Recurrence of Anti-glomerular Basement Membrane Antibody Glomerulonephritis

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Recurrence of anti-glomerular basement membrane antibody glomerulonephritis seems to be an unusual clinical phenomenon. We report a 57-year-old man with recurrence of anti-glomerular basement membrane antibody glomerulonephritis. He developed a rapidly progressive glomerulonephritis with anti-glomerular basement membrane antibody (anti-GBM Ab), and recovered with a combined treatment of prednisolone, anticoagulant and antiplatelet agents. After a 2-year remission, hematuria and proteinuria followed by renal functional deterioration occurred without any obvious cause. The second renal biopsy revealed cellular crescents with linear IgG deposition along GBM, a finding similar to the first one. The aforementioned combined treatment resulted in a gradual recovery from proteinuria and renal functional derangement.

Key words: Melbourne cocktail treatment, Rapidly progressive glomerulonephritis

In most patients with crescentic anti-GBM Ab glomerulonephritis, renal function rapidly deteriorates. Wu et al have reported that five of 40 patients with anti-GBM Ab glomerulonephritis showed a significant improvement in renal function (1). Two of these patients relapsed into anti-GBM Ab glomerulonephritis. To our knowledge, five cases with recurrent anti-GBM Ab glomerulonephritis have been reported, and three of them finally succumbed to renal failure (1-4). In most relapse cases, the recurrence was associated with infection. In this report, we describe a case with anti-GBM Ab glomerulonephritis who relapsed without an obvious cause after a 2-year remission and recovered by administration of combined therapy with prednisolone, heparin and dilazep hydrochloride.

CASE REPORT

A 55-year-old man was first admitted to the Hamamatsu University Hospital in September 1985, with complaints of microscopic hematuria, proteinuria and rapid renal functional deterioration. There was no history of hematuria, proteinuria or hypertension before admission. Also, he had not experienced hemoptysis, arthralgia, hydrocarbon exposure or prior viral prodome. Physical examination was normal except for a fine crackle heard in the right lower chest. Urine volume and urinary protein excretion were 600 ml/day and 1.1 g/day, respectively. The sediment contained numerous red cells per high-power field and some hyaline casts.

Chest X-ray demonstrated a mild fibrotic change in the lower field of the right lung, which had not significantly changed in the past 5 years. After the admission, the serum creatinine and blood urea nitrogen concentrations rapidly increased from 1.9 mg/dl to 8.6 mg/dl and from 21 mg/dl to 96 mg/dl respectively by hospital day 18. Serum anti-GBM Ab, estimated by use of a radioimmunoassay, was positive on days 38, 53, and 83. Serum complement, antinuclear antibody, circulating immune complex, and cryoglobulin were all within normal ranges. HLA-typing was not performed. Combined treatment was started with 80 mg/day of prednisolone.

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Fig. 1. Clinical course of a recurrent case of anti-GBM Ab glomerulonephritis. Scr, serum creatinine; U-prot, urinary protein excretion rate

Fig. 2. Glomerulus from the first biopsy showing a) fibrous crescent formation (PAS stain ×200) and b) linear deposition along the glomerular capillary walls (×260).

(Shionogi & Co., Ltd., Osaka), 12000 U heparin (Kodama., Co., Ltd., Tokyo), and 300 mg dipyridamole (Boehringer Ingelheim Japan., Co., Ltd., Kawanishi). One month later, the therapeutic course was interrupted by Carinii pneumonitis and gastrointestinal bleeding. Heparin was discontinued and the dose of prednisolone was tapered off to 15 mg/day. On hospital day 80, serum creatinine was decreased to 2.8 mg/dl, despite interrupted medication (Fig. 1).

A renal biopsy performed on hospital day 94 revealed fibrocellular crescents in 70% of 40 glomeruli obtained, and global sclerosis in 10%, and mild mesangial proliferation in the rest. Also, moderate interstitial mononuclear cell infiltration and tubular atrophy were found. Immunofluorescence staining demonstrated diffuse linear IgG and C3 depositions along the GBM (Figs. 2a, 2b and 3). A linear pattern of IgG was also demonstrated in sclerotic glomeruli. The patient was discharged in March 1986 with a maintenance dose of 10 mg/day of prednisolone. Thereafter, the prednisolone dosage was tapered off and eventually discontinued in June, 1986. He did well during the following sixteen months with 2.1 mg/dl of serum creatinine and normal urinalysis.

