Endoscopic ultrasound-guided transmural drainage of infected pancreatic necrosis developing 2 years after acute pancreatitis

Kyle Eliason, Douglas G. Adler

Department of Gastroenterology and Hepatology, University of Utah School of Medicine, Salt Lake City, Utah, USA

ABSTRACT

This is a case report of endoscopic ultrasound guided transmural drainage of a large infected pancreatic necrosis. The infected necrosis was treated by placement of a fully covered metal stent with subsequent endoscopic necrosectomy to remove solid debris. The case is notable for the fact that the patient developed infection of a long-standing and previously stable area of walled-off pancreatic necrosis 2 years after it formed. We believe this is the longest time ever reported between necrotizing pancreatitis and the development of infected pancreatic necrosis.

Key words: Infected pancreatic necrosis, pancreatic necrosis, stent, walled-off pancreatic necrosistransmural drainage

INTRODUCTION

Severe acute pancreatitis can often progress to pancreatitic necrosis. Patients with pancreatic necrosis are at risk for infection of the necrotic pancreatic bed, and these patients tend to have the poorest outcomes. Most patients with pancreatic necrosis develop infection within weeks of developing acute pancreatitis. We present a case of infected pancreatic necrosis that developed two years after an index episode of necrotizing pancreatitis and describe how this was treated by endoscopic ultrasound guided transmural drainage with endoscopic necrosectomy. This case may represent the longest time ever recorded between the development of pancreatic necrosis and infection.

CASE REPORT

In 2012, a 68-year-old white male with a history of recurrent acute pancreatitis developed an episode of severe necrotizing pancreatitis 4 weeks after recovery from a prior episode of mild acute pancreatitis. His pancreatitis was felt to be secondary to medications, either lisinopril (angiotensin converting enzyme inhibitor) or hydrochlorothiazide. He presented with severe abdominal pain with associated nausea and vomiting. He was found to have a lipase of 11,985 U/L (30-190 U/L). He had a lactic acidosis with a lactate of 4.5 mmol/L (0.7-2.1 mmol/L). His white blood cell count was 16.3 (3.2-10.6 k/µL) with 79% neutrophils and no bands. Creatinine was elevated at 1.5 (0.66-1.25 mg/dL). Treatment with NPO status and aggressive intravenous fluid hydration with a 4 L bolus of normal saline followed by 250 mL/h over a 48 h period resulted in resolution of his lactic acidosis, normalization of his leukocytosis and creatinine. His serum liver chemistries were normal and his calcium remained normal throughout the admission. Serum glucose remained normal. His medical history also

Access this article online

Quick Response Code:

Website:
www.eusjournal.com

DOI:
10.4103/2303-9027.163020

includes hypertension and an infrarenal abdominal aortic aneurysm for which he underwent endovascular repair.

He was observed in the surgical intensive care unit. Initially he was found to have a temperature of 36.9°C, blood pressure of 124/81 mmHg, respiratory rate of 19 with oxygen saturation of 97% on 3 L oxygen by nasal cannula. He was in moderate distress, no scleral icterus or jaundice, moist mucous membranes, lungs were clear and heart was regular rhythm with no tachycardia, there was moderate abdominal tenderness in the epigastric area with no guarding or rebound, no Cullen's or Grey-Turner sign, no peripheral edema.

A computed tomography (CT) scan revealed a large pancreatic fluid collection approximately 18 cm × 8.5 cm which caused gastric compression, partial gastric outlet obstruction, and chronic abdominal pain. The body and tail of the pancreas were largely absent on the CT scan and had been replaced by the pancreatic fluid collection which was felt to represent an acute necrotic collection [Figure 1]. There was significant pancreatic liquefactive necrosis associated with the fluid collection. There was rim enhancement of the fluid collection which was felt to represent pseudoepithelialization given the acuity of the formation of the fluid collection. His CT was not concerning for a hemorrhagic event. The patient was clinically stable and surgery declined to pursue operative necrosectomy at this point given the clinical stability of the patient and the acuity of the formation of the fluid collection. The primary surgical team opted for monitoring of the patient for any indication for urgent debridement and necrosectomy while awaiting maturation of the fluid collection. He was monitored as an outpatient by serial

CT scans. The fluid collection matured and remained stable in size on subsequent scans and given this and his stable vitals, the decision was made to not pursue surgical intervention with necrosectomy and drainage. He did have intermittent mild abdominal pain and early satiety during this period, but his weight was stable.

