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Brief report

Simultaneous pancreas-kidney transplant in two children with hemolytic-uremic syndrome

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Abstract. Simultaneous pancreas-kidney (SPK) transplantation has rarely been performed in the pediatric population. This report describes successful SPK transplantation in a 12-year-old girl and a 14-year-old boy with renal and pancreatic insufficiency secondary to postdiarrheal hemolytic-uremic syndrome. All reported cases of pediatric SPK transplantation are reviewed. SPK transplantation is a feasible option in selected pediatric patients with combined pancreatic and renal insufficiency.

Key words: Pancreas transplantation – Kidney transplantation – Hemolytic uremic syndrome – Diabetes mellitus

Introduction

Simultaneous pancreas-kidney (SPK) transplantation has been performed in adults since 1966, with 3,108 cases in the Unites States between 1 October 1987 and 31 May 1995 [1, 2]; however, only eight SPK transplants in pediatric patients have been reported to the International Pancreas Transplant Registry. This report describes two pediatric cases at the University of Minnesota. Unlike the typical adult SPK recipient who has insulin-dependent diabetes mellitus (IDDM), the renal failure and diabetes mellitus in these children were sequelae of hemolytic-uremic syndrome (HUS).

Case reports

Our first patient developed diarrhea-associated HUS at 2.5 years of age. Her course was complicated by chronic renal failure, transmural colonic infarction with subtotal colectomy, and pancreatic endocrine and exocrine insufficiency requiring insulin and pancreatic enzymes. Her renal function slowly declined, leading to initiation of hemodialysis at 6.5 years of age. Later that month, she received a 6/6 antigen-match cadaver kidney transplant at the University of Tennessee at Knoxville.

Her immediate postoperative course was uncomplicated. She had one episode of acute rejection 20 months posttransplant treated with high-dose steroids. Thirty months posttransplant, her creatinine increased from 1.1 to 1.6 mg/dl. Allograft biopsy revealed moderate chronic transplant nephropathy. Over the next year her creatinine increased to 2.0 mg/dl. Her renal function then stabilized. Pretransplant evaluation in June 1995 revealed a creatinine of 2.1 mg/dl and a creatinine clearance of 22 ml/min per 1.73m^2.

Her blood glucose levels were markedly labile with average values of 200–300 mg/dl and glycosylated hemoglobin levels between 10% and 17%. She had one admission for severe diabetic ketoacidosis in September 1994. Attempts at tighter glucose control resulted in multiple episodes of hypoglycemia.

The patient received a 1/6 antigen-match cadaver SPK transplant on 6 August 1995 at 12 years of age. The pancreas was drained via the bladder and the original kidney graft was not removed. Immunosuppression consisted of antithymocyte globulin (ATG) for 7 days, prednisone, azathioprine, and tacrolimus. She received insulin for 6 h postoperatively, after which she was normoglycemic.

She had three episodes of acute rejection, 10 days, 24 days, and 2 months post transplant. The first rejection episode was treated with 7 days of OKT3 plus a steroid taper. For the second episode of rejection she received 9 days of OKT3 and a steroid taper. She received a steroid taper alone for the third episode.

She currently has a serum creatinine of 1.1 mg/dl with a normal urine amylase level. Tacrolimus levels are being maintained between 5 and 10 ng/ml. She remains off insulin, but continues to require pancreatic enzyme supplementation.

Our second patient was diagnosed with postdiarrheal HUS at 23 months of age. His course was complicated by acute renal failure requiring 14 days of dialysis, hyperglycemia requiring insulin, and hypertension. Over the next few months, his creatinine normalized and his hyperglycemia improved, enabling him to stop insulin therapy. By age 5 years, his creatinine had increased to 0.9 mg/dl, his blood pressure was more difficult to control, and he had to resume insulin. A renal biopsy showed focal glomerular sclerosis and focal interstitial fibrosis, consistent with previous damage due to HUS. His renal function continued to slowly decline, and he was started on peritoneal dialysis in April 1995 at age 13 years.

