

## Serum complement component depression during acute adenovirus conjunctivitis

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**SUMMARY** Serum C1q, C3, C4, and C5 components of complement levels were measured in 35 healthy subjects and 29 patients with acute conjunctivitis due to adenovirus type 2, 7, and 8 infections. Serum C1q and C3 levels were found to be significantly low, and there was no change in serum C4 and C5 levels. A progressive decline in the serum complement level with the severity of disease was observed. The change in the complement levels in serum showed a tendency to reach normal levels with clinical improvement.

The complement system plays a role in defending the host against infection.<sup>1</sup> It consists of a group of proteins of 19 components that are normally present in a native or inactive state.<sup>2</sup> The complements may potentiate immunopathological injury as well as decrease replication in viral infection.<sup>3</sup> Activated complement is an important mediator of tissue inflammation.<sup>4</sup> The ocular tissue is known to contain components for both classical and alternate pathways of activation of complement.<sup>5</sup>

The serum and tear immunoglobulin profile has been studied in patients with acute adenovirus conjunctivitis.<sup>6</sup> However, no study has been reported on the serum complement component concentrations in this disease. Here we report observations on the complement levels in serum in patients suffering from acute adenovirus conjunctivitis, in the acute stage and in remission, which occurred in epidemic form during July and August 1981. The findings regarding adenovirus culture and serological titres have been described elsewhere.<sup>7</sup>

### Material and methods

The study was carried out among 35 healthy subjects and 29 patients with virologically confirmed acute adenovirus conjunctivitis attending the outpatient department of Guru Nanak Eye Centre, New Delhi. The control group comprised healthy subjects who had no evidence of ocular or systemic disease and who attended the Eye Centre during the same period

mainly for the purpose of refraction. In the control group were 28 males and 7 females with a mean age of 32.1 years, and the patients comprised 24 males and 5 females with a mean age of 31.2 years. The diagnosis of acute adenovirus conjunctivitis was established by detailed clinical examination including slit-lamp biomicroscopy, bacterial culture, viral culture, and specific serological studies. The patients were sub-grouped as mild, moderate, and severe according to the intensity of chemosis and congestion. Seventeen cases were due to adenovirus type 8, 5 to adenovirus type 7, and 8 to adenovirus type 2.

The samples of serum were stored at  $-20^{\circ}\text{C}$  until assayed. They were analysed for complement components by single radial immunodiffusion.<sup>8</sup> Monospecific goat antisera against human C3, C4, and C5 components of complement and their respective standards were obtained from Meloy Laboratories, Virginia, USA. Antihuman C1q complement component serum was obtained from Behring Institute, Frankfurt, West Germany. The levels of C1q component of complement in the samples of sera were compared with the WHO reference standard serum 67/97 and expressed in units per dl, the WHO reference standard serum being taken as 100 units per dl. In 10 patients the serum samples were collected during the stage of remission when there was no clinical evidence of the disease.

### Results

Serum C3, C4, C5, and C1q components of complement level in patients with acute adenovirus

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Table 1 Serum complement component levels in mg/dl (C3, C4, C5) and units/dl (C1q) in normal controls and acute adenovirus conjunctivitis

Complements	Normal control			Acute adenovirus conjunctivitis		
	Mean	SD	Range	Mean	SD	Range
C1q	134.2	35.2	65.9-195.6	95.8	23.9	55.5-155.3
C3	196.3	41.2	90.6-275.5	146.6	30.3	78.3-182.0
C4	37.3	12.9	19.5-64.5	33.7	11.3	17.8-60.0
C5	12.8	5.1	6.6-24.5	10.9	5.6	2.5-26.7

SI conversion: mg/dl  $\times$  10 = mg/l.

Table 2 Serum complement component levels in mg/dl (C3, C4, C5) and units/dl (C1q) in mild, moderate, and severe types of acute adenovirus conjunctivitis

Types	No. of patients	C1q		C3		C4		C5	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD
Mild	5	114.3	23.5	160.5	22.2	37.4	11.2	12.5	5.1
Moderate	19	94.6	20.7	150.3	25.7	33.4	12.1	10.9	5.9
Severe	5	82.1	29.0	118.8	41.3	31.2	8.7	9.1	5.7

SI conversion: mg/dl  $\times$  10 = mg/l.

conjunctivitis are given in Table 1. There was no significant change in serum C4 components ( $p > 0.3$ ) and C5 components of complement levels ( $p > 0.2$ ), while the serum C3 component ( $p < 0.001$ ) and C1q components of complement levels ( $p < 0.001$ ) fell significantly in comparison with the levels in the healthy subjects.

