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Iliac artery-enteric fistulas following failed pancreatic transplant

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ABSTRACT

Arterial-enteric fistulas occur from a multitude of causes, especially following surgical manipulation of vasculature. The development of an iliac artery-enteric fistula (IEF) occurs rarely in patients with failed pancreatic transplants. IEFs warrant urgent intervention due to the high mortality from hemorrhagic and septic shock. The diagnosis can be delayed by a lack of suspicion, the low sensitivity of diagnostic tests, and the nonspecific signs of fistulas on computed tomography. The management of IEFs is adapted from guidelines for arterial-enteric fistulas of other causes, with little consensus on ideal vascular reconstruction and postoperative antimicrobial management. The outcomes are limited to the short-term results from case reports and case series. We report two cases of IEFs in patients with a history of simultaneous pancreatic kidney transplant. Our patients underwent successful resolution of gastrointestinal bleeding and sepsis, with definitive management of fistula resection and interposition iliac artery bypass. The index of suspicion for IEFs should be high, and they should be considered as a source of anemia or gastrointestinal bleeding of an unknown source in patients with failed pancreatic transplant. Definitive management should be pursued in patients who can tolerate fistula resection, allograft explant, and arterial reconstruction. (J Vasc Surg Cases Innov Tech 2024;10:101427.)

Keywords: Arterio-enteric fistula; Iliac artery to small bowel fistula; GI bleed in failed pancreatic transplant

Arterial-enteric fistulas (AEFs) are an abnormal connection between an artery and the gastrointestinal (GI) tract. The suspected pathophysiology is that pressure against the bowel wall by a graft or pseudoaneurysm (PSA) with associated infection leads to erosion, necrosis, perforation, and, subsequently, the formation of a secondary AEF.[1] Most iliac-enteric fistulas (IEFs) occur from atherosclerotic aortic or iliac aneurysms (55%) or from PSAs from suture lines or grafts.[2] A few case reports and case series have described IEF formation after failed pancreatic transplants.[3-7] Given its rarity, the diagnosis is often delayed. This case series describes two cases of IEF formation in failed simultaneous kidney and pancreas (SKP) transplant and their operative management. The patients provided written informed consent for the report of their case details and imaging studies.

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CASE REPORT

Patient 1. Patient 1 is a 69-year-old woman with a medical history of type 1 diabetes mellitus, end-stage renal disease, antiphospholipid syndrome (treated by apixaban 2.5 mg twice daily and clopidogrel 75 mg daily). She underwent deceased donor kidney transplant in 2002 with subsequent failure, SKP transplant in 2006 with the pancreas anastomosed to the right external iliac artery (EIA) and enteric exocrine drainage (both allografts failed), and deceased donor kidney transplant to the left EIA and vein in 2017 (which failed). Her therapy continued receiving therapy with tacrolimus, sirolimus, and trimethoprim/sulfamethoxazole. The SPK was complicated by post-transplant lymphoproliferative disorder of the small bowel requiring treatment with rituximab.

She presented to the emergency department with an altered consciousness and hypotensive after a large bloody bowel movement during dialysis. Emergent endoscopy and colonoscopy to the distal ileum were negative for a source of the bleeding. Computed tomography (CT) angiography (CTA) of abdomen and pelvis indicated a partially thrombosed PSA from the distal right common iliac artery (CIA) with a possible AEF to the small bowel (Fig 1). Urgent endovascular management was used to temporize the hemorrhagic shock. The right hypogastric artery was coil embolized using Nestor coils (Cook Medical Inc). Next, a Viabahn balloon expandable 9-mm × 59-mm covered stent graft (W.L. Gore & Associates) was placed from the right CIA to the EIA. Intravenous piperacillin and tazobactam (Zosyn; Baxter International Inc) was started, with plans for lifelong suppressive antibiotics for *Escherichia coli* bacteremia found on admission.

