Nephrotic syndrome in a bone marrow transplant recipient after cyclosporine withdrawal

Sir,

Chronic graft-versus-host disease (GVHD) is one of the most frequent complications after bone marrow transplantation. Nephrotoxicity related to the use of cyclosporine (CsA) is common, but nephrotic syndrome has been reported rarely. Membranous glomerulonephritis has been found in the majority of patients [1–6], and in one case minimal change nephrotic syndrome was reported [7]. All these cases had chronic GVHD.

We describe a patient with nephrotic syndrome developing after CsA withdrawal, who failed to improve with prednisone but achieved remission on CyA.

A 59-year-old male was diagnosed with severe aplastic anaemia. He received an allogenic transplant from his HLA-identical brother. Cyclophosphamide and total lymphoid irradiation were used as conditioning, and a short-term methotrexate plus CyA as GVHD prophylactic treatment was given for 1 year. CsA was tapered and withdrawn after 14 months. One month later, he presented with nephrotic syndrome with 24 h urine protein of 5 g, serum albumin of 2.2 g, normal renal function (serum creatinine 0.8 mg/dl and creatinine clearance 120 ml/min). Hepatic enzymes increased and skin lesions consistent with GVHD appeared. Search for antinuclear antibodies, serology for hepatitis B and C and VIH was negative. A percutaneous renal biopsy revealed 10 glomeruli. Seven were optically normal, one sclerosed and two had slight ischaemic changes and a small sclerosed lesion coincidental with an area of interstitial fibrosis and inflammation. The rest of the glomeruli were optically normal. Direct immunofluorescence staining was negative for IgG, IgA, IgM, C3, C4, Clq and fibrinogen antibody. Electronic microscopy showed small homogeneous subepithelial electron-dense deposits without reaction of the basement membrane. These findings are characteristic of the diagnosis of early membranous nephropathy. The patient started with prednisone (60 mg), but 1 month later 24-h urine protein was 11 g and serum albumin 1.9 g/dl. He was then treated with CsA (4 mg/kg/day) and 20 mg prednisone. Four months later he had no clinical or laboratory features of GVHD or nephrotic syndrome. Prednisone was withdrawn and CsA tapered to 2 mg/kg/day during 12 months and to 1 mg/kg during 6 months. Currently he has a 24-h urine protein excretion of 600 mg, no clinical or laboratory features of GVHD and normal hepatic enzymes and renal function.

Our case underlines the importance of having optical and electronic microscopy to achieve a correct diagnosis and shows the occurrence of nephrotic syndrome immediately after CsA withdrawal reported with a good response to CsA re-introduction. Previous cases have been described in two patients who never received CsA [1], one during tapering [3] and four after discontinuation [2,6,7]. In one case, with improvement but not remission, a second biopsy [6] showed segmental sclerosis and again membranous nephropathy. Although autoantibodies were not present in most cases described in the literature, circulating or in situ immune complexes are responsible for membranous glomerulonephritis. However, cellular mechanisms may be implicated as sclerosis is also seen. Immunosuppression can easily control these manifestations. Our case report underlines the importance of CyA reintroduction in order to control GVHD-associated membranous nephropathy.

Conflict of interest statement. None declared.


DOI: 10.1093/ndt/gfg415

DOI: 10.1093/ndt/gfg389