Absence of Macroscopic Hematuria in a Case of IgA Nephropathy and Graves' Disease with Acute Renal Failure

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creatinine to 8.1 mg/dl in 2 days. The patient had experienced no macroscopic hematuria before admission.

On admission, the patient's blood pressure was 172/110 mm Hg and pulse 102 beats/min. The patient looked acutely ill and was disorientated. The thyroid was diffusely and moderately enlarged. No peripheral edema was found. Blood analysis gave the following readings: hemoglobin 15.2 g/dl, white blood cell count 14,100/mm³, total protein 6.2 g/dl, albumin 3.5 g/dl, BUN 270.3 mg/dl, creatinine 8.2 mg/dl, uric acid 31 mg/dl. Uri-nalysis results were as follows: protein 0.38 g/day, red blood cell count 15-20 per

Dear Sir,

The frequency of acute renal failure in IgA nephropathy has been reported to be 0.8-6.6% [1,2]. The etiology and pathogenesis of acute damage to renal function in IgA nephropathy, however, have not been fully elucidated. Bennett and Kincaid-Smith [3] have suggested that acute renal failure results from glomerular crescents, while the role of obstructive tubular red blood cell casts in the pathogenesis of reversible acute renal failure has been emphasized by other reports [4, 5]. Episodes of macroscopic hematuria are indeed frequently reported to precede the occurrence of renal failure, suggesting that macroscopic hematuria affects renal function. The authors have recently experienced a case in which reversible acute renal failure associated with IgA nephropathy was not accompanied by any evidence of macroscopic hematuria.

A 42-year-old man was admitted to this hospital suffering from acute renal failure. The patient had had an unknown type of nephritis with proteinuria and hypertension when tonsillectomy was performed at the age of about 10 years. The patient had remained well until 5 years ago, when proteinuria and hypertension were found during an annual medical examination. Eight days before admission, the patient experienced fatigue and a sore throat followed by vomiting after a picnic excursion with his family. After vomiting coffee ground materials, the patient was admitted to a nearby hospital, where intravenous fluid

administration was performed, but he did not recover. Blood urea nitrogen (BUN) increased to 221 mg/dl and serum

Fig. 1. Light microscopy of renal biopsy specimen with segmental mesangial proliferation and sclerosis. PAS. $\times 160$.

high-power field (hpf), white blood cell count 1-2/hpf, occasional hyaline cast. Antinuclear antibody was negative.

On the day of admission, 3-hour hemodialysis was performed. Daily infusion of 3,000 ml of electrolyte fluids was commenced. As the patient became lucid on the second day, dialysis was not performed, although BUN was 189.7 mg/dl and serum creatinine 6.5 mg/dl. On the third day, tarry stool was passed and an endoscopic examination revealed multiple gastric ulcers. Ranitidine and antacid drugs were prescribed. BUN and creatinine decreased gradually over the following 2 weeks, being 27.8 and

1.4 mg/dl, respectively, on the 15th day. A percutaneous renal biopsy was performed on the 50th day of hospitalization. Of 7 glomeruli present in the specimen, 1 showed global obsolescence and the rest segmental mesangial proliferation and sclerosis (fig. 1).

Glomeruli with crescents were not found. Focal areas of tubuli were atrophic with flattened tubular epithelial cells. Red blood cell casts were not noted. Focal areas of fibrosis and mild leukocyte infiltration were observed in the interstitium. On electron-microscopic observation, dense paramesangial deposits were noted. Immunofluorescent studies showed mesangial deposits of IgA, IgM, IgG and C3. From these findings, diagnosis of IgA nephropathy was made.

A thyroid function test on the 17th day of hospitalization revealed overt hyperthyroidism. Free T₄ was 3.3 ng/dl (normal 0.8-1.9), free T₃ 7.4 pg/ml (normal 2.6-5.4), TSH less than 0.1 μ U/ml (normal 0.6-4.9), anti-TSH-receptor antibody 37% (normal less than 10) and ¹²³I uptake 73.2%. Methimazole administration of 30 mg/day was begun, and the patient was discharged on the 63rd day.

The causes of acute renal failure associated with IgA nephropathy are controversial and unknown. Lupo et al. [6] have suggested that the pathogenesis of acute renal failure in IgA nephropathy is multifactorial and that it may result from both anatomic lesions and hemodynamic alteration. As most cases of acute renal failure in IgA nephropathy develop during episodes of macroscopic hematuria, hematuria per se may be associated with renal dysfunction [3-11]. Bennett and Kincaid-Smith [3] consider that episodes of macroscopic hematuria are a clinical indication of severe IgA nephropathy, in terms of increased incidence of crescent formation and worsened renal function. However, Prager et al. [5] have reported deterioration of renal function during episodes of macroscopic hematuria in IgA nephropathy. They concluded that the disturbance of renal function could be explained by the appearance of tubular necrosis associated with the presence of red blood cell casts [3]. Delclaux et al. [7] have described 6 cases of acute renal failure with macroscopic hematuria in IgA nephropathy. They also concluded that the possibility of acute tubular damage and/or tubular obstruction by red blood cell casts should be considered in all patients who develop acute renal failure soon after a hematuric episode [7]. In the present case, acute reversible renal failure in a patient with IgA nephropathy was not preceded or followed by episodes of macroscopic hematuria. Muscle exhaustion during a picnic excursion and dehydration induced by virus infection and vomiting were suspected to be clinically responsible for acute renal failure in

this case in which macroscopic hematuria was absent. Furthermore, this patient had hyperthyroidism which was not diagnosed until recovery from acute renal failure. Undiagnosed, untreated hyperthyroidism may have facilitated dehydration in this case. It is reported by Conn et al. [12] that dehydration facilitates the induction of acute tubular necrosis by myoglobin pigments in dogs. Therefore, in the present case, in which slight microscopic hematuria was seen, dehydration may have enhanced the nephro-toxicity may have enhanced the nephrotoxicity of hemoglobin, leading to acute tubular necrosis. Since renal biopsy was delayed in this case, it was not possible to secure histological evidence of acute tubular necrosis or red blood cell casts in the specimen.

In summary, an unusual case of IgA nephropathy with acute renal failure but without a preceding episode of macroscopic hematuria was seen. It was suggested that hemodynamic disturbance caused by dehydration and possibly by hyperthyroidism may have enhanced the toxicity of hemoglobin to renal tubular cells in this case.

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