At 4 months after the intervention, vascular surgery, with general surgery assistance, performed planned resection of the enteric fistula, concomitant resection of the right iliac artery

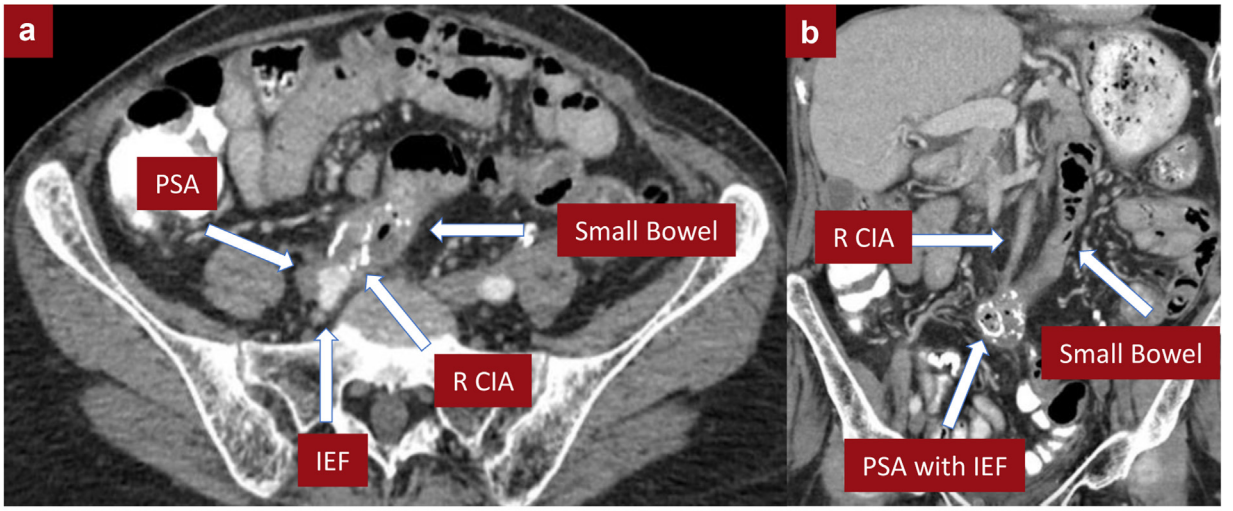

Fig 1. Axial (**a**) and coronal (**b**) views of computed tomography (CT) scan showing pseudoaneurysm (PSA) and iliac-enteric fistula (IEF) of the right common iliac artery (CIA) to the jejunum.

and stent, and right lower extremity revascularization for the recurrent transfusion requirements and *Enterobacter* bacteremia. A midline incision was made, and a portion of the involved jejunum ~100 cm away from the ligament of Treitz and an inflammatory mass were resected by general surgery. Using a transperitoneal approach for exposure of the iliac arteries, a cryopreserved iliac artery was anastomosed in end-to-end fashion from the distal CIA to the mid- EIA (Fig 2, *a*) by vascular surgery. An iliac vein injury was repaired primarily. The omentum was not long enough to lay into the pelvis where our vascular repair was. Suturing omentum over a vascular repair provides a layer of protection to minimize infections of the graft or recurrent fistulas to overlying bowel. The retroperitoneum was reapproximated over the bypass. Intra-abdominal cultures grew *Enterobacter cloacae, Enterococcus faecium,* and *Candida glabrata.* The patient completed her 7-day course of micafungin and meropenem. Apixaban 2.5 mg twice daily was restarted on postoperative day (POD) 5 and clopidogrel 75 mg daily on POD 7. The patient was discharged to a rehabilitation facility on POD 11 and then to home on POD 17. At 1 year postoperatively, there are no CT signs of fistula recurrence (Fig 2, *b*), and her hemoglobin remains stable.