Two years after developing the walled-off pancreatic necrosis (WOPN), he developed chills and rigors at home with subjective fevers. He also complained of nausea, vomiting, and decreased appetite with a 4 pound weight loss and presented again to our institution.

On evaluation, his vital signs were notable for mild tachycardia, otherwise normal. He was afebrile. He was pale and ill appearing. His abdomen was soft, with a palpable fullness over his left epigastric area that was tender to palpation. There was no rigidity or guarding. On laboratory testing, he had a normal total bilirubin, aspartate aminotransferase and alanine transaminase. Lipase was normal. A CT scan was obtained which again showed a well circumscribed, peripherally enhancing collection of WOPN, again essentially replacing the body and tail of the pancreas. Concerningly, the WOPN now contained many obvious gas bubbles, and the patient was felt to have developed infected pancreatic necrosis [Figure 2]. Surgery again declined to intervene operatively given the acutely infected fluid collection and his history of an aortic repair. The patient was admitted to the surgical ward at the hospital and IV meropenem was initiated given his CT findings. A nasojejunal feeding tube was placed and the patient was referred for endoscopic drainage.

Figure 1. Computed tomography showing large walled-off pancreatic necrosis replacing the body and tail of the pancreas
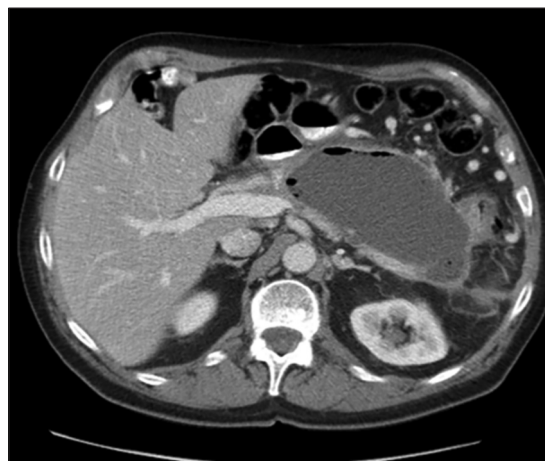

Figure 2. Walled-off pancreatic necrosis now with air bubbles consistent with infected pancreatic necrosis

On esophagogastroduodenoscopy (EGD), there was note of extrinsic compression in the stomach and second portion of the duodenum from the WOPN. Endoscopic ultrasound (EUS) demonstrated the lesion as a large, thick-walled fluid collection with turbid, heterogeneous solid and cystic contents [Figure 3]. No obvious communication with the pancreatic duct was noted, although there was very little remaining pancreatic parenchyma in the region of the lesion. The lesion measured approximately 20 cm by 9.6 cm in maximal cross-sectional diameter. There was a single compartment without septae. There was no associated mass. The cyst was then punctured with a 19 gauge needle under ultrasound guidance to create a cystgastrostomy. A 0.035" guide wire was inserted through the needle and coiled in the WOPN cavity under ultrasonic and fluoroscopic guidance [Figure 4]. The cystgastrostomy was dilated with a 6 mm biliary balloon dilator, after which purulent material was seen to begin to flow into the stomach. A 15 mm Axios (XLumena, Mountain View, CA, USA) fully covered metal stent advanced over the wire and across the cystgastrostomy. The stent was deployed under endoscopic and fluoroscopic guidance without difficulty [Figure 5]. Immediately following deployment, approximately 1.5 L of pus, cyst fluid and sold debris flowed through the stent into the stomach [Figure 6]. He was observed in the hospital overnight and discharged the following day on a 10 day course of oral levofloxacin.

Four weeks after stent deployment a follow-up contrast-enhanced CT scan demonstrated essential collapse and significant improvement in the size of the fluid collection, which now measured at 7.4 cm by 0.9 cm. EGD with direct examination and lavage of the cyst cavity was then performed. The cavity was lavaged with 500 cc of hydrogen peroxide with saline in a 3:1 ratio.

