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CASE REPORT | ENDOSCOPY

Endoscopic Ultrasound-Guided Treatment of Pancreaticocutaneous Fistulas

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ABSTRACT

Pancreaticocutaneous fistulas (PCFs) may be refractory to medical therapy or endoscopic retrograde cholangopancreaticography. Four patients underwent endoscopic ultrasound-guided management of refractory PCFs, which were internalized by endoscopic ultrasound-guided transmural puncture of the pancreatic duct (n = 2), fistula tract (n = 1), or both (n = 1), with placement of transmural stents providing internal drainage to the stomach (n = 3) or duodenum (n = 1). Drainage from PCFs ceased in all patients, and all percutaneous drains were removed; internal stents were left in place indefinitely. Endoscopic ultrasound-guided interventions may successfully treat PCFs, allowing removal of percutaneous drains, and are an attractive alternative for patients who might otherwise require pancreatic resection.

INTRODUCTION

Pancreaticocutaneous fistula (PCF) is a known adverse event of pancreatitis, pancreatic surgery or percutaneous management of peripancreatic fluid collections.[1-3] Endoscopic retrograde cholangopancreaticography (ERCP) is a standard endoscopic method for evaluating and treating PCF but may fail due to surgically altered anatomy,[4] impassable ductal strictures, or inability to effectively bridge a pancreatic duct disruption with a stent. Endoscopic ultrasound (EUS) can facilitate pancreatic duct access and stent placement.[3,5-8]

CASE REPORT

We retrospectively identified all 4 patients who underwent attempted EUS-guided management of a PCF at our institution and reviewed their medical records and imaging studies.

Case 1: A 71-year-old man underwent a Whipple procedure for resection of an inflammatory mass. A postoperative pancreatic duct leak was treated with placement of a percutaneous drain, which became a persistent PCF. Attempts at ERCP failed to identify the pancreaticojejunostomy, and percutaneous access to the pancreatic duct failed. Drainage of pancreatic juice (400 cc/d) persisted via the PCF despite a trial of total parenteral nutrition (TPN) with nil by mouth.

Endoscopic ultrasound showed that the pancreatic duct measured 3 mm in tail. Endoscopic ultrasound-guided pancreatography showed complete obstruction of the pancreaticojejunal anastomosis (Figure 1). A guidewire was inserted into the pancreatic duct via an EUS needle, the transgastric tract was balloon dilated, and a 7-French straight plastic stent was placed extending from stomach to pancreatic duct. Two additional straight plastic stents were placed in the same transgastric tract during a second endoscopic procedure several weeks later.

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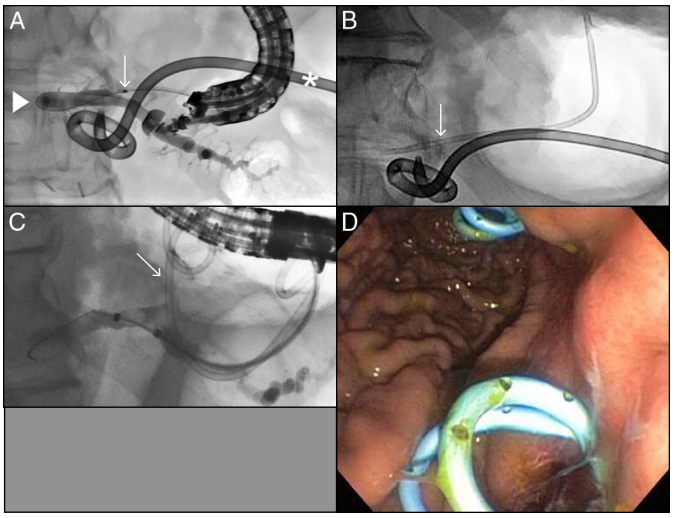

Figure 1. Endoscopic ultrasound-guided management of a PCF resulting from a percutaneous drain (asterisk) following pancreaticoduodenectomy in case 1. (A) Endoscopic ultrasound-guided pancreatography demonstrates a complete obstruction of the pancreaticojejunostomy (arrowhead). (B) A single plastic stent is placed draining the pancreatic duct to the stomach. (C and D) A guidewire and double pigtail stent was passed via the echoendoscope into pancreatic duct, then back into stomach via the original transgastric tract (arrows). The shafts of the stents traverse the pancreatic duct.

