Outcomes of renal transplantation in adult patients with primary FSGS: a single centre experience over forty years.

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Introduction: Primary focal segmental glomerulosclerosis (FSGS) is a common cause of nephrotic syndrome in adults and children and often leads to end stage kidney disease (1). The aetiology may be podocyte injury from a “circulating factor”; in these cases, 30-50% patients may develop recurrent FSGS following renal transplantation (2, 4). Genetic mutations affecting structural podocyte proteins may also cause FSGS; however many identified mutations confer a very low risk of recurrent disease. A more detailed understanding of the patient population is required in order to individualise pre-transplant counselling, and to identify patients at high risk of recurrence (3).

Methods: We performed a retrospective database search of all patients transplanted at our centre since 1981 (n=3908 transplants in n=3533 patients) with ESRF due to primary FSGS. A detailed case note review was undertaken to exclude patients with secondary FSGS. We evaluated the course of their native kidney disease, and their transplant outcomes including the incidence of recurrent FSGS and graft survival. The diagnosis of recurrent FSGS was made in patients with supportive transplant histology and proteinuria (1).

Results: We identified 106 patients with primary FSGS who were transplanted, representing approximately 3% of the transplant population. Detailed follow up data were available for 75 patients with a median follow up time of 84 months. 63% were male, reflecting the higher incidence of FSGS in men. Median age was 43 (+/- 18) years at time of transplantation, and where known, 30 years at the time of FSGS diagnosis. 67% were Caucasian. Genetic analysis identified mutations in 6 patients (ACTNS4, NPHS2, ACTN4, NUP107 and INF-2 (N=2)) but was not available for the majority of patients in our study. 52% of transplants were from deceased donors and 48% were from live donors. In all patients with functioning grafts, the median graft eGFR was 46 ml/min and urine ACR 9.3 at median 96 months post transplant. We identified recurrent FSGS in 13 (17.3%) of patients. Recurrent disease was more common in young, Caucasian men and typically occurred early post transplant (median 1 month) but was diagnosed as late as 3 years post-transplant. Recurrent disease was treated with plasma exchange (n=9) and/or rituximab (n=3) in addition to maintenance immunosuppression with calcineurin inhibitor, anti-proliferative and corticosteroids. Despite treatment, recurrent disease led to graft failure in 10/13 (77%) cases. No cases of recurrent disease occurred in patients with identified genetic mutation.

Discussion: Our study shows that the rate of recurrent FSGS observed in our centre over 40 years is much lower than published rates (17.3%) but that recurrent disease is likely to lead to graft loss. Recurrent FSGS occurred more commonly in young Caucasian men. This information will guide more individualised risk counselling prior to transplantation in our multi-ethnic population (3).