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Salvage of Graft Pancreas in a Simultaneous Pancreas-kidney Transplant Recipient With Splenic Artery Thrombosis, Infected Walled-off Necrosis, and Stenting of Y Arterial Graft Stenosis

Devprakash Choudhary, MS, MBBS,[1] Rajesh Vijayvergiya, MD, MBBS,[2] Ashish Sharma, MS, MBBS,[1] Anupam Lal, MD, MBBS,[3] Palanivel Rajan, MD, MBBS,[2] Ganesh Kasinadhuni, MD, MBBS,[2] Sarbpreet Singh, MS, MBBS,[1] and Deepesh B. Kenwar, MS, MBBS[1]

INTRODUCTION

Pancreatic allograft thrombosis (PAT) is among the leading causes of graft loss in simultaneous pancreas-kidney (SPK) transplantation.[1] Early PAT is multifactorial, and late PAT is mainly associated with rejection.[2] Predisposing factors for PAT include donor or recipient old age, donation after circulatory death, and prolonged ischemia time.[3] Collateral circulation within the pancreas prevents infarction in PAT if the occlusion affects one of the major arteries, viz, superior mesenteric artery (SMA) or splenic artery (SA).[4] PAT usually requires an allograft pancreatectomy. We describe salvage of pancreatic allograft in a SPK recipient with transplant pancreatic artery stenosis (TPAS) involving both limbs of Y arterial graft, complicated by isolated SA thrombosis with early acute graft pancreatitis (EAGP) causing walled-off pancreatic necrosis (WOPN). The transplanted pancreas was salvaged by optical coherence tomography (OCT) guided drug-eluting stenting (DES) of the Y arterial graft limbs.

CASE STUDY REPORT

A 47-y male (body mass index 22.5) with type I diabetes and end-stage renal failure underwent SPK. He was on an insulin pump for the last 10 y and on levothyroxine for hypothyroidism for the last 14 y; his visual acuity scores and fundoscopic examination were normal. The donor was a 42-y male (body mass index 24.6) whose organs were retrieved after brain death following head injury in a road accident. He was on triple inotropes with serum creatinine (sCr) of 1 mg/dL. During retrieval, histidine-tryptophan-ketoglutarate (HTK) was used. The kidney was transplanted first in the left iliac fossa with vascular implantation onto the left external iliac vessels, and the pancreas benching was performed. The pancreatic graft was placed intraperitoneally on the right side with head up and tail down. The portal vein was anastomosed to inferior vena cava with 5-0 prolene in a continuous manner; SMA and SA were sutured to arterial interposition Y graft, which was joined to the right common iliac artery with 6-0 prolene. Pancreatic exocrine drainage was established with proximal duodenojejunostomy with cold ischemia time of 7 h 5 min and a total operative time of 4.5 h. He received anti–thymocyte globulin as induction therapy (total of 225 mg over 3 d) and antimicrobial prophylaxis with broad-spectrum antibiotics and caspofungin. The recipient achieved euglycemia by postoperative day (POD) 3 with SCr of 1.2 mg/dL on POD 7. He received heparin until POD 7, followed by aspirin (75 mg once a day). There was poor visualization

of pancreas on protocol ultrasound, and the contrast-enhanced computed tomography (CECT) abdomen done on POD 15 showed patent pancreas allograft vessels with good contrast uptake. His immunosuppression comprised of tacrolimus, mycophenolate mofetil, and prednisolone.

Three months posttransplant, the patient presented with abdominal distention, fever, and leukopenia (total leucocyte count 2500–3000/mm³). CECT abdomen showed a large peripancreatic cystic collection (22 × 11 × 10.6 cm) with no contrast leak, decreased caliber of allograft SMA,

