Management of Graft Duodenal Leak in Simultaneous Pancreas Kidney Transplant—a Case Report from India and Review of Literature

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Abstract Pancreatic transplantation is currently the only effective cure for Type 1 diabetes mellitus. It allows long-term glycemic control without exogenous insulin and amelioration of secondary diabetic complications. In India, pancreas transplant has not yet established with only a single successful transplant reported so far in the literature. We report a 24-year-old Type 1 diabetic patient with renal failure who underwent a simultaneous pancreas kidney transplant. On postoperative day 15, he had leak from the graft duodenal stump for which a tube duodenostomy and proximal diversion enterostomy was done. He had a high output pancreatic fistula following the procedure which was managed conservatively. The tube duodenostomy was removed at three and half months and enterostomy closure with restoration of bowel continuity was done at 6 months. After a follow up of 7 months, patient is doing well with a serum creatinine of 0.8 mg/dl and normal blood sugars, not requiring any exogenous insulin or oral hypoglycemic drugs. Managing patients with graft duodenal complications after pancreas transplant is

challenging. Tube duodenostomy is a safe option in management of duodenal leak, although can lead to a persistent pancreatic fistula. A proximal diversion enterostomy allows early oral feeding and avoids the cost as well as the long term complications associated with parenteral nutrition.

Keywords Simultaneous pancreas kidney transplant · Duodenal leak · Type 1 diabetes mellitus · Complications after transplantation

Introduction

Pancreatic transplantation is currently the only effective cure for Type 1 diabetes mellitus, allowing long-term glycemic control without exogenous insulin and amelioration of secondary diabetic complications [1]. In patients with Type 1 diabetes complicated by end-stage renal disease, a simultaneous pancreas and kidney transplantation (SPK) can significantly improve their quality of life and long-term survival [2]. Over the years, the results of this procedure have improved with improvised surgical techniques and better management of the complications. Patient survival after SPK transplant is now over 95 % at 1 year posttransplant and over 83 % after 5 years. Graft survival after SPK is most favorable among all categories of pancreas transplantation with 86 % pancreas and 93 % kidney graft function at 1 year [2]. In India, pancreas transplant has not yet established with only a single successful transplant reported so far in the literature among the 20 odd transplants done so far in the country [3]. We report a 24-year-old Type 1 diabetic patient with renal failure who underwent SPK transplant which was complicated by graft duodenal leak and review the management of such a complication.

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Case

A 24-year-old male was diagnosed with Type 1 diabetes mellitus at the age of 10 years and was started on insulin. Eleven years later, he presented with features of diabetic nephropathy that progressed to end stage renal disease requiring renal replacement therapy. The patient was counseled regarding SPK transplant and was registered in the waiting list. He received SPK transplant from a 40-year-old male donor who had a body mass index of 25 kg/m², with no comorbidities and had sustained head injury and brain death after a road accident.

Retrieval Surgery The donor was taken up for multiorgan retrieval surgery and injection meropenem 1 g was given intravenously at the start of surgery. Standard surgical steps were followed to retrieve pancreas, liver, and the kidneys [4, 5]. Duodenum was washed with 10 % povidone iodine, amphotericin, and normal saline using a nasogastric tube. Pancreas was retrieved along with the spleen and C loop of duodenum whose both ends were transacted using a transverse stapler. The mesenteric vessels at the inferior border of pancreas were also stapled. Splenic artery, superior mesenteric artery (SMA), and portal vein were preserved for restoration of pancreatic blood supply. Donor iliac vessels were also retrieved for vascular reconstruction. The retrieval surgery was uneventful and the organs were perfused with histidine-tryptophan-ketoglutarate (HTK) solution (Custodiol; DR. FRANZ KOHLER CHEMIE GMBH, NeueBergstraße 3–7, 64,665 Alsbach-Hahnlein, Germany) and kept in ice slush till reimplantation.

