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Focal Segmental Glomerulosclerosis Recurrence in Allograft in a Young Bahraini Female- A Case Report

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Focal segmental glomerulosclerosis (FSGS) is not an infrequent cause of nephrotic syndrome in the young. The incidence is 5-15%. Renal morbidity is significant and the disease relentlessly progresses to renal failure. Failure due to steroid unresponsiveness and resistance to cytotoxic drug regimen necessitates renal transplantation. However, recurrence of the primary disease (FSGS) in the allograft poses a serious problem to the graft survival. We report a case of FSGS that recurred in the graft four months post transplantation in a sixteen year old Bahraini Female.

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Recurrence of the primary renal disease in the graft is well recognized and found in 10-20% of all recipients. However, graft loss due to recurrent disease is reported in less than 5% of all cases. The most frequent causes of recurrence are glomerulonephritis, membrano-proliferative GN type II, IgA nephritis and focal segmental glomerulosclerosis. Diabetic nephropathy is the commonest metabolic disorder linked to graft disease. Primary oxalosis is a rare disorder but is related to a very high risk of recurrent disease in the transplant[1].

Focal segmental glomerulosclerosis (FSGS) is a poorly understood cause of nephrotic syndrome that occurs in about 10% of patients. However, the pathobiology of the disorder in over 50% of the patients is associated with progressive renal dysfunction despite steroids and cytotoxic therapy. Transplantation is the treatment of choice, it is not free from complications especially the rapid recurrence of the primary disease.

The exact rate at which primary focal glomerulosclerosis (FGS) recurs in the transplant is somewhat difficult to determine, because the focal nature of the glomerular lesions can be due to sampling error in graft biopsies. The reported recurrence rate averages about 20 percent[2-4].

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A recent report shows that the relative risk for graft failure due to post transplant FSGS is 2.25%, membrano-proliferative glomerulo nephritis is 2.37% and for Hemolytic ureamic syndrome/ Thrombotic thrombocytopenic purpura (HUS/TTP) is 5.36%. There is higher graft failure and shorter half life in patients with recurrent FSGS[5].

Early detection of various related complications have become more feasible in the new renal transplant unit in Bahrain (February 1995) with the establishment of the allograft disease registry[6]. In this report we document a case of recurrent FSGS in one of our young allograft recipients.

THE CASE

A sixteen year old Bahraini female followed up for 3 years at the nephrology clinic of the Salmaniya Medical Complex for nephrotic syndrome.

Figure 1. Adequate renal biopsy showing characteristic focal segmental sclerosis H & E x 400

The renal biopsy carried out during this time revealed morphological features consistent with Focal segmental glomerulo sclerosis (FSGS) (Fig.1). SLE profile (anti dsDNA, ANA, anti Sm) was negative. Despite active treatment with steroids and cytotoxic agents, the patient developed end stage renal disease and underwent haemodialysis for two months prior to transplantation from live related donor (sister). The donor was HLA suitable and negative by cross matching. However, biopsy was not performed. Along with transplantation, bilateral nephrectomy was carried out. The histopathology of the native kidneys revealed marked tubulointerstitial loss with over 50% of glomeruli showing continued presence of FSGS with the remaining sclerosed globally. There were foci of dystrophic calcification and interstitial round cell infiltrates. The stromal scarring was significant. After successful transplantation, the patient developed Pulmonary oedema, from which she recovered following active intervention. Nearly four weeks later the patient became oliguric and the 24 hour urinary protein was 5.23gms. She had haemodialysis twice weekly which effectively improved the renal parameters. Persistent proteinuria and poorly controlled hypertension necessitated repeat graft biopsy five months later which showed features equivocal of FSGS (Fig.2). Stenosis of the transplant renal artery was not excluded. Even with adjustment of antihypertensive drugs and multi drug immuno-suppression, the patient showed further deterioration of renal functions following which permanent haemodialysis has become inevitable.

Figure 2. Graft biopsy showing glomerulis with focal segmental sclerosis chracterized by capillary obliterations, matrix increase H & E x 600

DISCUSSION

This report illustrates early recurrence of primary disease Focal Segmental Glomerulosclerosis (FSGS) in the allograft. Recurrence of FSGS is a serious threat to graft survival.

