Horseshoe Kidney and Membranous Glomerulonephritis with Cold Activation of Complement

Shouichi Fujimoto, Naoterae Hirayama, Toshihiro Uchida, Fumio Iemura, Yoshitaka Yamamoto, Tanenao Eto*, Hisanori Washimine and Akinobu Sumiyoshi**

A 48-year-old woman was admitted to our hospital because of proteinuria associated with persistent hypocomplementemia. Intravenous pyelography indicated the presence of horseshoe kidney without other abnormalities. Hypocomplementemia was caused by cold activation of complement. There were some findings suggestive of chronic liver disease (positive HCV antibody, hypergammaglobulinemia, low cholinesterase, etc.). Percutaneous renal biopsy showed the features of multiple evolitional phases of membranous glomerulonephritis. (Internal Medicine 31: 625-628, 1992)

Key words: chronic glomerulonephritis, anomalies of the genitourinary system, non-nephrotic membranous glomerulonephritis, HCV antibody

Introduction

Although patients with a horseshoe kidney may have multiple congenital anomalies, hydronephrosis, urinary tract infection or calculi as complications (1), there are a few case reports of such a patient with membranous glomerulonephritis (MGN) (2). On the other hand, cold activation of complement is noted in systemic disorders, such as systemic lupus erythematosus, chronic liver disease and cryoglobulinemia. Although a relationship between glomerulonephritis and cold activation is not still evident, a few cases with primary glomerulonephritis showing cold activation of complement are reported (3, 4).

We would like to describe a case of MGN with cold activation occurring in horseshoe kidney.

Case Report

A 48-year-old woman was admitted for evaluation of proteinuria associated with hypocomplementemia in September 30, 1990. Proteinuria had first been detected in August, 1989 by urinary tests performed as part of an annual health screening examination. One year later, she noticed mild pretibial edema and visited a local hospital. Urinalysis showed 2+ proteinuria but no hematuria. Laboratory findings for blood and serum were as follows: hemoglobin, 12.3 g/dl; white blood cell count, 4,200/mm³; BUN, 11.7 mg/dl; creatinine, 0.7 mg/dl; total protein, 7.6 g/dl; CH50, less than 5 U/ml. Dipyridamole, 300 mg/day, was prescribed, but proteinuria associated with hypocomplementemia persisted. She was referred to our hospital.

She was free from symptoms, and physical examination revealed blood pressure of 130/80 mmHg but no edema. She received blood transfusion at the delivery 21 years ago, but had never been pointed out liver dysfunction. There was no family history of renal or liver disease. Urinalysis showed proteinuria (0.6 g/day) with granular casts but no hematuria. Other laboratory findings for blood and serum are as follows. hemoglobin: 12.3 g/dl, white blood cell count: 3,600/mm³, platelets: 212,000/mm³, total protein: 8.24 g/dl (γ-globulin 2.25 g/dl), total bilirubin: 0.9 mg/dl, GOT: 30 IU/l, GPT, 21 IU/l; LDH: 320 IU/l, γ-GTP: 11 IU/l, ALP: 132 IU/l, cholinesterase: 362 IU/l (normal: 360–741), BUN: 17.2 mg/dl, creatinine: 0.7 mg/dl (Ccr 82 ml/min), sodium: 142 mEq/l, potassium: 4.1 mEq/l, chloride: 106 mEq/l, IgG: 2,410 mg/dl, IgA: 206 mg/dl, IgM: 241 mg/dl. Serum protein electrophoresis showed no "M" band. Serum concentrations of C3 and C4 components were 89 mg/dl (normal: 69–128) and 10 mg/dl (normal: 11–26) with very low serum hemolytic activities of component CH50 of less than 4 U/ml (normal: 30–40). However, the repeated evaluation for complement profile using plasma sample (EDTA treated) revealed C3 and C4 plasma levels of...
85 mg/dl and 9 mg/dl, and plasma CH50 of 33 U/ml. The antinuclear antibody, RA, HBs Ag and cryoglobulin were negative, but HCV antibody was positive. C1q binding assay disclosed a low level of circulating immune complex (CIC); less than 1.5 μg/ml (normal: less than 3.0). Raji cell test revealed the CIC level of 11 μg/ml (normal: less than 30). Abdominal ultrasonography, computed tomography, renal scintigraphy and intravenous pyelography indicated the presence of horseshoe kidney with no other abnormalities (Fig. 1).

