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Pathomorphologic Investigation of Intraorgan Arteries in Patients with Coarctation of the Aorta

E. E. Litasova, S. G. Chasovskikh, I. I. Semenov, and D. I. Indinok

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A stereotypic angiospasm develops in intraorganic arteries during coarctation of the aorta, which is characterized by different functional impacts: resistance in the basin of elevated vascular pressure and pressure and bloodflow regulation in the hypotension basin. The most marked structural changes are observed in the renal and coronary arteries. Changes in the small coronary arteries are mainly due to myocardial hypertrophy, whereas in the larger ones they are caused by the increased pressure transferred from the aorta. The degree of structural changes in the larger coronary arteries is greater than in the small arteries.

Key Words: *coarctation of the aorta; arteries; morphology*

Two circulatory basins with opposite hemodynamic regimens - hyper- and hypotension - appear in the organism during coarctation of the aorta (CA). The extracardiac (vascular) mechanisms of compensation in CA have been investigated mainly in experimental models [1,2,4,5,7-10, 12-17], except for a few works devoted to changes in the microcirculatory bed of the upper and lower extremities in patients [6].

This study was aimed at comparing the structural changes in the intraorgan arteries with opposite hemodynamic regimens in patients with CA.

MATERIALS AND METHODS

Material from 15 deceased patients with isolated preductal CA aged 5 to 52 years was used in the study. Three groups were distinguished in terms of age-specific vascular changes and physiological periods of life: the first comprising children and adolescents and the second and third adults aged under and over 35, respectively.

In order to elucidate the role of increased pressure in the aortic arch in the changes that develop in the coronary vessels, we selected a group consisting of 5 cases with congenital aortal stenosis involving fairly severe systolic overload of the left ventricle.

Specimens of tissues from the heart, brain, kidneys, spleen, and interdigital arteries of the extremities were taken for histological investigation. Paraffin embedding of the material and staining of tissues with hematoxylin-eosin and after Van Gieson (with additional resorcin-fuchsin staining of elastic tissues) were used.

Changes detected in the arterial wall were assessed using a previously proposed five-stage classification for the coronary vessels [3].

Research Institute of Circulation Pathology, Ministry of Health and the Medical Industry of the Russian Federation; Institute of Regional Pathology and Pathomorphology, Siberian Division of the Russian Academy of Medical Sciences, Novosibirsk

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TABLE 1. Structural Changes in Coronary Vessels and Myocardium in Patients with Coarctation of the Aorta (CA)

Parameter	Heart compartment	Age (years)			
		5-17	21-34	35-52	on the whole
Degree of changes in 6th-7th order coronary arteries (5-point scale)	LV	2.0	2.7	3.1	2.6
	RV	1.6	2.0	2.6	2.0
	LA	1.5	1.8	2.0	1.7
	RA	2.2	2.5	3.5	2.6
Ratio of cardiomyocyte diameter in CA to age-specific value, %	LV	169±6.3	199±5.3	152±9.1	273±8.2
	RV	117±8.6	150±6.4	163±6.0	143±8.4
	LA	136±7.4	153±6.0	125±9.1	138±7.3
	RA	149±3.4	124±6.1	105±7.3	126±5.8
Area occupied by myocardial connective tissue on slices, %	LV	10.0±0.6	19.3±0.3	24.2±0.4	17.8±0.4
	RV	9.1±0.6	11.2±0.4	12.0±0.5	10.8±0.5
	LA	7.6±0.8	10.1±0.5	19.4±0.6	12.4±0.6
	RA	15.0±0.9	19.8±0.3	25.1±0.7	19.9±0.6

Note. Here and in Table 2: left (LV) and right (RV) ventricles; left (LA) and right (RA) atria.

Cardiomyocyte diameter in various parts of the heart of patients with CA and controls (subjects who had died from causes other than cardiac) was measured in paraffin slices using an ocular micrometer. The data are represented as the ratio of cardiomyocyte diameter in CA to the age-specific value. For assessing the severity of sclerotic processes in the myocardium of various heart compartments, the area occupied by connective-tissue structures was measured by morphometric methods. The results of quantitative analysis were processed using methods of mathematical statistics.

