Letters to the Editor

Necrotizing crescentic glomerulonephritis with granulomatous vasculitis in a patient with familial Mediterranean fever and renal amyloidosis

Sirs,

Familial Mediterranean fever (FMF) is an autosomal recessive disease characterised by recurrent febrile inflammatory attacks of the serosal and synovial membranes (1). Secondary (AA) amyloidosis is the most common renal complication of FMF (2). Non-amyloid renal lesions have also been described. This is the first report of an FMF patient whose case was complicated by both secondary amyloidosis and necrotizing crescentic glomerulonephritis with granulomatous vasculitis.

The patient was a 51-year old woman who suffered from attacks of fever and abdominal and pleural pain since the age of 20. She was diagnosed with FMF at the age of 46, and placed on colchicine treatment. However, she did not take this treatment regularly. A sister and a brother also had FMF. She was admitted to our hospital because of painless macroscopic haematuria which had begun two weeks earlier. Her history was unremarkable with regard to drug use.

Her physical examination and laboratory studies were unremarkable except for ESR (75 mm/h) and CRP (17.7 mg/dL). In urinalysis, heavy proteinuria (6 g/24 h) was detected along with red blood cells, leukocytes and rare hyalen casts in the sediment. The glomerular filtration rate was 75 ml/min. The urine culture remained sterile for non-specific bacteria and mycobacteria. C3 and C4 levels were normal. Investigations for cryoglobulin and cryofibrinogen, HbsAg, anti-HCV, ANA and ANCA were negative. CT imaging of the thorax and paranasal sinuses were normal. Bilateral renal size and parenchymal echogenity were normal on ultrasound. Kidney biopsy revealed extensive glomerular sclerosis, abundant cellular crescent formation and



Fig. 1. A glomerule with partial crescent formation on the right and lymphocytic infiltration and a small granulomatous focus on the left.

evidence of granulomatous vasculitis (Fig. 1). Immunofluorescence studies were negative for immunoglobulins and complement components. Congo red stain was positive for amyloidosis which did not persist after potassium permanganate treatment; polarization microscopy revealed the typical green/yellow birefringence of amyloid.

She has been treated with colchicine 2 mg/day and azathioprine 100 mg/day for two years. In her recent follow-up examination, she was asymptomatic; serum creatinine was 0.8 mg/dl, urinalysis showed 1 to 2 red cells and 0.5 g/day protein excretion. Renal involvement is an important feature of FMF and the first identified renal lesion was secondary (AA type) amyloidosis which usually presents with permanent proteinuria without a nephritic urine sediment (1,2). Long-term colchicine treatment can prevent the development of secondary amyloidosis (2). In our patient, the delay in the diagnosis of FMF and poor drug compliance may have contributed to the development of amvloidosis.

Other renal lesions described in patients with FMF include mesangial proliferative glomerulonephritis, IgA nephropathy, IgM nephropathy, focal and diffuse proliferative glomerulonephritis, mesangiocapillary glomerulonephritis, membrano-proliferative glomerulonephritis and rapidly progressive glomerulonephritis (3-7).

Also, some of the non-amyloid glomerular lesions described in patients with FMF were associated with vasculitis (3, 5, 8). Some forms of vasculitic disorders are known to be associated with FMF; these include polyarteritis nodosa, Henoch-Schönlein purpura, protracted febrile myalgia and Behcet's disease (1, 3, 8).

Necrotizing crescentic glomerulonephritis with granulomatous vasculitis associated with FMF has not been described before. Although renal biopsy findings were strongly suggestive of Wegener's granulomatosis (WG), no other clinical, serological and radiological findings of WG or other systemic vasculitides were observed. Our patient showed a favourable response to moderate immunosuppressant treatment consisting of colchicine and azathioprine, and developed no other findings suggestive of extrarenal involvement of a systemic vasculitis during the two-year follow-up. We therefore consider that the renal findings of the present case, which mimick pauci-immune ANCA-related glomerulonephritis, may be a unique form within the spectrum of FMF-associated vasculitides.

The pathogenesis of non-amyloid glomerular diseases and vasculitis in FMF is still unknown. An immune complex mechanism may play an important role including type II rapidly progressive glomerulonephritis, IgM and IgA nephropathy (3, 4). But absence of immunoglobulins and complement in the biopsy specimens of our patient does not support this hypothesis. Another possible explanation is the entrapment of these substances as a result of mesangial dysfunction in clearing and processing of immunologically-irrelevant macro-molecular aggregates (7).

In conclusion, non-amyloid glomerular diseases should also be considered in the differential diagnosis of patients with FMF and renal involvement, especially when hematuria accompanies proteinuria. The contribution of vasculitis to the renal involvement in patients with FMF and its pathogenetic mechanisms remain to be elucidated.

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