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STANFORD MULTIDISCIPLINARY SEMINARS

Getting the Dead Out: Modern Treatment Strategies for Necrotizing Pancreatitis

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Case Presentation and Evolution

A 21-year-old male was brought to the emergency department with severe abdominal pain and vomiting. Low-grade fever and epigastric tenderness were noted on examination; laboratory values included a WBC of 11 K/μL and elevated amylase and lipase to 1,593 and >3,000 U/L, respectively. A CT scan was interpreted as showing an enlarged and ill-defined pancreas with heterogeneous parenchymal enhancement, consistent with pancreatitis. Several peripancreatic fluid collections extended bilaterally to the para-renal spaces, left para-colic gutter, and pelvis (Fig. 1). An ultrasound of the gallbladder was normal with no gallstones visualized. The patient had no other contributory past medical or social history. He was admitted to the medical service and initially developed a systemic inflammatory response (SIRS) to his idiopathic pancreatitis, with fever, tachycardia, and a white count peak to 16 K/μL. After several days of intravenous fluid resuscitation and bowel rest, he improved and was discharged home 10 days later tolerating a regular diet.

One week after discharge, the patient returned for an outpatient visit where he reported intermittent low-grade fevers and decreased appetite; he was able to tolerate only 50–60 % of his meals. Three days later (20 days after initial episode of pancreatitis), he returned to the emergency department for severe abdominal pain, vomiting, and dehydration. He was febrile and tachycardic with repeat CT scan interpreted as showing extensive pancreatic and peripancreatic necrosis, with acute necrotic collections (ANCs) extending to the spleen and tracking along the left paracolic gutter and retroperitoneum (Fig. 2). Bilateral pulmonary emboli were noted on CT scan, including an embolus within the right main pulmonary artery. A transthoracic echocardiogram demonstrated resultant right heart strain, and he was taken immediately to interventional radiology for thrombectomy and catheter-directed thrombolytic therapy; however, toward the end of the procedure, the patient suffered cardiogenic shock and cardiac arrest requiring resuscitative efforts and extracorporeal membrane oxygenation (ECMO). He had ensuing coagulopathy, and a hematocrit drop to 18 % that prompted a CT angiogram. Interval hemorrhage into the peripancreatic fluid collection was noted with no identifiable source; therefore, no intervention was required beyond transfusion. Ultimately, the patient spent the next 6 weeks in the hospital recovering. With respect to his necrotizing pancreatitis, although it was anticipated that intervention would likely be required for the extensive necrosis, given his recent cardiac events and clinical improvement over the hospitalization, treatment was deferred as long as the patient was asymptomatic and tolerating a regular diet, in order to maximize his nutritional status and his clinical status.

Two weeks after discharge, he returned to the surgery clinic reporting fevers to 102 °F and left flank pain. A CT scan (11 weeks after initial episode of pancreatitis) demonstrated interval development of gas within the fluid

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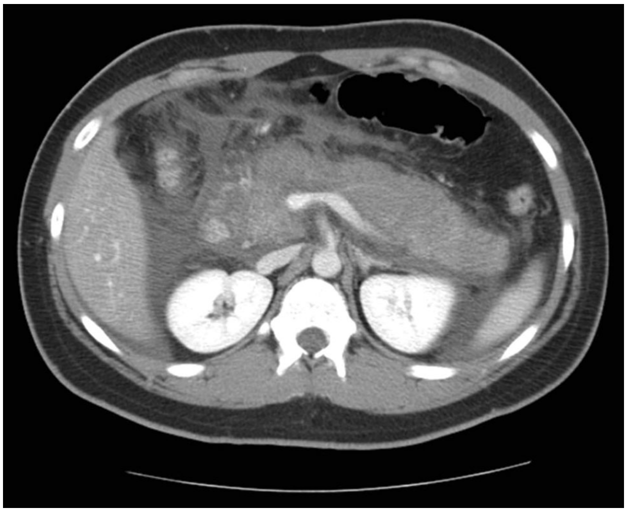