RESULTS

Moderate spiralization of the inner elastic membrane (IEM) without signs of its thickening was detected in the small intraorgan arteries of the brain. Thickening of the IEM was revealed in many arteries of a similar diameter (Fig. 1, *a*). Slight or moderate hypertrophy of smooth-muscle cells (SMC) was usually observed in the middle layer of small arteries. The adventitia of the vessels changed negligibly. Atrophy of the middle layer, leveling of the relief, and dilatation of the lumen were found in some patients of age group 3.

Clear-cut vascular changes were detected in the coronary arteries. A thickened and crimped IEM and hypertrophied SMC in the middle layer were seen in the small arteries of some patients. Sclerotic cufflike thickenings with hyperproduction of collagen were often observed periadventitially. Such changes occurred mainly in the small arteries of the left heart, mainly the left ventricle. Subendocardial and subepicardial small arteries of the right ventricle were observed in some cases, which were similarly characterized by a hypertrophic thickening of the media and spastic changes of the inner layer. Changes in the intima (crimped and thickened IEM) and media (hypertrophy) of the arteries of the 6th-7th order of branching were more expressed in the left versus the right ventricle. This was particularly manifest in patients aged under 17. Similar differences in the structural changes of the small coronary arteries were observed in the left and right atrial vessels.

TABLE 2. Comparative Characteristics of Structural Changes in the Coronary Arteries of Different Diameter in the Ventricles of Patients with Coarctation of the Aorta (CA) and Congenital Aortic Stenosis

Diameter of coronary arteries	Heart compartment	Degree of structural-hyperplastic changes in coronary arteries (for the whole group)	
		CA	congenital aortic stenosis
6th-7th order of branching	LV	2.6	3.0
	RV	2.0	1.7
	LA	1.7	2.0
	RA	2.6	2.1
4th-5th order of branching	LV	3.4	2.4
	RV	2.5	1.6

Note. Mean values for the group are presented, assessed using a 5-point scale.