and nonopacification of SA and vein (Figure 1A–D). The peripancreatic collection was drained under antibiotic cover with a 10F double J catheter; 1100 mL of pus was drained, which grew candida tropicalis on culture. The patient was treated with 2 wk of amphotericin B. Follow-up CECT abdomen done 2 wk after drainage showed a residual collection of size (9.1 × 5.1 × 4.8 cm) with stenosis of both limbs of interposition Y graft TPAS. The pigtail was upgraded from 10 to 18F, and saline wash was given to drain the debris. Endovascular intervention for TPAS was deferred because of active fungal infection, and
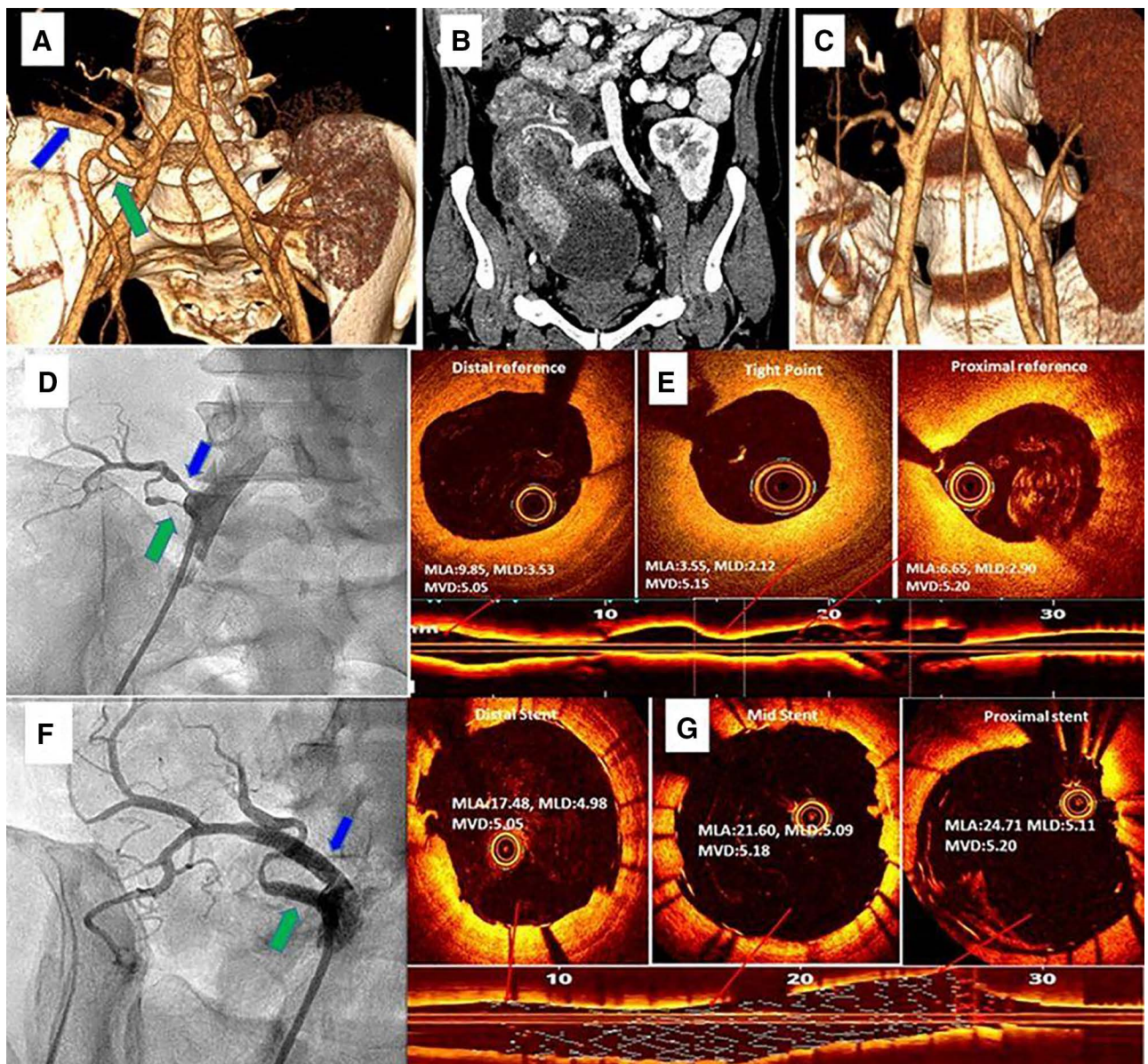
FIGURE 1. (A) 1-mo CT angiography showed patent TPA Y graft, including donor SMA (blue arrow) and donor SA (green arrow), and patent transplant renal artery. (B) 3-mo follow-up CT showed a large pancreatic pseudocyst and occluded distal SA. (C) 5-mo follow-up CT showed regression of pancreatic pseudocyst and ostial narrowing of SMA and SA. (D) Selective contrast angiogram showed ostial narrowing of SMA (blue arrow) and SA (green arrow) and total occlusion of distal SA. (E) OCT showed fibrous hyperplasia with a 60% diameter stenosis of SMA. Also depicted are the MLD in mm, MLA in mm², and MVD in mm. (F) Poststenting, a good flow was achieved in both SMA (blue arrow) and SA (green arrow), the right branch of the dorsal pancreatic artery supplying the head of the pancreas. (G) Repeat OCT of SMA showed well apposed and expanded stent. CT, computed tomography; MLA, mean luminal area; MLD, mean luminal diameter; MVD, mean vessel diameter; OCT, optical coherence tomography; SA, splenic artery; SMA, superior mesenteric artery; TPA, transplant pancreatic artery.

