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Determination of circulating immune complexes and complement levels in some allergic reactions

Aliyeva TR, Akbarov EC.

Azerbaijan Medical University, 1022, Baku, Azerbaijan

*Correspondence: Aliyeva TR.

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ABSTRACT

The aim of the investigation was a comparative study of changes in the level of the complement and concentration of circulating immune complexes (CIC) in blood and lymph at the Arthus and Overy phenomenon.

Experiments were conducted in three series. As a control group, the concentration of circulated immune complexes and level complement in the blood and lymph of intact animals was investigated. The concentration of immunocomplexes circulating in blood and lymph was investigated by the method of sedimentation of proteins by 3.5% poliethilenglucolum. For the definition of the titer of the complement in blood and lymph, the Reznikov's method is applied. At the statistical processing of the received data, methods of descriptive statistics, and rank criterion of Wilcoxon-Manna-Whitney are applied. The average value of received data is applied in a format of M±m (min-max) [11].

Results. Both in the sensitization and resolution stages of the Arthus and Overy phenomenon, the concentration of circulating immune complexes (CIC) increases, but this increase is more pronounced in animals with reproduced Arthus phenomenon. The complement titer decreased in the period of sensitization and in the period of the Artyus phenomenon. And in the period of Overy's phenomenon, it decreases more expressively.

Keywords: complement, atopical reactions, circulating immune complexes

It has been established that the cause of type III hypersensitivity reactions is complement-binding immune complexes consisting of antibodies, DNA, and other components of nucleosomes, which are deposited in kidneys, skin, joints, and vascular plexuses. The prolonged circulation of IC (immune complexes) in the bloodstream and their ability to deposit in the vascular walls and tissues are largely determined by the size of IC and the fact that they can fix complement [3]. Fixation of IC on endothelial cell receptors causes damage and desquamation of endothelial cells.

In diseases such as rheumatoid arthritis, systemic

lupus erythematosus, polymyositis, etc., the amount of immune complexes in the blood increases, and the systems responsible for their removal (mononuclear phagocytes, erythrocytes and complement) are overloaded, complexes are deposited in tissues. Immune complexes can trigger mechanisms of inflammatory processes. Directly interacting with basophils and platelets, they induce the release of vasoactive amines, stimulate macrophages, causing the release of cytokines TNFa and IL-1, activate the complement system with the formation of anaphylatoxins C3a and C5a, which stimulate the release of vasoactive amines, and the secretion of chemotactic factors by mast cells and basophils. This picture is particularly typical of autoimmune diseases, in which complement-activating immune complexes are deposited in tissues, leading to damage and resolution of body cells.

The data indicate that the complement system can influence the course of many immune processes: localization and preservation of the antigen (AG) in terminal centers, cellular cooperation, metabolism and functional activity of immunocompetent cells, and IC utilization [2]. Complement activation in many diseases is inadequate and a vicious circle occurs, leading to further tissue damage, increased inflammatory response, and chronic course of the disease.

Binding of complement cleavage products by specific receptors of immunocompetent cells affects their cooperation, induction of immune response, and maintenance of its activity [1].

Taking into account the above-mentioned, we investigated the changes in the level of circulating immune complexes (CIC) and complement activity in the experimental phenomenon of Arthus and Overy.

Materials and methods of research. Experiments were carried out in 3 series: In the I series of experiments, these parameters were determined in 9 rabbits with the reproduced Arthus phenomenon, and in the II series - with the phenomenon of Overy. CIC and complement titer in the blood and lymph of intact rabbits served as a control. To reproduce the Aratus phenomenon, rabbits were sensitized by subcutaneous injection of 1 ml of horse serum into the scapular region every 5 days; after the fifth injection, necrosis was observed in the area of horse serum injection. To reproduce the Avery phenomenon, the sensitized animal was injected subcutaneously with a permissive dose of horse serum, and Evans' blue was injected into the auricular vein. The area of injection is colored blue.

The blood necessary for the experiment was taken from the rabbit marginal vein, and lymph was taken from the thoracic lymphatic duct according to the method of A.A. Kornienko modified by M.H. Aliev and V.M. Mamedov [3]. CIC concentration was determined according to the Grinevich Y.A. and Alferov A.N. methods [6]. The method is based on the precipitation of antigen-antibody complexes with 3.75% polyethylene glycol solution followed by photometric determination of the optical density of the precipitate on a 450 nm wavelength spectrophotometer (Specol, Germany) and the conventional unit was indicated.

Reznikova's method (1967) was applied to determine complement activity in blood and lymph. The principle of the method is based on immune hemolysis of erythrocytes in the presence of hemolysin and complement followed by photometric determination of the optical density of the precipitate on a

450 nm wavelength spectrophotometer (Speckol, Germany) and the hemolytic unit is indicated [8].

The methods of descriptive statistics, the Wilcoxon -Mann-Whitney rank criterion were applied in statistical processing of the obtained data. The mean value of the obtained samples was applied in the format M±m (min-max) [4].