Fig. 1 Axial slice of CT scan from admission demonstrating severe acute pancreatitis. The pancreas is ill-defined with heterogeneous enhancement of the parenchyma. Peripancreatic fluid collections are seen extending to the pararenal spaces bilaterally

collection indicative of a superimposed infection (Fig. 3). The large area of infected pancreatic necrosis was now walled-off and primarily occupied the lesser sac with extension along the retroperitoneum, and caudally to the psoas and iliacus muscles, accounting for the patient's leg pain upon ambulation. Given the anatomic location of the necrosis, operative debridement was planned via a minimally invasive retroperitoneal pancreatectomy (MIRP). Two parallel 14F percutaneous drains were placed into the superior aspect of the necrotic collection by interventional radiology to serve as a guide for the MIRP (Fig. 4). Output from the drains was low at 50 mL over the next 24 h, indicating the bulk of the collections visualized with the CT scan was primarily necrotic debris rather than loculated fluid. To allow for operative debridement, the drains were exchanged and upsized to a 30F sheath using the Amplatz nephrostomy dilator set (Cook Medical, Bloomington, IN, USA) under fluoroscopic guidance (Fig. 5) to allow for an initial nephroscopic debridement (Fig. 6). Once enough retroperitoneal space was created, the sheaths were exchanged for radially dilating 12-mm laparoscopic ports (VersaStep, Covidien, Mansfield, MA, USA) for completion of the necrotic debridement via laparoscopy (Fig. 7). Two 28F chest tubes were placed into the necrotic cavity under fluoroscopy after debridement for continued drainage postoperatively.

He tolerated the procedure well, and by postoperative day 7, he was remarkably well-appearing and tolerating a regular diet. We downsized the chest tubes back to 14F pigtail drains for easier management at home. Since markedly diminished necrosis was noted radiologically, he

Fig. 2 Coronal slice of CT scan at 3 weeks after initial episode of pancreatitis. The pancreatic body and tail have been replaced with multiple multiloculated intra- and peripancreatic fluid collections, which extend to the spleen and track along the left paracolic gutter and retroperitoneum

Fig. 3 Coronal slice of CT scan at 11 weeks after initial episode of pancreatitis. There has been interval development of gas (*white arrows*) within the fluid collection indicative of superimposed infection

was discharged to home by postoperative day 9. On return to the surgery clinic for a postoperative outpatient visit, the patient had minimal complaints and demonstrated significant clinical recovery. A repeat CT scan at 3 weeks postoperatively demonstrated continued decrease in the remaining collections with minimal output from the percutaneous drains (Fig. 8). The drains were studied and exchanged over the next 6 weeks and sequentially removed in clinic. Although no specific etiology for his pancreatitis was discovered, the patient continued to recover with no further sequelae.

Discussion

Acute pancreatitis can be subdivided into two types: interstitial pancreatitis and necrotizing pancreatitis. Up to 40 % of patients with pancreatitis may develop severe pancreatic necrosis with superimposed infection [1]. Improved critical care management of these patients has reduced early deaths; however, late deterioration and progressive organ dysfunction in infected pancreatic necrosis are associated with significant morbidity and mortality [2]. The indications for intervention in pancreatic necrosis include infection, bleeding, and a "persistent unwellness" beyond the acute phase. The usual intervention is necrosectomy, which should be delayed until at least 3–4 weeks following the acute episode whenever possible until the area of necrosis is organized and walled-off to avoid higher mortality [3]. Although the traditional management of infected necrosis has been open surgical debridement for complete control of the infected necrosis, open necrosectomy is associated with significant morbidity, including high rates of pancreatic and enteric fistulas, incisional hernias, and pancreatic insufficiency with a published mortality approaching 25 % [4].

Given the morbidity of open necrosectomy, a variety of minimally invasive alternatives have been developed over the last decade. Newer approaches include percutaneous drainage alone [5] or in combination with another type of procedure as a "step-up" approach [6], endoscopic approaches to achieve trans-gastric or trans-duodenal drainage [7], laparoscopic methods (whether intra-peritoneal [8] or trans-gastric [9]), and various forms of retroperitoneal debridements [6], such as the video-assisted retroperitoneal debridement (VARD) [10] and the MIRP [11] (described in this clinical scenario). Minimally invasive approaches are thought to reduce physiologic stress as