Patient 2. Patient 2 is a 56-year-old man with a history of end-stage renal disease after robotic SKP transplant with enteric exocrine drainage of the pancreas and anastomosis to the left EIA in 2017. The kidney and pancreas failed 22 months later, and the patient's therapy was continued with tacrolimus and trimethoprim/sulfamethoxazole. At 6 years, 7 months after SPK transplant, the patient began having episodes of GI bleeding. The findings from esophagogastroduodenoscopy (EGD), push enteroscopy, colonoscopy, capsule endoscopy, and nuclear medicine scanning were negative. CTA demonstrated a blush contrast from the left EIA to the small bowel, concerning for an IEF (Fig 3). The patient underwent urgent exploratory laparotomy through a midline incision, allograft explanation, and resection of the involved small bowel and sigmoid colon with staple and handsewn anastomosis, respectively, by general surgery. Using the transperitoneal approach with bilateral groin cutdowns for distal control, a left iliofemoral bypass with a cryopreserved superficial femoral artery was performed by vascular surgery. An iliac vein injury was repaired with a bovine pericardial patch. The retroperitoneum was reapproximated over the bypass graft.

Postoperatively, the patient completed a 5-day course of intravenous piperacillin and tazobactam (Zosyn) in accordance with recommendations from infectious disease, and tacrolimus was discontinued by the transplant team. His postoperative course was complicated by dehiscence of the sigmoid anastomosis that required resection and end colostomy on POD 8. Additionally, the patient had a linear cryograft rupture from the portion under the inguinal ligament on POD 16. The graft was excised in its entirety and replaced with an 8-mm Hemashield graft (Getinge) impregnated with rifampin and covered with a large omental pedicle flap. The intraoperative cultures were significant for *Candida albicans*, and fluconazole was started on POD 19. On POD 25, the patient was taken emergently to the operating room to treat a PSA from the distal EIA with anastomotic dehiscence seen on CTA. The iliofemoral graft was partially transected, and an interposition 8-mm rifampin-soaked Hemashield graft was anastomosed. The intraoperative cultures of the hematoma grew *C. albicans* and vancomycin-resistant enterococci. He was discharged to a subacute rehabilitation on hospital day 48 with prescriptions for cefepime, oral metronidazole (Flagyl; Pfizer), fluconazole, and daptomycin, with plans for lifelong suppressive antibiotic and antifungal therapy. At 9 months after discharge, the bypass remains patent and his hemoglobin stable.

DISCUSSION

The pathogenesis of IEF formation is not well known. Few articles describe IEF formation associated with

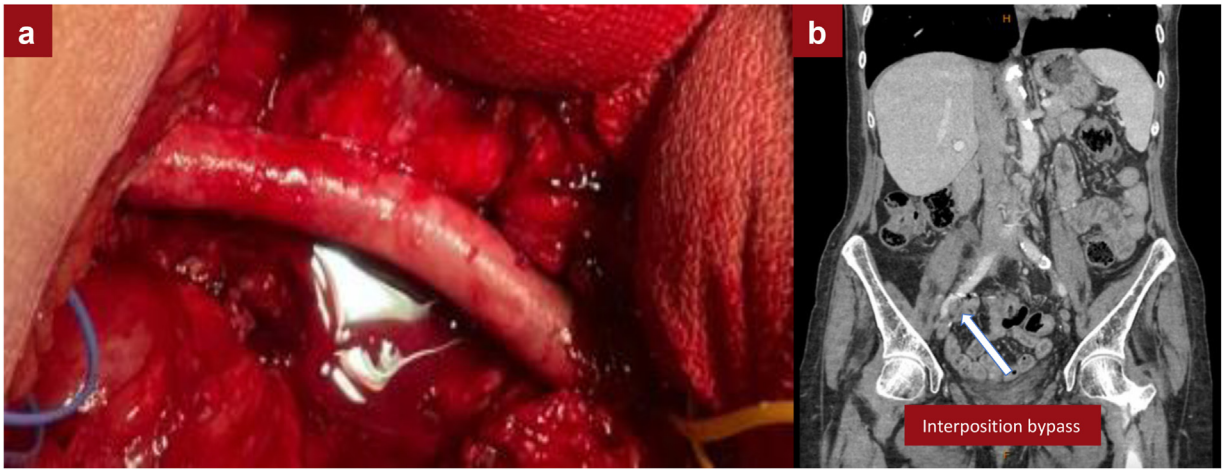

Fig 2. a, Right common iliac artery (CIA) to external iliac artery (EIA) cryopreserved bypass graft. **b,** Computed tomography (CT) of the interposition iliac artery bypass at 1 year of follow-up.