Backtable Surgery The tail of the pancreas was separated from spleen and splenic vessels were ligated at the pancreatic tail. Both the stapled ends of duodenum were oversutured with 4–0 prolene. Staple line over the root of mesentery was oversutured with 5–0 prolene. After checking the patency of internal arterial arcade of pancreas, gastroduodenal artery was ligated at the superior border of pancreas. Y-graft of donor iliac artery was used to reconstruct SMA and splenic artery using 6–0 prolene. Portal vein was lengthened using donor iliac vein graft using 5–0 prolene. All lymphatics and loose areolar tissue around the pancreas was ligated without injuring the pancreatic capsule. Figure 1 shows the pancreaticoduodenal graft after completed backtable surgery.

Recipient Surgery Induction immunosuppression comprised of single dose of tacrolimus 0.1 mg/kg, mycophenolate mofetil 1000 mg and injection antithymocyte globulin (ATG) 1 mg/kg given preoperatively. Intraoperatively, injection hydrocortisone 500 mg was given intravenously. Antimicrobial prophylaxis comprised of injection caspofungin 70 mg and injection meropenem 1 g and patient received heparin,

Fig. 1 Pancreaticoduodenal graft after completion of backtable surgery showing reconstructed artery and portal vein

dextran, and aspirin as thromboprophylaxis perioperatively. A midline vertical incision was given; left colon was mobilized to expose the left external iliac vessels. The graft kidney was transplanted first in the left iliac fossa and graft vessels were anastomosed to left external iliac vessels using end to side technique. Ureterovesical anastomosis was done using modified Lich Gregoir extravesical technique [6]. Good diuresis was observed after reperfusion of the kidney. Thereafter, pancreas was transplanted in the right iliac fossa. Right colon was mobilized to expose distal inferior vena cava (IVC) and right common iliac artery (CIA). Graft pancreas was placed in right paracolic gutter, graft artery was anastomosed to right CIA using 6–0 prolene, and graft vein was anastomosed to distal IVC using 5–0 prolene. After declamping, the pancreatico-duodenal graft perfused well and hemostasis was achieved. A 5 cm window was created in the right mesocolon and a loop of small bowel (around 30 cm proximal to ileocaecal junction) was brought to the right of window. Donor duodenum and small bowel loop were anastomosed in a side to side fashion in double layer using 4–0 polydioxanone (PDS). Total blood loss during surgery was around 500 ml and duration of the surgery was 6 h. Cold ischemia time (CIT, time from aortic clamping in the donor to reperfusion in the recipient) for the kidney and the pancreas was 7 and 8 h, respectively. Midline incision closure was done with no. 1 nylon loop suture over Jackson pratt drains.

Postoperative Course The patient remained hemodynamically stable with a urine output of 3600 ml, and blood sugars ranging between 66 and 227 mg/dl on the first day. Postoperative maintenance immunosuppression comprised of tacrolimus 0.1 mg/kg twice daily, mycophenolate mofetil 1000 mg twice daily, and two doses of injection ATG 1 mg/kg each on day 0 and day 1 of surgery. He developed bleeding from the drains on day 2 for which heparin infusion was stopped and reexploration was performed. However, no major bleeder was found and abdomen was closed after a thorough lavage. His serum creatinine decreased to 0.8 mg/dl and blood sugars remained between 100 and 150 mg/dl. On day 5, a

computerized tomographic angiography (CTA) was done which showed normal vascularity of the graft pancreas and kidney (Fig. 2). On day 10, patient developed fever with raised c reactive protein (CRP) which was attributed to a peripancreatic collection and was drained by placement of a pigtail drain which removed 50–100 ml of hemorrhagic fluid for next few days. The cultures from collection and blood were sterile. On day 11, another contrast enhanced computerized tomographic scan (CECT) of abdomen was done for fever which showed normal pancreatic vascularity with a small organized hematoma posterior to pancreas with pigtail drain in situ. On day 15, patient had enteric contents in the pigtail drain for which he was again re-explored and graft duodenal stump blow out was observed with a localized leak. Graft duodeno-ileal anastomosis was intact and the graft vessels were also healthy. A 14 F Foley's catheter was placed across the site of duodenal leak and brought out of abdominal wall as a tube duodenostomy and another portex drain was placed near the graft duodenum and a proximal loop enterostomy was performed. Postoperatively, he was kept on parenteral nutrition till day 25. The volume and infusion rate of parenteral nutrition was calculated according to the weight, total calorie requirement, and daily intake-output fluid balance. Serum albumin decreased to 2.2 g/dl during the hospital stay which improved to 3.5 g/dl with parenteral nutrition. He