In October 1987, hematuria and proteinuria
occurred again without any obvious cause. Urinary protein excretion gradually increased to 2.5 g/day and serum creatinine to 3.1 mg/dl. The patient was readmitted to our hospital in June 1988. A second renal biopsy revealed global sclerosis in 80% of 60 glomeruli and cellular crescents in others (Fig. 4). On electron microscopic observation, thinning and splitting of the GBM were observed, but there were no dense deposits. Immunofluorescent staining disclosed diffuse linear IgG and C3 depositions along the GBM, a finding similar to that in the first biopsy, although the depositions of IgG were fewer than those observed in the first biopsy specimens. Serum anti-GBM Ab was not detectable on days 14 or 45 by radioimmunoassay using a collagenase-soluble GBM antigen. He was started on treatment of 30 mg/day of prednisolone, 8000 U heparin and 300 mg dilazep hydrochloride (Kowa. Co., Ltd., Nagoya) from hospital day 35. Renal function gradually improved. The patient was discharged in September 1988 with a serum creatinine level of 2.4 mg/dl. Urinary protein excretion also was decreased to 0.2 g/day in March 1989.

DISCUSSION

We described a case of recurrent anti-GBM Ab glomerulonephritis. Renal functional deterioration and proteinuria was improved by administration of a combined therapy with prednisolone, anti-coagulant and antiplatelet agents.

Recurrence of idiopathic anti-GBM Ab glomerulonephritis seems rather unusual. Hind et al found only one relapse case in 44 patients with Goodpasture’s syndrome, in which anti-GBM Ab plays a causative role (5). Almkuist et al also reported a recurrent case of Goodpasture’s syndrome which rapidly elevated the titers of anti-GBM Ab within two weeks of the renal isograft, despite the fact that the titers had been undetectable for more than one year (6). To our knowledge, 6 recurrent cases of idiopathic anti-GBM Ab glomerulonephritis have been reported (1-4). In 4 of these patients, recurrence was associated with intercurrent infection; their prognosis was poor, and 4 of 6 patients rapidly progressed to renal failure. In our patient, neither suspected infection nor obvious abnormality was found at the recurrence time.

In our patient, it can not be completely excluded that re-exacerbation of renal damage was ascribed to the superimposition of other renal disease or to the non-immunological progression of glomerulonephritis, because of negligible serum anti-GBM Ab on the second admission, normal urinalysis during the first remission and the abrupt onset of hematuria. It is unlikely, however, as similar histological findings, active crescentic glomerulonephritis with diffuse linear IgG deposition, were disclosed by two sequential biopsies. A likely alternative is a recurrence of anti-GBM Ab glomerulonephritis.

It remains unclear as to why anti-GBM Ab was not detected on the second admission. A significant increase in the anti-GBM Ab titer may not be always

Fig. 3. Light microscopic appearance of the first biopsy specimen: interstitial monocellular infiltration and patchy tubular atrophies were observed (PAS stain ×60).

Fig. 4. Glomerulus from the second biopsy showing cellular crescent occupying almost all of the glomeruli (PAS stain ×200).
essential to the recurrence of anti-GBM Ab glomerulonephritis. Indeed, Rees et al found an increase in the serum anti-GBM Ab titer in only one of 16 relapses of Goodpasture's syndrome (7). The activity of the disease in our patient might not have been high enough to induce an increase in the serum anti-GBM Ab titer.

In summary, we reported a case of recurrent anti-GBM Ab glomerulonephritis after a two-year remission. Repeated renal biopsies revealed crescentic glomerulonephritis with linear IgG deposition along the GBM. Serum anti-GBM Ab was detected at onset but not at recurrence. Our patient achieved substantial recovery of renal function by a combined treatment with prednisolone, anticoagulant and antiplatelet agents.

REFERENCES