IMMUNOLOGICAL SPECIFICITY OF HUMAN AORTIC TISSUES IN ATHEROSCLEROSIS

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It has been shown [4-10] that the serum of patients with atherosclerosis, and also the serum of animals with experimental atherosclerosis possess specific features. Most investigators consider that the specific changes in the blood serum in this disease are associated with the β-lipoprotein fraction. It should be noted, however, that only isolated reports have been published of studies of the specific changes in the walls of the lower limb vessels [8, 10] and in the heart tissue of patients with atherosclerosis.

Bearing in mind that atherosclerotic changes are localized in the vascular system, and also the fact that the earliest and the most marked changes are found in the aorta, we have made an immunological study of the human aorta in atherosclerosis.

METHOD

Two methods were used in this investigation: the complement fixation reaction (CFR) at 50% titer [3] and the reaction of fixation of antiserum protein by antigen adsorbed on paper [1, 2]. Antisera were obtained from 13 rabbits. As antigens for immunization a mixture of aortic tissue from patients dying at the ages of 60, 64, and 82 years, with a diagnosis of atherosclerosis, and the aortic tissue from a clinically healthy person dying at the age of 28 years as a result of an accident, were used*.

The rabbits were immunized by intraperitoneal injection of homogenate of human aortic tissues in physiological saline in a dose of 2 ml (1:10) on alternate days for 8 days. Antisera were obtained on the 8th day after the last injection. Eight antisera were obtained against mixed tissues of aortas with marked signs of atherosclerosis, 5 against the tissue of the one aorta from the clinically healthy person dying accidentally. Saline extracts of human aortic tissues, prepared in a dilution of 1:10, were used as test antigens in the CFR at 50% titer. The doses of test antigens were estimated as protein, the total content of which was determined by Lowry's method.

RESULTS

The results of the serological study of the aortic tissues of a patient with marked signs of atherosclerosis and of the aortic tissues of the clinically healthy subject are given in Table 1 (prototype record of 26 experiments). Serum No. 57 was obtained against the aortic tissues of a patient with atherosclerosis, and serum No. 61 against the

*The aortas of the persons dying with a diagnosis of atherosclerosis were obtained from the Department of Pathological Anatomy, 2nd Moscow Medical Institute, and the aorta of the clinically healthy person from the Department of Pathological Anatomy, 1st Moscow Medical Institute.

TABLE 1. Quantitative CFR at 50% Titer with Sera against Aortic Tissues of Healthy Person (HA) and of Patient with Atherosclerosis (AA)

Antigens for immunization	Serum No.	Test antigen	Dilution of antiserum															
			1:10		1:20		1:40		1:80		1:160		1:320		1:640		KA	
			free	fixed	free	fixed	free	fixed	free	fixed	free	fixed	free	fixed	free	fixed	free	fixed
AA	57	AA	10,7	22,3	12,3	20,7	13,2	19,8	13,8	19,2	13,8	19,2	14,0	19,0	33,0	—	33,0	—
		HA	12,0	21,0	13,2	19,8	14,0	19,0	33,0	—	33,0	—	33,0	—	33,0	—	33,0	—
HA	61	AA	10,7	22,3	14,7	18,3	14,7	18,3	33,0	—	33,0	—	33,0	—	33,0	—	33,0	—
		HA	—	33,0	12,3	20,7	12,8	20,2	14,7	18,3	33,0	—	33,0	—	33,0	—	33,0	—
KC	№57		33,0	—	33,0	—	33,0	—	33,0	—	33,0	—	33,0	—	33,0	—	—	—
KC	№61		33,0	—	33,0	—	33,0	—	33,0	—	33,0	—	33,0	—	33,0	—	—	—
Complement control			33,0	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—

Note. Free—free units of complement, fixed—fixed units of complement.

TABLE 2. Fixation Reaction of Protein of Antiserum against Human Aortic and Heart Tissues from a Healthy Person and a Patient with Atherosclerosis.

Antigens for immunization	Serum No.	Test antigen	Specific increase in protein (μg)
AA	57	AA	140
		HA	110
HA	64	AA	160
		HA	380
AC	17	AC	210
		HC	105
HC	24	AC	52
		HC	104

Notes. 1. AA) Saline extract of atherosclerotic aortic tissue adsorbed on paper. 2. HA) saline extract of healthy aortic tissue adsorbed on paper. 3. AC) saline extract of atherosclerotic cardiac tissue adsorbed on paper. 4. HC) saline extract of healthy cardiac tissue adsorbed on paper.

aortic tissues of an apparently healthy person. Each serum was investigated with two test antigens—a saline extract of the aortic tissue from the cadaver of a patient dead from atherosclerosis and a saline extract of the aortic tissue of a clinically healthy person.

Analysis of the results shows that the sera against the atherosclerotic tissues reacted with the homologous test antigens (AA) in higher dilutions than with the heterologous (AH). A different picture was seen in the reaction between the sera against normal aortic tissue and the corresponding test antigens. For example, serum No. 57 reacted with test antigen of atherosclerotic aortic tissue in a dilution of 1:320, to fix 19 of the 33 units of complement taken in the experiment. The same serum, when reacting with aortic tissue from the healthy person, reacted in a dilution of 1:40, fixing 19 units of complement. Serum No. 61 reacted with homologous test antigen in a dilution of 1:80, whereas its reaction with heterologous test antigen terminated in a dilution of 1:40. It may be concluded from these results that the aortic tissues of the patient with signs of marked atherosclerosis were antigenically different.

The protein fixation reaction [1, 2] was used to investigate, not only sera against human aortic tissues, but also sera obtained against the heat tissues of patients with a diagnosis of atherosclerosis dying at the ages of 67, 80, and 83 years. The results are given in Table 2 (prototype record of 10 experiments).

In the protein fixation reaction the degree of reaction between antigen and antibody is expressed by the magnitude of the specific increase in protein, which is equal to the difference between the increase in protein of the antiserum during the reaction with the given antigen and the increase in protein of a nonimmune serum reacting with the same antigen. It follows from Table 2 that the specific increase in the protein of serum No. 57 against atherosclerotic aortic tissue reacting with homologous test antigen adsorbed on paper was 140 μg, whereas when reacting with heterologous test antigen, i.e., with adsorbed antigen of aortic tissue from a healthy person, the specific increase in protein was 110 μg. The specific increase in the protein of antiserum No. 64 to aortic tissues of the healthy person was 380 μg, and to atherosclerotic tissues it was 160 μg. A similar relationship was observed during the study of atherosclerotic human heart tissues.

On the basis of the results of the above experimental investigation of the antigenic changes in human aortic and cardiac tissues in atherosclerosis, and also of the results reported in the literature of the immunological investigation of sera [4-10] in this disease, it may be postulated that atherosclerosis is accompanied by a change in metabolism which leads to the appearance of substances in the wall of the aorta possessing antigenic properties different from those of normal human aortic tissue.

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