Recurrence of Glomerulonephritis Following Renal Transplantation (Part 2)*

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Secondary Glomerulonephritis

Systemic lupus erythematosus (SLE)

Before 1973, patients with SLE, especially those with acute deterioration of renal function and active extra-renal disease, experienced high mortality (20%) within 3 months of commencement of haemodialysis for end stage renal disease (ESRD). However, because of the concern for the poor long-term prognosis and because of the fear of recurrent disease, SLE was considered a contraindication to renal transplantation. After satisfactory 1 to 2 year results without recurrence were reported in 56 patients with SLE by the advisory committee to the renal transplant registry in 1975, patients with ESRD caused by SLE were more readily considered as candidates for renal transplantation. Renal transplantation for SLE patients with ESRD has now become more accepted, though it has been recommended that transplant hepatitis be postponed for at least 1 year after initiating maintenance dialysis and when there is no evidence of continued lupus activity. In a recent long-term study there was no recurrence in 32 SLE patients, where 69% of patients underwent < 1 year of dialysis prior to transplantation. There was no recurrence in an earlier report of 20 grafts in 18 patients, and the experience of the ANZDATA registry was similar with about 36 patients. Despite the fact that there is a genetic predisposition to the development of SLE, three allografts from HLA-identical siblings have been transplanted without adverse effects. SLE patients usually remain clinically and immunologically quiescent after transplantation i.e. hypocomplementaemia and evidence of circulating anti-double-stranded DNA antibody are negative. However, a non-specific positive FANA (diffuse or speckled type) is common and does not signify recurrent disease. Only five cases of recurrent lupus nephritis are discussed in the literature drawn from considerable numbers of patients transplanted over the last 15 years. These patients showed the pathological and immunohistochemical features of SLE nephritis, and three out of five had clinically active disease with extrarenal and serological manifestations. The weight of evidence favours the view that SLE recurs infrequently with an incidence of probably < 1:1000. When recurrence does occur, it is usually of minor clinical importance and is amenable to increased immunosuppressive therapy. There are several possible explanations for the lack of recurrence: 1. the disease may be burnt out by the time patient needs transplantation; 2. the cases of lupus with ESRD may represent less active disease (55% of the 66 cases from the transplant registry had no extrarenal manifestations of lupus); 3. the immunosuppressive therapy given after transplantation ameliorates the lupus disease process. SLE is compatible with long-term graft function.

Wegener’s granulomatosis

The results of renal transplantation in this rare cause of renal failure, though restricted, have been favourable, though extrarenal manifestations may be a problem. No graft failure from recurrence has been described in nine patients. Recurrence has been described, with a successful therapeutic response to a switch from azathioprine to cyclophosphamide (along with increased prednisolone dosage). Recurrence has been described despite the use of cyclosporin.

Haemolytic-uraemic syndrome

The haemolytic-uraemic syndrome (HUS), is a group of disorders whose mixed aetiology leads to unrestrained microvascular coagulation principally affecting the kidney, with thrombocytopenia, purpura, red cell fragmentation, renal failure, and
(usually) severe hypertension. It has been associated with a variety of clinical conditions including pregnancy, the use of oestrogen-containing oral contraceptives, virus infection, and exposure to other organisms. It is diverse in its manifestations and presentation, and this, combined with the similarity of the pathological lesion of HUS to that affecting small vessels in acute vascular rejection, cyclosporine toxicity, and malignant hypertension, are important considerations when considering recurrence. This heterogeneity is important to remember in considering risks to the graft, particularly since it seems that in some patients the tendency to develop an HUS in response to infections or other stimuli is inherited and lifelong, whereas in others it may be acquired and brief.

In children, HUS is a relatively common cause of renal failure (5%), but rare in adults.

The first report of a recurrence appeared 16 years ago. Folman et al. reported a child who lost three successive grafts from HUS, the first graft having been performed 5 months after the beginning of renal failure. The experience of Cameron was similar in two adult patients, both having received a transplant within 3 months of onset and both immediately losing two successive grafts with the reappearance of HUS. Since the early reports of recurrence, however, successful transplantation without recurrence has been reported by Broyer et al. in a series of eight children, and nine children in that of Potter et al. Cameron reported transplanting six patients after a delay of 6 months to 2 years without evidence of recurrent disease. A recent report from Leiden described the recurrence of HUS in two of eight patients; in one it was precipitated by the use of an oestrogen-containing oral contraceptive. An important review of the experience in Minneapolis with 14 patients with HUS has recently appeared. Seven of these patients had a definite recurrence of HUS in their renal allograft and three additional patients have probably had a recurrence (using carefully defined histological and clinical criteria). The increased frequency and severity of recurrence in this report compared with others is suggested by the authors to be possibly related to the frequent use of cyclosporin in those patients with definite recurrence. This led to their recommendation that cyclosporin (and Minnesota anti-lymphocytic globulin (ALG)) should not be used in patients with this condition. Leithner et al. had earlier reported finding recurrent HUS in a patient treated with cyclosporin but Hamilton et al. did not. Perhaps it is in those patients with an already defective prostacyclin production, which persists on dialysis, that problems may arise with intercurrent infections or other thrombogenic stimuli. Recurrence of HUS occurs quite frequently in patients who have received a graft from a living-related donor, compared with negligible recurrence in those receiving a cadaver graft. In the inherited forms of deficiency of endothelial prostaglandin I2 production, family members may be affected; Bergstein et al. reported two sisters, one of whom developed HUS in her remaining kidney after donating one to her sister who herself had HUS as cause of her renal failure. Lack of reports in the recent literature suggests that recurrence is rare and may be confined to the subgroup with persisting abnormalities of endothelial prostacyclin production. A delay of 6 to 12 months before transplantation seems best, on admittedly slender evidence.

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References
13. Oslen S, Bohman SO, Posborg-Petersen V. Ultrastructure of the glomerular basement membrane in


18Disney APS. Seventh report of the Australia and New Zealand combined dialysis and transplant registry (ANZ-DATA). Adelaide, South Australia: Queen Elizabeth Hospital, 1984: 35–36.


133 Cameron JS. Effect of the recipient’s disease on the results of transplantation (other than diabetes mellitus) *Kidney Int* 1983; 23: s24–s33.