Fig. 2 Coronal section of computerized tomographic angiography (CTA) of the patient on post operative day 5 showing normal graft pancreas and graft kidney

was also given injection fluconazole intravenously for 2 weeks. He developed a high output controlled pancreatic fistula on starting oral feeds and was started on injection octreotide, which was continued for 4 weeks. The patient required multiple courses of antibiotics for control of episodes of sepsis and even remained off all immunosuppression during one of such severe episode. The peripancreatic drain could be removed on day 78 and tube duodenostomy at three and half months following the transplant. At 6-month posttransplant, enterostomy closure was done and the bowel continuity was restored. At a follow up of 7 months patient is doing well, not requiring any medications for glycemic control with a serum creatinine is 0.8 mg/dl.

Discussion

Over the last few decades, SPK transplantation has emerged as a standard treatment of patients with end-stage renal disease resulting from Type 1 diabetes mellitus [1]. According to the International Pancreas Transplant Registry, over 35,000 pancreas transplants have been reported by the end of 2010. Of them, approximately 75 % were SPK, 18 % were pancreas after kidney (PAK) transplantation, and 7 % were pancreas transplantation alone (PTA) [2]. Although there has been an increase in the number of pancreatic transplants performed worldwide, it has so far trailed in India, despite India being home to nearly 1 lakh children with Type 1 diabetes due to various reasons [7]. As pancreas allografts are almost always retrieved from a deceased donor, the foremost requirement for pancreas transplantation is a well-established deceased donor organ transplant program.

Organ donation from deceased donors is gaining momentum in India but the program is still insufficient to meet the current organ shortage in the nation [8]. The pancreas donation is further limited by the narrow desirable range of donor's age, i.e., 10–45 years [9]. In addition, there are not many suitable recipients as most patients with Type 1 diabetes die as a result of the poor diabetic control and secondary complications of diabetes before they develop renal failure [10]. There is also a significant mortality risk associated with renal replacement therapy while waiting for the deceased organ which further limits the pool of available recipients. In our institute, there has been a significant increase in deceased organ donations over the last few years resulting in availability of donor organs for transplantation. This institute being a tertiary care center in North India also has a well-managed population of patients with Type 1 diabetes in whom longevity has been prolonged by better management of diabetic complications. These patients will invariably develop chronic renal failure after some years and the ideal treatment for them is SPK transplantation.

Since these patients will require immunosuppression for kidney transplant, combining a pancreas transplant along with kidney only adds to the surgical risk but significantly improves the quality of life and the long-term outcomes when compared to the kidney transplant alone [11].

However, there are significant surgical complications associated with pancreas transplant which cannot be taken lightly as was seen in our patient [12–14]. Most complications occur within the first 2 months of surgery and include graft pancreatitis (3–12 %), intra-abdominal infection/abscess (1–5 %), graft-vessel thrombosis (6–17 %), duodenal leak (4–10 %), and intra-abdominal hemorrhage (0–0.5 %) [12–14]. Prompt recognition and management of these complications are paramount as any delay can be fatal for the recipients. These complications may be associated with little clinical signs as the patients are on immunosuppressive medications. Therefore, there should be a very small threshold of doing radiological investigations to confirm these.

