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Serum complement C2 levels in patients suffering from cystic fibrosis (CF)

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Serum C2 complement levels were measured in 17 children suffering from CF, 17 with obstructive bronchitis, and 7 control children. No correlation was found between the C2 level and the clinical stage in Shwachman score, the HLA B7 or B18 antigens and the ventilation functional parameters. The mean serum C2 complement level did not differ in the three investigated groups, but in 5 of the 17 CF patients the serum C2 was diminished according to the possibility of C2 complement heterozygosity.

The CF patients with diminished C2 complement levels exhibited HLA B7, B12 or B35 antigens.

The serum C2 complement levels were significantly higher in the HLA B18 antigen-carrier CF homozygotes.

Complements C2 and C4 and Factor 8 are regulated by the MHC localized on the short arm of chromosome 6 (Alper, 1981 [1]). Pariser et al [11] described the null allele of the structural gene locus of complement C2. A significantly increased frequency of the HLA B18 antigen has been described in CF homozygotes by László [7]. This was the reason for our investigations. The synthesis of C2 is localized in the liver (Morris et al. [9]); the extrahepatic source is the mononuclear phagocyte. We have not found data about the levels of complement C2 in CF cases.

Investigated Groups and Methods

17 patients (children) suffering from CF, 17 children with obstructive bronchitis, and 7 children as controls, were investigated for serum complement C2 level. The C2 level in human serum was measured by the effective molecule titration method of Nelson et al [10].

HLA antigens were determined by the microlymphocyto-toxycity test of the NIH (Terasaki [15]). Correlations between the serum C2 levels and the clinical stage (in Shwachman score), the capnographic parameters and the Br-tests were investigated by the Wilcoxon test.

Results

The serum complement C2 levels are listed in Table I. There are no significant differences in the mean values. In one-third of the CF children, the complement C2 levels were extremely diminished, indicating the C2 heterozygous complement genostatus. Among the HLA antigens, B7, B12 and B35 were present in the CF pa-

TABLE I

Serum C2 complement levels

	1 Control group n=7	2 CF-homozygotes n=17	3 Obstructive bronchitis n=17
C2			
$\bar{x}$ =	1711.9	1533.68	1887.64
± S.D.	380.6	720.3	813.45
Minimum	1190.9	143.0	957.0
Maximum	2207.9	2493.0	3741.3
Median	1901.9	1650.0	1600.0

Difference between groups 1 and 2 Wilcoxon probe $p > 0.05$
Difference between groups 2 and 3 T-probe $p > 0.05$
Difference between groups 1 and 3 Wilcoxon test $p > 0.05$

tients with diminished complement C2 level.

In the presence of HLA B18 antigens, the complement C2 proved to be significantly higher than in the children without these HLA antigens. There was no correlation between the serum complement C2 level and the clinical stages in Shwachman scores, the ventilation functional parameters or the frequency of B7 or B18.

Discussion

The literature views regarding the quantitative and functional aspects of the complement system in CF are contradictory. An increased concentration of C3 in the sera of CF patients and gene carriers has been reported. The elevated levels in both healthy carriers and patients suggest a genetic mechanism for this increase, rather than simply a response to chronic infection. Polley and Rearn [12] reported a defective activation of the alternative pathway in serum exposed to inulin. Götz and Lubec [5] have shown that complement activation can occur via both the classical and alternative pathways during respiratory infection in patients with CF, and that immune complexes are formed.

The data of Strauss [14] indicated that the concentrations of classical complement components and the haemolytic activity of this pathway were similar in sera from CF patients and controls, and that the concentrations of C3 and Factor 8 were increased significantly in the sera from the patients, but that the level of C3b inactivator was nearly identical in patients and controls. Factor 8 was more readily activated in CF patient serum than in the control serum. A complement deficiency was not found. The significance of the easily activated Factor B is undefined.

Strunk et al [13] found depressed levels of complement C3 and C4 dur-

ing viral lower respiratory tract illnesses in the group of CF patients; these levels normalized after recovery. There was no clinical evidence of immune complex disease. It was postulated that antigen-antibody complex activation of complement may occur in CF homozygotes with viral lower respiratory tract illnesses.

The significance of complement changes in CF is unknown. Conover et al [4] have proposed that abnormalities of the complement system are directly related to the pathogenesis of CF. It is their contention that the ciliary dyskinesis factor of CF and the anaphylatoxin derived from C3 are closely related; and that C3a and perhaps other biologically active peptides accumulate in vivo to reach toxic concentrations because they are inefficiently catabolized due to decrease in arginine-peptidase and carboxypeptidase B. Lieberman [8] did not find any deficiency of carboxypeptidase B activity in patients with CF.

Ceder and Kolbert [3] have studied the uptake of acid hydrolases in 3 cell lines with different enzyme deficiencies. The intracellular enzyme activities increased when the cells were cultured in medium conditioned either by normal cells or by cells from cystic fibrosis patients. This indicates that the recognition marker on the CF enzymes is functioning normally when the enzymes are supplemented to cultured fibroblasts. Borgström et al [2] investigated the immunoreactive trypsin and the pancreatic secretory trypsin inhibitor in cord blood from infants with CF and reported that these pancreatic proteins were highly elevated. The lysosomal enzyme muramidase (lysozyme) is well known for its bacteriolytic activity. Hughes et al [6] did not find any significant difference between the serum levels of this enzyme in CF patients and controls. There was no correlation between the serum and salivary values and the age, sex or race of the subjects, the Shwachman-Kulczycki scores, colonization with Pseudomonas aeruginosa, Staphylococcus aureus or Haemophilus influenzae or white blood cell counts.

Wallwork et al [16] investigated various aspects of the immune status in CF homozygotes, and demonstrated that the serum IgG concentration was significantly increased or decreased in 10% of the cases, the IgA level fell transiently, while the serum IgM concentration was normal, and the IgE level was enhanced in 32%. The precipitating antibodies against the various antigens and allergens could be detected in the sputum, whereas their titre in the serum was extremely low or even zero. The serum C3 complement concentration was normal or mildly elevated.

In our experiments the C2 complement level was very low in 5 of the 17 CF patients; in all of these 5 cases relative antigens featured among the B locus antigens: B7, B35, and in one case B18. Of the A locus HLA-s, A11, A2, A9, A1 and A30 were confirmed. The lowest C2 complement levels were 144 IU/1 (HLA A2, 9; B12), 696 IU/1 (HLA A1, 30 B7, 35), 742 IU/1 (HLA A2, B7) and 906 IU/1 (HLA A2, B7).

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