Chance Finding of Proteinuria Leads to the Diagnosis of ANCA Associated Vasculitis

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Abstract: Microscopic polyangiitis (MPA) was recognised with a high early mortality rate and the renal involvement was characterised by segmental necrotizing glomerulonephritis with high positivity of antineutrophil cytoplasmic antibody (ANCA) and a broad spectrum of signs and symptoms including fever and malaise. We reported here a woman with ANCA associated with MPA diagnosed by a chance finding of proteinuria. To the best of our knowledge, early diagnosis of this disorder only by the presence of proteinuria has not been reported previously in the English literature.

INTRODUCTION

Microscopic polyangiitis (MPA) was recognised with a high early mortality rate and the renal involvement characterised by segmental necrotising glomerulonephritis and MPA is now defined as a systemic necrotizing vasculitis that affects small-sized vessels with high positivity of antineutrophil cytoplasmic antibody (ANCA) [1]. Patients with ANCA-associated MPA can present a broad spectrum of signs and symptoms including fever and malaise. We reported here a woman with ANCA associated with MPA, diagnosed by a chance finding of proteinuria. To the best of our knowledge, early diagnosis of this disorder only by the presence of proteinuria has not been reported previously in the English literature.

A 62-yr-old Japanese woman was admitted to one of our affiliated hospitals on November 1, 2004 for the regular health check-up with no symptoms. Her past medical history was unremarkable and the regular health check-up performed one year ago showed no findings including urinalysis without proteinuria. On physical examination, the patient had no remarkable physical signs with the following vital signs: blood pressure 124/70 mm Hg, regular pulse 78/min, temperature 36.5°C, and respiratory rate 20/min. The lungs were clear, the cardiac examination was normal, and there was no peripheral edema. The abdomen was nontender; hepatosplenomegaly was not present. The neurologic examination was unremarkable. The laboratory test results were: haemoglobin 12.4 g/dl, haematocrit 37%, white blood cell count 6,500/μl with 69% neutrophils, 25% lymphocytes, 3% monocytes and 3% eosinophils, platelet count 225,000/μl, sedimentation rate 12 mm/h, fasting blood sugar 89 mg/dl, blood urea nitrogen 23.3 mg/dl, creatinine 0.9 mg/dl, sodium 135 mmol/l, and potassium 4.5 mmol/l. Blood transaminases were within normal range. Urinalysis showed protein (2+) and no glucose. Urine microscopy was significant for 20-30 red blood cells/high power field 10-20 white blood cells/high power field, and 5-6 squamous epithelial cells/high power field. As she had no proteinuria by the regular check-up last year, urinalysis was conducted and found proteinuria (2+) again. Thus, myeloperoxidase-anti-neutrophil cytoplasmic antibody (MPO-ANCA) titer was examined in her blood and found that MPO-ANCA was positive (162EU). Then, this patient was admitted to our hospital on December 13, 2004 for further investigation of ANCA associated MPA. Proteinuria was quantified as 279mg/24 h and Ccr 58 ml/minutes. Immunologic workup revealed serum complement levels (C3 and C4) within normal range, negative anti-nuclear antibody and normal anti-double-stranded DNA. MPO-ANCA was 172 EU. The serum creatinine level was 0.9 mg/dl, and the blood urea nitrogen was 20 mg/dl. Renal biopsy was performed and showed focal necrotizing crescentic glomerulonephritis, involving more than half of the glomeruli (Fig. **1**). There was a marginal interstitial infiltrate consisting of lymphocytes and neutrophils. Small vessels showed fibrotic thickness and marginal levels of transmural infiltration. Immunofluorescence revealed no deposition of IgG, IgM, IgA and C3 in glomeruli. The patient was diagnosed with MPA on the basis of crescentic necrotising glomerulonephritis and vasculitis on renal biopsy along with MPO-ANCA positivity. She was treated with methyl-prednisolone pulse therapy (1 mg/kg) followed by oral prednisolone 40 mg/day and cyclophophamide (50mg/day). No serious side effects of the treatment were observed, and 3-weeks after the treatment, her MPO-ANCA level was improved from 172 to 48 EU and urinalysis revealed no proteinuria. The patient has been followed for more than 3-years to date, corticosteroid was gradually tapered to 8mg/day and cyclophosphamide (25mg/day) was continued as maintenance therapy, and no indications of relapse such as proteinuria or elevation of serum creatinine and MPO-ANCA are apparent so far.