A percutaneous renal biopsy was performed. Of 14 glomeruli obtained, global sclerosis was found in 1, segmental sclerosis in 1, and mild adhesion in 3. In the other 9 glomeruli, neither capillary-wall thickening nor changes in the mesangium were evident, and glomerular capillary lumens were widely patent on light microscopy. Segmental tiny spike formation and a vacuolated appearance of tangentially cut portions of glomerular basement membrane were noted on PAM stain (Fig. 2). Immunofluorescence study revealed granular deposits of IgG and a small amount of IgM and C3 along the glomerular capillary walls, but no deposits of IgA (Fig. 3). Electron microscopy showed small, scattered electron-dense deposits in the subepithelial and intramembranous regions (Figs. 4, 5). Spike and dome formation and translucent areas were also found in areas. Although electron-dense deposits (majority were in intramembranous regions) were sparse, the diagnosis of MGN at stage III was made.

**Discussion**

Chen and Ko (2) recently reported a case of MGN in a horseshoe kidney. MGN occurs most commonly in middle-aged adults with primary glomerulonephritis. Horseshoe kidney, however, is one of the most common anomalies of the genitourinary system (1). Therefore, the concurrence of these two diseases in a given patient may be due to chance. Abson et al (5) reported a case of a horseshoe kidney complicated by the development of a focal and sclerosing glomerulonephritis. They also considered that the association of these two renal pathologies in their case was by coincidence.

The majority of patients with MGN show nephrotic
Membranous GN in Horseshoe Kidney

syndrome. However, some show a benign clinical course associated with asymptomatic proteinuria. In these cases, light microscopy, as in the present patient, may occasionally show absence of spikes or absence of thickening of the glomerular basement membrane, while electron microscopy shows sparse, electron-dense deposits which usually present features of multiple evolutionary phases of MGN (6, 7). These histological alterations are considered as a milder form rather than as an early stage of MGN. Cases of concurrent MGN and segmental glomerulosclerosis (FSGS) have been reported (8, 9). Because MGN with focal sclerosing lesions, including hyalinoses and adhesion, is frequently found (10, 11), MGN with the lesions of FSGS does not necessarily indicate concurrence of two glomerular diseases. Furthermore, the present patient showed no evidence of vesicoureteral reflux, which is often noted as a complication of horseshoe kidney and may produce reflux nephropathy show-
ing features of FSGS.

This present case had cold activation of complement; the serum separated at a cold temperature showed a very low CH50 level, while plasma containing EDTA showed a normal CH50 level. In this case, there was no confirming evidence of systemic disorder such as systemic lupus erythematosus or chronic liver disease, and cryoglobulin-activating complement in cold temperature was not detected. Although there were no pathological or radiological findings of liver disease, the findings of hyper-gammaglobulinemia, low normal level of cholinesterase, positive HCV antibody and cold activation of complement may suggest the presence of chronic liver disease. There are a few reports stating that patients with primary glomerulonephritis show cold activation of complement (3, 4). A relationship between glomerulonephritis and cold activation of complement is still not evident. In this case, infectious antibody of HCV (viral antigenemia), in spite the lack of an increase in CIC levels, may be related to the pathogenesis of MGN as well as HBe positive MGN (12, 13). Further studies will be necessary to determine whether MGN is one of the complications of horseshoe kidney and if there is any relationship between glomerulonephritis and cold activation of complement.

References