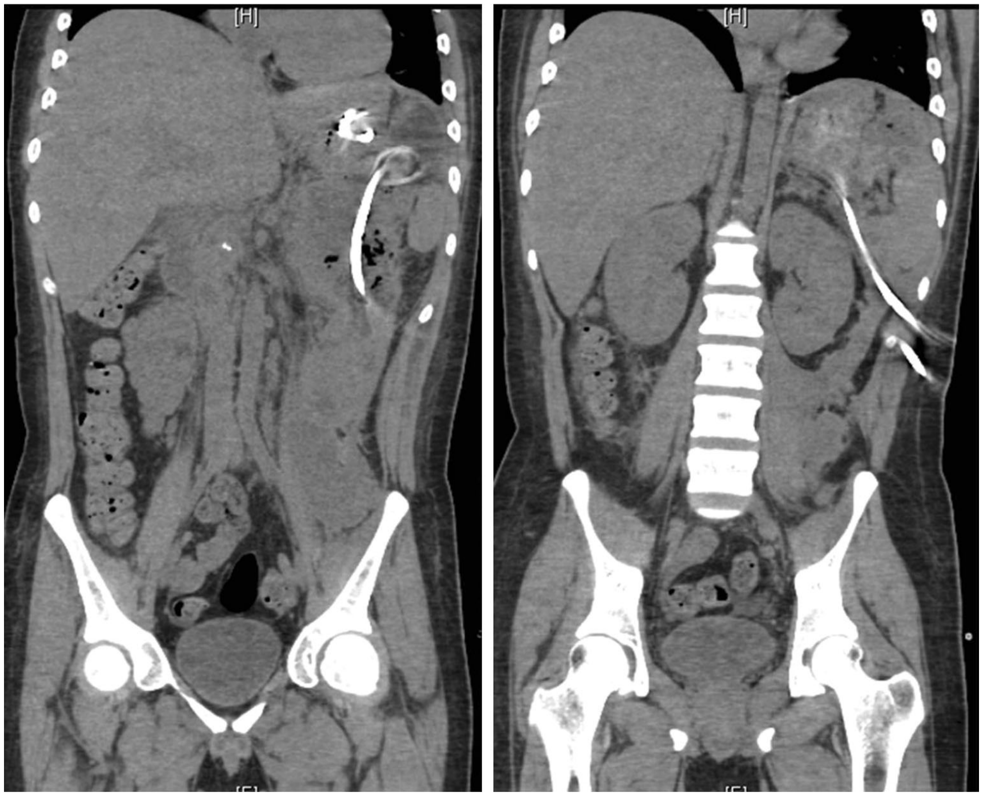

Fig. 4 Coronal slide of CT scan demonstrating placement of two parallel 14F percutaneous drains by interventional radiology. The drains are aimed superiorly from the left flank toward the splenic hilum and serve as a guide for subsequent minimally invasive retroperitoneal pancreatectomy

compared with open surgery and thus decrease mortality. Published reports are generally single-institution series; however, the high success rates reported from tertiary care centers have facilitated increasing application of these procedures. The newer approaches also suffer limitations, notably lengthy hospitalizations, the need for repeated procedures, and prolonged treatment periods (inpatient and outpatient) for complete debridement [5, 12], because many do not allow at a single procedure the same extensive necrosectomy offered by open surgery.

For this patient, an operative intervention was required given the presence of infection. The timing of intervention was at 11 weeks after his initial presentation, and therefore, the collection had organized and become walled-off necrosis (WON). The CT scan indicated that this was not a liquefied collection of infected fluid, and therefore, the pancreatic necrosum required surgical debridement, rather than simple drainage alone. The largest collection was located immediately behind the stomach, so the thought of performing a laparoscopic trans-gastric necrosectomy was entertained as an option; however, given the added anatomic consideration of the large column of necrosis extending along the left retroperitoneum, the concern was that this second area would not be accessible by a trans-gastric approach alone. For this reason, the strategy of utilizing a retroperitoneal debridement (MIRP) through the left flank and extending superiorly toward the splenic hilum would allow a one-stage procedure to clear the cavity and debride both areas of necrosis.

This case highlights the importance of recognizing the breadth of techniques available for pancreatic necrosectomy and further individualizing the appropriate intervention—whether via an open or minimally invasive approach—according to clinical presentation, morphology of necrosis, and patient anatomy. The pattern and extent of fluid collections by location (pancreatic, peripancreatic, and retroperitoneal), the nature of content (solid, liquid), and the presence of surrounding wall are all necessary for the accurate diagnosis and treatment of these local complications. The 2012 revision of the Atlanta classification of acute pancreatitis provides four definitions in a standardized fashion, based on the presence or absence of necrosis and time from injury [13]. These are acute peripancreatic fluid collection (APFC), pancreatic pseudocyst, ANC, and WON.

