Outcome of Primary Glomerular Disease in Pediatric Renal Transplantation: A Single-Center Experience

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ABSTRACT

Introduction. The recurrence of primary disease in transplantation is a well-known problem. We report our single-center experience to assess the frequency of the recurrence of primary glomerulonephritis in children after renal transplantation.

Patients and methods. Medical reports of 14 children with primary glomerular disease were evaluated. Among the 14 grafts were 10 from living related and four from cadaveric donors. Ten were diagnosed as focal segmental glomerulosclerosis (FSGS), two membranoproliferative glomerulonephritis (MPGN), and two polyarteritis nodosa (PAN). The original diagnosis was biopsy-proven in every case. All patients were treated with calcineurin-based immunosuppressive therapy.

Results. The mean age was 15.5 ± 5.4 years. The median transplantation duration was 47 months; however, one of the FSGS patient had hyperacute rejection. Five years later she received a second graft with a serum creatinine of 0.7 mg/dL at 7 years after transplantation. Posttransplant recurrence of FSGS was confirmed in two patients (20%), who were treated with plasmapheresis with no improvement of proteinuria, two FSGS patients had thromboses after transplantation. One had a cardiac thrombosis with heterozygote MTHFR mutation and one, a renal artery thrombosis and loss of graft with prothrombin 20210A mutation. They all have functioning grafts except these two. We did not observe recurrence of PAN or MPGN in patients.

Conclusion. Although the number of patients is quite small, our recurrence rate was compatible with the previous reports. Additionally, we strongly recommend evaluation of all risk factors for thrombosis and give appropriate anticoagulation.

RECURRENT GLOMERULAR DISEASE is a significant issue in pediatric renal transplantation. The 2004 annual report of the North American Pediatric Renal Transplant Cooperative Study (NAPRTCS) group demonstrated that glomerular diseases with a high risk of recurrence accounted nearly 30% of all pediatric renal disease leading to the need for transplantation. In fact, recurrent disease accounts for about 8% of all pediatric graft losses, it is the fifth most common cause of graft loss among pediatric renal transplant recipients. Depending on the type of glomerulonephritis, the recurrence rate and prognosis are different.[1,2]

The most frequent disease resulting in end-stage renal failure in children is focal segmental glomerulosclerosis (FSGS), accounting for 8.3% of the chronic renal insufficiency patients, 14.3% of the dialysis patients, and 11.4% of transplant recipients.[3] Recurrence of FSGS has been reported to range between 20% and 40%.[4]

Renal transplantation remains the final therapeutic option for the majority of patients with membranoproliferative glomerulonephritis (MPGN) II. MPGN II has been reported to recur in 18% to 100% of renal allografts, rates of graft failure as a result of disease recurrence have ranged from 0% to 100%.

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Additionally, despite the potential for relapse and the lack of characteristics that predict the risk, transplantation is an advisable mode of therapy for patients with renal failure caused by antineutrophilic cytoplasmic antibodies (ANCA)-positive microscopic polyarteritis nodosa (PAN).

The aim of this study was to assess the frequency and clinical implications of recurrence of the original renal disease in children after kidney transplantation.

PATIENTS AND METHODS

Among the 70 pediatric kidney transplantation patients, medical reports of 14 children with primary glomerular disease were reviewed for clinical data, including demographic information, disease history, physical examination, and laboratory results. Ten of them were diagnosed as FSGS, two MPGN, and two PAN. The original diagnosis was biopsy, proven in every case. The grafts were ten from living related ($n = 10$) or cadaveric donors ($n = 4$). All recipients were immunosuppressed with either cyclosporine or tacrolimus, azathioprine or mycophenolate mofetil plus, and steroid. Recurrence of FSGS was treated by plasmapheresis according to protocol recommended by Cochat et al[5] with cyclosporine. Ten sessions of plasmapheresis were performed over 2 weeks, then one session per week for 2 months.

RESULTS

The mean age was 15.5 ± 5.4 years. The median transplantation duration was 47 months (7 to 84 months). One FSGS patient had hyperacute rejection. Five years later, she received a new graft and has a serum creatinine of 0.7 mg/dL at 7 years after the second transplantation.

