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ORIGINAL ARTICLE

C3 and C4 Complements in Glomerular Disorders in Children*

by

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Abstract

Seventy children who were hospitalized for kidney diseases in the Nephrological ward Department of Child Health, University of Indonesia, Jakarta were used in this study.

Thirty seven patients suffering from acute poststreptococcal Glomerulonephritis (A.G.N.), 3 patients with Membranoproliferative Glomerulonephritis (M.P.G.N.) and 30 patients with Nephrotic Syndrome due to other causes were examined for complement concentration.

A total of 80 samples were examined for C3 and 25 samples for C4 concentration using the immunediffusion plates.

Almost all patients with A.G.N. and M.P.G.N. showed depression of C3. C4 concentration was normal except in 2 patients, 1 with A.G.N. and the other with M.P.G.N.

This suggest activation of complement at the C3 level by the alternating pathway in most of the patients.

C3 concentration in A.G.N. patients returned to normal after 8 - 10 weeks. In MPGN the depression was persistent in 2 patients, while in 1 patient it returned to normal level after 3 months of Immunosuppressive treatment.

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Introduction

The concentration of different complement components in various forms of Glomerulonephritis has been reported by several workers (Gewurz et al., 1968; Brandis et al., 1975).

Its importance in the pathogenesis and management of glomerulonephritis had also been established (West et al., 1964; Cameron et al., 1973).

Due to the simplicity of plasma concentration measurement, this method had been widely adopted in research laboratories (OGG et al., 1968).

Three types of glomerulonephritis associated with consistent changes in the plasma concentration of complement components are :

1. Acute glomerulonephritis (AGN) occurring after streptococal infection
2. Lupus glomerulonephritis
3. Membranoproliferative glomerulonephritis (MPGN) (Gewurz et al., 1968; Cameron et al.,1970).

Rarer glomerular diseases associated with alteration in complement concentration include glomerulonephritis associated with subacute bacterial endocarditis (Herdman et al., 1970) and infected juguloatrial shunt for hydrocephalus (Black et al., 1965).

Recently it has been recognized that besides the classical activation of complement by the early component C1, C4 and C2, the C3 may be triggered by an alternate pathway (Vallota et al., 1970).

The measurement of different complement components proves useful in distinguishing the mechanism of complement activation in the plasma.

The purposes of this study are:

1. To investigate the complement profile, namely C3 and C4 concentration in several kinds of glomerular disorders.
2. To know which kind of complement activation is operating in our patients,
3. To look for the possibility of using this examination as a diagnostic aid in the differential diagnosis in certain kinds of glomerular disorders.

Material and Method

Seventy children hospitalized in the nephrological ward Department of Child Health, University of Indonesia, Jakarta, from June 1975 to June 1976, consisting of 37 patients with AGN post streptococcus, 3 patients with MPGN and 30 patients with Nephrotic syndrome due to other causes were enrolled in this study.

Fifteen normal children served as control.

A total of 80 samples were examined for C3 (measured as β_1 A), 25 samples for C4 concentration.

The C3 was examined in our Laboratory using the Behring Werke Partigen Immune diffusion plates while the C4 was examined in the subdivision of Clinical Immunology, Department of Pathology, Royal Perth Hospital, Perth, using the same method.

Result

The plasma C3 concentration in 15 normal children can be seen in fig. 1.

Almost all patients showed C3 concentration between 80 - 140 mg%, concentration considered as within normal limits. In 2 patients it was above 140 mg%.

Fig. 2 showed the C3 concentration in different kinds of nephrotic syndrome.

In all 18 patients with minimal changes, 4 patients with mesangial proliferative glomerulonephritis, 3 patients with focal glomerulosclerosis and 4 patients with membranous nephropathy no depression of C3 concentration were detected. In 4 patients with minimal changes and 1 patient with membranous nephropathy the C3 concentration were above normal. The significance of this finding was not known.

Fig. 3 showed us the C3 concentration in 37 patients suffering from AGN post streptococcus. Except in 2 cases, all other patients showed low concentration of C3 in the acute stage (2nd week) of the disease. Repeated examinations after 8 weeks in 10 patients showed a return of C3 to normal concentration.