The patient's fistula output ceased immediately, and his percutaneous drain was removed. He did well for 11 months but then developed recurrent episodes of postprandial pain and pancreatitis. Repeat computed tomography demonstrated that the transgastric stents had migrated out and were no longer present. Endoscopic ultrasound was repeated, and the pancreatic duct was punctured from stomach at a different site. A guidewire was passed via the new puncture site into the pancreatic duct, then back into the stomach via the original transgastric duct drainage site, which was stenosed but still patent. Two double pigtail stents were placed bridging these drainage sites, with their pigtails in the stomach and their shafts traversing the pancreatic duct (Figure 1). The patient subsequently did well.

Case 2: A 30-year-old woman underwent ERCP for removal of a bile duct stone. Endoscopic retrograde cholangopancreaticography was complicated by pancreatitis requiring a 3-week hospitalization. A large pancreatic fluid collection developed and was drained percutaneously. Drainage of 200 cc/d of pancreatic juice persisted via the percutaneous drainage catheter. Trials of TPN and octreotide were unsuccessful. During ERCP, pancreatography (Figure 2) revealed a complete obstruction of the pancreatic duct, which could not be crossed with a guidewire.

Endoscopic ultrasound showed a percutaneous drain between stomach and pancreatic tail, with its pigtail in a small intrapancreatic collection. The percutaneous drain blocked access to the pancreatic duct, preventing drainage of the duct via the stomach. The percutaneous drain tract itself was punctured from the fourth portion of duodenum under EUS guidance, at a site where the drain abutted the duodenum. A single 7-French double pigtail drain was placed, extending from duodenum into the percutaneous drain tract and reaching the intrapancreatic collection. At a subsequent endoscopy 2 weeks later, additional 7-French and 10-French double pigtail stents were placed alongside the first stent, and the percutaneous drain was removed.

Case 3: A 65-year-old woman underwent Whipple procedure for resection of high-grade liposarcoma. Surgery was complicated by a pancreatic leak and bleeding requiring reexploration. A percutaneous drainage catheter was placed, with persistent drainage of 300 cc/d of pancreatic juice. Computed tomography showed a gap between the remaining pancreas and the jejunum suggesting dehiscence of the pancreaticojejunal anastomosis, as well as a local recurrence of her liposarcoma (confirmed by percutaneous biopsy). Endoscopic retrograde cholangopancreaticography was attempted but failed to identify the pancreaticojejunostomy.

Endoscopic ultrasound showed a nondilated pancreatic duct in tail measuring 1.5 mm, which was punctured from the stomach with a 19-gauge needle. Pancreatography showed a

