Letters

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Lobular membranoproliferative glomerulonephritis with organized microtubular monoclonal immunoglobulin deposits associated with B cell small lymphocytic lymphoma

Sir,

Fibrillar glomerulonephritis (FGN) and immunotactoid glomerulopathy (ITG) are well known glomerular diseases with Congo-red-negative deposits [1–4]. While FGN is characterized by randomly arranged microfibrils around 20 nm in diameter with no underlying systemic disorder, ITG is defined by orderly arranged microtubular deposits, usually >30 nm in diameter with a hollow core; patients with ITG tend to have underlying lymphoproliferative diseases.

Microtubular monoclonal immunoglobulin deposits with a diameter smaller than that commonly observed in ITG have been described in a few patients with lymphoproliferative disorders, and Touchard et al. coined the term ‘GOMMID’

for such glomerulonephritis with organized microtubular monoclonal immunoglobulin deposits [5,6]. We report here a patient with nephrotic syndrome due to GOMMID following B-cell malignant lymphoma associated with IgG-κ monoclonal gammopathy. Interestingly, although the patient developed AL amyloid deposition (κ type) in a cervical lymph node, no amyloid was recognized in the kidney.

Case. A 46-year-old Japanese man presented with lymph node swelling and IgG-κ monoclonal gammopathy. The lymph node biopsy revealed small lymphocytic lymphoma cell infiltration with amyloid deposition in the vessel walls and interstitium. The lymphoma cells were positive for CD5, CD20 and CD23, and κ light chains were detected in the cytoplasm of plasma cell-differentiated lymphoma cells. Amyloid deposits were also positive for κ light chains. He developed nephrotic syndrome 5 months later from the lymph node biopsy. Serum immunoglobulin concentrations at renal biopsy were as follows: IgG was 1410 mg/dl, IgA was 93 mg/dl and IgM was 51 mg/dl. Although serum cryoglobulin was weakly positive, its type was not determined due to insufficient concentration. Renal biopsy was performed and light microscopic studies revealed membranoproliferative glomerulonephritis with lobular accentuation (Figure 1a). Congo red staining was negative in the renal biopsy specimens. Immunofluorescence microscopic studies demonstrated positive staining for IgG, C3 and κ light chain in the mesangium and glomerular capillaries, and IgG1 was dominantly positive among the IgG subclasses. Electron microscopy showed expanded mesangial areas containing orderly arranged microtubular deposits with an average external diameter of 15 nm (Figure 1b).

Discussion. GOMMID was proposed to include the following criteria: (i) the presence of organized microtubular deposits (15 nm in width) in glomeruli without thrombi in the glomerular capillaries and/or renal arterioles; and (ii) monotypic immunoglobulin deposits, irrespective of the presence of detectable monoclonal immunoglobulin in patient serum and/or urine, type I cryoglobulinaemia or immunoproliferative disorder [5]. Our case satisfies these criteria and features both pathological and clinical aspects of GOMMID.

The relationship between malignant lymphoma and GOMMID is not fully understood. Touchard et al. [5] showed that leukaemia/lymphoma cells were the major source of glomerular immunoglobulin deposits from immunofluorescence and electron microscopic studies. In the present case, although we failed to observe lymphoma cells with electron microscopy, their role was strongly suggested by the correspondence of the isotype of monotypic immunoglobulin deposited in the glomeruli with that of the serum paraprotein. On the other hand, the different patterns of Congo red staining, positive in the lymph node and negative in the glomeruli, were remarkable in this case. It would be suggested that each immunoglobulin deposition was related to the production of amyloid- or non-amyloid-forming κ light chains derived from different plasma cell clones. Diversity of the tissue microenvironment might also explain such different patterns of immunoglobulin deposition [7].

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1Department of Second Internal Medicine Kei Matsushita1
2Department of Pathology Kiyotaka Nagahama2

Yoshiaki Inayama2

Fig. 1. Pathological findings of renal biopsy specimens. (a) Light microscopy. A glomerulus showing membranoproliferative glomerulonephritis with lobular accentuation. Periodic acid–Schiff, original magnification ×400. (b) Electron microscopic examination. Marked mesangial widening is noted with microtubular deposits (original magnification ×10,000). Inset: high power view of microtubular deposits in the mesangial area. Bar=100 nm (original magnification ×30,000).
Sir,

We read with interest the report by Ferraro et al. [1] on the effectiveness of rituximab in refractory Wegener’s granulomatosis (WG). We report a case of relapsing WG with remission under rituximab, whereas cyclophosphamide was contra-indicated.

WG was diagnosed in February 2002 in a 57-year-old hypertensive patient with fatigue, renal failure (creatinine 334 μmol/l), haematuria and serum PR3-ANCA at a titre of 1090 U/ml (positive >20). Renal biopsy disclosed nephroangiosclerosis and necrotizing glomerulonephritis. High dose corticosteroids and 12 cyclophosphamide pulses resulted in remission, but renal insufficiency led to dialysis. Maintenance therapy with azathioprine was given from August 2002 to July 2003. In February 2004, relapse occurred with fatigue and haemoptysis related to alveolar haemorrhage, with positive PR3-ANCA at a titre of 200 U/ml. Corticosteroids and a first cyclophosphamide pulse were administered but stopped because platelet count fell at 74,000/mm³. The alkaline phosphatase level was 334 UI/l (normal <100). Portal hypertension was demonstrated with grade II oesophageal varices due to veno-occlusive disease associated with nodular regenerative hyperplasia of the liver, probably induced by azathioprine. The patient received four weekly administrations of 375 mg/m² of rituximab, inducing complete remission. Mycophenolate mofetil (1.0 g/d) was subsequently administered as maintenance therapy. No relapse has occurred to date.

This case highlights the interest of rituximab in WG, in the case of contra-indication of cyclophosphamide. A few case reports show that rituximab is effective in WG [1–3], but prospective studies are necessary in order to evaluate its indications, since rituximab seems favourable as compared to other drugs.

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