Peripancreatic fluid that develops in the early phase (<4 weeks) of acute interstitial pancreatitis without associated necrosis constitutes an APFC. On contrast-enhanced CT (CECT) imaging, these APFCs are homogenous and

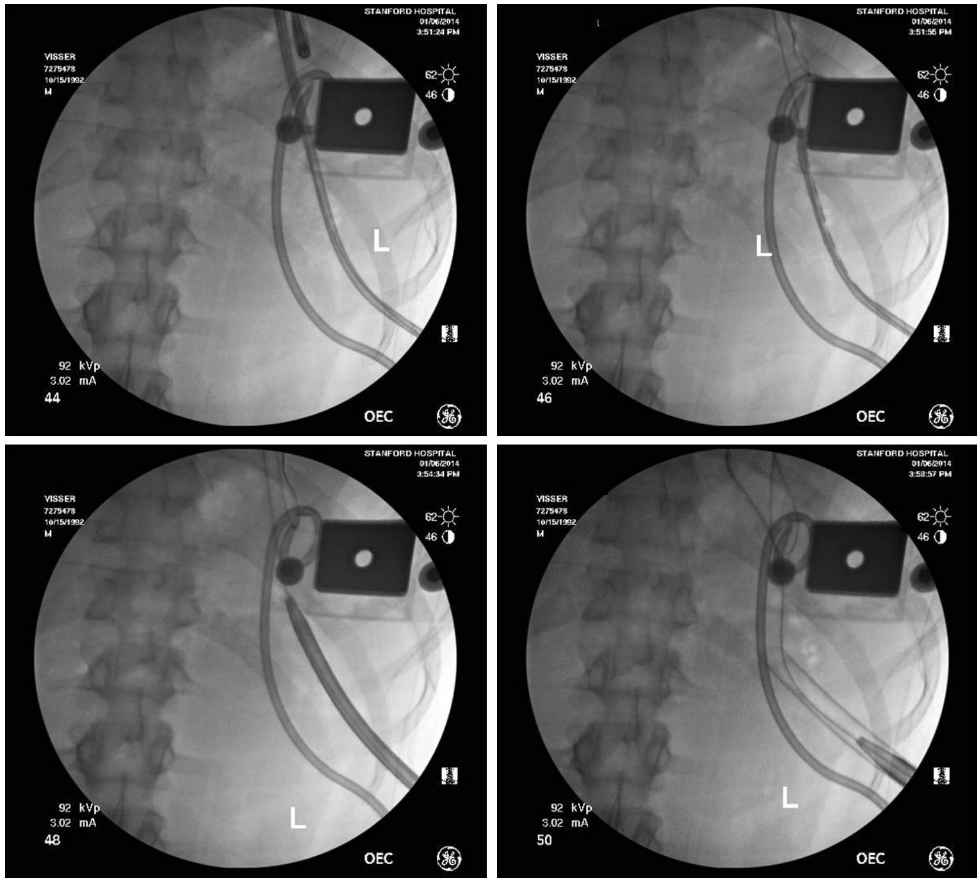

Fig. 5 Intraoperative fluoroscopic images illustrating the exchange and upsize of the 14F percutaneous drains over wire guidance to 30F nephroscope sheaths

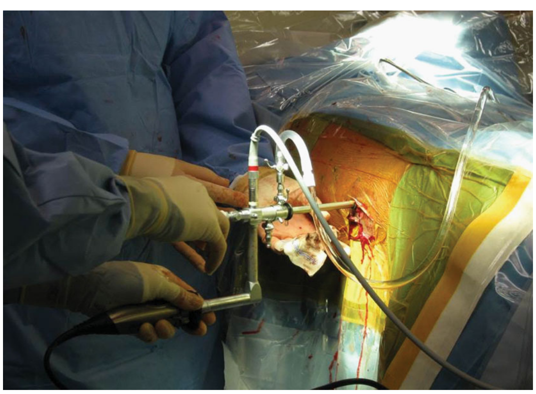

Fig. 6 Intraoperative pancreatic necrosectomy with a nephroscope aiming at creating adequate space within the necrotic cavity

without a definable wall; many will remain sterile and resolve spontaneously without intervention. When a localized APFC persists beyond the acute phase, it may develop into a pancreatic pseudocyst, specifically, a collection that is peripancreatic or intrapancreatic, surrounded by a well- defined wall, and containing predominantly liquid material [13]. Pancreatic injury with disruption of the main pancreatic duct or the intra-pancreatic branches results in consequent leakage of pancreatic juice into a persistent fluid-filled cavity; aspiration of the pseudocyst