Various risk factors for surgical complications include older donor age, cardiocerebrovascular cause of donor death, hemodynamic instability, pancreas overperfusion at retrieval, and prolonged preservation time [12–15]. Prolonged preservation time of pancreas can cause reperfusion pancreatitis which if severe will necessitate graft pancreatectomy [15]. Although there are reports in literature with successful pancreatic transplants with CIT of more than 15 h, it is generally advisable to limit acceptance of organs where CIT is anticipated to be more than 12 h [15]. Thrombosis of pancreatic vessels is not an uncommon complication as it is a low flow organ and some thrombus invariable occurs at the distal ligated ends of splenic and mesenteric vessels. Perioperative anticoagulation is an important strategy to prevent this complication but may result in increased rate of reexploration for bleeding as was seen in our patient. Monitoring by thromboelastography (TEG) has been shown to be helpful in assessing coagulation status and can reduce the increased risk of bleeding after pancreas transplant [16].

Graft duodenal leaks are among the most common surgical complications after pancreas transplant with an incidence of 4–10 % and can result in graft loss in some cases [17]. Typically, early duodenal leaks are anastomotic leaks, either at the duodenovesical (in bladder drained pancreas transplant) or duodenoenteric (in enteric drained pancreas transplant) anastomosis. Late leaks (after 4 weeks post transplant) arise more frequently from the oversewn or stapled duodenal stumps [17, 18]. In a study involving 284 pancreas transplants, the incidence of duodenal leak was 6.3 % of which 94 % cases had duodenal stump leaks [17]. In the early period after transplantation, duodenal leaks are often related to graft preservation injury, technical reasons, and recipient's atherosclerosis [17–19]. Long-term immunosuppression in PAK transplant is

a risk factor for duodenal leaks. Late duodenal leaks have been related to duodenal perforation secondary to infectious or ischemic ulcers. Rejection and cytomegalovirus (CMV) infection are the other possible risk factors for duodenal leak [20]. The cause of duodenal leak in our case could be a reperfusion injury or graft pancreatitis as the patient had abdominal signs along with fever and raised inflammatory markers with negative initial cultures.

Treatment of such leaks usually mandate surgical exploration; however, management depends on the size of the leak, location, viability of the surrounding tissue, infective, or non-infective cause of leak and general condition of the patient. If the graft duodenum is not compromised, the leak is well circumscribed and there is no peritonitis then a primary repair can be attempted [17–19]. Before attempting for graft salvage, one need to ensure that there is no evidence of distal obstruction, undrained infection, or bowel ischemia as the cause of the leak. Moreover, rejection or CMV infection must be ruled out as a cause of the leak. That can be done by an excisional biopsy of the surrounding duodenal tissue followed by primary closure. Some localized duodenal leaks can also be managed conservatively by prolonged parenteral nutrition therapy but in our setup, it was thought to be safer to resume oral nutrition early [21]. Therefore, a proximal enterostomy was done along with the tube duodenostomy as has been described, although infrequently, in management of such leaks [22]. This procedure is based on pyloric exclusion technique used in the management of pancreatoduodenal injuries [22]. A high output pancreatic fistula can complicate tube duodenostomy but can be controlled with octreotide as was done in this patient [23]. There are reported cases of graft salvage after duodenal leaks/necrosis with total duodenectomy and drainage of pancreatic duct to bowel or bladder or occlusion of pancreatic duct with a polymer [19, 24, 25]. Another option described after a duodenal leak is Roux-en-Y graft duodenojejunostomy [19, 21]. Graft pancreatectomy should be considered to salvage the patient in the situation of duodenal segment leaks with abdominal sepsis or prolonged morbidity with non healing leakage [26].

Although SPK transplant is the treatment of choice for patients with Type 1 diabetes presenting with end stage renal failure, it can be associated with significant surgical complications. Managing patients with surgical complications after pancreas transplant is challenging. Duodenal graft complications can occur early after transplantation and are often a result of preservation injury or technical reasons. Tube duodenostomy is a safe option in management of duodenal leak, although can lead to a persistent pancreatic fistula. A proximal diversion enterostomy would allow early oral feeding and can avoid the long-term complications associated with parenteral nutrition.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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