Circulating Immune Complex in Glomerular Diseases

by

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Abstract

Circulating Immune Complex (CIC) in the serum have been studied in 75 patients with glomerular diseases. The highest positive rate in patients with post streptococcal glomerulonephritis and lupus nephritis were respectively 83.3% and 75%.

In nephrotic syndrome: 33.3% (5/15) was positive in diffuse mesangial proliferative cases, and in all 3 patients with membranoproliferative glomerulonephritis, membranous nephropathy and focal glomerulosclerosis. All of them had detectable immune deposits in the glomeruli.

In minimal lesion nephrotic syndrome (MLNS) without glomerular immune deposits, CIC was positive in 2 out of 17 cases (12%). This support the hypothesis that in MLNS a humoral immune mechanism might take part in the pathogenesis of the disease.

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Introduction

A subject of considerable scientific interest and importance to nephrologist, as well as immunologist was the recent development of techniques for the detection of Circulating Immune Complex (CIC) in the serum.

Studies performed in animals and humans have established the important role of antigen antibody complexes in the pathogenesis of immune mediated glomerulonephritis. The glomerular deposition of CIC has been studied by light, immunofluorescence and electron microscopy in various animal models and in human renal diseases (Wilson and Dixon 1976).

Mc Cluskey et al. (1960) could induce glomerulonephritis by injection of preformed immune complexes in mice.

Due to these observations, there seems to be some hope that CIC detection might serve as a new clinical tool for the diagnosis, prognosis as well as management in glomerular diseases.

However, up till now there is still inconsistency on the relationship between the occurrence of glomerular deposition and the demonstration of CIC in human subjects. For instance despite morphologic evidence of glomerular immune complex deposition in patients with membranous glomerulonephritis and IgA nephropathy, CIC have been difficult to demonstrate in these patients, even in studies where serial serum samples were obtained (Fussell et al, 1978).

On the otherhand in a number of patients with minimal change nephrotic syndrome and some patients with idiopathic crescentic glomerulonephritis despite severe renal damage and no detectable glomerular immune deposits, CIC examination in the serum showed positive results (Stuchura, et al, 1981).

Due to these discrepancies, a study of CIC in the serum was conducted in 75 children suffering from glomerular diseases seen during an interval of two years, to correlate the finding of CIC and the deposits in renal biopsy tissue and the severity of the clinical picture of the disease.

Materials and methods

Circulating immune complex examination of the serum was conducted in 75 children, 40 cases suffering from acute glomerulonephritis and 35 from nephrotic syndrome, during a period of two years, namely from June 1980 until June 1982. The age of the patients were between 1½ and 12 years old, comprising of 29 girls and 46 boys.

Serum samples for CIC examination were obtained on the day of admission and renal biopsy were performed on the first or second week of hospitalization and was sent for pathological examination by means of light, immunofluorescence and in some patients for electron microscopy examination.

Circulating immune complexes were examined by detecting the inhibition effect on the capacity of RF (rheumatoid factor) to agglutinate latex particles coated with human immunoglobulins (IgG).

The procedure was a modification to the method describe elsewhere (Luhurra, et al, 1976).

Briefly, 5 μl of two fold dilutions of the patient serum was mixed (V/V) with RF containing serum of optimal dilution and incubated at 37°C for 15 minutes.

The mixture (5 μl) was then tested for inhibition effect by mixing V/V with indicator particles, namely latex particles coated with human immunoglobulins on a glass slide. The agglutination pattern was evaluated after 2-5 minutes at room temperature.

The titer of CIC was determined as the reciprocal of the dilution of the patient serum providing significant inhibition, represented by subagglutination pattern.

Patients with a clinical entity of acute glomerulonephritis, were consisted of: 36 cases with post streptococcal glomerulonephritis, 3 cases of SLE nephritis and 1 case with Henoch Schönlein nephritis.

All patients with post streptococcal GN showed elevation of ASO titer and lowering of the C3 complement. Serum CIC examination showed positive results in 83% of these cases.

In the SLE patients, beside the low C3 examination, antinuclear factor was positive and clinically a butterfly rash was detected.

CIC was positive in 2 out of 3 cases of the SLE patients and on the single patient with Henoch Schönlein nephritis it was negative.

<table>
<thead>
<tr>
<th>Etiology</th>
<th>No cases</th>
<th>CIC</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post strept</td>
<td>36</td>
<td>30</td>
<td>6</td>
</tr>
<tr>
<td>S L E</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Henoch Schönlein</td>
<td>1</td>
<td>----</td>
<td>1</td>
</tr>
<tr>
<td><strong>T o t a l</strong></td>
<td>40</td>
<td>32</td>
<td>8</td>
</tr>
</tbody>
</table>

Renal biopsy of the nephrotic syndrome patients showed:

- minimal lesion in 17 cases, diffuse mesangial proliferative in 15 cases, membranoproliferative G.N. in 1 case, membranous nephropathy in 1 case and focal and segmental glomerulosclerosis in 1 case.

In patients with minimal lesion 2 cases (12%) showed CIC positive, while
in several proliferative cases it was generally mild, and focal glomerulosclerosis was minimal. The overall positive rate in non-membranous cases was 58% (Table 2).

**TABLE 2**: CIC finding in nephrotic syndrome

<table>
<thead>
<tr>
<th>Membranous Pred G. N.</th>
<th>Membranoprolif G. N.</th>
<th>Minimal lesion</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No case</td>
<td>15</td>
<td>17</td>
<td>32</td>
</tr>
<tr>
<td>1</td>
<td>10</td>
<td>5</td>
<td>15</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>15</td>
<td>25</td>
</tr>
<tr>
<td>33</td>
<td>12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Discussion**

In a case who was hospitalized due to AGN, renal failure, and disseminated intravascular coagulation, the general condition was further deteriorated, necessitating a peritoneal dialysis intervention. Prior to dialysis, the coagulation abnormalities, and third dialysis performed.

Due to a lack of control, the dialysis procedure was not monitored properly, using the C1q deviation as a positive control (18 of 52 cases), which may have been due to the examination of the glomerular diseases.

Many different CIC assays have been developed, including the following:

- C1q deviation
- Total CIC
- Membranoproliferative
- Membranous
- Minimal

For instance, in cases of membranoproliferative glomerulonephritis (MGN), using C1q only positive cases, there were 10 cases of membranoproliferative glomerulonephritis (MGN) with only positive cases compared to 15 cases of membranous glomerulonephritis (MGN) with only positive cases.

In this study, which is the first to use the injection of IgG to detect C1q, the overall positive rate in non-membranous cases was 58% (Table 2).

The positive rate in this study was 75% in patients with proliferative glomerulonephritis, 82% in patients with membranous glomerulonephritis, and 63% in patients with minimal change disease (Table 2).

The positive rate in the SLE patients was 75% compared to 82% in the proliferative glomerulonephritis cases and 63% in the minimal change disease cases (Table 2).

Other explanation for the discrepancy between CIC in the serum and in the glomeruli is that CIC may be detected in the serum before it is formed in the glomeruli. CIC in the serum is detectable even in patients with early membranous glomerulonephritis. Therefore, CIC detection in the serum may be an early marker of membranous glomerulonephritis.
Despite this, we think that it is too early to take any definite conclusion at this moment. Further study should be made to confirm this assumption.

REFERENCES