Figure 3. 7.5 MHz endoscopic ultrasound image of infected pancreatic necrosis with turbid, heterogeneous contents
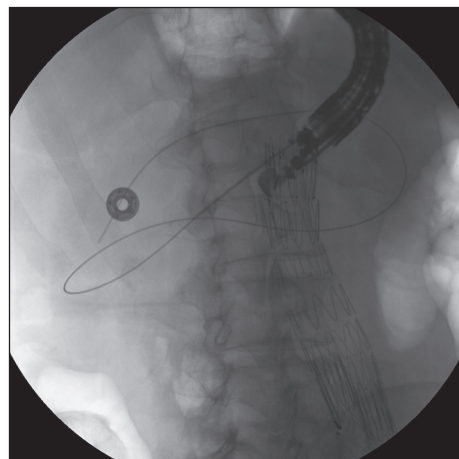

Figure 4. Guidewire passed through 19 gauge endoscopic ultrasound fine-needle aspiration needle and looped in infected necrosis
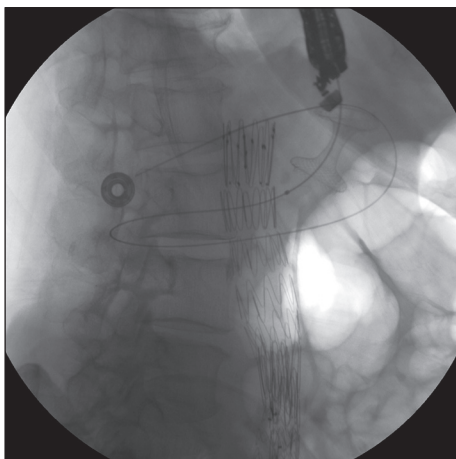

Figure 5. Fluoroscopic image of Axios stent following deployment. The patient also has an aortic graft
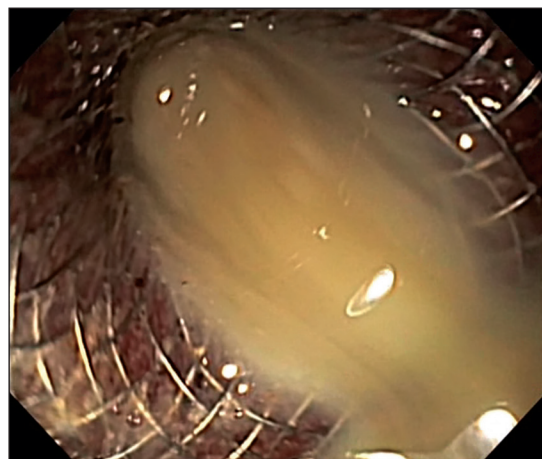

Figure 6. Purulent material draining through Axios stent following deployment

The cavity was markedly smaller and almost totally collapsed, consistent with drainage of the infected collection. The lining of the cyst cavity appeared healthy with good granulation tissue [Figure 7]. Residual solid material was removed with polypectomy snares, nets, and rat-toothed forceps.

Six weeks following stent placement, a CT was again obtained. This demonstrated further improvement with the fluid collection measuring 7 cm by 0.8 cm [Figure 8]. The following day repeat EGD was performed with lavage of the cyst cavity and a final endoscopic transmural necrosectomy was performed. The pancreatic fluid collection cavity was markedly smaller than previously noted and almost totally collapsed, consistent with his imaging. Repeat lavage and endoscopic necrosectomy was again performed on any residual necrotic tissue. At the conclusion of the procedure, there was no visible necrotic tissue noted within the cavity. The cavity was flushed and aspirated to collapse. Stent removal was accomplished with a rat-toothed forceps. There was rapid closure of the cystgastrostomy tract. The patient was sent home with a short course of antibiotics. He is now pain free and tolerating a general diet.