The C3 concentration in 3 patients with MPGN proved by light microscopy and immunofluorescence examination of the renal biopsy specimen were depressed. After 3 months of repeated examinations of C3,2 patients showed persistent depression, while in 1 patient it returned to normal level after immunosuppressive treatment. The clinical course of this patient showed also remarkable improvement. (Fig. 4).

The C4 concentration in AGN and MPGN and other kinds of nephrotic syndrome showed normal concentration except in 2 patients, 1 with AGN and the other with MPGN. This means that almost in all patients the alternate pathway of C3 complement activation was operating.

Discussion

The finding of temporary depression of C3 concentration in AGN post Streptococcus and persistent depression in MPGN was already confirmed in the literature (Gewurz et al., 1968; Cameron et al., 1973).

The result of C3 examination in our patients showed depression of C3 concentration in 35 out of 37 cases with AGN post streptococcus in the acute stage, which returned to normal level after 8 weeks.

Dodge (1972) reported 45 out of 46 cases and Brandis (1975) 5 out of 6 cases with AGN post streptococcus had low concentration of C3.

In Brandis' patients some of the C3 concentration have returned to normal level after 10 to 14 days. This suggests making an early examination of C3 within 2 weeks of the acute stage in AGN in order to have a better parameter in the diagnosis of this disease. The fin-

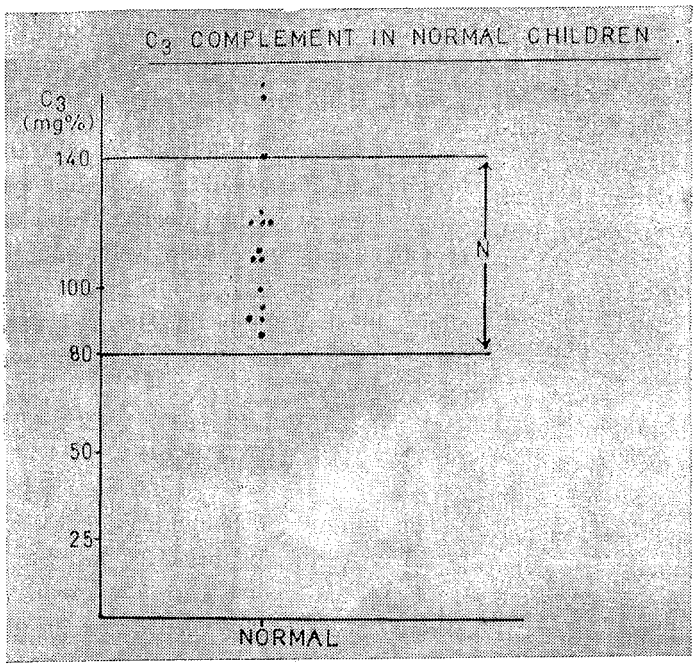

C3 COMPLEMENT IN NORMAL CHILDREN
C3 (mg%)
140
100
80
50
25
N
NORMAL

FIG. 1.

