Case Report

Successful transplant of a kidney with focal segmental glomerulosclerosis

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Introduction

The gap between the number of kidneys available for transplantation and the number of recipients awaiting a kidney is growing. Consequently there is increasing interest in the donation of marginal kidneys [1]. Kidneys have been successfully transplanted from donors with known polycystic kidney disease [2], diabetic glomerulosclerosis [3], and horseshoe kidneys [4]. The reuse of a transplanted kidney has also been described [5]. Resolution of glomerular disease has been reported after transplantation of organs with diabetic glomerulosclerosis [3] and mesangial IgA deposits [6]. The presence of nephrotic syndrome in the donor has been considered a contra-indication to transplantation; even a recent study of transplantation of pairs of ‘extended criteria’ donor kidneys excluded potential donors with greater than 3 g/24 h proteinuria [7]. We have been able to identify only one previous report of transplantation of kidneys from donors with nephrotic syndrome, and involving successful transplantation of kidneys from a donor with minimal-change nephropathy; proteinuria rapidly resolved following transplantation [8]. Primary focal segmental glomerulosclerosis (FSGS) is thought to be caused by a circulating factor [9] and would therefore be expected to resolve following transplantation. We report successful renal transplantation, with resolution of proteinuria, from a cadaveric donor with FSGS who had nephrotic syndrome for 38 years.

Case

The donor was a 51-year-old female who had had nephrotic syndrome since the age of 13, with incomplete response to corticosteroids. A renal biopsy when she was 23 showed FSGS; proteinuria persisted despite cyclophosphamide. At the age of 31 she remained nephrotic; a repeat renal biopsy showed FSGS with patchy tubular atrophy and fibrosis. Twenty-four hours protein excretion varied between 7.5 and 1.09 g but fell to <0.2 g after addition of an ACE inhibitor for hypertension 4 years before the donor’s death, when creatinine clearance was measured at 67 ml/min. The donor had undergone removal of a benign brain tumour 5 years prior to death, which had resulted from subdural haemorrhage. Serum creatinine was 93 μmol/l on admission, rising to 154 prior to pronouncement of brain-stem death; dipstick urinalysis showed 3+ proteinuria. A pre-implantation biopsy showed acute tubular necrosis and vacuolation of tubular cells consistent with tubular injury, mild foci of tubular atrophy and interstitial fibrosis, and segmental lesions consistent with FSGS in 2 of 9 glomeruli.

Recipient A was a 67-year-old man who had been on CAPD for 45 months and whose primary disease was reflux nephropathy. He had a history of ischaemic heart disease and was awaiting an exercise tolerance test. The kidney was a 1A, 1B, 1DR mismatch; cytotoxic and FACS cross-matches were negative. The kidney functioned immediately after transplantation. Initial immunosuppression was with antithymocyte globulin, cyclosporin, and prednisolone. The post-operative course was complicated by severe steroid psychosis on day 3, leading to withdrawal of prednisolone and conversion to tacrolimus and mycophenolate mofetil, in the hope of minimizing the risk of acute rejection which might have required further steroid treatment. The graft functioned immediately, serum creatinine falling to a nadir of 208 μmol/l on day 7, followed by a rise to 271 μmol/l on day 10, prompting a transplant biopsy which disclosed segmental hyalinosis with tuft adhesions in two of eight glomeruli, increased mesangial matrix in the remainder, and hypertensive vascular changes similar to the appearances pre-implantation, and with no evidence of acute rejection. Serum creatinine fell to the previous baseline with reduction of tacrolimus doses, but rose to 268 on day 58, when a further biopsy showed similar glomerular and parenchymal changes but with marked hyaline arteriolar sclerosis. Protein excretion was 5.9 g/24 h on day 8,
3.1 g/24 h on day 10, 0.9 g/24 h on day 21, and 35 mg/mmol creatinine at 1 year post-transplant. Serum creatinine has remained stable at around 200 µmol/l; creatinine clearance (Cockcroft and Gault) 30 ml/min.

Recipient B was a 53-year-old man with end-stage renal failure due to reflux nephropathy, who had been on haemodialysis for 2 years. The kidney was a 1A, 1B, 0DR mismatch; cytotoxic and FACS mismatch were negative. The graft functioned immediately. Immunosuppression was with tacrolimus and prednisolone. On day 27 a transplant biopsy was performed for graft dysfunction and showed segmental sclerosis in one of five, global sclerosis in one of five, and normal appearances in three of five glomeruli, with mild focal tubular atrophy and interstitial fibrosis but no evidence of acute rejection. Serum creatinine fell to a nadir of 204 µmol/l and has remained at this level subsequently, with a measured creatinine clearance of 31 ml/min. Protein excretion was 1.8 g/24 h 2 years pre-transplant, 1.23 g/24 h on day 4, 2.09 g/24 h on day 24, 0.6 g/24 h at 1 year post-transplant.

Discussion

FSGS is considered to be a contra-indication to donor transplantation. However, it is increasingly accepted that this condition is due to a circulating factor, resulting in increased glomerular permeability and sclerosis; 30–40% of patients with FSGS suffer from recurrence when treated with a kidney transplant leading to graft failure in half of them. Treatment with plasmapheresis can suppress the proteinuria in the short term. Savin and colleagues tested serum samples from patients with FSGS in an in-vitro assay of glomerular permeability to albumin. The patients who had developed recurrent FSGS following transplantation had serum with significantly higher permeability to albumin than controls or patients with FSGS who had not relapsed. Plasmapheresis significantly reduced the permeability and the proteinuria for a short while [9]. Attempts to isolate and identify the circulating factor have so far been unsuccessful. Whether its action is mediated immunologically or by direct injury is still not certain.

The two recipients described here had successful engraftment with resolution of proteinuria and reasonable excretory function. It would have been of interest to obtain late biopsies to look for resolution of the histological changes of FSGS, but in our view this would be unethical in the absence of other indications for biopsy. It is also possible that the haemodynamic effects of calcineurin inhibitors contributed to the reduction in proteinuria. This experience suggests that primary FSGS should not be considered a contra-indication to organ retrieval if excretory renal function is well preserved.

References


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