Transplantation Proceedings

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Experience With 13 Segmental Pancreas Transplants in Cyclosporine-Treated Diabetic Patients Using Ethibloc for Duct Obliteration (Surgical Aspects)

W. Land, W.-D. Illner, D. Abendroth, and R. Landgraf

SINCE August 1979, 18 segmental pancreas transplantations in 17 diabetic recipients with end-stage renal failure have been performed at our institution (17 combined pancreatic and renal allotransplantations, one pancreatic retransplantation). The course and outcome of simultaneous pancreatic and renal transplantations in the first three patients receiving conventional immunosuppressive therapy have been published elsewhere.[1-3] This article presents our experience with 13 segmental pancreatic allotransplantations in 12 patients treated with the new immunosuppressive agent cyclosporine (Sandimmune, Sandoz Ltd., Basel, Switzerland). As details of patient selection, postoperative management, and long-term follow-up are presented by our group elsewhere in this issue,[4,5] we will mainly concentrate on surgical aspects in this report.

MATERIALS AND METHODS

Twelve type I diabetic patients in end-stage renal failure (aged 25 to 49 years) have been accepted for treatment. Combined pancreatic and renal allotransplantation was performed in all 12 patients, pancreatic retransplantation alone in one patient.

Donor Pancreatectomy

The technique of pancreas harvesting has been described previously.[2] Recently, we modified our technique slightly: (1) Hypothermic in situ perfusion of the pancreas with Euro-Collins' solution was provided by an intraaortally situated catheter via the celiac axis. (2) The celiac axis, including an aortal patch and the portal vein, respectively, were used for anastomosis exclusively. Harvesting of the pancreas was combined with the removal of the kidneys (all cases), the removal of the heart (three cases), and the removal of heart/lung (one case). Organ harvesting was performed either at our own clinic or at external hospitals. Transportation of the organs was provided by helicopters or emergency cars. Cold ischemia time never exceeded five and one half hours.

Special Donor Criteria

Special donor criteria for pancreas harvesting were used at our institution: age, 15 to 40 years; stable circulation; blood sugar and serum amylase, normal/subnormal; no obesity; negative crossmatch; and blood group compatibility.

Duct Obliteration

The duct obliteration procedure was started immediately before transplantation; under hypothermic in vitro conditions, the duct was cannulated (Abbocath cannula). Between 3.5 and 6 mL of Ethibloc (prolamine, alcoholic amino acid solution) were injected throughout the ductal system under x-ray control. Duct obliteration was considered to be efficient when first signs of overinjection appeared as revealed by x-ray. After occlusion, the ductal orifice, as well as the parenchyma near the cut surface, were ligated.

Recipient Operation

Our technique of pancreatic transplantation has been slightly modified recently. The segmental pancreas graft was situated (in an upside-down position) extraperitoneally in the right iliac fossa by positioning the distal 2/3 intraperitoneally. Circulation was established by end-to-side anastomosis of the portal vein to the right external iliac vein and the celiac axis (plus patch) to the right external iliac artery. The wound was drained for two to four days either by a silicon rubber drain or Penrose drain (Fig. 1). Following closure of this wound, a renal graft from the same donor was placed in the left iliac fossa using the standard technique.

Immunosuppressive Protocol

Basic immunosuppression consisted of intravenous (IV) cyclosporine 3.5 to 5 mg/kg/d over the first ten days posttransplant. Cyclosporine was administered orally (15 mg/kg) until the end of one month, when it was decreased

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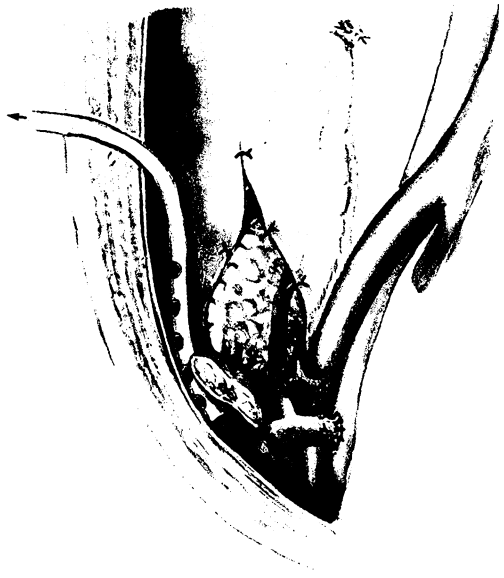

Fig. 1. Technique recently used in segmental pancreatic transplantation: partially extra/interperitoneal position of the graft. For anastomosis, the portal vein as well as the celiac axis (plus an aortal patch) are used. The operation is done at the right iliac fossa.

by 2 mg/kg monthly to a maintenance level of 6 to 8 mg/kg monthly to a maintenance level of 6 to 8 mg/kg body wt.

Steroids (methylprednisolone) were begun at 500 mg IV intraoperatively by decreasing the daily dose to 30 mg during the first two weeks posttransplant. During the next two months, methylprednisolone was slowly decreased to a daily dose of 8 mg and maintained at that level.

Antirejection treatment. Antirejection treatment consisted of three IV bolus injections of 500 mg methylprednisolone during the first rejection episode. The second and third rejection episodes were treated by administration of antithymocyte globulin (ATG, Fresenius, Frankfurt, FRG) in a dose of 4 to 7.5 mg/kg daily over a period of seven days in combination with methylprednisolone in a dose of 120 mg IV daily until reversal.