DISCUSSION

Pancreatic fluid collections (including both walled off necrosis and pseudocysts) occur after about 10% of episodes of acute pancreatitis or after an acute exacerbation of chronic pancreatitis.[1] There have been recent changes to the classification of pancreatic fluid collections. In 2013 there was revision of the Atlanta classification of acute pancreatitis to include both early and late fluid collections. Acute collections include acute peripancreatic fluid collections, acute necrotic collections, pseudocysts, and WOPN.[2] Acute necrotic collections occur within 4 weeks from episode of acute pancreatitis in the setting of necrotizing pancreatitis and contain both solid and liquid material. Pseudocysts are fluid-filled collections that persist for >4 weeks from episode of acute pancreatitis and contain no solid material and have a defined wall. WOPN, as our patient had, occurs >4 weeks after episode of acute pancreatitis and contains solid and liquid material from the necrotic pancreas within a defined, encapsulated wall.[2] While there are no universally accepted guidelines for management of these fluid collections, the majority of these lesions will resolve spontaneously without the need for interventions; some reports have shown up to 60% of walled-off fluid collections resolve without intervention.[3-6] Conservative management usually entails antibiotic treatment and monitoring with serial imaging, with earlier imaging if pain, chills, jaundice, fevers, or early satiety from duodenal or gastric compression occurs.[7-11]

There have been many well-described complications of pancreatic fluid collections including pain, gastric outlet obstruction, biliary obstruction and vascular occlusion secondary to expansion of the fluid collection, pleural or pericardial effusion secondary to fistula formation into pleural space or pericardium, spontaneous infection, and pancreatic ascites (which may be chylous or hemorrhagic).[8,9,12,13] Digestion of adjacent vessels can result in pseudoaneurysm formation, and the rupture of such a lesion or the erosion of the collection into a vessel can lead to hemosuccus pancreaticus.[14,15]

Figure 7. Endoscopic image obtained during necrosectomy

Figure 8. Computed tomography scan showing collapsed area of necrosis prior to Axios stent removal

Current recommended treatment consists of a "step-up" approach involving percutaneous, endoscopic, and/or surgical drainage depending on both the acuity and the characteristics of the infected pancreatic necrotic fluid collection.[16-18] Indications for intervention include suspicion of, or documented, infected pancreatic necrosis, organ failure, gastric outlet obstruction and/or biliary obstruction, persistent pain, and disconnected duct syndrome (transected pancreatic duct in presence of pancreatic necrosis).[9] Generally, intervention is delayed until the collection has walled off and allowed to mature; most sources advocate waiting at least 4 weeks after the acute onset of pancreatitis.[9]

There is a significantly higher risk of mortality when patients develop infected necrosis, thus early intervention is recommended in this setting.[2,16,19,20] It is presumed that the source of many of these infections is from the gut as analysis has shown that the predominant organisms are gram-negative (most frequently *Escherichia coli*).[19,21] There has also been shown to be an increased risk of infected necrosis in patients with previous bacteremia.[19] Prior separate infections from other sources, such as pneumonia, have not been shown to increase the risk of infected pancreatic necrosis.[19] Our patient had no other sources of infection or recent infections, so the infected WOPN in our patient was likely from a gastrointestinal (GI) source, although the exact source is unknown.[19-21]

Endoscopic intervention requires close proximity of the fluid collection to either the gastric or duodenal wall for transmural drainage to be performed. As such, 75-80% of necrotic collections that ultimately require intervention can be approached endoscopically, as was the case in our patient.[2,9,10] EUS-guided therapy of pancreatic fluid collections has been shown to be associated with a lower risk of adverse events and greater success rates when compared with non-EUS guided endoscopic therapy.[22] EUS-guidance is recommended for initial puncture and drainage to assure a safe tract without interposed vessels.[2,9,10] Once the cystenterostomy tract has been made and dilated, placement of multiple large-bore double-pigtail stents, metal biliary stent(s), covered esophageal stents, or covered metal stents specifically designed for PFC drainage is typically performed to allow for the contents to drain to the GI tract and to further the formation of a mature tract.[18,23] Endoscopic necrosectomy has also been well-described with irrigation of the WOPN cavity with saline or hydrogen peroxide/

saline solution followed by necrosectomy with use of standard endoscopic equipment such has Roth nets, large forceps, baskets and balloons reported for use in endoscopic necrosectomy.[18,20,24]