Table 2 shows the serum C1q, C3, C4, and C5 components of complement levels in mild, moderate, and severe types of acute adenovirus conjunctivitis. The serum C1q component of complement level showed a significant fall in moderate ( $p < 0.001$ ) and severe ( $p < 0.001$ ) types of disease, while its level in the mild type ( $p > 0.2$ ) remained unaltered in comparison with the levels in the healthy subjects. The serum C3 component of complement level, however, showed a significant fall in all types of the disease ( $p < 0.005$ ,  $p < 0.001$ ,  $p < 0.001$  in mild, moderate, and severe types respectively). Serum C4 component of complement ( $p > 0.99$ ,  $p > 0.3$ ,  $p > 0.2$  in mild, moderate, and severe types respectively) and C5

component of complement levels ( $p > 0.95$ ,  $p > 0.3$ ,  $p > 0.2$  in mild, moderate, and severe types respectively) did not show any change in the severity of disease when compared with the levels in healthy subjects.

Table 3 shows the serum complement levels in patients with acute adenovirus conjunctivitis during the acute and remission stages. There was a significant rise in serum C1q components of complement level ( $p < 0.001$ ) and C3 components of complement level ( $p < 0.001$ ) in the stage of remission. The levels of the 2 complements C1q and C3 almost reached the normal values. However, no alteration was seen in the serum C4 ( $p > 0.8$ ) and C5 component of complement levels ( $p > 0.6$ ).

## Discussion

Viral diseases associated with serum complement depression have been recognised in man during hepatitis type B, Epstein-Barr infection, dengue haemorrhagic fever, and subacute sclerosing pan-encephalitis.<sup>9</sup> Viral-antigen-antibody complex activates the complement system, resulting in inflammatory injury.<sup>10-12</sup> It has been shown in ocular inflammation that activation of complements either by the classic or alternate pathway may be involved.<sup>13,14</sup> C1q, C3, and C4 components represent acute phase reactant in human serum.<sup>15</sup> These 3 complement components in serum were normal or raised during the acute phase and normal in the convalescent phase in patients with Epstein-Barr infection.<sup>16</sup>

C3 component acts as a focal point for activation of

Table 3 Serum complement component levels in mg/dl (C3, C4, C5) and units/dl (C1q) in acute and remission stages of acute adenovirus conjunctivitis

Complements	Acute stage		Remission stage		p value
	Mean	SD	Mean	SD	
C1q	97.3	16.2	127.6	17.6	<0.001
C3	143.6	23.3	181.7	27.1	<0.001
C4	36.6	12.4	38.2	10.8	>0.8
C5	11.1	4.5	12.2	3.9	>0.6

the terminal complement component leading to membrane damage and lysis.<sup>17,18</sup> A significant depression of C3 component in serum has been observed in the present study in patients with acute adenovirus conjunctivitis. The role of complement in conjunctivitis has not so far been studied. However, depression of C3 component in serum has been reported in patients with acute viral lower respiratory tract illness<sup>19</sup> and Argentine haemorrhagic fever.<sup>20</sup> The C3 deficiency is of particular importance because it participates in a variety of biological phenomena and is also situated at the pivotal point between the classical or alternate pathway.<sup>21</sup>

Viral lysis initiation is reported to be carried out by C1q component of complement.<sup>22</sup> A significant depression of serum C1q component level in patients with adenovirus conjunctivitis has been observed in the present study. C1q component level in serum was reported to be low in Junin virus haemorrhagic fever.<sup>20</sup> C1q component is reported to be depressed or absent in severe combined immunodeficiency.<sup>23</sup> An increased catabolism of C1q component is probably secondary to low levels of IgG in patients with immunodeficiency.<sup>24</sup> The present report is in agreement with these findings, for low serum IgG levels have been reported in acute adenovirus conjunctivitis in our earlier report.<sup>6</sup>

Low C1q and C3 component levels in serum may be due to the activation of the classical/alternate pathway, transient depression of complement component synthesis, increased catabolism, or the presence of inhibitors of complement action. The reversal of complement components (C1q and C3) in serum in the remission stage, as is evident from Table 3, is interesting, and it is obvious that serum complement component levels tend to attain the normal level as the disease recedes.

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