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Arterio-Enteric Fistula in Failed Enteric-Drained Pancreas Transplants: An Impending Danger

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Abstract

Keywords

- ▶ arterio-enteric fistula
- ▶ enteric-drained pancreas transplant
- ▶ gastrointestinal bleeding
- ▶ endovascular stenting
- ▶ allograft pancreatectomy

Enteric drainage is the preferred method of exocrine diversion in simultaneous kidney-pancreas transplantation. Because of improvements in immunosuppression, enteric drainage has become the preferred method of pancreas transplantation in general. Although associated with less potential complications than bladder-drained pancreas, potentially lethal arterio-enteric fistulas in the setting of nonfunctioning allografts represent a constant threat. We herein present a case report, a review of the literature, and a call for caution.

Pancreas transplantation allows for a euglycemic state in the absence of exogenous insulin. Exocrine pancreatic drainage can be achieved via the gastrointestinal or urinary tracts. Arterio-enteric fistulas constitute an infrequently encountered but potentially fatal complication associated with failed enteric-drained pancreas transplants.

Case Report

Our patient is a 58-year-old woman who is presented with hematemesis. Work up inclusive of esophagogastroduodenoscopy (EGD), colonoscopy, and capsule endoscopy did not identify any site of hemorrhage. After a 48-hour observation period with no further bleeding, the patient was discharged home. Twenty days later, she was presented to an outside hospital with a severe recurrent gastrointestinal bleed, prompting an emergent transfer to our institution for further diagnosis and treatment.

Her past medical and surgical histories were significant for type 1 diabetes mellitus and renal failure, for which she had undergone an isolated living donor-related kidney

transplant 5 years before presentation. She underwent a cadaveric pancreas after kidney transplant, 2 years later. The methods of pancreas transplantation utilized were enteric exocrine drainage and systemic venous drainage. The pancreatic allograft functioned well initially, and the patient maintained euglycemia for 2 years. At that point, 1 year before presentation, the pancreatic allograft had failed because of chronic rejection. Her kidney allograft was still functioning normally. Her immunosuppressive regimen consisted of the following: mycophenolate mofetil 250 mg oral, twice a day; tacrolimus 3 mg oral, twice a day; and prednisone 5 mg oral, once a day.

The patient was admitted to our intensive care unit and transfused 6 units of packed red blood cells and 2 units of fresh-frozen plasma with an adequate hemodynamic response. A bedside EGD showed large amounts of blood in the stomach and duodenum with no apparent source. On the basis of these findings, it was decided to proceed with an emergency angiogram to identify the source of bleeding and control it, possibly by endovascular approach. While in the radiology department, as the procedure was about to be

performed, she developed massive hematemesis and acute persistent hypotension.

Because of her critical status, and the yet unknown diagnosis, the angiogram was aborted and the patient was emergently rushed to the operating room for an exploratory laparotomy. On entering the abdomen, the entire gastrointestinal tract was found to be distended with blood. A gastrotomy failed to demonstrate any source of bleeding in the stomach or duodenum. Profuse back-bleeding from the small bowel was noted. Inspection of the abdominal cavity showed the region of the failed pancreas transplant with direct jejunal anastomosis (as opposed to Roux-en-Y) in the right lower quadrant as the possible source of bleeding. Opening of the transplant duodenum to native jejunum, anastomosis demonstrated active bleeding from a fistula between the transplanted pancreatic arterial supply, originating in the right external iliac artery, and the gastrointestinal tract. The bleeding was controlled and an allograft pancreatectomy was performed. On gross inspection, the pancreas appeared fibrotic, necrotic, and nonfunctional. The transplanted duodenum to native jejunum, anastomosis was resected and the arterial supply to the fistula was ligated. Given the patient's critical condition, evidenced by her hypothermia, pressor requirements, and coagulopathy, a decision was made to place an abdominal vacuum assisted closing dressing, leaving the stapled blind intestinal segments in discontinuity to be addressed at a subsequent take-back procedure.

Three days later, the patient underwent reinforcement of the vascular repair with a covered stent encompassing the external and common iliac arteries. The abdominal cavity was washed out and the intestinal continuity restored. The abdominal wound was subsequently closed with Vicryl (polyglactin 910, Ethicon, Somerville, NJ) mesh and a jejunostomy feeding tube placed. Despite an initial period of improvement, the patient slowly deteriorated over the next month. She underwent tracheostomy; but, was never able to achieve independence from mechanical ventilation. Eventually, she had two episodes of cardiac arrest with return of spontaneous circulation after advanced cardiac life support protocol was performed. After discussion with her family, care was withdrawn and she expired.

Discussion

Common complications following all pancreatic transplants include arterial and venous graft thrombosis occurring in approximately 6% of cases.¹ Prophylaxis with anticoagulants and antiplatelet agent regimens are variable based on institution. Infectious complications due to immunosuppression are similar to other transplants and occur in approximately 10% of cases. Postoperative pancreatitis is also common following transplantation, and is felt to be caused by manipulation and ischemia injury incurred during procurement. Treatment is supportive.

Pancreatic transplant exocrine drainage can be achieved via the small bowel or the urinary bladder. Bladder drainage allows for easy and prompt measurement of pancreatic amylase levels, which can be checked to monitor for rejection.¹ The drawback of bladder drainage is that it is frequently

complicated by dehydration, acidosis due to exocrine bicarbonate losses, urethritis, hematuria, bladder calculi, and recurrent urinary tract infections. These complications occur in approximately 50% of cases, with 10% of cases significant enough to require conversion to enteric drainage.^{1,2} Because of these complications, as well as improvements in immunosuppressive monitoring, most centers currently opt for enteric drainage.²⁻⁶

A rare but potentially fatal complication of enteric-drained pancreas transplants is the formation of an arterio-enteric fistula. The patient will present with gastrointestinal bleeding that can be rapid and massive. The severe episode of bleeding is often preceded by a herald bleed, seen weeks before that is self-resolving. Arterio-enteric fistulas are most often found in pancreas transplants that have failed. Similar types of fistulas are not seen in bladder-drained pancreas transplants.