In this case, we describe infection arising in a large, but stable area of WOPN 2 years after the lesion initially formed. Such a long period is highly unusual. We believe this represents the longest time from development of WOPN to infection ever reported. For the most part, infections in pancreatic necrosis occur early on in the course of the disease and delayed infections, especially occurring more than 3 months after WOPN formation are exceedingly rare.[2,16,19,25] Reports suggest the infection of pancreatic necrosis is relatively common, occurring in up to 12% of patients who develop acute pancreatitis and up to 40% of patients with necrotizing pancreatitis.[19-21] One large cohort study showed that the infection occurred within the range of 17-37 days and with a mean of 26 days.[19] Another group analyzing benefits of conservative versus surgical treatment followed 204 patients for 35 months from time of acute nectrotizing pancreatitis. They found that the 27 patients, whom ultimately developed infection, did so at a mean of 21 days with a range of 10-48 days.[26] None of these patients developed infection after a long period of time as our patient did.

There is a greater risk of infection when larger areas of the pancreas undergo necrosis, and our patient had a very large area of necrotic pancreas. Again, this risk described is, usually, within the first several weeks.[19,21,25] There was a study that took 60 patients presumed to have infection and used CT-guided FNA to confirm a true infection in 36 of those patients, they found that infection actually occurs earlier than previously thought, within 14 days in 20 of the 36 patients; all patients were found to have infected necrosis at an early stage.[27] In another prospective study that included 114 patients, bacterial contamination rates of acute necrotizing pancreatitis were 24% within the first 7 days from the time of the attack and rose to 71% at week 3, then rapidly declined to 33% at week 4.[21] A separate study done to evaluate the clinical value of EUS-FNA as a means of early detection of infected pancreatic necrosis was done with 193 patients, of which 33 were found to have infected necrosis a mean of 13 days from onset of abdominal symptoms (pain/pancreatitis) with a range of 3-44 days.[28] Infected necrosis is not uncommon early in the disease course, as is the high mortality rate in necrotizing pancreatitis, which is

likely related to the high rates of early infection and mulit-organ system failure with some reports suggesting 40% of deaths occur within the first 2 weeks from onset of symptoms which goes along with the noted early infected necrosis.[29] As reviewed, above, infected necrosis most often occurs very early in the course of disease after acute necrotizing pancreatitis. There is significant mortality with infected necrosis, and early intervention is recommended in infected necrosis.

Overall our patient did well with EUS-guided transmural drainage and subsequent necrosectomy, but the case highlights the fact that infections can occur very late following an episode of pancreatic necrosis.