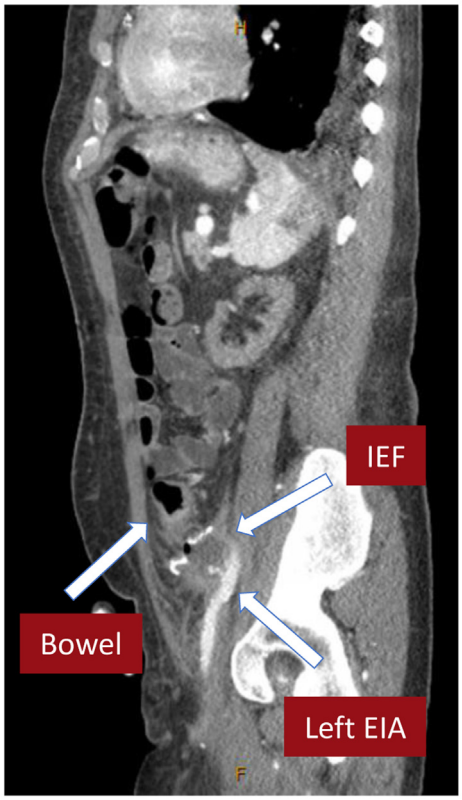

Fig 3. Left external iliac artery (EIA) pseudoaneurysm (PSA) with associated iliac-enteric fistula (IEF).

pancreatic transplant.[3-7] This phenomenon has been associated with a few factors. First, IEFs are frequently found in conjunction with mycotic infections. However, the rate is not higher in pancreatic transplant compared with other transplants.[3,5] Second, studies show that 80% of IEFs in pancreatic transplants occur in failed pancreatic allografts.[5-7] This is anticipated to be from the release of digestive enzymes and rejection events.[5] Fridell et al[6] reported five AEFs in a retrospective review of 346 pancreas transplants, four after a failed allograft and three after immunosuppression discontinuation. However, both of our patients had maintained immunosuppression therapy after documented graft failure. Finally, most IEF formations in pancreatic transplants are associated with previous or concurrent kidney transplant, as was seen in our patients.[5] This likely occurred from the added risk of trauma from the additional surgery, inflammation from potential kidney allograft failure, and an increased risk of fungal and bacterial inoculation with prior abdominal surgery in patients requiring kidney transplants.

AEFs should remain high in the differential diagnosis for patients with GI bleeding and a history of pancreatic transplant. An expedited diagnosis is required to prevent life-threatening bleeding. A minor bleeding episode can precede a catastrophic hemorrhage in as few as 4 days.[8] Workup of AEFs is usually lengthy due to the low sensitivity of the current diagnostic tools. Deijen et al[8] observed that the diagnosis of AEF was made after a median of 6 days (range, 4-92 days). EGD and colonoscopy are the gold standards for evaluating GI bleeding, and, thus, one of the first tests completed. However, these tests were found to only detect one quarter of secondary AEFs.[5,8-10] CT is considered one of the most accurate and sensitive, noninvasive diagnostic procedures for AEFs.[10,11] However, CTA might not identify AEF in periods without active bleeding. If bleeding persists and clinical suspicion for an AEF is high, it has been proposed that repeat CTA might be of better utility than repeat EGD.[9] We propose this is especially relevant for patients with IEFs, in whom the fistula is more likely to have formed to part of the GI tract not accessible by scope (ie, the iliac artery and jejunum in our patient) compared with the higher rates of duodenal involvement in AEFs. Another

useful diagnostic tool can be blood cultures, positive 50% to 63% of the time in patients with AEFs, and most often growing *E. coli*.[1]

