Whole Organ and Pancreaticoureterostomy in Clinical Pancreas Transplantation

J.M. Gil-Vernet, L. Fernández-Cruz, A. Caralps, J. Andreu, and D. Figuerola

PANCREAS transplantation for the treatment of diabetes mellitus in humans has proven increasingly successful in recent years. However, the surgical procedure still remains partly experimental since no one single technique or method has been universally accepted. The technical problems in pancreas transplantation are the management of exocrine secretions and vascular thrombosis. Sutherland[1] has recently published the number of cases and current number of functioning grafts according to the technique of pancreas transplantation from July 1, 1977, to June 30, 1983. Of 16 cases using urinary drainage (ducto-, cysto-, or ureterostomy), five are still functioning. One of the major complications independent of the failure to establish adequate and safe exocrine drainage is vascular thrombosis, occurring within the first days or weeks after surgery. The high rate of vascular thrombosis seen in pancreatic grafts may be explained by the disproportion between the blood flow provided by the splenic artery to the possibilities of outflow through the venous pancreatic network, which is particularly reduced in segmental grafts.[2] We attempted to obviate this problem by using a whole pancreas technique, with anastomosis of the papilla of Vater to a divided ureter, so that the pancreatic exocrine secretions were diverted into the bladder. As shown by Sollinger et al,[3] and with our technique of pancreaticopyelostomy,[4] the rejection process seems to effect exocrine tissue more severely than islet cells, so that a significant drop in urinary amylase might be a sensitive index of early pancreatic rejection.

MATERIALS AND METHODS

Our total experience from February 1983 until June 1984 comprises nine cadaveric renal and pancreatic transplants, with both organs provided by the same donor. The recipients were seven men and two women. All suffered from juvenile diabetes of long standing (14 to 32 years); their age range was 29 to 54 years. One patient (male, 34 years old) with a segmental graft, in which the pancreatic duct was injected with prolamine has had excellent graft function for over 16 months. Four cases received a segmental pancreas, with pancreatico-pyelostomy drainage. Two patients functioned for over five and nine months; one is currently functioning for more than 14 months. In three cases (47, 31, and 32 years old, respectively), the whole pancreas was transplanted without the duodenum, but preserving the sphincter of Oddi, with a circular layer (0.5 cm) of duodenal wall, which was used to drain the exocrine secretion to a divided ureter. The whole organ included celiac artery, intact splenic artery, common hepatic artery distal to the origin of the gastroduodenal artery, distal end of mesenteric vein, and portal vein. The whole organ graft vessels (celiac artery and portal vein) were anastomosed to the patients' right iliac artery and vena cava. Pancreaticoureterostomy was accomplished by telescoping the papilla of Vater into the ureter by means of one-layer anastomoses with interrupted 6-0 Prolene between the duodenal wall, 0.5 cm away from the edge of the papilla, and the ureter (Fig 1). The renal graft was then anastomosed to the left iliac vessels extraperitoneally. In two patients, immunosuppression consisted of azathioprine and prednisone, and in another, azathioprine was replaced by cyclosporine. Rejection was treated with 0.25 to 1.00 g doses of methylprednisolone given intravenously over several days.

RESULTS

All grafts demonstrated good initial function, with cessation of exogenous insulin administration. One patient died following an acute myocardial infarct, 72 hours after transplantation, with both the kidney and pancreas functioning. Urinary amylase in the 24-hour urine was checked at regular intervals after transplantation. From the day after operation, in all cases, graft function was excellent,

From the Department of Urology, Hospital Clinic I Provincial, Barcelona, Spain.

Address reprint requests to Dr J.M. Gil-Vernet, Departmento de Urology, Hospital Clinic I Provincial, c/o Casanova 143, 08036 Barcelona, Spain.