He received a living-related simultaneous kidney and segmental pancreas transplant from his mother on 15 August 1995 at 14 years of age. The pancreas was drained via the bladder and the native kidneys were not removed. Immunosuppression consisted of ATG for 7 days, prednisone, mycophenolate mofetil, and tacrolimus. He required no insulin post transplant.

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Table 1. Data on pediatric simultaneous pancreas-kidney transplants

Patient no.	Age at transplant (years)	Date of transplant	Institution	Etiology of pancreas and kidney failure	Follow-up
1	13	5/23/81	Queen Elizabeth Hospital Birmingham, UK	IDDM GN	Both grafts functioning at 14-month follow-up
2	16	1/4/89	University of Louvain, Saint-Luc Hospital, Brussels, Belgium	IDDM PUV	Both grafts lost to chronic rejection Retransplanted with a kidney alone
3	16	2/19/90	University of Iowa	HUS	Both grafts functioning
4	16	3/31/90	University of Texas, Galveston	WS	Both grafts lost to chronic rejection Dies 10/93 from complications of WS
5	14	3/14/94	Wilford Hall Medical Center Lackland, Texas	IDDM Diabetic nephropathy	Both grafts functioning
6	14	4/21/94	Royal Liverpool Hospital Liverpool, UK	IDDM Diabetic nephropathy	Both grafts functioning
7	12	8/6/95	University of Minnesota	HUS	Both grafts functioning
8	14	8/15/95	University of Minnesota	HUS	Both grafts functioning

IDDM, Insulin-dependent diabetes mellitus; GN, glomerulonephritis; PUV, posterior urethral valves; HUS, hemolytic-uremic syndrome; WS, Wolfram syndrome

He has had no episodes of rejection and currently has a creatinine of 1.1 mg/dl, with a normal urine amylase level. Tacrolimus levels are being maintained between 5 and 10 ng/ml and he remains off insulin.

Discussion

There have been eight pediatric SPK transplants reported to the International Pancreas Transplant Registry (Table 1). The first patient was included in a previous report on SPK transplantation [3]. Patients 1, 2, 5, and 6, similar to almost all adult SPK recipients, had IDDM. In the first two patients, however, kidney failure was not due to diabetic nephropathy. Patient 1 had glomerulonephritis and patient 2 had posterior urethral valves and reflux nephropathy. Two of the patients, 5 and 6, were reported to have diabetic nephropathy as the etiology of their renal failure. Although progressive diabetic renal lesions have been reported in adolescence [4], renal failure secondary to diabetic nephropathy rarely occurs before adulthood.

Patient 4 suffered from Wolfram syndrome, a hereditary neurodegenerative disorder which is also known by the acronym DIDMOAD (diabetes insipidus, diabetes mellitus, optic atrophy, and deafness). Urinary tract abnormalities are common [5].

Patients 3, 7, and 8 had diarrhea-associated HUS as the underlying etiology for both kidney failure and diabetes mellitus. Pancreatic endocrine insufficiency has been reported as a sequelae of postdiarrheal HUS in 4%–15% of patients, and may resolve spontaneously or persist [6]. Pancreatic exocrine insufficiency is a very rare complication, occurring in less than 1% of patients [7]. The decision to anastomose the pancreas to the bladder in these patients was based on the greater technical difficulty of enteric drainage. Bladder-drained transplants have a 19% higher 1-year graft survival than enteric-drained transplants, due to a lower rate of technical failure [2]. Our first patient (no. 7, Table 1) currently has good weight gain with minimal steatorrhea on low-dose enzyme supplementation. Conversion to enteric drainage remains a viable option if her pancreatic exocrine insufficiency worsens.