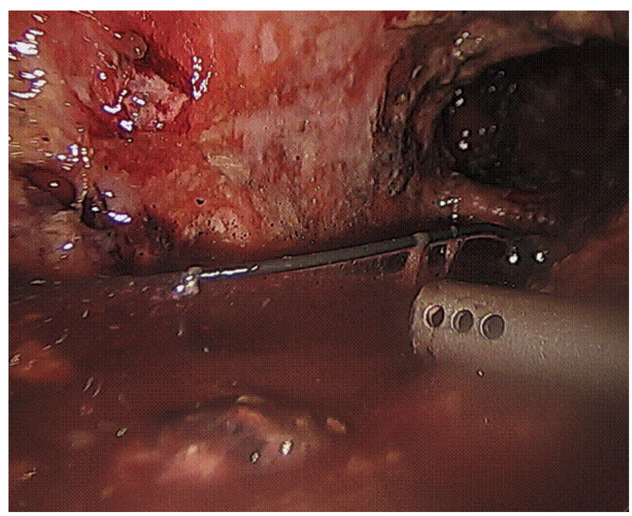

Fig. 7 Intraoperative view of the necrotic cavity during MIRP debridement and lavage. After nephroscopic debridement, the nephroscopic sheaths are exchanged for laparoscopic ports to introduce working instruments for debridement under direct visual guidance

will reveal an elevated amylase level in the cyst fluid. Asymptomatic pseudocysts can be expectantly observed; symptomatic, enlarging or infected pseudocysts have been treated with endoscopic or surgical cystogastrostomy,

Fig. 8 Coronal slice of CT scan at 3 weeks postoperatively after MIRP demonstrating good resolution of the retro-gastric and retroperitoneal pancreatic necrosis

provided there is a well-encapsulated rim around the collection [14]. Instances during which a pseudocyst may arise in the setting of necrotizing pancreatitis are as a result of "disconnected duct syndrome" from necrosis of the pancreatic neck or from localized leakage of the disconnected duct after surgical necrosectomy [15].

During the first 4 weeks of necrotizing pancreatitis, a collection containing varying amounts of fluid and solid necrotic debris involving the pancreatic parenchyma or the peripancreatic tissues is termed an ANC [13]. CECT imaging will show lack of parenchymal enhancement by intravenous contrast agent, and fluid collections are heterogeneous in different locations with no definable wall encapsulating the collection. Within the first week of severe acute pancreatitis, differentiating APFC from ANC is often difficult; therefore, serial imaging is used to characterize the demarcation and extent of necrosis and associated acute collections. Sterile ANCs almost never require intervention early in the course of disease and in the later phase (>4 weeks), only in the case of disabling symptoms or significant mechanical obstruction (gastric outlet or biliary). Infection of ANCs may occur at any time during the clinical course of necrotizing pancreatitis, with a peak occurrence of 2–4 weeks after presentation [12]. Infection is strongly suspected when there is gas evident in the ANC on CT imaging or there is clinical development of SIRS, sepsis, or organ failure in a previously stable patient. With the high morbidity and mortality associated with invasive surgical interventions for early infected ANCs, minimally invasive percutaneous or endoscopic transmural drainage procedures have emerged to effectively treat fluid collections as a temporizing measure in septic patients [6]. Poorly organized ANCs are more difficult to manage by any method compared with necrosis with a well-encapsulated rim [14]. A mature, encapsulated collection of pancreatic/peripancreatic necrosis with development of a well-defined inflammatory wall (4–6 weeks after onset of necrotizing pancreatitis) has become WON [13]. By CECT criteria, WON is heterogeneous with liquid/nonliquid density and varying degrees of loculations that can be both intrapancreatic and extrapancreatic. Asymptomatic WON does not mandate intervention regardless of size and extension of collection, with some even resolving spontaneously over time. Symptomatic WON generally requires intervention late in the disease course (>4 weeks) in the case of intractable pain, obstruction, or infection [12]. The anatomic location and accessibility to the area of WON are important considerations in selecting the optimal procedure for debridement.

It is important to emphasize that successful management of necrotizing pancreatitis is not defined by avoidance of surgery. The goals of any strategy for debridement and drainage should be to minimize procedural morbidity and mortality, avoid multiple procedures and lengthy hospital stay where possible, and expedite recovery to the patient's prepancreatitis health. There is certainly not one universal approach that is applicable to all patients, but the treatment strategy should be tailored with respect to clinical status of the patient, timing of intervention, "quality" of the necrosis (the continuum from pseudocyst to solid necrosum), and anatomic considerations (location and accessibility).

Key Messages

- The management of patients with necrotizing pancreatitis remains challenging, and despite recent advances, this condition is associated with significant morbidity and mortality.
- The early phase is associated with a SIRS response to pancreatic injury whereas the late phase is associated with local or systemic complications, including infected necrosis that requires drainage/debridement.
- A variety of minimally invasive techniques for managing pancreatic necrosis have been developed with the

intent to decrease the physiologic stress in comparison with open surgery.

- The treatment strategy for each patient should be individualized with respect to clinical stability, timing of intervention, and anatomic considerations of necrosis.

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