Proliferative Endo- and Extracapillary Glomerulonephritis and Benign Monoclonal IGM Gammopathy

J.		Lima ^a
M.		Monteagudo ^a
M.		Valles ^b
F.		Garcia-Bragado ^a
M.		Carrera ^c
M.		Vilardell ^a

Services of ^aInternal Medicine and ^bNephrology, Hospital General 'Valle Hebron', and ^cService of Pathology, Hospital 'Principes de España, Barcelona, Spain

J. Lima, Service of Internal Medicine, Hospital General "Valle Hebron", Paseo Valle Hebron S/N, E-08035 Barcelona (Spain)

Dear Sir,

Renal involvement in benign monoclonal gammopathy (BMG) is rare [1]. Although the histological findings in renal biopsies are very varied, we found only 1 case of BMG and glomerulonephritis (GN) with endo- and extracapillary proliferation [2]. We studied a patient with IgM BMG and GN, in whom endo- and extracapillary proliferation was revealed by renal biopsy. Renal function improvement with immunosuppressive treatment is stressed.

A 76-year-old man was admitted because of bilateral leg edema of 2 months duration. He had no previous medical history. Physical examination showed no particular abnormalities except for malleolar swelling. Blood analysis revealed an erythrocyte sedimentation rate of 118 mm/h, hemoglobin 7.44 mmol/l (12 g/l), serum creatinine 225.4 $\mu\text{mol/l}$ (2.55 mg/dl), serum total protein 61.6 g/l and albumin 0.43 mmol/l (2.8 g/dl). Serum immunoelectrophoresis showed a monoclonal IgM κ spike. Serum IgM levels were 30 g/l (3,000 mg/dl), while the other immunoglobulin values remained normal. Leukocyte and platelet counts, results of liver function, antinuclear antibody, rheumatic factor, cryoglobulins, hepatitis B surface antigen and complement were all normal or negative. Urinalysis revealed 80 red blood cells/high-power field and 6 g proteinuria in a 24-hour urine collection. Urine immunoelectrophoresis detected a small homogeneous IgM κ spike; no free light chains were detected. Skeletal survey and studies for occult neoplasia were negative. Bone marrow biopsy revealed 5% mature plasma cells.

Percutaneous kidney biopsy yielded 20 glomeruli. Optic microscopy demonstrated segmentary mesangial proliferation with subendothelial deposits; 40% of glomeruli had crescents (fig. 1); 8 glomeruli showed diffuse sclerosis. There was moderate interstitial fibrosis with slight round cell infiltration. Immunofluorescence showed marked segmentary granular capillary and scanty mesangial deposits of IgM (fig. 2). Anti-IgG, anti-IgA and anti-C3 were absent. Stains for amyloid were negative. Serum creatinine level rose to 397.8 $\mu\text{mol/l}$.

Fig. 1. Segmental hypercellularity with epithelial reaction and sinechiae. Interstitial fibroedema with tubular basement membrane sclerosis. Periodic acid-Schiff. $\times 200$.

> ; “ ,
f * *

Fig. 2. Segmentary parietal deposits. Anti-IgM. x 500.

458

Lima/Monteagudo/Valles/Garcia-Bragado/Carrera/Villarde

(4.5 mg/dl). Treatment with 6-methylprednisolone, 1 mg/kg/day, and chlorambucil, 0.150 mg/kg/day, was initiated. After 12 months treatment, serum creatinine values remain stable at 176.8 $\mu\text{mol/l}$ (2 mg/dl) and 24-hour urine protein less than 1 g. Serum monoclonal gammopathy has decreased to 17 g/l and has disappeared in urine. There is no evidence of an infectious, solid or hematologic proliferative process.

Excluding amyloidosis and mixed essential cryoglobulinemia as causes of glomerulopathy and BMG have been reported since 1971 [2–6]. Although all kinds of glomerular lesions have been described, proliferative GN is the most common change. Several hypotheses attempt to explain the relationship between BMG and GN [7], but this remains unknown. Avasthi et al. [5] failed to prove that in vitro paraprotein has antibody activity against glomerular components. In malignant monoclonal gammopathy, Meiner et al. [8] postulated that the monoclonal component plays a major role in the glomerular change, triggering a leukocyte- or macrophage-mediated inflammatory reaction. This reaction produces severe lesions in the basal membrane which in turn allow fibrin to reach the Bowman space, leading to epithelial proliferation. Renal studies by immunofluorescence, together with the presence of IgM in serum, establish a highly probable close pathogenic relationship between the monoclonal gammopathy and the glomerular lesion. In patients affected by malignant monoclonal gammopathy, renal function improved with immunosuppressive therapy [8]. In contrast, most patients with BMG and GN suffer progressive loss of renal function leading to a stage of renal failure despite immunosuppressive therapy. However, in our patient the nephrotic syndrome disappeared with corticosteroid and immunosuppressive therapy, and renal function remains stable. A further interesting factor is the finding of an IgM paraprotein in urine. This protein is not filtrable, and its presence in urine is very uncommon [9]. We attribute the presence of IgM-k in urine to a severe capillary alteration which improved with treatment.

This case suggests that, when BMG is associated with proliferative glomerular nephropathy in close relationship with the monoclonal spike, immunosuppressive treatment could be considered.

References

- Kyle RA: Monoclonal gammopathy of undetermined significance. *Am J Med* 1978;64:814–826.
- Kebler R, Kithier K, McDonald FD, Cadnapaphornchai P: Rapidly progressive glomerulonephritis and monoclonal gammopathy. *Am J Med* 1985;78:133–138.
- Verroust P, Mery JP, Morel-Maroger L, Clauvel JP, Richet G: Glomerular lesions in monoclonal gammopathies and mixed essential cryoglobulinemias IgG-IgM. *Adv Nephrol* 1971; 1: 161–194.
- Jensen H, Wick A: Monoclonal immunoglobulinemia associated with glomerulopathy. *Acta Med Scand* 1975; 197: 265–269.
- Avasthi PS, Erickson DG, Williams RC, Tung KSK: Benign monoclonal gammaglobulinemia and glomerulonephritis. *Am J Med* 1977;62:324–329.
- Mallick NP, Dosa S, Acheson EJ, et al: Detection, significance and treatment of paraprotein presenting with 'idiopathic' proteinuria without myeloma. *Q J Med* 1978; 196:145–175.
- Beaufils M, Morel-Maroger L: Pathogenesis of renal disease in monoclonal gammopathy: current concepts. *Nephron* 1978; 20:125–131.
- Meyrier A, Simon P, Mignon F, Striker L, Ramee MP: Rapidly progressive (crescentic) glomerulonephritis and monoclonal gammopathies. *Nephron* 1984;38:156–162.

Crossman ME, Bia MJ, Goldwein MI, Hill G, Goldberg M: Giant kidneys in Waldenström's macroglobulinemia. Arch Intern Med 1977;137:1613–1615.