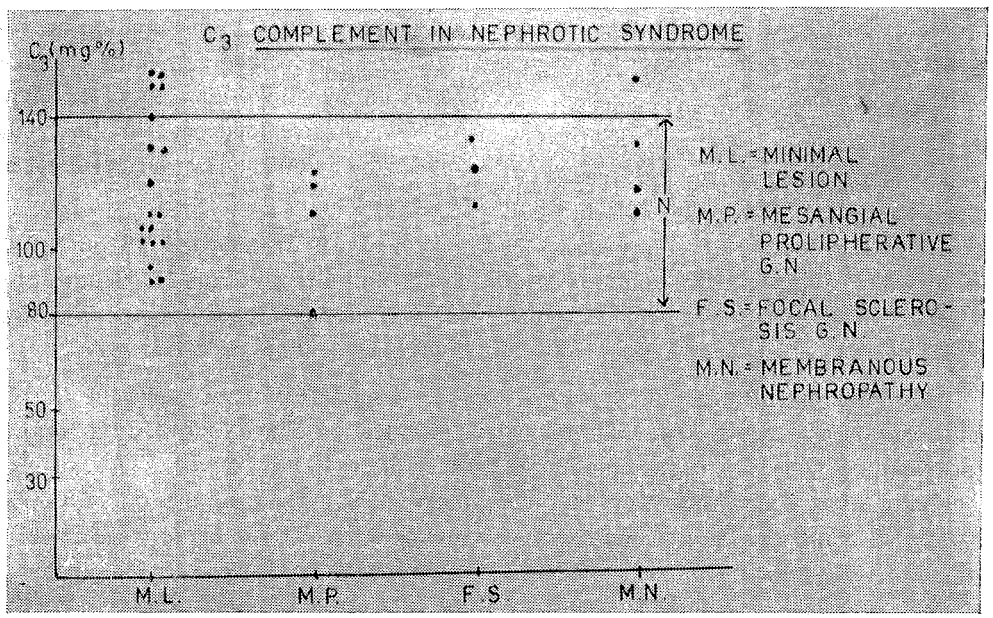

C3 COMPLEMENT IN NEPHROTIC SYNDROME
C3 (mg%)
140
100
80
50
30
N
M.L.
M.P.
F.S.
M.N.
M.L. = MINIMAL LESION
M.P. = MESANGIAL PROLIPHERATIVE G.N
F.S. = FOCAL SCLEROSIS G.N
M.N. = MEMBRANOUS NEPHROPATHY

FIG. 2.

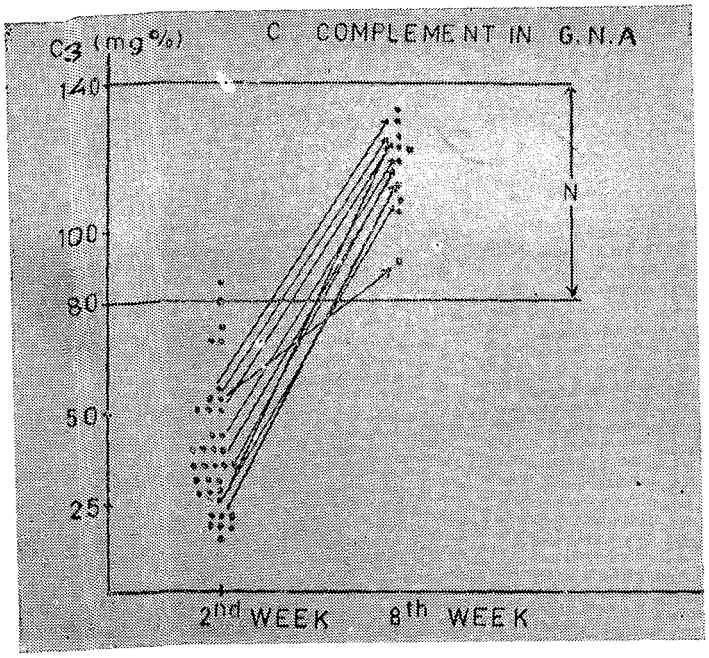
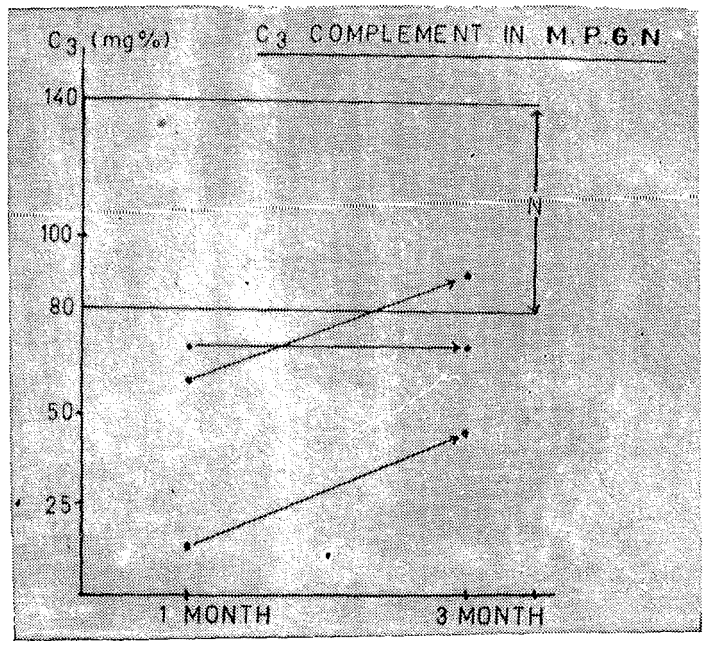

C3 (mg%)
C COMPLEMENT IN G.N.A
140
100
80
50
25
N
2nd WEEK
8th WEEK

FIG. 3.