The success rates of living-related donor (LRD) transplants are clearly superior to those obtained with cadaver donors. However, caution should be exercised when considering LRD transplantation for a condition which has an increased chance of recurring after transplantation and causing ultimate graft failure. The recurrence rate of FSGS in the allograft is 20-40%, with graft failure resulting in 40-50% of these cases. Once a first transplant fails due to recurrent disease, the risk of recurrence in the second transplant approaches 80%. LRD transplant should be avoided[7] in patients at high risk for recurrence.

The susceptibility of the donor kidney appears to be an important factor in the development of chronic renal damage. This may play a role in the long-term functional changes seen after clinical renal transplantation[8].

Neither the course of FSGS nor the recurrence in the graft are reliable predictors of prognosis. Several factors such as early age of onset, rapid renal dysfunction, mesangial prominence, duration of dialysis, HLA compatibility have all been suggested with no significant statistically acceptable status. However, results of a study conducted to investigate the role of serum immunoglobulin sub classIgM in predicting the response to therapy in FSGS, suggested that higher IgG/ IgM ratios may be associated with better clinical response and these changes may reflect dysregulation of immunoglobulin class in patients with FSGS[9].

There is a subgroup in which the disease recurs in about 50% of the cases. These patients, who almost certainly have primary FSGS, tend to be less than 20 years of age and have a rapid clinical course, with the interval from the diagnosis of FSGS to end-stage renal disease (ESRD) being less than three years[10].

The primary form can be considered when there is nephrotic syndrome without other causes. The origin of primary FSGS has not yet been determined. Several factors including genetic, racial, developmental, macrophage, viral and others are being explored which have encouraging results[11].

There is convincing evidence that primary FSGS is pathogenetically related to circulating humoral factors and are attributed to the augmented membrane permeability. Two recent reports appear to confirm this hypothesis[12,13]. Serum from some patients with FSGS increased the permeability of isolated glomeruli to albumin. Furthermore, testing pre-transplant sera with this in vitro system can be used to predict recurrence after transplantation[12].

Use of regenerating protein adsorption column and to a lesser degree plasma exchange can dramatically, although transiently, reduce protein excretion in patients with recurrent FSGS in the transplant[13]. The factor removed, which is not an immunoglobulin, increased protein excretion when injected into rats.

Both studies suggest that the circulating factor is a non-immunoglobulin with a molecular weight of approximately 50 Kilodaltons[12,13]. However, the nephrotoxin has not yet been identified.

Treatment with plasma exchange can lead to complete remission of proteinuria and relapsing patients may respond to repeated sessions. Best results are obtained when plasma exchange is started early with the onset of proteinuria and when there are no visible lesions on light-microscopy[14].

Though FSGS morphologically is uniform, pathologically and etiologically the disorder may be divergent. It is now being currently accepted that FSGS is possibly not a homogenous entity. It has increasingly been recognized to occur in a familial pattern. Reports document the development of biopsy-confirmed FSGS and subsequent ESRD in live related kidney donors, who were proved to have family members with ESRD secondary to FSGS. These kidney donors were apparently healthy by routine physical examination, urine analysis, and serum creatinine at the time of evaluation[15].

Some patients develop proteinuria and FSGS in the transplant even though they did not have primary FSGS in their native kidneys. This form of FSGS, occurring for the first time has a different pathogenesis from recurrent disease[16]. Occurring first time FSGS in renal allografts most often is diagnosed in association with chronic allograft nephropathy, it presents late after transplantation and in association with arterial hyalinosis, suggesting that these lesions may be related to chronic cyclosporin toxicity[17]. The onset of proteinuria is delayed and more indolent, generally occurring 3 months or more after transplantation[18,19].

In the present case, nephrotic syndrome ending in early ESRD in a three years period is prognostically related to poor outcome. Further, the renal biopsy carried out 4 weeks

following transplantation showed subintimal basophilic degeneration in medium size blood vessels indicating hypertension which is an important factor underlying early deterioration of graft function. For long time survival of graft, compliance to immunosuppression along with control of hypertension are considered important.

CONCLUSION

This case illustrates recurrence of FSGS in an adult female. It is recommended with rapid deterioration in renal function that living-related donor transplantation should generally be avoided in patients at high risk for recurrence, those with rapid progression of the primary disease and those with recurrence in a prior allograft. Use of cadaver kidney, on the other hand, is not precluded.

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