The goal of treatment is to control hemorrhage, control infection, and maintain distal perfusion via targeted antibiotic therapy, graft removal, late transplant removal, arterial reconstruction, and bowel repair.[1,3] Revascularization can be completed with extra-anatomic femoral-femoral bypass or anatomic bypass with rifampin-soaked grafts.[11,12] The treatment options include a single-stage procedure, whether the extra-anatomic bypass is completed first to prevent arterial reconstruction in an infected field, followed by resection of the fistula, involved bowel and artery, and transplant graft; or by removal of the involved structures, followed by in situ arterial reconstruction using an autogenous conduit, an allograft, or prosthetic conduits soaked in rifampin.

Surgical treatments can also be completed as a two-stage procedure with stent graft placement of the iliac artery as a temporizing measure for unstable patients to allow time for recovery from hemorrhagic shock, followed by definitive surgery as the second stage. However, definitive repair, as described, is required to minimize the risk of recurrent infection or new fistulation.[11] Endovascular intervention alone can be offered to patients who would not be able to tolerate an open procedure or have a low life expectancy, because it is associated with recurrent infection and bleeding. It has an in-hospital mortality rate of 0% compared with 35% after open intervention in one study.[13] One study noted an incidence of infection or recurrent bleeding in 44% after endovascular management alone and a mortality rate of 29% at a mean of 13 months after an AEF diagnosis.[8]

The long-term results of rifampin-soaked grafts or allografts have shown low reinfection rates.[12] Rare complications of allografts include early or late allograft rupture as seen in our patient.[14] It is suspected that rupture of our cryopreserved allograft was a technical defect in the graft due to its linear appearance and location under the inguinal ligament. Adjunct maneuvers should be used to reinforce vascular anastomoses in these infected fields where tissue could be friable and the risk of anastomotic degeneration or recurrent fistulization is high. The techniques described include folding the donor arterial edge to create a double layer to suture to or using autologous tensor fascia lata in a similar fashion to a felt strip to buttress the anastamosis.[15] Additionally, omental flaps can be used when the native vascular wall or periarterial tissue cannot be used. The flap is created by dividing the omentum in an avascular plane (usually 10-15 cm in width) in a direction perpendicular to the transverse colon, usually based on the left omental artery and using the splenic flexure as the base of the flap, because it is a constant anatomic finding and allows the remainder and major part of the omentum to be left in place. It is then secured in place with interrupted silk sutures and a running 3-0 silk suture to secure the edge of the flap to the mesocolon to prevent any herniation between the transverse colon and omentum.[16] The use of an omental flap during the initial operation of our second case or flap coverage of the distal anastomosis during reintervention after cryograft rupture vs extra-anatomic bypass could have helped prevent the subsequent complications and reinterventions.

Whether temporizing or definitive management is pursued, antibiotic therapy should be an adjunct, although few data are available regarding the most appropriate duration. In a retrospective analysis by Omran et al,[1] postoperative intravenous antibiotic and antifungal agents were administered to patients in one series for 6 weeks with excellent outcomes. The need for oral suppressive antibiotics after 6 weeks of therapy was determined by the clinical and laboratory parameters.[1] It is important to note that intra-abdominal cultures are positive 75% to 100% of the time, most often with *Candida* spp.[1] Both of our patients were treated with either a short-course or lifelong antifungal agents due to their intraoperative culture findings.

CONCLUSIONS

The development of an IEF is rare, except in the patient population that has undergone pancreatic transplant. An IEF should be considered as a source of GI bleeding in patients with failed pancreatic transplant for an expeditious diagnosis. Definitive management should be pursued for patients who can tolerate the procedure.

DISCLOSURES

None.

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