the step-up approach was planned for the pancreatic collection.[5] Subsequent drain and blood bacterial and fungal cultures were sterile. Cytomegalovirus viral load was negative. Serum amylase and lipase remained normal throughout the hospital stay. Drain fluid carcinoembryonic antigen (1.16 ng/mL), CA 19-9 (11 units/mL), and cyst wall sample for malignant cytology were negative. The patient did not require insulin during the hospital stay. His fasting blood sugar was 90 mg/dL, c-peptide 1.2 ng/mL, and hemoglobin A1c 5.2%. The patient was discharged with a drain in situ, which was removed after 2 mo with no residual collection on CECT abdomen.

At 6 mo posttransplant, the patient presented with fasting hyperglycemia >130 mg/dL, though his c-peptide was normal. The patient was taken up for endovascular intervention for TPAS. Digital subtraction angiography revealed significant stenosis of both limbs of the Y graft. The SA limb was stented despite the thrombosed tail of the pancreas because one of its branches was supplying the head of the pancreas (Figure 1F). Through a 7-Fr Judkins right guiding catheter, the SMA lesion was crossed with balloon middleweight coronary wire and predilated with a 3 × 15 mm noncompliant (NC) balloon. OCT revealed a fibrotic lesion causing stenosis. The lesion was stented with a 5 × 22 mm DES and postdilated with a 5 × 8 mm NC balloon. The SA had a proximal 90% lesion predilated with a 3 × 15 mm NC balloon, stented with 4.5 × 12 mm DES. Postprocedural OCT showed a well-apposed stent without any residual stenosis, check angiogram showed good graft flow without any complications (Figure 1E–G), with the resolution of fasting hyperglycemia. At 2-y follow-up postintervention, his hemoglobin A1c is 5.6% with fasting blood sugar of 90 mg/dL, c-peptide 1.5 ng/mL, and sCr 1.1 mg/dL.

DISCUSSION

According to United Network for Organ Sharing data, SPK is the most common multiorgan transplantation being performed in the United States. This case highlights the compound effect of late-occurring isolated SA thrombosis due to TPAS or EAGP complicated by WOPN. The TPAS was managed using a multidisciplinary step-up clinical approach requiring endovascular intervention with subsequent resolution of pancreatic allograft dysfunction.[5] To the best of our knowledge, this is the first case reported in the literature for TPAS-related allograft dysfunction, with salvage of graft using DES stenting of both limbs (SMA and SA) of Y arterial graft. PAT and graft pancreatitis are the 2 most common complications following SPK (Table 1).[1] Complete PAT presents as hyperglycemia with or without allograft site tenderness and is primarily managed surgically.[6] In PAT, the pancreatic allograft's survival depends on the Intraparenchymal pancreaticoduodenal arcades ("splenocephalic anastomoses"). The Kirks arcade (the right branch of the dorsal pancreatic artery joins the anterior superior pancreaticoduodenal artery) plays a vital role in this collateral supply.[4] Prophylaxis for PAT is based mainly on anticoagulation in the immediate postoperative period; however, there is a lack of consensus regarding various

prophylactic regimens to prevent PAT.[7] At our center, SPK recipients receive heparin in the immediate postoperative with aspirin on discharge untill 6 mo posttransplantation. In the index case poststenting, the patient was kept on a dual antiplatelet agent for 6 mo.

In 60%–70% of cases, EAGP is caused by vascular thrombosis and manifests clinically as graft site tenderness with systemic inflammatory response.[1] The preservation solution HTK has been highlighted as a risk factor for graft pancreatitis.[1,8] However, the first world consensus on pancreas transplantation recognizes that HTK could be used at low perfusion volumes when cold ischemia time is >10 h.[9] The use of HTK as a perfusion solution remains popular because of its lower cost.

