Membranous Nephropathy after Bone Marrow Transplantation in Ciclosporin Treatment

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Dear Sir,

We report here the occurrence of membranous nephropathy (MN) in a 20-year-old patient with severe aplastic anaemia during treatment with cyclosporin (CS-A) after bone marrow grafting from his HLA-identical brother. Conditioning therapy was performed on days -5 to -2 before bone marrow transplantation (BMT) using cyclophosphamide 50 mg/b.w./day. To prevent graft-versus-host disease (GvHD), CS-A was given from day -1 on as usual [1]. As infectious disease prophylaxis he received trimethoprim and sulfamethoxazole, as well as anti-CMV hyperimmunoglobulin, acyclovir and amphotericin B, as described in detail earlier [1]. Four weeks after BMT, a trilinear take was documented. Skin GvHD grade I appeared 10 days after BMT and was successfully treated with prednisolone 1 mg/b.w./day.

Seven months after BMT, proteinuria was detected for the first time and the patient developed a nephrotic syndrome (maximal proteinuria of 30 g/day). Histological, immunohistological as well as electron microscopical analysis of a renal biopsy revealed MN stage I [2]. Furthermore, signs of CS-A toxicity in proximal tubular epithelial cells were observed. In addition, interstitial cellular infiltrates characterized by specific monoclonal

1 Supported by the Deutsche Forschungsgemeinschaft DFG, Mu 523/3-2 and SFB 120. antibodies were shown to consist mainly of CD4 + /CD8 + T lymphocytes with a CD8 + /CD4 + ratio of 1.9, as well as of a large number of monocytes/macrophages. Expression of different MHC class II products on renal epithelial cells and on vessels did not differ from those of the normal kidney. At the time of renal biopsy, cholestatic enzymes were elevated; anti-nuclear and anti-IgM antibodies against rubella, but no anti-DNA antibodies were found in the patient's serum.

Since CS-A toxicity had been documented by renal biopsy, CS-A therapy was stopped and MN was treated with chlorambucil and prednisolone [3]. During three therapeutic cycles, proteinuria declined rapidly to 2.5-5.0 g/day. At the end of the third cycle the patient presented with a relapse of proteinuria (9.0 g/day). The therapeutic regimen was changed to CS-A and low-

dose prednisolone leading to a residual proteinuria of 2.0 g/ day, which has now been stable for more than 1 year. Currently the patient is in excellent condition.

In this patient, MN could have occurred de novo or in association with GvHD after BMT. The presence of interstitial cellular infiltrates, especially of CD8+ T lymphocytes (not detected in MN [pers. observation]), indicated GvHD-mediated renal lesions. However, MHC class II antigen expression on proximal tubular epithelial cells as another sign of GvHD was lacking. As known from experiments in mice [4], treatment with CS-A might have hindered the induction of MHC class II antigen expression on renal tubular cells of this patient. Although CS-A is used to treat MN [5], this drug did not prevent our patient from contracting MN.

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