Tubulointerstitial nephritis with anti-neutrophil cytoplasmic antibody following indomethacin treatment

Sir,

Tubulointerstitial diseases including tubulointerstitial nephritis (TIN) have an impact on overall renal function and eventual prognosis of renal diseases [1]. However, the detailed pathogenesis of human TIN has not been fully studied. Renal involvement in anti-neutrophil cytoplasmic antibody (ANCA)-associated diseases shows mainly glomerular lesion, especially necrotizing crescentic glomerulonephritis [2]. However, TIN with minor glomerular lesion in ANCA-associated diseases is rare. We herein describe a case showing TIN following indomethacin treatment and developed interstitial pneumonitis and pulmonary haemorrhage associated with high levels of myeloperoxidase (MPO)-ANCA.

Case. An 83-year-old man was admitted to Kanazawa University Hospital because of renal dysfunction in February 1998. He was suffering from ossification of the posterior longitudinal ligament and had been treated with indomethacin for 1 month (February 1998). Urine analysis showed proteinuria of 0.7 g/day and microscopic haematuria. The urine sediment showed clustering of leukocytes and cellular casts. Urine culture and cytology were negative. Haematological laboratory test results were haematocrit 29.1%, red blood cell count 3.19 × 10^6/ml, haemoglobin 9.6 g/dl and white blood cell count 16 900/ml. Serum blood urea nitrogen and creatinine (Cr) levels were increased from 53.3 mg/dl and 2.3 mg/dl to 75 mg/dl and 4.9 mg/dl, respectively within 1 month in spite of discontinuance of indomethacin (Figure 1). Urinary β₂-microglobulin and N-acetyl-β-D-glucosaminidase were elevated to 31 250 μg/l (normal; 5–253 μg/l) and 16 U/l (normal; 0.97–4.17 U/l), respectively. Serum C-reactive protein was 21.0 mg/dl (normal; 0–0.7 mg/dl) and erythrocyte sedimentation rate was 103 mm/h. Serum antinuclear antibody was negative and the complement fractions were normal. MPO-ANCA was elevated up to 117 EIA units (normal; <10 EIA units). Renal biopsy revealed that five out of six glomeruli showed minor abnormalities and that the other glomerulus was totally obsolescent. The interstitium was diffusely infiltrated by small round cells accompanied with few eosinophils. In addition, tubulitis was detected. Necrotizing arteritis was not detected in the interstitium. The immunofluorescence microscopic findings revealed no deposition of immunoglobulins or complements in the kidney. Methylprednisolone pulse therapy (1000 mg/day, 3 days) was administered twice accompanied by oral daily prednisolone (20 mg). These treatments led to the improvement of renal function and decrease of MPO-ANCA titres (Figure 1). However, 1 month after methylprednisolone pulse therapy, Cr was increased from 2.7 mg/dl to 6.1 mg/dl. Chest X-ray and computed tomography showed active interstitial pneumonitis and pulmonary haemorrhage in accordance with the exacerbation of MPO-ANCA titres.

In parallel with deteriorated renal function and lung lesions, MPO-ANCA had risen to 116 EIA units. Finally the patient died from sepsis.

Comment. We observed a case of TIN with ANCA following indomethacin treatment. The relation between the drug and TIN is tentative and the pathogenic role of ANCA in the genesis of the tubulointerstitial lesion requires further studies.

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