The Index patient presented in systemic inflammatory response with WOPN. Drainage fluid grew candida tropicalis, the most common fungal infection seen in acute pancreatitis following surgical intervention and is associated with an increased mortality rate of up to 80% in the transplant population. Invasive fungal infections due to graft pancreatitis are rare but are a significant cause of graft loss, with dismal patient survival.[10]

It is also essential to correctly identify a cystic pancreatic neoplasm versus a pseudocyst or WOPN; misdiagnosing can lead to graft loss and poor recipient outcomes. We did not perform KRAS and GNAS mutations with TP53 and PIK3CA or PTEN mutations, because neoplasm in the immediate posttransplant period is less likely.[11]

The endovascular approach has a high technical success (>95%) in evading hepatic artery thrombosis following hepatic artery stenosis in orthotopic liver transplantation with an excellent primary assisted patency and decreased need for reintervention.[12] However, literature on the use of stents in TPAS remains scarce. In the index case, both Y limbs of arterial graft (SMA and SA) were severely stenosed, reducing vascular flow to the pancreatic allograft. The percutaneous endovascular intervention reported in the literature for graft salvage in TPAS or venous thrombosis or pseudoaneurysms of graft pancreas has had a limited success.[13-16]

Successful stenting for TPAS was beneficial in index case. Challenges included assessing the appropriate balloon's size and stent choice, given the intricate anatomy, and it was overcome using OCT to measure the vessel diameter at stenotic segments. Intravascular imaging using OCT is commonly used in coronary artery disease to assess plaque morphology and luminal narrowing, thus guiding the angioplasty and mitigating and identifying complications. DES was used in both Y limbs, because it has decreased in-stent restenosis compared with bare metallic stent in native renal artery stenting.[17] OCT in this patient revealed severe luminal narrowing with a circumferential fibrotic plaque and was vital in deciding the stent dimension leading to an excellent outcome.

CONCLUSION

Conservative treatment of posttransplant peripancreatic collections is feasible in selected patients. TPAS is catastrophic and can lead to graft loss. The endovascular intervention of TPAS is safe and can improve pancreatic allograft function.

TABLE 1.

Factors predisposing to pancreas allograft thrombosis—index case factors[a]

PAT factors and Virchow's triad

Hypercoagulability	Endothelial injury/activation	Abnormal blood Flow
• **_Diabetes_** • Acute surgical stress Inherited thrombophilic disorders (deficiencies of protein C, and protein S, genetic mutations of factor V Leiden, and prothrombin) • Hyperlipidemia, homocysteinemia • Donor/recipient (smoking, _obesity_) Malignancy • Heparin-induced thrombocytopenia	• _Ischemic reperfusion injury_ • _Procurement and implantation injury_ • Calcineurin inhibitors **_Perfusion fluid (HTK)_** _Longer cold ischemia time (>12 h)_ • _Delayed graft function_ • Uncontrolled hypertension • **Graft pancreatitis** Preexisting vascular disease • Immunologic factors—graft rejection • **Infections**	• **Altered vascular flow (inflow _and_ outflow _obstruction_)** Prolonged immobility • Congestive heart failure/atrial fibrillation/myocardial infarction/atherosclerotic vessels

Other donor-related factors

- Old age, peritoneal dialysis
- **_Hemodynamic instability_** _and massive fluid resuscitation during the procurement_
- _Suboptimal back table preparation_
- PDRI

Other recipient-related factors

- Segmental pancreas transplantation
- Left-sided pancreatic graft
- **Intraoperative vasopressor use**, hypotension in postoperative
- **Enteric exocrine drainage**
Posttransplant acute graft pancreatitis
- Previous thrombotic events
Ischemic heart disease, peripheral vascular disease, retinopathy/neuropathy

Graft pancreatitis factors

Donor	Recipient
• Age • **_Excessive inotropic requirements_** • _Donation after circulatory death_	• _Enteric Exocrine drainage_ • _Infection (cytomegalovirus_, **fungal, eg, candida**) • Oddi's sphincter dysfunction secondary to rejection

[a]Highlighted in bold. common factors for PAT in bold
Risk Factors present in the index case.
HTK, histidine-tryptophan-ketoglutarate; PAT, pancreatic allograft thrombosis; PDRI, Pancreas Donor Risk Index.

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