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Vascular complications following bladder drained, simultaneous pancreas-kidney transplantation: the University of Miami experience

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Abstract Vascular complications remain a significant nonimmunologic source of pancreas allograft loss. From February 1993 through January 1998, we performed 98 simultaneous pancreas-kidney transplantations (SPK) using pancreatic exocrine bladder drainage in patients with type 1 insulin-dependent diabetes mellitus and end-stage renal disease. They originally received quadruple immunosuppression, and since May 1997 triple immunosuppression protocol (tacrolimus, mycophenolate mofetil, and steroids). The patients' mean age was 37 years (range 24–53 years), including 50 women and 48 men with a mean follow-up of 42 months. The overall rate of vascular complications was 6% (5 patients). The vascular complications were as follows: late thrombosis of the Y with persistent pancreas allograft function ($n = 1$), rupture of a pseudoaneurysm of the superior mesenteric artery (PSMA) with an arteriovenous fistula (AVF) ($n = 1$), thrombosis of the splenic vein (SV) ($n = 3$), complete thrombosis of the superior mesenteric vein (SMV) and splenic vein ($n = 1$). The patient with PSMA underwent surgical correction of the AVF and PSMA with preservation of the allograft pancreas function. The other patient with late thrombosis of the Y-graft required no treatment. All 3 patients with SV thrombosis were systemically heparinized followed by oral anticoagulation. The patient with complete thrombosis required surgical thrombectomy of the SMV and SV followed by heparinization and oral anticoagulation. All 6 patients including the 4 with thrombosis had preservation of the pancreas function. Serial pancreas ultrasound showed resolution and improvement with recanalization of the splenic vein and superior mesenteric vein in those patients with thrombosis. We describe our vascular experience with salvage of the pancreatic allograft function. Surgery seems to be the best treatment option in the case of AVF or complete thrombosis of the allograft. Intravenous heparin followed by oral anticoagultion could be a conservative approach for SV thrombosis.

Key words Vascular complications · Pancreas-kidney transplant · Thrombosis

Introduction

Improvement in surgical techniques and immunosuppression has resulted in significantly better outcomes in pancreatic transplantation [1]. However, complications are frequent and occasionally life-threatening [2]: arterial and venous thrombosis, arterial stenosis, hemorrhage, and mycotic pseudoaneurysms [3–7]. We report

our outcome and management of pancreatic vascular complications after simultaneous pancreas-kidney (SPK) transplantation.

Patients and methods

From February 1993 through January 1998, we performed 98 SPK using pancreatic exocrine bladder drainage in patients with type 1 insulin-dependent diabetes mellitus and end-stage renal disease. The patients' mean age was 37 years (range 24–53 years), including 50 women and 48 men with a mean follow-up of 42 months.

Donor and recipient operation

The donor operation generally included procurement of the liver, both kidneys, whole pancreas, and duodenum. Our method of procurement is standard, the pancreas, duodenum, and spleen are harvested en bloc. All mesenteric connections are divided between silk ligatures to minimize bleeding following reperfusion. The duodenum is divided in its first and third portion using a GIA staple. In the absence of a right replaced hepatic artery the superior mesenteric artery (SMA) is divided at the level of the aorta; if a right replaced hepatic is present, the SMA is divided above its take-off. The superior mesenteric vein is ligated in the mesentery below the inferior border of the pancreas. The portal vein is divided at the superior border of the pancreas to give an adequate length of the portal vein for the liver. The back table dissection involved: (1) Shortening the duodenal segment, staple dividing both proximal and distal ends, and oversewing each with interrupted silk or Prolene (Ethicon Suture, Sommerville, NJ) 4–0 sutures; (2) the splenic artery and vein are ligated, and the spleen is removed; (3) the portal vein is dissected proximal to the junction with the splenic vein to obtain extra length for anastomosis with the recipient iliac vein; (4) fashioning the Y graft of the donor (internal, external, and common iliac artery) and anastomosing the internal iliac to the splenic artery of the pancreas and the external iliac artery to the superior mesenteric artery of the pancreas, both using running 6–0 Prolene.

Following recipient midline incision, the pancreas-duodenal allograft was usually performed first and revascularized on the right side as follows: (1) The portal vein was anastomosed to the external iliac vein (5–0 Prolene) that was completely mobilized, in order to avoid any tension and allow mobility of the anastomosis during positioning or swelling of the pancreas; (2) the common iliac artery of the 'Y'graft was anastomosed to the recipient external or common iliac artery (6–0 Prolene). The duodenum was opened to allow drainage and prevent distention. A pancreaticoduodenocystostomy was performed using the two-layer hand-sewn technique. The outer layer was done with running 4–0 Prolene and an inner full-thickness running layer with 4–0 Vicryl (Ethicon Suture). The kidney was revascularized next on the left side as follows: (1) The renal vein was anastomosed to the common or external iliac vein; (2) the renal artery was anastomosed to the common or external iliac artery. A modified Politano-Leadbetter ureteroneocystostomy anastomosis (shorter submucosal tunnel) was performed. No drains were used.