These cases demonstrate the feasibility of SPK transplantation in selected pediatric patients with combined pancreatic and renal insufficiency. SPK transplants have been quite successful in the adult population. Between October 1987 and April 1995, 1-year patient survival was 91%, while graft survival was 84% for the kidney and 77% for the pancreas [2]. Graft survival has shown steady improvement, with 1-year pancreas graft survival in SPK transplants increasing from 70% in 1987 to 81% in 1993 [2]. Pancreas graft loss due to rejection is quite low in SPK transplants, with only 9% rejected at 1-year and 15% at 4 years [2]. In contrast, graft loss due to rejection in the pancreas after kidney transplant and pancreas transplant alone was much higher, with 33% and 37% rejected at 1 year and 59% and 68% by 4 years [2]. Adult recipients of SPK transplants are often at increased postsurgical risk, due to long-standing complications of IDDM. This is not the case in the pediatric population, which may account in part for the good results obtained in six of the eight patients. Potential causes of combined renal and pancreatic failure in children include diarrhea-associated HUS, IDDM with non-diabetic renal failure, IDDM with onset in infancy, and Wolfram syndrome. The potential gain in quality of life achieved by providing pancreatic function to those with hyperlabile diabetes mellitus must be weighed against the risks of surgical complications and the availability of living-related versus cadaveric organs.

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Literature abstracts

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Angiotensin converting enzyme gene polymorphism and renal hemodynamic function in early diabetes

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An insertion/deletion (I/D) of the human angiotensin converting enzyme (ACE) gene is a major determinant of circulating ACE levels. Recent studies suggest that the ACE I/D polymorphism may influence the risk of developing nephropathy in patients with insulin dependent diabetes mellitus (IDDM), although the mechanism responsible for the effect is unknown. Since an early increase in glomerular filtration rate (GFR) may also be a risk factor for the development of diabetic nephropathy, we sought to determine if the ACE I/D polymorphism influenced renal hemodynamic function in patients with IDDM. Genomic DNA was obtained from 39 normotensive male and female patients with uncomplicated IDDM (mean duration 3.4 years; range 1 to 6 years), and from 20 non diabetic control subjects. The ACE I/D polymorphism was determined using the polymerase chain reaction. Subjects were divided into three groups based on their ACE genotype. Values for GFR, renal plasma flow (ERPF), filtration fraction, and renal vascular resistance were determined in both groups using classic inulin and paraaminohippurate clearance techniques. Blood glucose was maintained between 4 to 6 mmol/liter in the patients with IDDM using a modified euglycemic clamp technique. Mean values for GFR were significantly greater in patients homozygous for the I allele (143 ± 7 ml/min/1.73 m^2) compared to patients homozygous for the D allele (121 ± 3 ml/min/1.73 m^2, $P < 0.01$), while the mean GFR values for the heterozygous patients were intermediate. ERPF was also significantly greater in patients homozygous for the I allele (850 ± 103 ml/min/1.73 m^2) compared to patients homozygous for the D allele (672 ± 31 ml/min/1.73 m^2, $P < 0.04$), while there were no differences in the values for mean arterial pressure, glycosylated hemoglobin, or albumin rates amongst the groups. There was no dominant effect of the ACE gene I/D polymorphism in the control group. These results suggest that: (1) the ACE gene I/D polymorphism influences glomerular filtration and renal plasma flow rates in patients with early uncomplicated IDDM; and (2) differences in renal hemodynamic of diabetic nephropathy offered by the I allele.

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Unilateral multicystic dysplastic kidney: the case for nephrectomy

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Management of unilateral multicystic dysplastic kidneys (MCDK) presents physicians and surgeons with a significant dilemma. Recent studies have indicated that the incidence of short term complications of MCDK is low and many authors have recommended conservative non-operative treatment. Surgery has been proposed by some because of the potential complications of hypertension, infection, and malignant change. Three children with hypertension secondary to MCDK seen at this institution in the past four years, one of whom had been discharged from follow up as a result of "disappearance" of the cystic kidney on ultrasound examination, are reported. We believe that the risks of hypertension secondary to MCDK have been understated, and that based on the conclusions of these studies, many children may be receiving suboptimal follow up. We currently favour elective nephrectomy as the treatment of choice for this lesion.