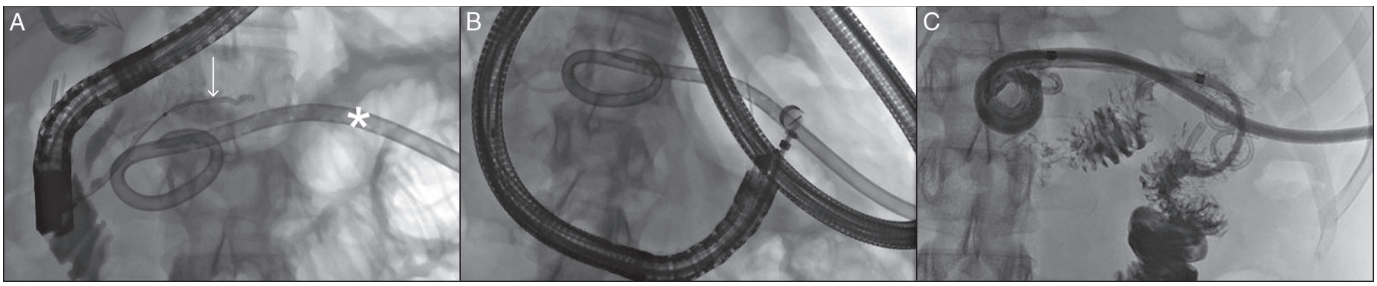

Figure 2. Endoscopic ultrasound-guided management of a PCF arising after percutaneous drainage of pancreatic necrosis in case 2. (A) Endoscopic retrograde cholangopancreaticography demonstrates a complete obstruction of pancreatic duct (arrows) by the percutaineous drain (asterisk) (B) Endoscopic ultrasound-guided transmural puncture of the percutaneous drain from the fourth portion of the duodenum. (C) Multiple internal double pigtail plastic stents were placed to drain the fistula tract and pancreas into the duodenum.

Table 1. Demographic, clinical, interventional, and follow-up data for 4 patients undergoing EUS-guided management of PCF

Age (years)	Gender	Cause of PCF	Prior Therapy Attempted	Duration of Fistula Before EUS (days)	Fistula Output per day (mL)	Amylase in Fistula Fluid (U/L)	Internal Drainage Site	Target of Internal Drainage	Number of Endoscopic Procedures	Maximum Number of Internal Stents	Follow-Up After Removal of Percutaneous Drain (days)
71	M	Postoperative (pancreatico-duodenectomy)	ERCP, TPN, percutaneous drainage of pancreatic duct	233	400		Stomach	Pancreatic duct	4	3	390
30	F	Pancreatitis with disconnected duct	ERCP, TPN, octreotide	202	200	>17 600	Duodenum	Percutaneous fistula track	2	2	265
65	F	Postoperative (pancreatico-duodenectomy)	ERCP	88	300	>13 000	Stomach	Pancreatic duct and percutaneous fistulas track	3	3	448
59	F	Postoperative (pancreatico-duodenectomy)	ERCP, octreotide	206	500	>17 000	Stomach	Pancreatic duct	1	2	718

Note: Dependent variable: Federal Government Investment in Public Works per capita, in thousand Argentine pesos, deflated using INDEC's construction index prices. Unstandardized regression coefficients. Standard Errors reported in parenthesis.
$^{*}p < 0.100$; $^{**}p < 0.050$; $^{***}p < 0.010$.

complete obstruction of the pancreatic duct at the surgical resection margin, with a leak into the percutaneous drain. A 0.035-inch wire was passed via the needle into the pancreatic duct, then out the duct leak and through the percutaneous tract. Two 7-French internal transgastric stents were then placed, each traversing the stomach wall and pancreatic duct and entering the percutaneous tract. After EUS, pancreatic drainage ceased immediately and her percutaneous drain was removed. She subsequently began chemotherapy for her recurrent liposarcoma and felt well at the time of last clinical follow-up.

Case 4: A-59 year-old woman with multiple endocrine neoplasia type 1 and multiple pancreatic neuroendocrine tumors underwent a pylorus-preserving Whipple procedure for a large pancreatic head gastrinoma. During surgery, a smaller pancreatic tail gastrinoma was also enucleated. Her course was complicated by a pancreatic leak treated with placement of a percutaneous drainage catheter and development of a persistent PCF. Endoscopic retrograde cholangopancreaticography failed to visualize the pancreaticojejunostomy.

Pancreatic duct diameter was 2 mm in the tail. Endoscopic ultrasound-guided pancreatography showed a complete obstruction of the pancreaticojejunostomy, and plastic stents were placed from stomach to pancreatic duct. Percutaneous drainage decreased from 300 to 50 cc/d but did not resolve. A second EUS was performed a month later. This showed a stenosis of the pancreatic duct near tip of pancreatic tail, upstream from the transgastric stents, at the surgical enucleation site. This stenosis obstructed a segment of pancreatic duct in the tip of the tail, which was not drained by the transmural plastic stents and was leaking into the PCF. The pigtail of the percutaneous drain lay next to this stenosis. An EUS-guided transgastric puncture was performed at a new site, with placement of 2 transgastric stents into the tract of the percutaneous drain. The percutaneous drainage catheter was removed.