Immunosuppression

Until July 1994, induction immunosuppression consisted of 10–14 days of murine monoclonal antibody OKT3 (5 mg/day), methylprednisolone (1 g on the date of surgery tapered to 0.1 mg/kg/day over 3 months), azathioprine (2 mg/kg/day tapered to 1 mg/kg/day over 2 weeks). Cyclosporine (CsA) was started when the serum creatinine was below 4 mg/dl at a maintenance oral dose of 10 mg/kg/day and adjusted according to whole blood therapeutic levels. After July 1994, OKT3 and tacrolimus (instead of CsA), azathioprine, and methylprednisolone were used as the induction regimen. Tacrolimus (T) was started immediately after surgery by continuous intravenous (iv) infusion at doses of 1 mg/24 h, and continued for a mean of 6 days (range 4–8 days). The iv dose was adjusted with an oral dose of T (0.1–0.2 mg/kg/day) to maintain a trough level of 10–15 ng/ml. Recently, we have also introduced mycophenolate mofetil (MMF) (1 g twice a day) to our regimen.

Since May 1997, a triple immunosuppression protocol (tacrolimus, mycophenolate mofetil, and steroids) without antibody therapy induction has been introduced as a new regimen.

Results

The overall rate of vascular complications was 6% (5 patients). The vascular complications were as follows: Late thrombosis of the 'Y' with persistent pancreas allograft function ($n = 1$), rupture of a pseudoaneurysm of the SMA with an arteriovenous fistula (AVF) ($n = 1$), thrombosis of the splenic vein (SV) ($n = 3$), complete thrombosis of the superior mesenteric vein (SMV) and SV ($n = 1$).

The patient with PSMA underwent surgical correction of the AVF and PSMA with preservation of the allograft pancreas function. The other patient with late thrombosis of the 'Y'graft required no treatment. All 3 patients with SV thrombosis were systemically heparinized followed by oral anticoagulation. The patient with complete thrombosis required surgical thrombectomy of the SMV and SV followed by heparinization and oral anticoagulation. All 6 patients including the 4 with thrombosis had preservation of the pancreas function. Serial pancreas ultrasound showed resolution and improvement with recanalization of the splenic vein and superior mesenteric vein in those patients with thrombosis.

Discussion

An AVF involving the SMA and SMV as a complication has only recently been reported in the pancreas allograft [8]. The possible causes in our patient include congenital malformation or the possibility of needle injury during procurement, back table preparation, or hemostasis during reperfusion in the recipient. Doppler ultrasound is indicated if the endocrine function deteriorates or if there is hematuria and pain over the graft, and should specifically look for abnormal flow in the pancreatic head. The presence of an AVF in our case was suggested by nuclear imaging, which showed a large vascular blush over the recipient iliac artery immediately following injection of isotope. A Doppler ultrasound confirmed ab-

normal flow in the region of the head of pancreas, suggestive of an AVF with a pseudoaneurysm. The operative approach consisted of vascular checking of the iliac vessels or the 'Y' arterial graft. We placed loops around the recipient iliac artery and vein and the 'Y'graft but did not need to occlude inflow, avoiding further ischemic injury to the pancreatic graft. The AVF was successfully corrected by directed surgical ligation. The intrapancreatic SMV was tamponaded from within by a Foley catheter balloon while dissecting it from the pancreatic head to get enough vein to effect a tension free closure of the SMV.

Complete venous thrombosis remains a major cause of graft loss after pancreas transplant, but rarely a cause of mortality [9]. Attempts to salvage the transplanted pancreas have been uniformly disappointing [10, 11]. Thus, an immediate reoperation to avoid life-threatening sequelae has been advised [12], and different techniques of thrombus removal have been described, whether through a previous anastomosis, through a longitudinal venotomy in the portal vein [10], or resecting a thrombotic segment of the pancreas graft [13]. Two issues are noteworthy in our case: (1) The thrombectomy was performed within 4 h of the clinical event (sudden hematuria), at which time the pancreas was dusky but salvageable; (2) the technique used has not been previously described and consisted of opening the SV at the level of the pancreas tail and the SMV at the level of the mesentery, avoiding as much as possible anastomosis manipulation or a longitudinal venotomy in order to reduce factors that may induce new thrombosis. Then, clots were removed through these openings with a Fogarty catheter balloon. Proximal recipient venous control during the thrombectomy is important to prevent dislodgement of the clot and subsequent pulmonary embolus.

These patients should be closely monitored after surgical thrombectomy, and there should be no hesitation in removing the graft if the patient's condition deteriorates [10, 14].

Systemic anticoagulation is well accepted when SV thrombosis is documented by Doppler ultrasound [15], but there are different viewpoints about the need for anticoagulation in pancreas transplant. Sollinger suggests that the use of systemic anticoagulation not only does not reduce the incidence of venous thrombosis, but may enhance postoperative bleeding which may compress either the SV or portal vein, thereby increasing the risk of venous thrombosis [16]. However, others have reported a decrease in the incidence of venous thrombosis after systemic anticoagulation in patients with SPK transplant [15], transplantation from live donors [17], and with pancreas transplant alone [18]. We obtain a thromboelastogram and use heparin if there is evidence of hypercoagulability to minimize the chance of postoperative thrombosis [19].

In the case of late thrombosis of the 'Y'graft, pancreas function was possibly maintained by collateral flow or neovascularization between the donor graft and recipient vessels [20]. In summary, we present our experience with vascular complications with salvage of the pancreatic allograft function. Surgery seems to be the best treatment option in the case of AVF with PSMA and complete thrombosis of the allograft. Intravenous heparin followed by oral anticoagulant could be a conservative approach in the case of SV thrombosis.

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