Results and discussions. As a result of the study, it was established that both in the sensitization and resolution stages of the Arthus and the Overy phenomenon, the concentration of circulating immune complexes (CIC) increases, but this increase in animals with reproduced Arthus phenomenon was more pronounced. The complement titer decreases during the period of sensitization and the Arthus phenomenon. And in the period of the Overy phenomenon, it decreases more expressively.

Thus, if at the stage of sensitization of the Arthus phenomenon (5th day), the complement titer in the blood decreases in comparison with intact animals by 1.4 times, equal to 29.0 c.u., at the stage of development of the Arthus phenomenon, the complement titer sharply decreases. If at the stage of sensitization (5th day) of the Arthus phenomenon, related to immunocomplex reactions, the complement titer in the blood decreased in comparison with intact animals 1,1 times and was equal to 36,4 c.u., then in the resolution period, the complement titer sharply decreased and was equal to 4,8 c.u.

The concentration of CIC in the blood compared to control figures increased 4.5 times ($p<0.001$) at the stage of sensitization (day 5), and at the stage of the Arthus phenomenon (day 25), there was an increase in the concentration of CIC 11.8 times ($p<0.001$), i.e., more than in intact animals (38.14 mmol/l.). In some animals at the stage of the Arthus phenomenon, the area of injection is slightly hyperemic and the area of necrosis is small. And in others, on the contrary, strong hyperemia and necrosis were observed.

Table 1. Complement titer and CIC concentration in the blood during the Arthus and Overy phenomenon

Number of animals n = 18	Overy phenomenon				Arthus phenomenon			
	Day of sensitization, CIC concentration	Overy phenomenon period,CIC concentration	Day of sensitization, complement titer	Overy phenomenon period, CIC concentration	5th day of sensitization, CIC concentration	Arthus phenomenon period, CIC concentration	5th day of sensitization, complement titer	Arthus phenomenon period, complement titer
M±m	6.16±0.14	15.37±0.33	27.4±0.4	11.3±0.4	14.60±0.39	38.14±0,44	36.4±0.3	4.8±02
Min	5.5	13.2	25.9	9.9	12.8	36	34.6	4
Max	7	16.3	30.1	13.8	16.1	40,1	37.8	6
p	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001

In the period of sensitization of the Overy phenomenon the complement titer in blood decreased by 1.5 times in comparison to intact animals and was equal to 27.4 u.u., the concentration of circulating immune complexes (CIC) increased by 1.9 times and was equal to 6.16 mmol/l ($p < 0.001$). Compared to blood, these parameters' changes were somewhat less pronounced in lymph.

During the sensitization period of the Overi phenomenon in the lymph, the complement titer decreased by 1.5 times compared to intact animals and was equal to 27.4 ($p < 0.001$) c.u., then the concentration of circulating immune complexes increased by 1.9 times ($p < 0.001$). In animals with the reproduced Overy phenomenon, the complement titer decreased by 3.6 times compared to intact animals and was equal to 11.3 c.u. ($p < 0.001$), the level of CEC during this period increased by 4.0 times higher than that of intact ones (Table No. 2). At the same time, the concentration of CEC and complement titer increased 2.6 times ($p < 0.001$) in comparison to intact animals and was equal to 1.92 mmol/l in animals with the reproduced Arthus phenomenon.

Table 2. Complement titer (in c.u.) and CIC concentration (mmol/L) in lymph at Arthus and Overy phenomenon.

Number of animals n =18	Overy phenomenon				Arthus phenomenon			
	Day of sensitization, CIC concentration	Overy phenomenon periods, CIC concentration	Day of sensitization, complement titer	Overy phenomenon period, CIC concentration	5th day of sensitization, CIC concentration	Arthus phenomenon period, CIC concentration	5th day of sensitization, complement titer	Arthus phenomenon period, complement titer
M± M ±m	4,84 ±0,17	10,07 ±0,17	22,6 ± 0,3	10,4 ±0,8	5,76±0,12	27,16± 0,73	20,7 ±0,3	3,8±0,4
Min	3,6	9,2	20,9	6,9	5,2	22,1	19,8	1,8
Max	5,3	10,9	24	14,4	6.2	29,1	23,1	5,4
p	0,001	0,001	0,001	0,001	0,001	0,001	0,001	

Discussion

Studies have found that, in the Arthus phenomenon, the concentration of CICs is elevated during both the sensitization and resolution stages [1]. Some researchers have observed low CIC values, which correlated with high titer of the C4 component of complement and increased serum IgE concentration for atopic course of allergic disease [10]. Our studies showed increased CIC leads and a moderate decrease in the Arthus phenomenon [2]. Some authors have noted a correlative relationship between the content in the blood of CIC, the complement system, and the severity of the course of atopic diseases [10]. It has been shown that people with congenital defects of the complement system are predisposed to the development of IC diseases [11].

Thus, our studies have shown that:

1. In the Arthus phenomenon, complement titer decreases both in the sensitization and Arthus phenomenon periods.
2. In animals, reproduced by the Overy phenomenon, the complement titer decreases more pronouncedly.
3. In both allergic reactions the concentration of CIC is increased, but in the Arthus phenomenon, this increase is more pronounced.

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