Table 1. Results of Simultaneous Pancreatic and Renal Transplantation Under Cyclosporine Therapy (12 Patients)

Patients in the Consecutive Series (age)	Survival Time (mo)		
	Pancreas	Kidney	Patient
4. H. S.* (36 yr)	(Venous thrombosis)	27	27
5. P. K. (41 yr)	26	26	26
6. A. B. (33 yr)	16	16	16
7. G. L. (26 yr)	6	6	6
8. K. F. (49 yr)	1	1	1†
9. R. J. (25 yr)	2 (Rejection)	2 (Rejection)	6
10. H. K. (42 yr)	6	6	6
11. F. S. (40 yr)	5	5	5
12. U. S. (33 yr)	2	2	2
13. S. K. (27 yr)	(No function)	2	2
14. M. S. (36 yr)	1.5	1.5	1.5
15. G. S. (33 yr)	1	1	1

*Retransplantation: second occurrence of venous thrombosis.

†See Table 2, same patient.

RESULTS

The overall results of 12 combined pancreatic and renal transplantations (and one pancreatic retransplantation) are shown in Table 1. One patient died of acute liver failure (acute yellow liver necrosis) posttransplant. The other patients are currently alive. Eight of 13 pancreatic grafts, as well as ten of 12 renal grafts, are currently functioning (August 1983); pancreatic grafts after 26, 16, 6, 6, 5, 2, 1½, and 1 month; renal grafts 27, 26, 16, 6, 6, 5, 2, 2, 1½, and 1 month. Four of 13

Table 2. Early (Local) Complications Following Simultaneous Organ Transplantation

Patient	Complications	
	Pancreas	Kidney
4. H. S.	Venous thrombosis (twice)	None
5. P. K.	Transient fistula	Rupture after biopsy (led to operative repair)
6. A. B.	Peripancreatic fluid collection	Wound hematoma (led to evacuation)
7. G. L.	Transient fistula	Wound hematoma (led to evacuation)
8. K. F.	None	None
9. R. J.	Fistula; infection (rejection)	Rejection
10. H. K.	Peripancreatic fluid collection	None
11. F. S.	Peripancreatic fluid collection	Wound hematoma (led to evacuation)
12. U. S.	Transient fistula	None
13. S. K.	No function: infection (led to exploration)	Distal ureter necrosis (led to operative repair)
14. M. S.	Fistula	None
15. G. S.	None	None

pancreatic grafts failed because of acute irreversible vascular rejection,[1] acute posttransplant venous thrombosis,[2] and no primary function.[1] Concerning the last case, an abnormal blood supply of the body and tail of the donor pancreas has to be discussed (only a few nutritive branches arising from the splenic artery without any parenchyma presentation were shown by angiography). We observed a relatively high incidence of early postoperative local complications on both sites of the grafts as shown in Table 2. At the site of the pancreatic graft, peripancreatic fluid collection requiring repeated needle aspiration and transient pancreatic fistula, respectively, were encountered most frequently; at the site of the renal graft, deep wound hematomas requiring surgical evacuation was observed.

Rejection episodes of both organs proved to be almost mild under cyclosporine treatment. There was only one acute vascular-type rejection not responding to antirejection treatment. Normally, all rejection episodes could be reversed either by methylprednisolone (IV bolus) alone or by combined administration of methylprednisolone and ATG.

DISCUSSION

Our current technique of combined segmental pancreatic and renal grafting using cyclosporine as posttransplant immunosuppressant has been associated with (1) low mortality, (2) an acceptable morbidity, (3) rare immunologic graft loss, (4) a relatively high incidence of early local complications, and (5) a reasonable rate of functioning pancreatic grafts (at the present time, August 1983: 61.5%).

We assume and discuss that this high rate of functioning pancreatic grafts is primarily a result of the strong immunosuppressive potency of the new agent cyclosporine, which reduces the events of irreversible allograft rejection. This observation is in accordance with our results obtained in cadaveric renal transplantation using cyclosporine as basic immunosuppressive therapy; the one-year graft survival rate of renal allografts has improved by 20% (to 80%) compared with our historic controls using conventional immunosuppressive therapy.[6]

The clinical use of cyclosporine may also have led to the low rate of mortality in our recent series, although other contributing factors, such as better selection and improved management of the patients, and the gaining of experience within the transplant group may play some role.

The morbidity observed in our patients after combined transplantation certainly is higher than in kidney-transplanted patients but it seems acceptable. This morbidity mainly concerns the incidence of early local complications such as peripancreatic fluid collection and transient pancreatic fistula at the site of the pancreatic graft, as well as severe wound hematomas at the site of the renal graft.

Indeed, the incidence of complications from residual function of the exocrine system of the duct-occluded pancreatic graft worries us. We believe that these local complications probably arise from a too-early reabsorption of the occlusion substance Ethibloc (Ethicon, Raritan, NJ) before the acini are completely atrophied (a decisive difference between Ethibloc and neoprene used by the Lyon group and others). It is worthwhile to mention that the administration of somatostatin did not prevent these local complications from arising from residual exocrine secretion. On the other hand, this property of early reabsorption may be the reason for the good long-term function of the pancreatic grafts as discussed by us elsewhere in this issue.[4] If it is suggested that a remaining foreign body causes increased fibrosis in the graft over a longer period of time, then the early reabsorption of ethibloc would imply a beneficial effect (as far as long-term function is concerned) because of a milder fibrosis-inducing effect. A completely intraperitoneal position of Ethibloc-occluded pancreatic grafts might reduce this kind of local complication.

The incidence of wound hematoma at the site of the renal graft is obviously a result of

our aggressive regimen of early postoperative anticoagulation (heparinization). This protocol was applied to prevent venous thrombosis of the splenic vein of the pancreatic graft. In fact, this complication can be prevented completely by aggressive anticoagulation therapy according to our experience. Nevertheless, a new therapeutic concept of posttransplant anticoagulation is being worked out at the present time.

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