The diagnostic work up for gastrointestinal bleeding in pancreatic transplant patients with enteric drainage must include, in addition to the standard differential diagnoses, the possibility of arterio-enteric fistulas. Gastrointestinal bleeding can be seen in the early postpancreas transplant period as a result of technical complications, infections, anticoagulation, leakage of digestive enzymes, and percutaneous procedures. In some instances, arterial pseudoaneurysms or disruption of the vascular suture line can potentially be associated with delayed bleeding, hematomas, or arteriovenous or arterio-enteric fistulas.^{2,6} This represents a challenging problem in pancreas recipients, since in enteric-drained organs, endoscopic access to the duodenal portion of the graft is difficult. Most often, it is the timing of the endoscopy that makes the diagnosis difficult. When endoscopy is performed at the original diagnosis of the herald bleed, the bleeding source may not be identified because it has already self-remitted. When endoscopy is performed in the acute phase of the secondary presentation, the volume of hemorrhage in the gastrointestinal lumen is often too massive to clearly visualize the exact bleeding source.⁷ Gastrointestinal bleeding in transplant patients may also be secondary to *cytomegalovirus* infection. Such bleeds however, are usually mild or moderate and patients tend to be stable enough to allow for a diagnostic work up and treatment.^{8,9}

The presence of an arterio-enteric fistula with massive gastrointestinal bleeding represents a challenging situation. This late complication has been associated with failed allografts and is thought to be due to the release of digestive enzymes and rejection events.^{10,11} The failed or chronically rejected pancreas graft becomes fibrotic, causing the intestinal anastomosis to fall over the devitalized pancreas and rest on the arterial anastomosis. This malpositioning allows for the formation of an arterio-enteric fistula.

Arterio-enteric fistula is a rare complication, the knowledge of which is based on case reports and single center experiences. A review of the literature revealed 11 cases of iliac-enteric fistulas in failed enterically drained pancreas transplant recipients.¹¹⁻¹⁴ The results of these cases are listed below (► **Table 1**).

Table 1 Published cases of arterial-enteric fistulas in cases of failed pancreatic transplants

	Age, y/gender	Failed allograft	Presentation	Treatment	Outcome	Herald bleed
Gritsch et al ¹⁰	47/M	Yes	Lower GI bleed	Transplant pancreatectomy	Survived	Yes
Lopez et al ¹¹	37/M	Yes	Lower GI bleed	Coil embolization, followed by transplant pancreatectomy	Survived	Yes
Higgins et al ¹²	34/F	Yes	Lower GI bleed	Angioembolization x2, expired after 3rd episode of bleeding	Expired	Yes
	38/M	Yes	Upper GI bleed	Covered stent, followed by transplant pancreatectomy	Survived	Yes
Semiz-Oysu ¹³	42/M	Yes	Lower GI bleed	Covered stent	Survived	Yes
Fridell ²⁰	20/M	Yes	Upper GI bleed	Transplant pancreatectomy/fem-fem bypass	Survived	Yes
	21/F	Yes	Upper GI bleed	Transplant pancreatectomy	Survived	Yes
	61/M	Yes	Upper GI bleed	Endovascular stenting followed by transplant pancreatectomy	Survived	Yes
	37/F	Yes	Upper GI bleed	Endovascular stenting followed by transplant pancreatectomy	Survived	Yes
	48/M	No	Upper GI bleed	Endovascular stent	Expired	Yes
Molmenti ⁶	58/F	Yes	Upper GI bleed	Transplant pancreatectomy	Expired	Yes

Open emergency approaches as well as endovascular techniques such as coil embolization and covered stents have been described in the treatment of this condition in the setting of both functioning and nonfunctioning grafts.^{14–17} Given the very limited number of cases, there is yet no definite evidence to determine the best approach. Rebleeding,¹⁸ graft infarct with abscess development,¹⁹ and graft loss,²⁰ have been reported with endovascular techniques. Endovascular treatment may be very useful as an initial bridging approach in the acute setting,^{9–12,19} followed by a transplant pancreatectomy under stable conditions.

A high clinical suspicion for this entity should direct the diagnostic work up in any patient with a history of pancreas transplant and gastrointestinal bleeding. In all reported cases, including ours, the massive gastrointestinal hemorrhage was preceded by a herald bleed. Most cases were also associated with graft failure or rejection. The only case not associated with graft failure was a fistula caused by clamp injury to the common iliac artery that fistulized to the donor duodenum. Immunosuppression should be maintained to avoid further complications of rejections even in cases of failed solitary pancreas transplants. An accurate and prompt diagnosis should allow delivery of appropriate care. Involvement of a multidisciplinary team is strongly advised, given that these complex patients in critical condition require the collaboration of diverse specialties.

The high mortality associated with the potential of an arterial-enteric fistula, as well as the high risk of complications associated with endovascular therapy as the only treatment have prompted some to advocate transplant pancreatectomy as the standard of care for failed organs. Others find such an approach not entirely safe, given the potential for complications of any surgical intervention coupled to the possibility of associated mycotic arterial aneurysms.¹⁸ Irrespective of the surveillance and/or treatment methods, these patients should be followed up with extreme caution and all bleeding should be carefully evaluated.

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