0041–1345/85/1704–0025$03.00/0

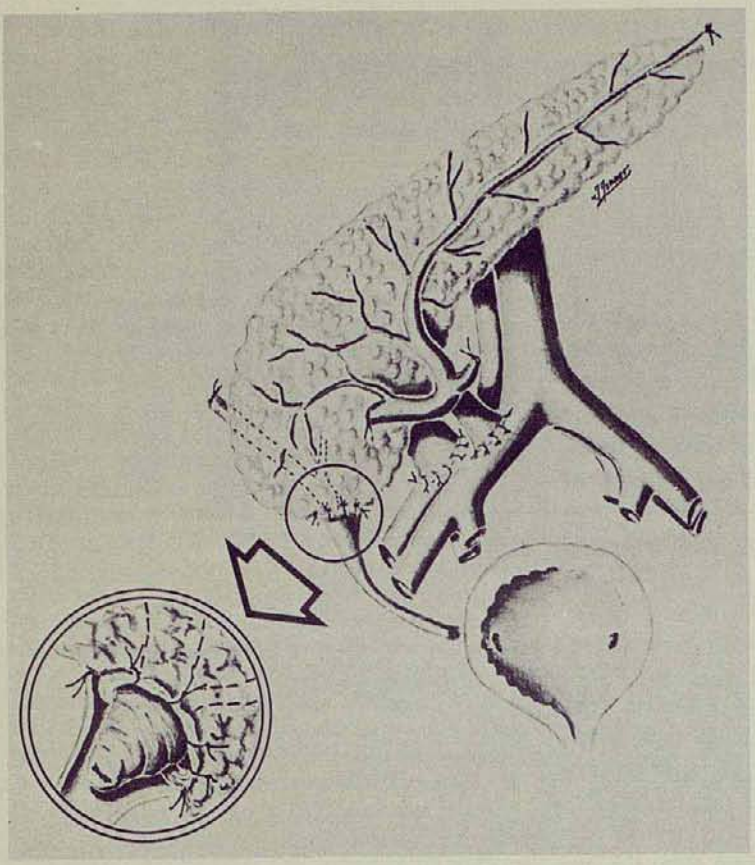

Fig 1. Whole organ and pancreaticoureterostomy technique.

secreting a large amount of amylase into the urine, ranging between 1,122 and 5,909 U/24 h. The increase in serum creatinine levels, was used as an early determinant of rejection, initiating a standard immunosuppressive therapy. Postrejection urinary amylases reached higher values than the initial levels. The gradual increase of the urinary amylase secretion after antirejection therapy could be the result of healing of an ischemic injury. A progressive increase and higher levels of urinary amylase were reached after graft stabilization. One patient exhibited a second episode of kidney rejection, with a rise in serum creatinine levels, coinciding with a concomitant decrease in urinary amylase levels. After antirejection therapy, this patient had a progressive increase in urine amylase until graft stabilization (Table 1). This patient has had good function in both organs for over seven months (Fig 2). Another patient developed irreversible kidney graft rejection three days after transplantation, with only pancreatic juice draining into the bladder. This patient also presented a clinical picture of intestinal ischemia two weeks postoperatively. Graft nephrectomy and an intestinal resection of 100 cm of necrotic jejunum were performed (at the time of laparotomy, the mesenteric vessels were patent). After this episode, the patient had a significant decrease in the quantity of pancreatic juice drained through the

Table 1. Patient A.M.

	Urinary Amylase (U/24 h)	Serum Glucose (mg/dL)
Before first rejection*	1,224 ± 144	113 ± 16
Interval	34,716 ± 22,978	103 ± 21
Before second rejection*	8,810 ± 745	83 ± 2
Present status at 7 mo	96,143 ± 25,219	112 ± 13

*Two days before the period of rejection.

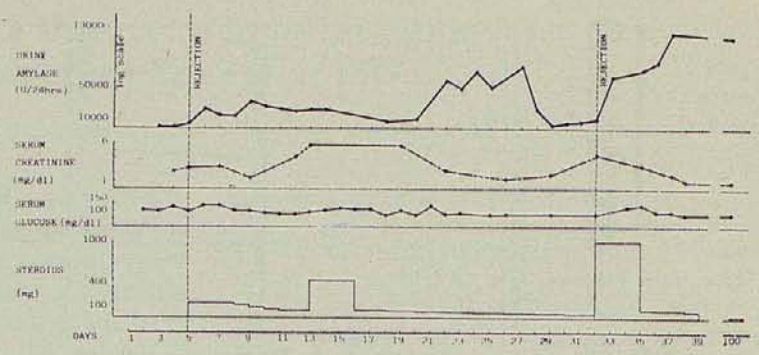

Fig 2. Male, 31 years old (case No. 7). Note the decline or urinary amylase before the rejection episode. After antirejection therapy, the patient experienced progressively increased urinary amylase levels until graft stabilization.

bladder, and in the levels of urinary amylase. In this patient, urine lipase output per 24 hours was also measured. The changes in output of this enzyme into the urine were parallel to the amylase levels. These values were even lower after an episode of pancreatic graft rejection associated with high fever and abdominal pain. Endocrine function was normal at all times. There was a gradual increase in pancreatic juice flow and urinary amylase after antirejection therapy (Table 2). The mean pancreatic juice flow was 400 to 500 mL/d and the urinary amylase never reached prerejection levels (Fig 3). Although this patient has had normal glucose levels for over two months, the exocrine tissues were evidently severely damaged.

DISCUSSION

The results of pancreatic allografting in humans remain disappointing, and the chief stumbling block is the lack of a safe and reliable surgical technique. Graft failures with increased morbidity and mortality have also been associated with the failure to establish adequate and safe exocrine drainage.[5–8] In 277 cases reported to the Pancreas Registry (D.E.R. Sutherland[1]) between July 1, 1977, and June 30, 1983, duct injection seems to continue to be the most popular technique, with 35 cases performed during the first six months of 1983, compared with only 19 enterically drained segmental grafts; 11 grafts used urinary drainage; two were done with open ducts; two pancreaticoenteric grafts were drained enterically, and three were unclassified. Duct injection with polymers has the advantage of being relatively safe, but long-term follow-up of such patients has shown severe fibrosis, resulting in graft failure.[5] Pancreaticoenterostomy provides physiologic drainage, but leakage from the anastomotic site often leads to intra-abdominal sepsis.[6] The open-duct method seems to work in some patients, but the development of pancreatic ascites in others may force removal of the pancreatic graft.[5] Urinary tract diversion has the advantage of allowing monitoring of the exocrine pancreas. Deterioration of renal function was a consistent and early sign of rejection processes in both organs in one of our patients. In another patient, pancreatic rejection occurred 12 days after irreversible kidney rejection. As the rejection process seems to effect exocrine tissue more severely than the islet cells, a significant drop in urinary amylase level may be a sensitive index of early pancreatic rejection.