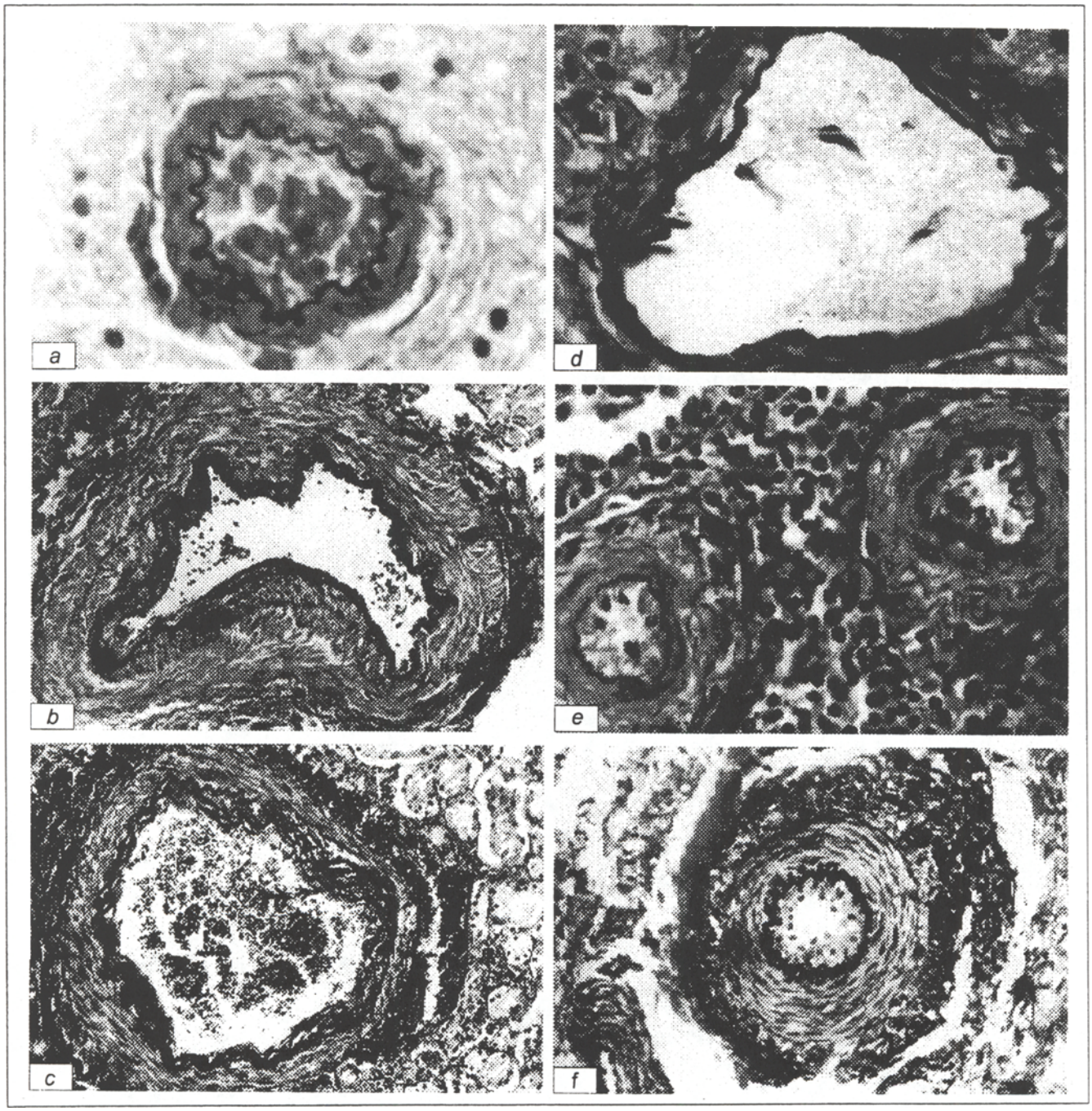

Fig. 1. Compensatory changes in the intraorgan arteries in coarctation of the aorta (CA). *a*) spiralization and negligible thickening of the inner elastic membrane (IEM) in a small artery of the brain in CA; *b*) hypertrophy of the muscle layer, elastofibrosis of the intima of 4th-order coronary artery in the right ventricle; *c*) thickening and increase of the number of elastic fibers in the intima of the renal arciform artery; *d*) atrophic thinning of the wall and dilated lumen of the intralobular artery of the kidney in a patient aged 52; *e*) hypertrophy of the media and angiospastic thickening of the intima in follicular arteries of the spleen; *f*) perivascular sclerosis, hypertrophy of the media, thickening of the IEM, and angiospastic thickening of the intima of an interdigital artery of the hand. *a-c*: Van Gieson staining with fuchseline; *d-f*: Van Gieson staining. *a*, *d*, *e*: ×640; *b*, *c*, *f*: ×200.

Cardiomyocyte hypertrophy in the left ventricle, which is functionally under a greater load in this condition, was somewhat more expressed than in the right (Table 1). The hypertrophic changes of cardiomyocytes were more pronounced in children and adolescents. In subjects aged over 35 cardiomyocyte hypertrophy in the left ventricle was somewhat lower. Hypertrophic changes in the left atrium were most expressed in groups 1 and 2. In the right atrium cardiomyocyte hypertrophy steadily lessened with age.

The time course of sclerotic processes in the organ tissue is an important factor which helps clarify

the relationships between changes in cardiomyocytes, stroma, and arterial vessels supplying the myocardium. Quantitative assessment of cardiomyofibrosis showed that fibrosis of the stroma slackens with age. On the other hand, myofibrosis is appreciably enhanced in the left ventricle of patients aged over 15. In the atria, particularly in the right one, myofibrosis intensifies with age.

