IMMUNOLOGICAL SPECIFICITY OF HUMAN HEART TISSUES IN ATHEROSCLEROSIS

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Despite the great importance of this problem, little attention has been paid to the immunological investigation of the heart tissue in atherosclerosis. Only isolated immunological studies of the serum proteins have been made.

For instance, the method of immune precipitation revealed the presence of a β-lipoprotein fraction in the serum of dogs receiving thiourea and cholesterol which was not present in the serum of healthy animals. Antisera obtained during immunization of rabbits with lipoproteins isolated from the serum of persons with coronary atherosclerosis have been found to differ in their immunological properties from normal sera [7]. The precipitation reaction has demonstrated specific differences between the sera of patients with coronary atherosclerosis and the sera of clinically healthy persons. The immunoelectrophoretic investigation of the serum of persons suffering from atherosclerosis has revealed the presence of an antigenic substance not found in persons with no clinical signs of atherosclerosis [3]. Immunization with β-lipoprotines isolated from the blood of animals kept on a high cholesterol diet has been found to prevent the development of atherosclerosis in rabbits and cocks fed on cholesterol. The complement fixation reaction has revealed specific properties of blood vessels from human subjects showing atherosclerotic changes [4, 5, 8]. In the present paper the results of an investigation of human heart muscle tissue from persons with atherosclerosis are described.

EXPERIMENTAL METHOD

Three preparations of heart tissue from persons dying from atherosclerosis at the ages of 67, 80, and 83 years were used.* As normal controls 2 preparations of heart muscle were obtained from persons dying from road traffic accidents at the age of 18 and 28 years.

Antisera were obtained by injecting a tissue homogenate in physiological saline (1:10) into rabbits. Immunization was carried out every other day for 8 days. Blood was taken on the eighth day after the last injection.

Eleven antisera were obtained and investigated: 4 sera against mixed heart tissue from the 2 "healthy" subjects, 3 sera against mixed heart tissue from 2 patients with signs of marked atherosclerosis, and 4 sera against the heart tissue of one patient. Saline extracts of heart muscles in a dilution of 1: 10† were used as test antigens. The doses of the antigens were determined as protein, the total concentration of which was estimated by Lowry's method [6].

The serological activity of the tissues was determined by the complement fixation reaction in a 50% titer[1]. Altogether 25 experiments were performed.

* The heart muscles of persons dying from atherosclerosis were obtained from the Department of Pathological Anatomy, Second Moscow Medical Institute, and the "healthy" heart muscles from the Lefortovo morgue.
† In the subsequent description the sera obtained against muscle tissues with marked atherosclerosis are designated AC sera, and those obtained against "healthy" heart tissues HC sera; the antigens are similarly designated.

Quantitative Complement Fixation Reaction in a 50% Titer with Sera Against Heart Tissue of a Healthy Person and of a Patient with Atherosclerosis (in Units of Complement)

Immune antigen	Antiserum No.	Units of complement / Heart tissue	Dilution of antisera 1:10 Free	1:10 Fixed	1:20 Free	1:20 Fixed	1:40 Free	1:40 Fixed	1:80 Free	1:80 Fixed	1:160 Free	1:160 Fixed	1:320 Free	1:320 Fixed	Antigen control Free	Antigen control Fixed	Antiserum control Free	Antiserum control Fixed
AC	27	AC	6,6	18,4	7,2	17,8	7,5	17,5	9,0	16,0	11,4	13,6	25,0	—	25,0	—	25,0	—
		HC	6,0	19,0	6,4	18,6	7,0	18,0	25,0	—	25,0	—	25,0	—	25,0			
AC	75	AC	6,0	19,0	6,8	18,2	7,3	17,7	7,8	17,2	12,0	13,0	25,0	—	25,0	—	25,0	—
		HC	5,8	19,2	6,6	18,4	25,0	—	25,0	—	25,0	—	25,0	—	25,0	—		
HC	33	AC	6,6	18,4	25,0	—	25,0	—	25,0	—	25,0	—	25,0	—	25,0	—	25,0	—
		HC	6,0	19,0	6,2	18,8	6,8	18,2	7,8	17,2	25,0	—	25,0	—	25,0	—		
HC	24	AC	5,5	19,5	6,9	18,1	7,3	17,7	25,0	—	25,0	—	25,0	—	25,0	—	25,0	—
		HC	—	25,0	4,5	20,5	5,8	19,2	6,2	18,8	6,9	18,1	25,0	—	25,0	—		
Complement control			25,0	—														

Note. Free) Free units of complement; fixed) fixed units of complement.

EXPERIMENTAL RESULTS

The results of tests of 4 antisera by the complement fixation reaction with two test antigens are shown in the table. Both antisera tested in this reaction with homologous test antigens showed serological activity. Sera Nos. 27 and 75 and sera Nos. 33 and 24, for instance, reacted with the homologous antigens in dilutions of 1: 160 and 1: 80.

Cross reactions between the antisera and test antigens revealed that the antisera under investigation reacted differently with the HC and AC antigens. Whereas sera Nos. 27 and 75 reacted with AC antigen in a titer of 1: 160, fixing in these conditions 13.6 and 13 units of complement from 25 units taken in the experiment, with antigen from the "healthy" heart the reaction ended in one case in a dilution of 1: 40, and in another case—1: 20. The opposite principle was observed in all the experiments undertaken with serum obtained against HC muscles, whereas serum No. 33 reacted with HC antigens in a dilution of 1: 80, fixing 17.2 units of complement, and serum No. 24 in a dilution of 1: 160, fixing 18.1 units of complement of the 25 units taken for the experiment, when AC antigen was tested the reaction with serum No. 33 was completed in a dilution of 1: 10, and with serum No. 24 in a dilution of 1: 40. A similar pattern was observed in all the experiments carried out. The titer of the reaction between AC antiserum and antigens from AC tissue was always greater than the titer of the reaction with antigens from HC tissue. The reaction between HC antiserum and the homologous antigen took place at a higher dilution than the reaction with AC antigen.

The results of the study of the antisera and antigens by the complement fixation reaction in a 50% titer thus revealed antigenic differences between the muscles of a heart with marked signs of atherosclerosis and the muscles of a clinically healthy heart. Apparently specific changes take place in the human heart muscle in atherosclerosis which are not found in the heart muscle of healthy persons. Whether these changes are the result of the characteristic metabolic disturbances found in atherosclerosis or whether they arise in the course of aging are problems for special examination.

SUMMARY

A method of quantiative complement fixation reaction in a 50% titer was used to study sera against the heart tissues of patients with atherosclerosis and healthy individuals. Cross experiments demonstrated that heart tissues differed immunologically in patients with atherosclerosis and healthy individuals.

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