REFERENCES

1. O'Malley VP, Cannon JP, Postier RG. Pancreatic pseudocysts: Cause, therapy, and results. *Am J Surg* 1985;150:680-2.
2. Banks PA, Bollen TL, Dervenis C, *et al*. Classification of acute pancreatitis-2012: Revision of the Atlanta classification and definitions by international consensus. *Gut* 2013;62:102-11.
3. Mouli VP, Sreenivas V, Garg PK. Efficacy of conservative treatment, without necrosectomy, for infected pancreatic necrosis: A systematic review and meta-analysis. *Gastroenterology* 2013;144:333-40.e2.
4. Vitas GJ, Sarr MG. Selected management of pancreatic pseudocysts: Operative versus expectant management. *Surgery* 1992;111:123-30.
5. Yeo CJ, Bastidas JA, Lynch-Nyhan A, *et al*. The natural history of pancreatic pseudocysts documented by computed tomography. *Surg Gynecol Obstet* 1990;170:411-7.
6. Jacobson BC, Baron TH, Adler DG, *et al*. ASGE guideline: The role of endoscopy in the diagnosis and the management of cystic lesions and inflammatory fluid collections of the pancreas. *Gastrointest Endosc* 2005;61:363-70.
7. Muddana V, Whitcomb DC, Papachristou GI. Current management and novel insights in acute pancreatitis. *Expert Rev Gastroenterol Hepatol* 2009;3:435-44.
8. Whitcomb DC. Clinical practice. Acute pancreatitis. *N Engl J Med* 2006;354:2142-50.
9. Working Group IAP/APA Acute Pancreatitis Guidelines. IAP/APA evidence-based guidelines for the management of acute pancreatitis. *Pancreatology* 2013;13 4 Suppl 2:e1-15.
10. Tenner S, Baillie J, DeWitt J, *et al*. American College of Gastroenterology guideline: Management of acute pancreatitis. *Am J Gastroenterol* 2013;108:1400-15. Erratum in: *Am J Gastroenterol* 2014;109:302.
11. Adler DG, Chari ST, Dahl TJ, *et al*. Conservative management of infected necrosis complicating severe acute pancreatitis. *Am J Gastroenterol* 2003;98:98-103.
12. Fulcher AS, Capps GW, Turner MA. Thoracopancreatic fistula: Clinical and imaging findings. *J Comput Assist Tomogr* 1999;23:181-7.
13. Steinemann DC, Dindo D, Clavien PA, *et al*. Atraumatic chylous ascites: Systematic review on symptoms and causes. *J Am Coll Surg* 2011;212:899-905.e1.
14. Risti B, Marincek B, Jost R, *et al*. Hemosuccus pancreaticus as a source of obscure upper gastrointestinal bleeding: Three cases and literature review. *Am J Gastroenterol* 1995;90:1878-80.
15. Adler DG, Petersen BT, Gostout CJ. Hemosuccus pancreaticus. *Gastrointest Endosc* 2004;59:695.
16. van Santvoort HC, Besselink MG, Bakker OJ, *et al*. A step-up approach or open necrosectomy for necrotizing pancreatitis. *N Engl J Med* 2010;362:1491-502.
17. Freeman ML, Werner J, van Santvoort HC, *et al*. Interventions for necrotizing pancreatitis: Summary of a multidisciplinary consensus conference. *Pancreas* 2012;41:1176-94.
18. Trikudanathan G, Attam R, Arain MA, *et al*. Endoscopic interventions for necrotizing pancreatitis. *Am J Gastroenterol* 2014;109:969-81.
19. Besselink MG, van Santvoort HC, Boermeester MA, *et al*. Timing and impact of infections in acute pancreatitis. *Br J Surg* 2009;96:267-73.
20. Gardner TB, Coelho-Prabhu N, Gordon SR, *et al*. Direct endoscopic necrosectomy for the treatment of walled-off pancreatic necrosis: Results from a multicenter U.S. series. *Gastrointest Endosc* 2011;73:718-26.
21. Beger HG, Bittner R, Block S, *et al*. Bacterial contamination of pancreatic necrosis. A prospective clinical study. *Gastroenterology* 1986;91:433-8.
22. Park DH, Lee SS, Moon SH, *et al*. Endoscopic ultrasound-guided versus conventional transmural drainage for pancreatic pseudocysts: A prospective randomized trial. *Endoscopy* 2009;41:842-8.
23. Antillon MR, Bechtold ML, Bartalos CR, *et al*. Transgastric endoscopic necrosectomy with temporary metallic esophageal stent placement for the treatment of infected pancreatic necrosis (with video). *Gastrointest Endosc* 2009;69:178-80.
24. Abdelhafez M, Elnegouly M, Hasab Allah MS, *et al*. Transluminal retroperitoneal endoscopic necrosectomy with the use of hydrogen peroxide and without external irrigation: A novel approach for the treatment of walled-off pancreatic necrosis. *Surg Endosc* 2013;27:3911-20.
25. Beger HG, Rau B, Mayer J, *et al*. Natural course of acute pancreatitis. *World J Surg* 1997;21:130-5.
26. Büchler MW, Gloor B, Müller CA, *et al*. Acute necrotizing pancreatitis: Treatment strategy according to the status of infection. *Ann Surg* 2000;232:619-26.
27. Gerzof SG, Banks PA, Robbins AH, *et al*. Early diagnosis of pancreatic infection by computed tomography-guided aspiration. *Gastroenterology* 1987;93:1315-20.
28. Rau B, Pralle U, Mayer JM, *et al*. Role of ultrasonographically guided fine-needle aspiration cytology in the diagnosis of infected pancreatic necrosis. *Br J Surg* 1998;85:179-84.
29. McKay CJ, Imrie CW. The continuing challenge of early mortality in acute pancreatitis. *Br J Surg* 2004;91:1243-4.