Antineutrophil Cytoplasmic Autoantibody-Positive Crescentic Glomerulonephritis Associated with Thiamazole Therapy

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Dear Sir,

Antineutrophil cytoplasmic autoantibodies (ANCA) have been described as serologic markers related with vasculitic disorders [1]. Dolman et al. [2] reported 6 patients with ANCA-positive vasculitis associated with propylthiouracil (PTU) therapy, and Vogt et al. [3] added 2 patients with ANCA-positive crescentic glomerulonephritis after the same treatment. Indeed, reports on ANCA-related syndrome associated with PTU treatment have been increasing in Japan also, but there has never been a report on cases of ANCA-related syndrome associated with thiamazole (MMI), another antithyroid drug, therapy. We describe ANCA-positive crescentic glomerulonephritis with pulmonary involvement in association with treatment with MMI.

In 1987, a 49-year-old man was diagnosed as having Graves' disease. He was given MMI 5-10 mg daily for 6 years and had been euthyroid since. In October 1993, when he was found to have slight hypofunction of thyroid, administration of MMI was discontinued. In January 1994, MMI (5 mg/day) was resumed because of relapse of hyperthyroidism. In order to perform the 'block and replace therapy', which is a combination therapy of MMI and thyroxine, the dose of MMI was increased to 30 mg/day in May 1994 and 2 months later, to 45 mg/day. Around that time, fever, cough and proximal myalgia of lower extremities developed. He was admitted to our hospital in August 1994. He had lost 3 kg in 6 months. On physical examination, he had fine crackles in bilateral lower lung fields. The chest radiograph and computed tomography (CT) scan showed interstitial shadows in the lower lobes on both

Fig. 1.

Fig. 1. Renal biopsy specimen showing fibrotic crescent formation and collapsed glomerular tufts. Periodic acid-Schiff stain. $\times 50$. detectable (398 EU and 116 EU respectively).

After withdrawal of MMI, myalgia disappeared but serum creatinine level rose to 2.7 mg/dl and protein excretion to about 1.0 g/day. After initiating prednisolone (PSL) 50 mg/day, he became afebrile and renal function began to improve. On hospital day 93, we performed a percutaneous renal biopsy. The specimen revealed crescentic glomerulonephritis (fig. 1). Immunofluorescence study was negative. After MMI therapy was discontinued, the patient was treated with radioiodine, and thyroid function became normal. When he was discharged. Serum albumin concentration was 2.5 g/dl. Blood urea nitrogen concentration was 12 mg/dl and serum creatinine level was 1.2 mg/dl. Urinalysis revealed microscopic hematuria (11-30 erythrocytes per high-power field) and protein excretion was 0.52 g/day. Creatinine clearance was 27.8 ml/min. The serum free-thyroxine (FT4) level was 1.02 ng/dl and TSH 0.062 µU/ml. Antinuclear antibodies were positive at a titer of 1:640. Antibodies to thyroid microsomes and thyroglobulins were detected at titer 1:240 and 1:2,400, respectively. ANCA with both p-ANCA (anti-MPO) and c-ANCA (anti-PR3) pattern were

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charged in December 1994, at PSL dose of 25 mg daily, serum creatinine level was 2.1 mg/dl and protein excretion was below 0.5 g/day. Interstitial pneumonitis showed improvement on CT scan, and both p-ANCA and c-ANCA turned negative.

This case suggests that MMI can induce ANCA-related pulmonary-renal syndrome. The exacerbation of the disease was in parallel with the increment of the dose of MMI.

Agranulocytosis associated with MMI is observed in patients taking more than 30 mg daily, while no such dose-related side effect is found in PTU therapy [4, 5]. Therefore, it is inferred that even MMI, when administered at a high dose, can give rise to the ANCA-related syndrome.

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Induced by Thiamazole Therapy