Cyclosporin and Prednisolone: Do They Prevent Recurrence of Focal Segmental Glomerulosclerosis?

J.R. Burke
R.J. Rigby
Renal Unit, Princess Alexandra Hospital, Brisbane, Australia

Dear Sir,

Patients with renal failure from focal segmental glomerulosclerosis (FGS) have a high incidence of recurrence in transplant kidneys. The recurrence is estimated at approximately 30% in first renal allografts and 75% in second renal allografts [1]. We wish to report the possible prevention with cyclosporin of nephrotic syndrome from FGS in a child receiving a second cadaver allograft where the first renal transplant failed because of recurrent FGS. In addition, this case illustrates the interaction between cyclosporin and drugs which induce hepatic P450 enzymes – in this instance sodium valproate.

A 5-year-old girl presented in 1977 with nephrotic syndrome. Total serum protein was 52 g/l, albumin 20 g/l, 24-hour urine protein 4.7 g and serum creatinine 0.07 mmol/l. There was no response to prednisolone 2 mg/kg/day for 6 weeks and cyclophosphamide 3 mg/kg/day for 8 weeks; renal function deteriorated, and she commenced haemodialysis 15 months later. Bilateral nephrectomy because of severe hypertension was performed in 1979. In 1980, a renal cadaver transplant (HLA-A zero mismatch, HLA-B and HLA-DR 2 mismatches) was performed with prednisolone and azathioprine as immunosuppression. Recurrence of nephrotic syndrome was documented within 3 weeks (serum albumin 26 g/l, 24-hour urine protein 6.9 g/l, serum creatinine 0.06 mmol/l. A biopsy at 4 weeks after transplant showed 1 glomerulus with segmental hyalinosis and no evidence of rejection. Renal function deteriorated and she recommenced dialysis after 11 months.

In January 1985, she received a second cadaver allograft (HLA-A 1 mismatch, HLA-B zero mismatch, HLA-DR 2 mismatches). Sodium valproate 25 mg/kg/day was being administered for epilepsy.

Pre-operatively, intravenous cyclosporin 25 mg/kg and methylprednisolone 15 mg/kg were given. In the postopera-

6 month
12.5
505
0.20
0.11

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tive period, cyclosporin 25–30 mg/kg/day was given intravenously for 5 days and then orally (20–25 mg/kg/day) for 5 months. Prednisolone 2 mg/kg/day was given for 1 week and then reduced to 1 mg/kg/day for 2 weeks. Two rejection episodes at 8 and 18 days, confirmed by renal biopsies, were treated with methylprednisolone, 20 mg/kg/day, for 3 days. There was no evidence of FGS on either biopsy. Cyclosporin levels (whole blood RIA) ranged from 360 to 1,750 ng/ml. Hypertension has been severe – presumably from cyclosporin and required captopril for control. At 6 months after transplant there has been no evidence of recurrence of nephrotic syndrome (serum albumin 36 g/l, 24-hour urine protein 0.2 g/day, serum creatinine 0.12 mmol/l). Treatment is now cyclosporin 12.5 mg/ kg/day (cyclosporin level 505 ng/ml) and prednisolone 0.2 mg/kg/day (table I).

The pathogenic mechanisms in FGS are unknown, but recurrence of the disease with heavy proteinuria can occur within hours after transplantation [2]. Cyclosporin exerts its immunosuppressive effect mainly by reducing T-helper cell activity. Particularly it inhibits the production and release of various lymphokines including inter-feron and interleukin 2. High-dose cyclosporin was given in a deliberate attempt to prevent recurrence of FGS, as there were major problems on dialysis with vascular and peritoneal access. Induction of cytochrome P-450 by some anti-convulsants increases the hepatic elimination of cyclosporin. This effect not previously reported with sodium valproate would have contributed to this child’s tolerance of high-dose cyclosporin. This girl could be in the group of the 25% patients who do not develop recurrent FGS in the second graft, but we would suggest further trials with this regimen.

References