A high incidence of graft vascular thrombosis has been seen in pancreatic transplantation.[6,7] One explanation of this may be the abnormal hemodynamic situation of the segmental pancreatic vessels, where the large

Table 2. Patient R.R.

	Urinary Amylase (U/24 h)	Serum Glucose (mg/dL)
Before first rejection*	5,909	124 ± 20
Interval	29,740 ± 18,802	119 ± 34
Before second rejection*	8,801 ± 4,308	97 ± 13
Present status at 7 mo	3,606 ± 2,780	150 ± 18

*Two days before the period of rejection.

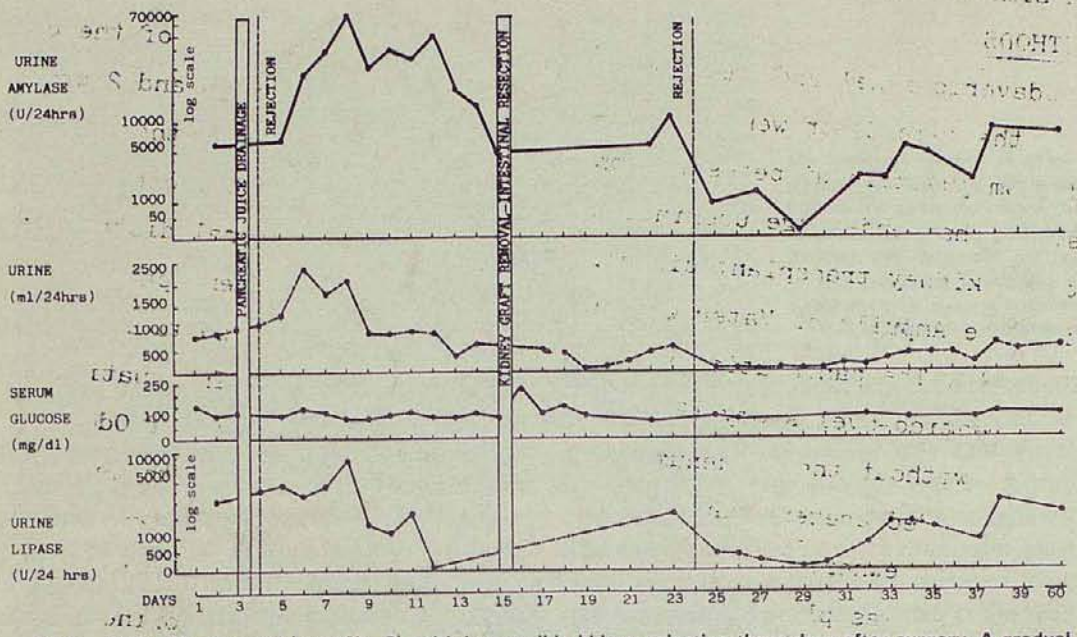

Fig 3. Male, 32 years old (case No. 8), with irreversible kidney rejection three days after surgery. A gradual increase of urine amylase, pancreatic juice flow, and urine lipase after antirejection therapy was seen. A drop in these parameters was seen after an episode of rejection, although serum glucose was normal at all times.

splenic artery is drained via the small pancreatic vessels. With the whole organ technique, all pancreatic vessels are preserved, along with the splenic, common hepatic, and gastroduodenal arteries. This procedure also includes a larger number of islets in the transplant, resulting in a greater reserve (compared with segmental grafts) for residual function if fibrosis or rejection episodes reduce the beta cell mass.[5]

REFERENCES

1. Sutherland DER: World J Surg 8:270, 1984

2. Calne RY, McMaster P, Rolles K, et al: Transplant Proc 11:51, 1980

3. Sollinger HW, Cook K, Kamps D, et al: Transplant Proc 17:749, 1985

4. Gil-Vernet JM, Fernández-Cruz L, Andreu J, et al: Transplant Proc 17:342, 1985

5. Sutherland DER, Chin PL, Goetz FC, et al: World J Surg 8:244, 1984

6. Groth CG, Tyden G, Lundgren G, et al: World J Surg 8:257, 1984

7. McMaster P, Michael J, Adu D, et al: World J Surg 8:253, 1984

8. Dubernard JM, Traeger J, Bosi E, et al: World J Surg 8:262, 1984