STATUS OF COMPLEMENT SYSTEM IN INDIAN CHILDHOOD CIRRHOSIS (ICC)

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ABSTRACT

The mean value of C3, C4, C3PA and CH50 in the serum samples of Indian Childhood Cirrhosis was considerably low as compared to normal controls. These differences were statistically significant. The mean percentage decrease was to the extent of 27.6%, 35%, 12.6% and 22.9% respectively. Moreover, the activation product of C3 i.e. C3b was also found in the serum samples of these patients.

INTRODUCTION

Clinical syndrome generally referred to as Indian Childhood Cirrhosis (ICC) is a distinct entity of fatal liver disease affecting infants and young children of Indian subcontinent often below the age of 4 years. Its etiopathogenesis is obscure and its nature and evolution is still inadequately understood. From time to time, malnutrition, toxic agents, metabolic defects and viruses have been incriminated in ICC. Dermatoglyphic and epidemiological data point out to a genetic predisposition.

Children suffering from ICC manifest a paucity of immune responses and hence are more susceptible to certain antigenic insults. Earlier work indicates that there may be an immunological involvement. Although quite a few workers have studied the changes in the levels of complement components in various liver diseases in adults, only two reports on C3 levels in ICC patients are available in the literature. Even these are variable and conflicting. The present study reports the serum levels of complement components, total haemolytic complement (CH50) and C3 activation product in patients with ICC.

MATERIALS AND METHODS

Serum samples from the patients of ICC were obtained from out-patient's departments and wards of the All India Institute of Medical Sciences, New Delhi. Patients usually had enlarged liver with sharp leafy margins and in the advanced stage of disease developed jaundice, oedema or ascites. The diagnosis was confirmed by histopathological examination.

Normal healthy subjects with no history of any liver disease formed the control group. C3, C4 and C2PA levels were estimated by single radial immunodiffusion technique using monospecific antisemum (Behringwerke, West Germany). CH50 was estimated by the method of Mayer. The presence of C3b, the activation product of C3 was determined by two-dimensional cross electrophoresis using monospecific rabbit anti human C3.

Statistical analysis was done by students' t test. All the parameters were estimated in fresh samples.

RESULTS AND DISCUSSION

Table 1 gives the mean values of C3, C4, C3PA and CH50 levels in the serum samples of normal controls and patients with ICC. Mean values of C3, C4, C3PA and CH50 in ICC samples were considerably low as compared to controls. These differences were statistically significant. In one patient there was drastic lowering in the levels of both C3 and C4, the values being 21.0 mg% and 5.0 mg% respectively. In this particular sample C3PA level was also low, although the decrease was not as pronounced as with C3 and C4.

| Table 1 C3, C4, C3PA and CH50 levels in the serum samples of ICC and normal controls |
| --- | --- | --- | --- |
| C3 (mg%) | C4 | C3PA | CH50 (units/ml) |
| Indian Childhood Cirrhosis | |
| n | 40 | 40 | 40 | 40 |
| Mean | 74.0 | 17.4 | 13.8 | 25.9 |
| S. D. | ±20.9 | ±7.0 | ±3.3 | ±7.0 |
| P | <0.01 | <0.01 | <0.01 | <0.05 |
| Normal controls | |
| n | 56 | 44 | 40 | 23 |
| Mean | 102.3 | 26.8 | 15.8 | 33.6 |
| S. D. | ±16.9 | ±6.6 | ±3.4 | ±5.7 |

n = number of samples; S. D. = standard deviation.
Figures 1a and b. Cross-electrophoretic pattern of C3 from a. normal human serum, b. serum of ICC patient. In each frame left arc is C3 and right arc is C3b.

Cross electrophoretic pattern revealed the presence of C3b, the activation product of C3 in the samples of ICC patients studied (figure 1).

The present results clearly show significantly reduced C3, C4, C3PA and CH50 levels in ICC samples. Moreover C3b, the breakdown product of C3, was also found in these samples. These observations indicate the possible activation of both the classical as well as alternate pathways in ICC patients. However, the lowering of C3 levels can also be attributed to its impaired synthesis, as it has been proved conclusively that the liver is the principal site of C3 synthesis and ICC is the disease which affects the liver cells.

Reduced complement levels have been reported in a number of liver diseases in adults. However, only two reports on C3 levels in ICC samples are available in literature. Chandra suggested a significant lowering of C3 levels in ICC samples. In 30 ICC samples he found that C3 levels were 1/3rd of those in normal healthy controls. On the other hand, Sehgal et al. reported no significant difference in C3 levels between patients and controls in a study conducted on 45 children suffering from ICC.

Both the studies mentioned above provide contradictory observation. These workers, however, did not study the levels of other complement components and were therefore not in a position to comment on the involvement of complement system in ICC and the mode of activation leading to such a lowering in C3 levels.

The present findings suggest that the activation of complement system via the classical as well as alternate pathway in ICC might contribute to the modulation of some immunological processes and mediation of tissue injury in this disease.

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