**Letters**

**Minimal-change nephrotic syndrome associated with mixed connective-tissue disease**

Sir,

Mixed connective-tissue disease (MCTD) is a rheumatological disorder which has combined features of systemic lupus erythematosus, systemic sclerosis (SSc), polymyositis/dermatomyositis, and rheumatoid arthritis (RA) with antibodies to U1 small nuclear ribonucleoprotein (U1snRNP). Although renal involvement was considered to be rare in the initial description [1], several studies demonstrated that renal disease was found in 10–50% of patients with MCTD [2,3]. However, to our knowledge, nephrotic syndrome due to minimal-change glomerulopathy has not been reported in patients with MCTD. Here we would like to report a MCTD patient who developed minimal-change nephrotic syndrome (MCNS).

**Case.** In November 1999, a previously healthy 31-year-old Japanese woman presented with fatigue, swollen fingers, and joint pain. Initial investigations showed: urinalysis, no proteinuria without haematuria; renal and liver function within the normal range; serum protein, 8.2 g/dl; albumin, 4.2 g/dl; blood cell count within the normal range; erythrocyte sedimentation rate, 13 mm/h; and C-reactive protein, 0.1 mg/dl. Antinuclear and anti-U1snRNP antibodies were positive, and anti-dsDNA, anti-Sm, anti-Jo-1, and anti-Scl-70 antibodies were negative. The patient was diagnosed as having MCTD on the basis of Raynaud’s phenomenon, swollen fingers, polyarthritits, sclerodactyly, muscle weakness, and positive anti-U1snRNP antibody. She was followed up in our out-patient clinic and was not given non-steroidal anti-inflammatory agents, steroids, or immunosuppressive drugs.

In February 2000, 3 months after her initial presentation, the patient noticed persistent oedema on the lower extremities, and was found to have heavy proteinuria. She was admitted to the Nephrology Unit of the Osaka Rosai Hospital on 9 February 2000. The physical examination revealed swollen fingers and hands with typical sclerodermatous skin changes, facial erythema, and pitting oedema on lower extremities. Her blood pressure was 90/60 mmHg, the pulse was 92 b.p.m., and temperature was 37.2°C. Laboratory evaluation showed haemoglobin, 15.5 g/dl; and a leukocyte count, 6100 mm3 with normal differentiation; thrombocytes $12.7 \times 10^9$ mm³; blood urea nitrogen, 15 mg/dl; serum creatinine, 0.7 mg/dl; normal Na and K concentrations; serum protein, 6.4 g/dl; serum albumin, 1.7 g/dl; total cholesterol 223 mg/dl; aspartate aminotransferase, 53 IU/l; alanine aminotransferase, 42 IU/l; lactate dehydrogenase,
many patients with MCTD satisfy the diagnostic criteria of other connective-tissue diseases and that the clinical features of MCTD patients shift to proper features of SSc or RA during their clinical course. Our case fulfilled all three sets of criteria for MCTD, which were proposed by the International Symposium on Mixed Connective Tissue Disease and Anti-nuclear Antibodies [5]. In addition, severe pulmonary hypertension, a common cause of death in MCTD, was recognized in our patient. In conclusion, this case represents the first patient to our knowledge with MCNS associated with MCTD.

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Fig. 1. A glomerulus showing lack of increased cellularity and the normal capillary walls (periodic acid-silver magnification, × 100).

506 IU); and creatine kinase 207 IU). The level of serum IgG was elevated to 4062 mg, IgA was 300 mg, and IgM was 269 mg/100 ml. Complement, cryoglobulin, and anti-neutrophil cytoplasmic autoantibodies were normal. Urinalysis showed heavy (4+) proteinuria with trace haematuria. Twenty-four-hour urinary protein excretion rate was 12 g/day, and creatinine clearance was 84 ml/min. Urine cultures for bacteria and mycobacteria were negative. The chest X ray showed no evidence of pleural effusion on cardiomegaly. The electrocardiogram showed right axis shift and P-pulmonale. Doppler cardiac ultrasonography revealed tricuspid regurgitation with pulmonary hypertension. Mean pulmonary artery pressure and pulmonary capillary wedge pressure, measured by a Swan–Ganz catheter, were 42 and 20 mmHg respectively. Histological examination of a percutaneous renal biopsy revealed 32 glomeruli without light-microscopic aberrations (Figure 1). In an immunofluorescence study, no significant deposits of immunoglobulins or complement were found. Electron-microscopic examination showed effacement of foot processes of epithelial cells without electron-dense deposits along capillary walls. These findings were compatible with a diagnosis of MCNS.

The patient was treated with one cycle of steroid pulse therapy, which consisted of 3 consecutive days of 1000 mg methylprednisolone, and thereafter with 60 mg/day of prednisolone. She also received temocapril, beraprost, and warfarin because of pulmonary hypertension and severe Raynaud’s phenomenon. The proteinuria disappeared within 10 days and the general state was improved. One month later, her pulmonary artery pressure, estimated by Doppler cardiac ultrasonography, was decreased from 70 mmHg to 42 mmHg, and drugs were tapered. On 19 June she was discharged from our hospital. After discharge, her urinary protein excretion was consistently below 0.1 g/day and her renal function remained normal.

Comment. MCTD is principally treated with steroids and non-steroidal anti-inflammatory agents. It is widely recognized that the use of the latter may be complicated in MCNS. In our case, proteinuria developed without drugs and disappeared immediately after treatment with steroids. Kitridou et al. [2] reported proteinuria (>0.5 g/day) in 11 of 30 patients with MCTD, and nine of them developed nephrotic syndrome. However, patients with MCTD usually showed a form of membranous glomerulonephritis when they developed nephrotic syndrome [4]. It is well known that