The patient initially did well but presented 391 days later with complaints of left upper abdominal discomfort. Computed tomography showed no evidence of pancreatitis or fluid collection, but one of her transgastric stents extended close to the abdominal fascia in the former percutaneous drain tract. Endoscopy was repeated, and the offending stent was removed from the stomach with fluoroscopic assistance, leaving her other transgastric stents in place. After this, her discomfort resolved.

Outcomes: Patient information and outcomes are presented in Table 1. The 4 patients have been followed for a median of 328 days (range 265–718) since their percutaneous drains were removed. All patients had resolution of pancreatitis and catheter-associated pain and resumed a normal diet; their

body weight stabilized or increased. None developed pancreatic exocrine or endocrine insufficiency at time of last follow-up. Internal stents were left in place indefinitely in all cases. Adverse events following EUS-guided intervention included mild postprocedure pancreatitis (1 patient) and transient postprocedure abdominal pain (3 patients) requiring hospitalization after the initial EUS-guided intervention for a mean of 1.7 days (range 1–2).

DISCUSSION

Pancreatic fistulas may be external or internal,[4] and may occur as complications of pancreatitis, malignancy, pancreatic drain placement, or pancreatic surgery. Internal fistulas are usually inflammatory and are often associated with pancreatic duct obstruction and leakage. If duct disruption occurs anteriorly, a pancreaticoenteric fistula may form;[9] disruption into the peritoneal space may result in pancreatic ascites; and pancreaticopleural or mediastinal fistulas may result from tracking of pancreatic juice into the thoracic cavity.[10] External fistulas are also called PCFs.

Medical therapy for pancreatic fistulas may include bowel rest, TPN, and somatostatin analogues such as octreotide; however, there is limited evidence of benefit for these interventions. A metaanalysis evaluating the role of somatostatin analogues for the treatment of pancreatic fistula found no benefit,[11] and use of TPN in pancreatitis has been associated with higher rates of infection.[12] Endoscopic retrograde cholangopancreaticography is the primary endoscopic modality for treatment of internal or external pancreatic fistulas, and placement of a pancreatic duct stent that bridges the ductal disruption often successfully resolves the fistula.[13] However, ERCP may fail in patients with disconnected pancreatic duct syndrome (in which a segment of pancreatic duct in tail is completely disconnected from the downstream duct in pancreatic head) and has a very low success rate of pancreatic duct cannulation after prior Whipple procedure.[14] Pancreatectomy may be required to treat patients who fail medical therapies and ERCP.[15]

Endoscopic ultrasound-guided pancreatic duct access enables treatment of symptomatic pancreatic duct obstruction that is not amenable to ERCP. The EUS-guided "rendezvous technique" involves placement of an EUS needle into the pancreatic duct, with passage of a guidewire via the needle and across the ductal obstruction to the gut lumen, facilitating pancreatic stent placement via ERCP. Endoscopic ultrasound-guided "transmural stent placement" similarly involves placement of a pancreatic guidewire via an EUS needle. The trans-gastric or trans-duodenal tract to pancreatic duct is then dilated, and a stent is placed via the tract into the pancreatic duct.[3,5,16-17]

Endoscopic ultrasound-guided treatment of a PCF poses particular technical challenges. The pancreatic duct is decompressed by the fistula and usually narrow in caliber, and there is no fluid collection to access. Prior publications describe attempted EUS-guided therapy of 4 PCF cases, with failure in 2 cases,[7,8] success by rendezvous technique in 1 case,[17] and an unclear outcome in 1 case.[6] Irani et al pioneered a combined EUS/interventional radiologic technique for placement of internal stents in PCF patients, in which the fistula tract rather than the pancreatic duct is drained, and much of the manipulation is performed percutaneously with endoscopic or EUS guidance.[18] This is the first case series to describe techniques of successful EUS-guided internalization of refractory PCFs by endoscopic methods alone.

