Renal protection in immunoglobulin-A nephropathy

Sir,

I applaud the timely reminder by Nagy et al. [1] that good control of hypertension can do much to ameliorate the course of immunoglobulin-A nephropathy. There are some good antiproliferative agents coming along. Only I wish to point out that we have forgotten [2] the potential of anti-thromboxanes [3], which will surely be synergistic to angiotensin-converting enzyme or angiotensin-receptor blocker inhibitors. After all, thromboxane A2 partly mediates the action of angiotensin II [4].

Conflict of interest statement. None declared.

London, UK Edwin N. Wardle
Email: nigel@edwinwardle.freeserve.co.uk


doi:10.1093/ndt/gfi260

Crescentic transformation of membranous glomerulopathy: a reversible condition

Sir,

Crescentic transformation of membranous nephropathy (MN) has been described previously [1–4], but only one reported case has responded to treatment (intravenous methylprednisolone) [4]. We report a patient with stable MN who developed an acute crescentic glomerulonephritis (CGN), associated with a rapidly deteriorating renal function, which responded well to oral prednisolone and cyclophosphamide.

A 59-year-old male presented to this unit in January 2000 with nephrotic syndrome and a normal serum creatinine (85 μmol/l). A full autoimmune screen was negative, including anti-glomerular basement membrane (anti-GBM) antibodies. A native renal biopsy was performed and was reported as being normal on light microscopy; however, electron microscopy subsequently revealed changes consistent with early MN (Figure 1). The patient was commenced on oral prednisolone (60 mg od). Response to the steroid therapy was minimal and after 4 months it was tailed off.

In July 2001, the patient developed a worsening in his symptoms and serum creatinine had risen to 407 μmol/l. A full autoimmune screen was, again, negative. Renal vein thrombosis was excluded by venography.

A second percutaneous renal biopsy was performed and was reported to show the morphological and immunological features of membranous glomerulonephritis with crescentic transformation (Figure 2). Electron microscopy again confirmed the presence of background changes consistent with MN (Figure 3). Prednisolone was therefore restarted (60 mg od) and, in addition, the patient was commenced on oral cyclophosphamide (200 mg od).

On review after 3 weeks of treatment, renal function had improved significantly with creatinine down to 192 μmol/l. At this stage the dose of cyclophosphamide was reduced (50 mg od) and the steroids were also gradually reduced down to a maintenance dose of 10 mg od. Cyclophosphamide was stopped in April 2002. The patient currently remains well on a low maintenance dose of prednisolone (5 mg alternate days).

The mechanism of conversion of MN to CGN is unknown. Some case reports have noted an association with the presence of anti-GBM antibodies [1,2] that may or may not play a role in the pathogenesis. In this case, anti-GBM antibodies were not detected.

Previous theories on the patho-physiology of both MN and anti-GBM-mediated CGN, based on experimental evidence

Fig. 1. Electron micrograph of the first renal biopsy (2000) showing subepithelial deposits consistent with early membranous nephropathy (magnification: x14 400).
from animal models, have suggested a common mechanism, with the development of antibodies to fixed antigens in the glomerulus thought to be central [5]. These antibodies form in situ antigen–antibody complexes (Ag–Ab), leading to activation of complement and resulting in damage to the integrity of the GBM. The histopathological and clinical differences between the two diseases have been explained by such factors as differences in kinetics of antibody deposition, the role of complement and neutrophils and subsequent changes in the glomerular filtration barrier [5].

The development of glomerular crescents requires disruption of the GBM integrity sufficient to allow the efflux of cells and macromolecules into Bowman’s space [6].

More recent work has called these older theories into question, with emerging evidence that MN may be due to circulating rather than in situ Ag–Ab complexes, involving immunoglobulin subclass IgG4 [7]. It therefore remains unclear at present whether transformation of MN to CGN represents an increase in severity of a common underlying pathology or the development of a second separate process.

In summary, given the previous case described [4] and the case we present here, conversion of MN to CGN should be considered a potentially reversible condition with appropriate immunosuppression therapy. Further research is required to clarify optimum treatment regimes.

Conflict of interest statement. None declared.


doi:10.1093/ndt/gfi259

Advance Access publication 6 December 2005

Altered expression of nuclear factor-κB in peripheral blood mononuclear cells in chronic haemodialysis patients

Sir,
Uraemia is associated with a pro-inflammatory and pro-oxidant state that may contribute to a heightened risk of atherosclerosis and malnutrition [1]. The activation of the oxidant-sensitive nuclear factor (NF)-κB transcription factor family is one of the major pathways resulting in inflammation [2]. We hypothesized that, in haemodialysis (HD) patients, NF-κB activation in peripheral mononuclear cells (PBMCs)