Marked compensatory hypertrophy of the left-ventricular myocardium develops in patients with congenital aortic stenosis, similarly as in those with CA, but the pressure in the aortic arch is not as high. Changes in the small coronary arteries (of the 6th-7th order of branching) in these two groups of patients are similarly expressed. Comparison of the structural changes in the walls of larger arteries (4th-5th order of branching) showed them to be more expressed in the left versus the right ventricle in CA and less expressed in congenital aortic stenosis. It is noteworthy that in the arteries of the 6th-7th order of branching in CA such changes were more marked than in larger arteries (of the 4th-5th order of branching, Fig. 1, *b*). In congenital aortic stenosis the changes were more pronounced in the small than in the large arteries (Table 2).

Assessment of the relationships between structural and hyperplastic changes in the coronary vessels and the time course of compensatory processes in the myocardium permitted us to make several assumptions. Changes in the intracardiac hemodynamics (pressure rise in the cardiac cavities with their blood content increased) and the specific features of the coronary bloodflow affect myocardial compensation in heart diseases. Structural changes in the coronary arteries are associated with increasing cardiomyocyte hypertrophy in the majority of heart defects. The major changes involve the small muscular arteries (arteriolar barrier). In CA the high systolic and diastolic pressure transferred from the aorta appreciably affects the more proximal muscular elastic arteries. Apparently, it is this factor that leads to an appreciable arteriosclerosis of the vessels supplying not only the left, but also the right heart.

Some authorities [11] explain the more expressed signs of decompensation of the functionally less loaded right compartments of the heart in comparison with the left in CA by desynchronization of the work of the left and right heart in patients with a "hypertensive" heart. Without ruling out the effect of this component, we believe that CA involves a dissociation of the adaptive reserve, which is weakly expressed in the right compartments and surpasses the necessary level of blood supply. As a result, with the bioenergetics at a low ebb, the adaptive reserve becomes depleted sooner and the transition to the stage of decompensation is hastened. This is clearly seen in the right atrium in the form of a very low and progressive drop of the level of cardiomyocyte hypertrophy and, with age, maximal myofibrosis.

In the arteries of the hypotension basin the greatest changes were observed in the renal vessels. The IEM was folded and thickened in the interlobular arteries of different diameter. In the middle layer of the vessel a hypertrophy of SMC was observed. Sometimes the number of elastic membranes in the intima and a thickening of the hypertrophied middle layer of the arciform arteries of the organ were clearly seen (Fig. 1, *c*), often associated with elastofibrosis of the adventitia. The structural changes (more pronounced in the intima) progressed to stages 3-4 in almost half the observations. Despite the appreciable changes in the vessels of the cortical layer of the kidneys, sclerotic changes here were less expressed than in the medullary layer. Sclerotic glomeruli were rather few and dystrophic changes in the epithelium of twisted canaliculi were moderately expressed. On the whole, we may speak about chronic angiospasm of the system of arteries in this organ.

An opposite development of structural hyperplasia was observed in the renal arteries at later stages of the disease: signs of moderate hypertrophy of SMC and even its reduction in the middle layer, as well as a general thinning of the layer; the IEM either remained slightly thickened or looked atrophic. The arterial lumen was dilated, and the internal relief of the intima devoid of its usual folds (Fig. 1, *d*). Changes in the renal vessels were observed in all cases, this distinguishing the kidneys from all other organs in patients with this congenital defect.

Among the other organs of the hypotension basin, arterial changes were found in the spleen. A slight hypertrophy of the smooth-muscle layer, slight foldedness, and a negligible thickening of the IEM were detected. Signs of angiospasm of the intrafollicular artery (Fig. 1, *e*) with a "cushionlike" sclerotic thickening of the intima and stenotic lumen were revealed in one 22-year-old patient.

Interdigital arteries of the upper and lower extremities were examined in some patients. In group 1 the changes were observed mainly in the small arteries of the hands: IEMs were crimped, with densely disposed endotheliocytes, as well as sclerosis and hypertrophy of the media (Fig. 1, *f*).

Hence, the pattern of changes in the intraorgan arteries was on the whole similar to that in experimental CA [12], but the angiospastic signs were more expressed in the experiment, which might be due to the greater plasticity of vascular walls in the earlier stages of circulatory disorders.

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