MPA is defined as necrotising vasculitis affecting small vessels (capillaries, venules, or arterioles) with few or no immune deposits (pauci-immune). Several characteristic fea-

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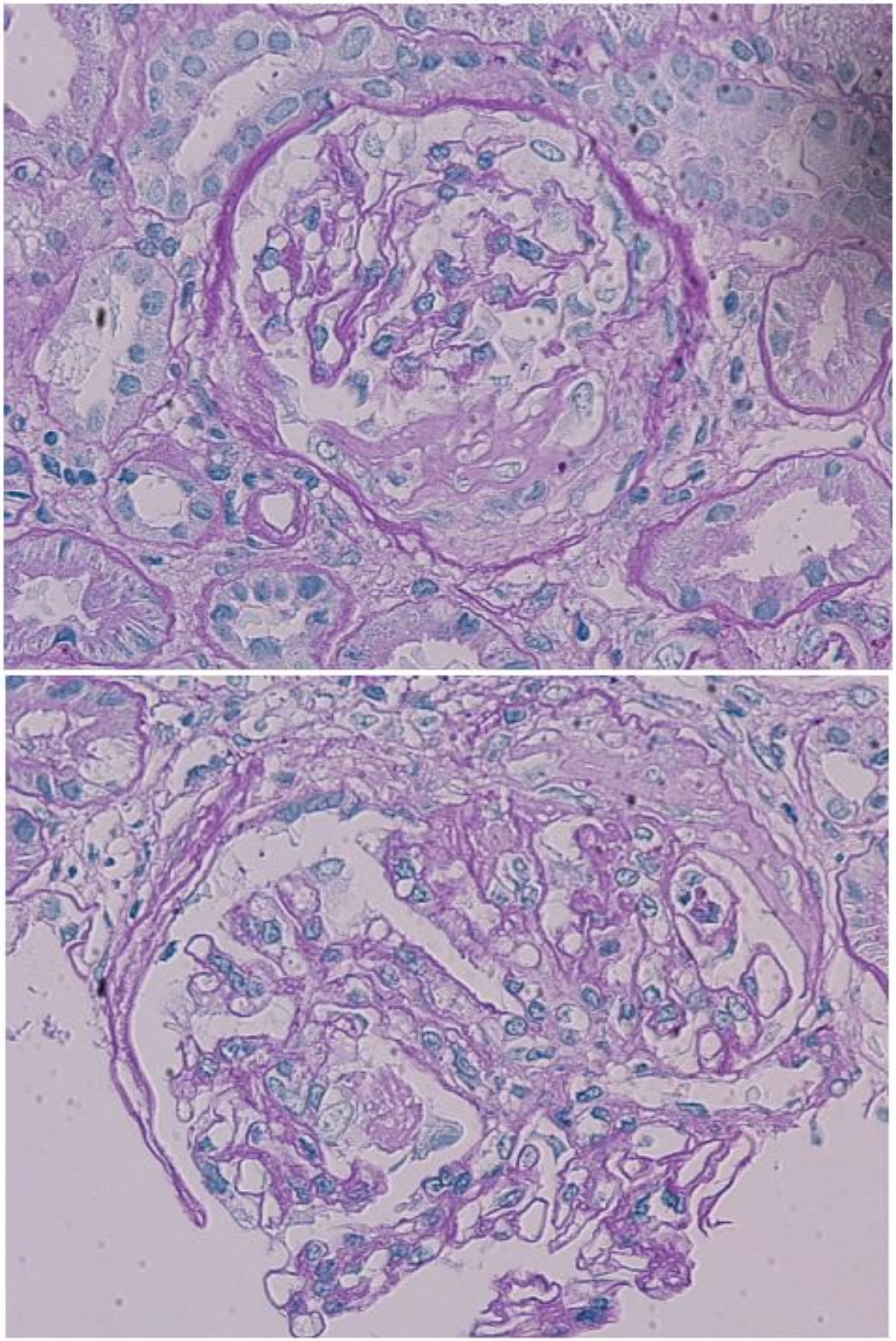

Fig. (1). Glomeruli contain crescentic cell proliferation. (Periodic acid Schiff stain; original magnification ×400).

tures of MPA include pauci-immune focal necrotizing crescentic glomerulonephritis, pulmonary capillaritis, and circulating MPO-ANCA, and it sometimes involves the cutaneous, musculoskeletal, gastrointestinal, and neurologic systems [2-4]. About 60% of microscopic polyangiitis patients have MPO-ANCA and 30% have proteinase 3 ANCA [4]. The prognosis of the disease can be improved, if the condition is recognised early and treated with corticosteroids and cytotoxic agents including cyclophosphamide, which induce remission in approximately 80% of patients. It has been reviewed that diagnosis of MPA is usually preceded by a prodromal phase of several months of constitutional symptoms, including polymyalgia [5].

In summary, the presented patient appeared with chance findings of proteinuria, as an initial clinical sign, indicative of vasculitis in small vessels. Early recognition and treatment of this disease may be important for preventing the development of life-threatening organ damage including end stage renal failure, thereby protecting quality of life and survival of patients with MPA. The presence of ANCA was associated with renal involvement and pulmonary haemorrhage, and to a lesser extent with vasculitis of the skin and mononeuritis multiplex [6]. Although rare, proteinuria may indicate the presence of MPA, hence early testing for ANCA may be warranted to exclude or support this possibility.

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