FIG. 4.


C3 (mg%)
C3 COMPLEMENT IN M.P.G.N
140
100
80
50
25
N
1 MONTH
3 MONTH

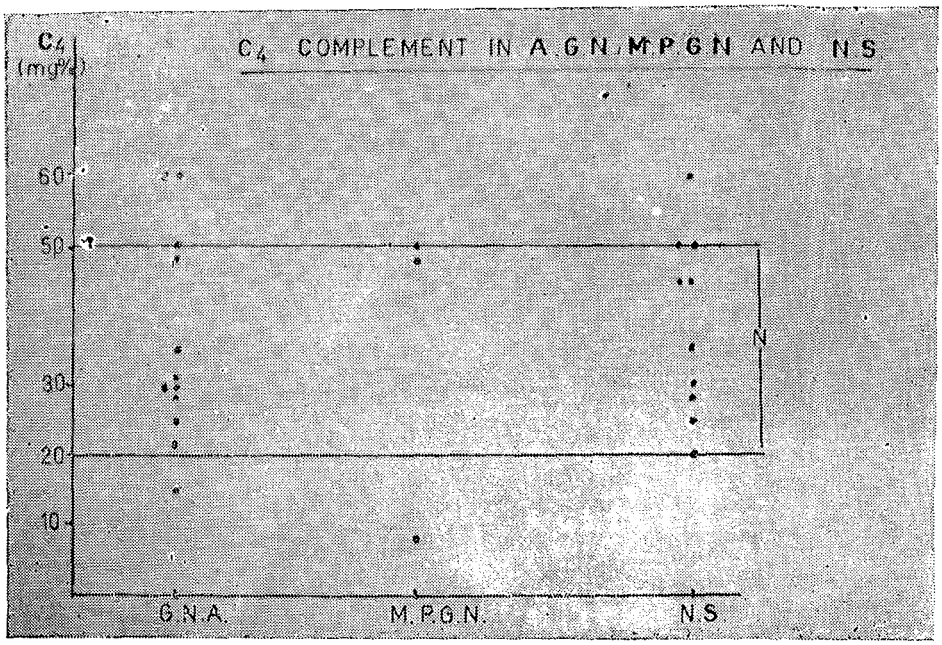

C4 COMPLEMENT IN A.G.N./M.P.G.N. AND N.S
C4 (mg%)
60
50
30
20
10
N
G.N.A.
M.P.G.N.
N.S

FIG. 5.

ding of AGN due to streptococcal infection would suggest a good prognosis in children with a 90% cure rate (Dodge et al., 1972).

Differentation of MPGN and AGN post streptococcus is very important because MPGN usually has a bad prognosis, requiring a longterm management and follow up. In AGN post streptococcus the depression of C3 occurs in 2 to 8 weeks, while in MPGN C3 is low for months or years (Cameron et al., 1970).

In our 3 cases of MPGN 2 showed persistent depression after 3 months and in one it returned to normal after immunosuppressive treatment.

In this study the C3 examination proved to be a useful method in the diagnosis of post streptococcal AGN and in the differentiation of AGN with MPGN.

The finding of normal levels of C4 in most of our AGN and MPGN cases was in accordance with the report in the literature (Cameron et al., 1973).

This suggests the alternate pathway of C3 complement activation and against the initially assumed hypothesis that in post streptococcal AGN the classical pathway is operating.

Substances involved in the activation of C3 by the alternate pathway are :

— properdin, glycine rich glycoprotein (Gewurz, 1971).

— C3 breakdown product C3b.

— C3 nephritic factor which is found in the serum of some patients suffering from MPGN and AGN. (Spitzer et al., 1969; Vallota et al., 1970).

C4 is depressed in lupus nephritis and also in a small proportion of AGN and MPGN suggesting that the classical pathway is taking place (Cameron et al., 1973).

In our patients it was only depressed in 2 cases, 1 with AGN and the other with MPGN. None of them had lupus nephritis. So although in most cases the alternate pathway of C3 activation is taking place in some patients of AGN and MPGN the classical pathway is also operating.

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