The mean age at the onset of FSGS was 4.7 ± 2.2 years. The median duration of FSGS prior to reaching end-stage renal disease (ESRD) was 60 months (17 to 120). All patients except one were dialyzed before transplantation. Patient characteristics are detailed in Table 1. Biopsy-proven recurrence of disease occurred in 2 of 10 patients with FSGS, leading to graft loss and requirement for hemodialysis despite plasmapheresis. One of them had cardiac thrombosis with heterozygote MTHFR mutation and underwent successful thrombectomy with a functioning graft. One of them experienced renal artery thrombosis and graft loss with prothrombin 20210A mutation. Both of them have had additional risk factors for thrombosis.

Two MPGN type II patients have functioning grafts with last visit creatinine levels 0.72 and 0.68 mg/dL and transplantation durations of 16 and 32 months.

Two patients with ANCA-positive microscopic PAN also have functioning grafts with the last creatinine levels of 0.88 and 0.92 mg/dL, respectively, and transplantation durations of 54 and 60 months, respectively.

DISCUSSION

Glomerulonephritis is the underlying cause of endstage renal failure (ESRF) in 30% of pediatric kidney transplant recipients. These patients are at risk of recurrence of their original diseases. Risk factors for recurrence are largely unknown and prediction remains difficult.[1]

FSGS is the third most common primary diagnosis leading to ESRD in children. Recurrence of FSGS has been reported to range between 20% and 40%.[4]

Recurrent FSGS after transplantation is unpredictable, and clear risk factors have not been idendified. The most common risk factors proposed were: younger age at original disease onset, shorter duration of the disease from onset to ESRF, and the presence of mesengial hypercellularity in native renal biopsies.[6]

Evidence-based treatment options for recurrent FSGS do not exist. High-dose cyclosporine, tacrolimus, cyclophosphamide, ACE inhibitors, and steroids have been tried with varying success. The most successful treatment for recurrent FSGS appears to be plasmapheresis with or without cyclophosphamide.[7] Biopsy-proven recurrence of disease occurred in 2 of 10 patients with FSGS leading to graft loss and requirement for hemodialysis despite plasmapheresis. Pretransplantation prophylactic plasmapheresis has been reported to be successful, unfortunately, these two patients did not receive pretransplant plasmapheresis.[5]

Table 1. FSGS Patient Demographics

	Patient									
	1	2	3	4	5	6	7	8	9	10
Age at onset of initial NS (y)	3	1	2	4	6	3	6	2	8	10
Sex	F	M	M	F	M	F	F	F	M	M
Duration of original NS prior to ESRD (mo)	12	60	68	120	46	106	58	84	17	62
Duration of dialysis (mo)	19	48	36	80	1	–	10	2	12	11
Donor (type)	CD	CD	LD	CD	CD	LD	LD	LD	LD	CD
Acute rejection in first 3 (mo)	–	–	–	–	+	–	–	–	+	–
Duration of transplantation (mo)	54	40	60	84	12	18	52	–	7	14
Creatinine (mg/dL)										
First year	0.37	0.67	0.59	0.64	0.66	0.81	0.7	–	–	2.7
Third year	0.39	0.82	0.61	0.66	–	–	0.79	–	–	–
Last visit	0.41	0.89	0.87	0.71	–	–	0.88	–	3.4	3.6
Recurrence	–	–	–	–	–	–	–		+	+
Graft loss	–	–	–	–	–	–	–	+	+	+

NS, nephrotic syndrome; ESRD, end-stage renal disease; CD, cadaveric donor; LD, living donor.

According to the NAPRTCS, vascular thrombosis (11.6%) has become the most common cause of graft loss among pediatric renal transplantations. Furthermore, renal allograft recipients with thrombophilia are at higher risk for early allograft loss.[8]

Although the number of our patients was small, our recurrence rate (20%) was compatible with previous reports. Additionally, we strongly recommend the evaluation of all risk factors for thrombosis and administer appropriate anticoagulation.

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