pancreas is the mainstay of treatment for infected pancreatic necrosis or abscesses. Percutaneous drainage is primarily a bridging technique for patients that are not stable enough to undergo surgical debridement, although about 35% of patients can be managed with percutaneous drainage alone. Percutaneous drainage compared with open pancreatic debridement in select cases has shown decreased new onset multi-system organ failure, incisional hernias, and interval development of diabetes. This had no significant effect on mortality. In general, CT guidance is used to establish percutaneous access into the pancreatic fluid collections using a transperitoneal route if available to avoid solid organs, intervening bowel, or vasculature. The limitations to this approach are due to location of the space that requires drainage, catheter diameter, viscosity of the fluid, and the amount of debris present. Due to these limitations, the drainage catheter generally requires meticulous maintenance as well as frequent replacement.

Endoscopic debridement for infected necrosis has been described via a transgastric approach but is limited to patients who are stable and have developed WOPN. The overall approach is similar to that of pseudocyst drainage. Once a cystgastrostomy has been established, direct endoscopic debridement can be performed using a forward viewing endoscope. Following mechanical debridement, double pigtail stents are placed in the cavity, and some experts suggest placing a nasocystic tube along side the stents for post procedure irrigation. Serial imaging can be used at 2-week intervals until resolution of necrosis is achieved. Similar to percutaneous drainage, data suggest that 33% of patients treated with endoscopic debridement will eventually need open surgical debridement.
Vascular Complications

The incidence of vascular complications related to acute pancreatitis is not known, though it has been speculated to have an incidence nearing 25% in acute pancreatitis cases.39 The most common complications are pseudocyst hemorrhage, erosions of the gastrointestinal vessels, venous thrombosis, variceal formation, and pseudoaneurysm formation. The pathogenesis of vascular complications is multifactorial, but the predominant mediators are local spread of inflammation, irritative effects of activated pancreatic enzymes, and pressure necrosis due to fluid collection or inflammatory debris on surrounding structures. The mortality related with hemorrhage associated with these complications of acute pancreatitis has been reported to occur in up to 14.5% of the time, and there does appear to be a correlation with severity of underlying illness.40–42

Pseudoaneurysm

A pseudoaneurysm is a collection of blood and blood clot that has formed outside of a vessel. Pseudoaneurysms have been reported to occur in 3.5%–10% of patients with pancreatitis.43 Arteries most commonly involved are the splenic, gastroduodenal, and pancreaticoduodenal. These vessels are involved in approximately 90% of all pseudoaneurysms related to acute pancreatitis.44,45 Rupture of pseudoaneurysms is a serious complication of pancreatitis and have been known to bleed into the pseudocyst, the gastrointestinal tract, peritoneal cavity or pancreatic parenchyma.46 The diagnosis is not always clear as the patient may have hemodynamic instability or multiple organ dysfunction related to severe pancreatitis. The patient may present with abdominal pain, signs of exsanguinating blood loss, or slow intermittent bleeding. A sudden exsanguinating process, which leads to death within minutes to hours, has been reported in 7.5% of patients with pseudoaneurysm ruptures.47

Regardless of size, non-bleeding pseudoaneurysms do not require treatment and are usually observed and diagnosed based on dynamic contrast-enhanced CT scan. The gold standard for diagnosis and preferred method of treatment of ruptured pseudoaneurysms in stable patients is angiography. Angioembolization has been used extensively in the treatment of visceral artery pseudoaneurysms and is considered much less invasive than surgical options. The advent of newer catheters, embolic material, and improvement in technical expertise has been demonstrated with increasing success over the past decade (as high as 67%–100%).48

Percutaneous ultrasound guided thrombin injections have also been used successfully in treatment of pseudoaneurysms.49 This technique has been described as first-line management or as adjuvant treatment with arterioembolization. However, to date, there are no large, prospective studies that compare the efficacy of thrombin injection to arterioembolization in pancreatic pseudoaneurysms.

Surgical management of pseudoaneurysms has been limited to patients with hemodynamic instability and/or failure of radiologic techniques. The most common surgical procedure is suture ligation of the bleeding point; however, recurrence of bleeding has been reported to be high. Due to excellent collateral circulation of the pancreas and peri-pancreatic structures, it is optimal to ligate the artery proximal and distal to the pseudoaneurysm. Primary resection of the pseudoaneurysm with or without pancreatic resection may be required if ligation of the proximal and distal ends of the bleeding vessel are not achieved.50,51

Venous Thrombosis

Venous thrombosis may be observed in acute pancreatitis and is related to acute inflammatory processes of the pancreas adjacent to venous structures. Isolated splenic vein thrombosis is the most common type, and, in some case series, has had a reported incidence as high as 42% in acute pancreatitis cases.52 Less commonly, portal and superior mesenteric vein thrombosis can occur as a results of pancreatitis. The pathogenesis is related to intimal injury and compression as a result of the close proximity of the venous vasculature to the pancreas, most specifically the splenic vein. Stasis of blood flow occurs from these intrinsic and extrinsic factors and eventually leads to thrombosis. Development of venous stasis has been hypothesized to occur as a result of compression by pseudocyst and/or enlarged edematous pancreatic parenchyma. Splenic vein obstruction can be seen of the pseudocyst tail in nearly 30% of cases.53

Splenic vein thrombosis (SVT) may be silent or present as gastrointestinal bleeding (anemia, hematemeses, melena, or hematochezia). Occasionally thrombocytopenia, pancytopenia, and/or abdominal pain can occur due to splenomegaly.54 SVT is asymptomatic in the majority of cases and may present as an incidental finding on CT scan. Dynamic-enhanced CT scan can be done with a sensitivity of 71% in detecting SVT.
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Venography is the gold standard for diagnosing SVT. Many patients with SVT develop silent collaterals without gastric or esophageal varices and are extremely unlikely to bleed.