DISCLOSURES

Author contributions: All authors designed the manuscript, analyzed the data, and critically revised the article. A Haseeb and MD Topazian wrote the article. MD Topazian is the article guarantor.

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Informed consent was obtained for this case report. The Mayo Clinic Rochester IRB approved the protocol.

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REFERENCES

1. Blatnik JA, Hardacre JM. Management of pancreatic fistulas. *Surg Clin North Am*. 2013;93(3):611–7.
2. Zinner MJ, Baker RR, Cameron JL. Pancreatic cutaneous fistulas. *Surg Gynecol Obstet*. 1974;138(5):710–2.
3. Fujii LL, Topazian MD, Abu Dayyeh BK, et al. EUS-guided pancreatic duct intervention: Outcomes of a single tertiary-care referral center experience. *Gastrointest Endosc*. 2013;78(6):854–64.e1.
4. Kozarek RA, Traverso LW. Pancreatic fistulas: Etiology, consequences, and treatment. *Gastroenterologist*. 1996;4(4):238–44.
5. Bataille L, Deprez P. A new application for therapeutic EUS: Main pancreatic duct drainage with a "pancreatic rendezvous technique." *Gastrointestinal Endosc*. 2002;55(6):740–3.
6. Ergun M, Aouattah T, Gillain C, et al. Endoscopic ultrasound-guided transluminal drainage of pancreatic duct obstruction: Long-term outcome. *Endoscopy*. 2011;43(6):518–25.
7. Kinney TP, Li R, Gupta K, et al. Therapeutic pancreatic endoscopy after Whipple resection requires rendezvous access. *Endoscopy*. 2009; 41(10):898–901.
8. Mallery S, Matlock J, Freeman ML. EUS-guided rendezvous drainage of obstructed biliary and pancreatic ducts: Report of 6 cases. *Gastrointest Endosc*. 2003;59(1):100–7.
9. Wolfsen HC, Kozarek RA, Ball TJ, et al. Pancreaticoenteric fistula: no longer a surgical disease? *J Clin gastroenterol*. 1992;14(2):117-21.
10. Rockey DC, Cello JP. Pancreaticopleural fistula. Report of 7 patients and review of the literature. *Medicine* (Baltimore). 1990;69(6):332–44.
11. Gans SL, van Westreenen HL, Kiewiet JJ, et al. Systematic review and meta-analysis of somatostatin analogues for the treatment of pancreatic fistula. *Br J Surg*. 2012;99(6):754–60.
12. Marik PE, Zaloga GP. Meta-analysis of parenteral nutrition versus enteral nutrition in patients with acute pancreatitis. *BMJ*. 2004; 328(7453):1407.
13. Telford JJ, Farrell JJ, Saltzman JR, et al. Pancreatic stent placement for duct disruption. *Gastrointest Endosc*. 2002;56(1):18–24.

14. Chahal P, Baron TH, Topazian MD, et al. Endoscopic retrograde cholangiopancreatography in post-Whipple patients. *Endoscopy*. 2006; 38(12):1241–5.
15. Lin JW, Cameron JL, Yeo CJ, Riall TS, Lillemoe KD. Risk factors and outcomes in postpancreaticoduodenectomy pancreaticocutaneous fistula. *J Gastrointest Surg*. 2004;8(8):951–9.
16. François E, Kahaleh M, Giovannini M. EUS-guided pancreaticogastrostomy. *Gastrointest Endosc*. 2002;56:128–33.
17. Mavrogenis G, Kisoka P, Dehaeck G, et al. Single operator endoscopic ultrasound-assisted rendezvous for the treatment of pancreaticocutaneous fistula. *Pancreatology*. 2013;13(3):316–7.
18. Irani S, Gluck M, Ross A, et al. Resolving external pancreatic fistulas in patients with disconnected pancreatic duct syndrome: using rendezvous techniques to avoid surgery (with video). *Gastrointest Endosc*. 2012; 76(3):586-93.e1-3.