Alteration of C3 Nephritic Factor in a Patient with Membranoproliferative Glomerulonephritis Type II

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Dear Sir,

C3-nephritic factor (C3NeF) is often found in patients with membranoproliferative glomerulonephritis (MPGN) type II [1]. In plasma, low levels of C3, caused by activation of the alternative pathway of complement, are accompanied by relatively normal levels of C1, C4, and C2 [2]. Performing immunohistological studies, C3 deposition is also frequently observed in the glomeruli. However, the relationship between C3NeF, hypocomplementemia, and immunological renal lesions is still controversial.

We observed a case with MPGN type II who developed chronic renal failure and whose C3NeF level decreased and disappeared with progression of chronic renal failure and reappeared after starting hemodialysis. The relation between CH₅₀/C3 and C3NeF levels was completely reciprocal during the clinical course of this patient.

A 7-year-old girl presented with facial edema and oliguria 2 weeks after catching a common cold in 1975. Heavy proteinuria and slight microhematuria were pointed out by her doctor. There was no family history of any medical diseases. In 1977, a renal biopsy specimen was obtained because of a persistent proteinuria. She was diagnosed as having MPGN by light microscopy, showing lobular formation with mesangial and endocapillary proliferation in all glomeruli. However, the study by electron microscopy demonstrated no dense deposits in the glomerular basement membrane, but only lamellation of the lamina densa. In 1982, a second renal biopsy specimen was obtained because heavy proteinuria and nephrotic syndrome had continued.

Electron

microscopy revealed typical dense deposits of MPGN type II on the lamina densa in all glomerular basement membranes [3].

A detailed complement profile of this patient was first studied in 1983. Then renal function tests revealed values within normal ranges: serum creatinine 0.6 mg/dl, blood urea nitrogen 11 mg/dl, and creatinine clearance (C_{cr}) 96 ml/min. Complement assays showed extremely reduced CH₅₀ (15 U/ml) and C3 (10 mg/dl) levels (fig. 1), a high titer of C3d, and a normal C4 titer (34 mg/dl).

C3NeF was strongly positive by the methods of EC3bBb stabilization and C3 conversion test, and the serum levels were followed up by using the ELISA method which we had newly developed [1]. The titer for C3NeF is expressed as stabilizing units per milliliter (SU/ml) compared with the standard curve in which 0.1 mg IgG purified from the serum of this patient was set at 100 U/ml. The C3NeF assay for time course was performed in triplicate at the same time, using frozen samples.

In spite of methylprednisolone pulse therapy and the treatment with cyclophosphamide, the C3NeF values in her serum remained strongly positive (95-100 SU/ml). In 1986, however, C3NeF began to decrease with progression of the renal dysfunction and became negative (< 10 SU/ml) when her C_{cr} was 14 ml/min in 1990. Serum CH50 and C3 levels were increasing during this period and were within the normal range (CH50 36 U/ml; C3 74 mg/dl) in 1990. The relationship between C3NeF and CH50 was completely reciprocal.

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lignant clinical course [7]. On the other hand, Klein et al. [8] reported that the serum levels of C3 and C3NeF serve as reliable indicators of the ultimate outcome of this disease. Our results may give the answer to support the latter for this discrepancy and may explain the fact that MPGN type II is easily relapsed in the transplanted kidney [9, 10].

However, C3NeF reappeared slightly but distinctly (24 SU/ml), and the CH50/C3 levels decreased (CH50 24 U/ml; C3 49 mg/dl) after start of hemodialysis (fig. 1).

The clinical course suggests that C3NeF is an only or main activator of complement in this patient. Furthermore, the relation between the disappearance of C3NeF and the progression of renal tissue damage also suggests that the C3NeF autoantibody may be directed to the neoantigen of C3bBb deposited in the glomeruli.

The changes of the general condition in a patient with chronic renal failure may affect the humoral immune systems. It is reported that in patients with systemic lupus erythematosus, the disease activities decrease associated with the progression of chronic renal failure [4]. Actually, it should be thought that immunological activities may decrease in this patient, while the change of serum IgG levels was not related to the alterations of the C3NeF levels.

C3NeF may be trapped by kidney or other organs, leading to its decrease in the circulation. However, if it was true, the serum complement levels should remain reduced because C3NeF deposited in organs is thought to be a stronger activator of complement than in the fluid phase [5].

After starting hemodialysis therapy, the level of C3NeF increased slightly but distinctly, and simultaneously the serum levels of CH50 and C3 decreased (fig. 1). These phe-

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1980

Fig. 1. Time course of C_{cr} (•) and serum levels of C3 (○), C3NeF (■) and IgG (□).

nomena suggest that the complement activation by the membrane for hemodialysis [6] may present the neoantigenic stimulation of the C3bBb convertase to induce B cells to produce C3NeF again.

It was reported that the prognostic significance of the presence of C3NeF was doubtful, because it was equally detected in both groups of MPGN type II with benign or ma-

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