Management of SVT should be focused on observation due to the possibility of variceal formation and subsequent risk of upper gastrointestinal hemorrhage in the future. However, data suggest that variceal formation is unlikely if they were not present at the time of diagnosis. At this time, there are no guidelines for the routine surveillance of interval variceal development. Patients who develop bleeding related to gastric or esophageal varices can be temporized endoscopically with variceal band ligation. Splenectomy is curative, and the treatment of choice in symptomatic patients that are surgical candidates. In patients that are at high surgical risk or have technically difficult to excise spleens, radiographic arterioembolization may be a possible alternative or bridge to surgery. The role of splenectomy in asymptomatic SVT associated with gastric varices remains controversial. Long-term observations show that bleeding risk in patients with SVT over time exceeds the risk of elective splenectomy due to post splenectomy sepsis; thus, prophylactic splenectomy may be useful. Opposing expert opinion suggests that observation followed by splenectomy after the first episode of variceal bleeding may be a reasonable approach, as bleeding appears to be uncommon with a reported incidence of only 4% in asymptomatic patients with gastric varices in association with SVT. However, there is no definitive way to accurately predict the risk of variceal hemorrhage, and thus, the possibility of life-threatening bleeding cannot be excluded with certainty. Bleeding risk is greater in patients with larger varices or when red wale markings are observed during endoscopy, which may be beneficial in decision making. Patients with hypersplenism presenting as pain or cytopenias may also have a greater justification for undergoing prophylactic splenectomies to prevent bleeding.

Other Bleeding Complications

Other bleeding complications include postnecrosectomy bleeding, which can be a result of overly aggressive debridement and placement and/or use of noncompliant drainage tubes next to a vascular structure resulting in pressure necrosis and direct erosion into a vessel. In some cases, incomplete debridement can result in sepsis and erosion into vascular structures as well. Data
suggest that bleeding complications are significantly more common in interventions that occur in the acute phase versus after delayed interventions.\textsuperscript{59} Radiologic arterioembolization is the mainstay of management with surgery reserved for refractory cases or for patients with hemodynamic instability. Rarely, bleeding can occur into the pancreatic duct, which is known as hemosuccus pancreaticus; however, this is more typically seen as a complication of chronic pancreatitis. Intermittent, low-grade gastrointestinal bleeding up to exsanguinating bleeding has been described as a result of hemosuccus pancreaticus. Due to rare occurrence, there are limited data on its management. Options include radiographic arterioembolization versus surgical vessel suture ligation with or without distal pancreatectomy. Mortality rates associated with surgery have been reported as high as 20\%–25\%, though re-bleeding rates are significantly lower than that of arterioembolization.\textsuperscript{60}

Other Complications of Pancreatitis

Isolated splenic complications of acute pancreatitis are uncommon. Intrasplenic pseudocysts, splenic infarction, necrosis, rupture, and hematoma have all been reported as possible complications. Some of these complications can be life threatening and require emergent splenectomy, and if necessary, distal pancreatectomy as definitive treatment.\textsuperscript{61} Bowel compression has been reported as a result of pressure necrosis from inflammatory debris from the tail of the pancreas. This may result in signs and symptoms of partial or complete obstruction and may even result in fistulization of the small or large bowel. The left colon is the most common site of compression and fistulization.\textsuperscript{62} Decompression of the obstructing lesion can be done percutaneously, endoscopically, or surgically depending on the type of lesion. After fistulization has occurred, treatment is limited to surgical repair or resection.

Common bile duct obstruction may be a complication of acute pancreatitis. This is normally seen in the early symptomatic phase of illness and is related to the inflammatory mass in the head of the pancreas, pseudocyst, or fluid collections. Typically, the distal common bile duct is affected and subsides with clinical improvement of underlying illness. In patients who develop biliary sepsis or intractable pruritus, management options include endoscopic, surgical, or percutaneous decompression. Endoscopic or percutaneous decompression is associated with lower morbidity and should be considered first-line therapy. Patients generally need short-term decompression with stents or catheters as resolution is almost always seen once clinical improvement of the underlying illness occurs.

CONCLUSION

In conclusion, acute pancreatitis is an aggressive inflammatory process which may have variable regional and remote organ involvement. Local complications of pancreatitis are many and may result in varying degree of morbidity and or mortality. The onset of complications may occur at any time during the course of the acute illness. Careful monitoring of patients taken to rapidly recognize complications can ultimately change the course of disease. Management of complications is dictated by the identification and understanding of specific complications and also on the knowledge and availability of local expertise.

References

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