Renal Transplantation Under Cyclosporine and FK 506 for Hemolytic Uremic Syndrome

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HEMOLYTIC uremic syndrome (HUS) is known to be a leading cause of acute renal failure in children. When seen in adults, it may often be sporadic, or familial.[1] The results of renal transplantation with cyclosporine (CyA) in patients with HUS as the cause of end-stage renal disease (ESRD) have been reported in many series.[2-4] We previously reported our experience with renal transplantation for HUS under FK 506 (Prograf) immunosuppression.[5] In this article, we describe our overall results of kidney transplantation for renal failure due to HUS treated with either CyA or FK 506 (Prograf) as the main immunosuppressive agent.

PATIENTS AND METHODS

All patients who underwent renal transplantation with a diagnosis of HUS as the cause of renal failure were studied. Seven adults and four children received a total of 16 kidneys. One child received two cadaveric kidneys; the first graft was treated with CyA and the second with FK 506. A second patient received five cadaveric transplants. CyA was used for the third and fourth transplants, while the fifth was performed with FK 506 (the first two transplants were with azathioprine and prednisone). The fourth kidney was transplanted elsewhere and lost to a technical error at 1 week. This graft, plus the first two transplanted kidneys were excluded from analysis.

All other patients received a single kidney; three were from living donors, and six were from cadaveric donors. Five cases received CyA as the main immunosuppressive agent, with FK 506 as the primary agent in eight cases. The immunosuppressive regimen consisted of CyA or FK 506 and prednisone, with or without azathioprine (AZA). Two patients received OKT3 for induction therapy at the time of retransplantation with FK 506.

The clinical features are described in Table 1. A diagnosis of recurrent HUS was made if the following features were present: progressive thrombocytopenia; and hemolytic anemia and a rising serum creatinine without evidence of rejection by histological examination of a kidney biopsy.

RESULTS

Children

Four children received a total of five cadaveric kidneys. All were treated with FK 506; in addition, one child received a

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Table 1

Patient	Age at Dx HUS	Age at Tx	Type of Tx	Family Hx	Onset of Disease	Drug Therapy	Outcome
1	3.5 mo	11 mo	CAD	yes	5 d	CyA	dialysis
	3.5 mo	4.5 y	CAD	yes	5 d	FK 506	dialysis
2	7 y	8.5 y	CAD	no		FK 506	GF at 3.5 y
3	16 mo	3 y	CAD	no	—	FK 506	GF at 3.3 y
4	23 mo	10 y	CAD	no	—	FK 506	GF at 4.3 y
5	22 mo	18 y	LRD	no	—	FK 506	GF at 2.8 y
6	28 y	28.8 y	CAD	no	—	CyA	GF at 8.7 y
7	22 mo	29 y	LRD	no	—	CyA	Graft loss to pyelonephritis and CR at 4.9 y
8	25 y	26 y	LUD	no	19 days	CyA	Graft loss at 4.5 mo, died at 1.2 y
9	38 y	42 y	CAD	no	—	FK 506	GF at 2.9 y
10	37 y	41 y	CAD	yes	4 wk	FK 506	Graft loss at 1 mo died at 1.7 y
11	13.5 y	14 y	CAD × 5	no	—	Imuran	Graft loss at 10 y (CR)
		25 y				Imuran	Graft loss at 3 wk (PNF)
		25 y				CyA	Graft loss at 2 y (CR)
		29 y				CyA	Graft loss at 1 wk (Tech)
		32 y				FK 506	GF at 4 y

LRD = living related donor, LUD = living unrelated donor, CAD = cadaveric donor, GF = good function, PNF = Primary nonfunction, Tech = technical.

first graft under CyA immunosuppression. Both kidney transplants in this child (performed at ages 11 months and 4.5 years) failed due to recurrent HUS documented by day 5 posttransplantation. Allograft nephrectomies led to resolution of the hematologic abnormalities. No rejection was reported at the time of recurrence of the disease. This child had a maternal aunt who died of HUS at 1 year of age.

The remaining three patients (75%) are well 3.3 to 4.3 years posttransplantation without any evidence of recurrent HUS and with good graft function (Table 1).

Adults

Seven adults received a total of eight kidneys for analysis. Patient number 11 was transplanted initially at age 14 years, and at age 32 she received her fifth kidney transplant (grafts 1, 2, and 4 were excluded from analysis). All kidneys were cadaveric in nature. The remaining 6 adults each underwent a single kidney transplant (Table 1).

Two adults developed recurrent HUS documented by renal biopsy. One recipient gave a family history of HUS in two first cousins and developed recurrent HUS by 4 weeks posttransplantation under FK 506 therapy. Having returned to dialysis, she died from secondary septicemia and thrombotic thrombocytopenia purpura (TTP) 1.7 years posttransplantation. A second adult died; recurrence of HUS was seen by day 19 posttransplantation under CyA immunosuppression. After multiple unrelated complications, this patient died at 14 months posttransplantation, and 9.5 months after allograft nephrectomy.

The remaining five adults (71%) remain free of recurrent disease. Two patients were treated with CyA and three received FK 506 immunosuppression (one patient received CyA with a previous graft). One CyA-treated patient lost her graft after 4.9 years due to severe pyelonephritis and chronic rejection. Patient number 11 developed no recurrence of HUS with either CyA or FK 506 therapy.

DISCUSSION

The recurrence of hemolytic uremic syndrome after kidney transplantation with cyclosporine, and more recently with FK 506, has been reported. When we compare the outcome of 11 patients treated with either CyA or FK 506, we find that two of five grafts were lost to recurrent HUS under CyA therapy (40%), and two of eight grafts were lost with FK 506 immunosuppression (25%). Although our numbers are small, the recurrence of this disease seems to correlate more with a positive family history for HUS than with the type of immunosuppression used. One patient, without a family history of HUS, developed recurrent disease at 3 weeks posttransplantation. Having received a kidney from an unrelated donor, the onset of early rejection after transplantation could have been a contributing factor in her disease onset. However, no rejection was documented at the time of recurrent HUS.

Although our experience suggests that HUS can reoccur with either CyA or FK 506 immunosuppressive therapy, the incidence is seemingly (but not statistically) lower with FK 506. The familial form of HUS appears to have a poorer outcome (two of two patients) than the spontaneously acquired form (one of nine patients). The overall 1-year graft survival for this patient population remains at 70%.

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