Renal transplantation; Membranous nephropathy

AN EARLY CASE OF DE NOVO MEMBRANOUS NEPHROPATHY ON A RENAL TRANSPLANT PATIENT

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INTRODUCTION

Second to chronic allograft dysfunction, membranous nephropathy (MN) is the most frequent cause of nephrotic syndrome in renal transplantation (1). This pathology can be caused by recurrence of the primary renal disease, the development of de novo glomerulopathy or by a transplanted glomerular disease (present but unrecognized in the donor) (2). De novo MN was first described more than 25 years ago (3) and is the most common de novo disease after engraftment. It has an incidence of 2-9% in most series, with the highest rates being reported by centres who perform routine graft biopsies (2, 4). De novo disease tends to present later than the recurrent forms, and typically occurs two years post-transplantation, although cases have been described at four months (2).

CASE REPORT

Emergency haemodialysis was started on an 18 year old female Caucasian (HLA A 22, 28; B 8, 18; DR 3, 5) who presented with severe uremia. There was no past history of disease, namely she denied oedema, frothy urine, hypertension or other urinary symptoms. Biopsy was not performed due to small regular kidneys.

Aged 21 she received a cadaveric renal allograft from a CMV IgG positive donor. The CMV status of the patient was unavailable at this stage. The back-table donor biopsy showed a normal kidney with mild intersticial oedema and occasional atrophic tubules. Immunossupression was started and consisted of cyclosporine A, azathioprine and prednisone. There was immediate function, with serum creatinine of 1,8 mg/dl on the 2nd day, which dropped to 1.3 mg/dl at discharge on day 15.

One month post-transplant, a rise in serum creatinine to 3,9 mg/dl led to a graft biopsy being performed, which showed a mild acute cellular rejection. Treatment with methylprednisolone 500 mg x 3 was attended by return to previous

creatinine value of 1,4 mg/dl. At this time, CMV immediate early antigen (IEA) became positive. She was treated with anti-CMV hyperimmune globulin and gancyclovir. Despite this, CMV antigenemia (positive IEA) was present until month 5. At this time, a positive dipstick for protein led to a 24-hour collection being performed, which showed 3.6 g of proteinuria to be present. Although serum creatinine remained stable at 1.0 mg/dl, a second biopsy was performed and showed MN of the graft. Immunoperoxidase staining with monoclonal serum for CMV was negative. After review of month one biopsy with adequate staining it was thought that thickening of the basal membranes was already present, alongside acute rejection.

At month 8 serum creatinine is 0.8 mg/dl, proteinuria is absent and the patient is oedema free. The most frequent causes of secondary MN have been excluded (drug-induced, tumour-associated, auto-immune, infection-related).

Four weeks after the first positive IEA result, the patient was CMV IgM negative and IgG positive. Ten weeks later she became IgM positive and IgG positive. These findings were present after twelve more weeks.

COMMENTS

MN of the graft was found one month post-transplantation. Although histological examination of the patient's native kidneys was not possible, gender, age, and absence of a history of nephrotic syndrome or hypertension, make primary membranous nephropathy very unlikely as the primary renal disease. We therefore assume de novo disease to be present in the graft. The persistence (3.5 months) of CMV antigenemia makes a causal relationship likely, despite the immunoperoxidase findings.

The patient´s B18 and DR3 haplotypes have been associated with a very high risk for the occurrence of primary MN (5). In fact, there may be a relative risk of 12

for developing MN if DR3 is inherited (6). We suggest that the risk conferred may apply to development of de novo disease in a renal graft.

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