# MORPHOLOGY AND PATHOMORPHOLOGY

# Morphogenesis and Variants of Remodeling of Atherosclerotic Heart

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Morphogenesis of atherosclerotic heart is presented on the basis of complex pathomorphological analysis of 1000 autopsies. Special attention was paid to the dilatation and hypertrophic variants and to structural mechanisms of heart and coronary vessel remodeling under conditions of atherosclerotic process. Predominant remodeling of atherosclerotic heart and coronary arteries by the dilatation variant determines unfavorable prognosis of heart failure. Compensatory and adaptive processes (cardiomyocyte hypertrophy and collateral circulation) developing in the heart compensate for functional insufficiency of the organ for some time.

**Key Words:** *atherosclerosis; dilatation and hypertrophic remodeling; cardioventriculography; coronarography; morphological methods*

Atherosclerotic heart (AH) is a chronic dysfunction developing as a result of relative or absolute reduction of arterial blood supply to the myocardium. According to the International Statistical Classification of Diseases and Health-Related Problems (10th revision; 1995), AH is a form of chronic coronary heart disease (CHD). Atherosclerotic heart is a disease standing out from the group of coronarogenic diseases because of high incidence, complex pathogenesis, polymorphic clinical pathomorphological manifestations, and severe complications [5].

Statistical interpretation of AH corresponds to that of nosological entities included in the group of chronic CHD (denoted as chronic or lasting for more than 8 weeks). The term AH (as a clinical pathomorphological variant of chronic CHD) is equivalent to the term "atherosclerotic cardiosclerosis" widely used in clinical practice. These terms are synonymous because of common etiology and pathogenesis, disease manifestations, and acknowledged statistical analysis.

Analysis of the main manifestations of AH hemodynamic disorders persuasively indicates nosological universality of such notions as atherosclerotic heart disease, atherosclerotic cardiosclerosis [14], ischemic heart [12], ischemic cardiomyopathy [13], or chronic ischemic cardiomyopathy [11]. The type of pathomorphological changes in AH myocardium and coronary system, patho- and thanatogenesis factors, and causes and mechanisms of death of the patients confirm common nosology.

We carried out a complex pathological study of AH with the analysis of the incidence of the involvement of the main coronary arteries (CA), causes of death, distinguishing the main variants of heart remodeling and compensatory adaptive changes in the coronary vessels.

## MATERIALS AND METHODS

The study was carried out on the hearts of dead patients with AH. Detailed retrospective analysis

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was carried out in group 1 (600 observations; 440 men and 160 women, mean age 68.2±0.8 years, mean duration of disease 12.2±0.4 years). This analysis included studies of case histories, evaluation of the results of paraclinical examination and autopsy protocols, and comparative analysis with archive histopreparations. Complex pathomorphological analysis including studies by modern methods was carried out in group 2 (400 observations; 260 men and 140 women, mean age 72.4±0.8 years, mean disease duration 16.6±0.2 years). In parallel, clinical pathomorphological analysis of pathomorphological data and results of vital functional tests (mainly echocardiographic) was carried out.

Control group included 100 hearts obtained at autopsy of age-matched subjects (accidental deaths) without atherosclerotic changes and aneurysms in CA (pathomorphological data).

The following studies of AH were carried out: postmortem contrast cardioventriculography, X-ray studies; separate weighing of the heart, volume/weight and planimetric cardiometry; postmortem contrast coronarography; biopsy of the myocardium; histological, histochemical, morphometric, electron- and polarization microscopy of the myocardium [7,8].

## RESULTS

Macroscopic study showed increased size and weight of AH (Fig. 1, *a*); the hearts were elongated, with "impending" atria. Macroscopic examination of the myocardium showed more intense pattern of the stroma and numerous small cicatricial formations, more often seen in the subepicardial compartments of the left ventricle and ventricular septum.

Postmortem coronarography showed the most frequent involvement of the anterior interventricular branch of the left CA; the right CA ranked second, and the circumflex branch of the left CA was rarely involved in obstructive atherosclerotic process [9,10].

Obstructive atherosclerotic lesions were mainly observed in the proximal segments of CA: in segments I and II (segment I was involved in 74.5%, segment II in 60.3%, segment III in 36.9%, and segment IV in 24.6% cases). The main type of involvement were stenosis (in 46.6% cases in segment I, in 39.0% in segment II, in 23.8% in segment III, and in 15.0% cases in segment IV); occlusions of the main CA ranked second (20.5, 16.2, 10.7, and 8.4% cases, respectively), and CA thrombosis ranked third (7.4, 5.1, 2.4, and 1.2% cases, respectively). The incidence of thrombosis in all segments of the anterior interventricular branch of the left CA was 2-fold higher than in the right CA.

Calcinosis occupied a special place among complicated atherosclerotic lesions of AH CA (Fig. 1, *b*). Detailed study of calcinosis incidence in the three main CA in AH showed a decrease in the incidence of involvement in the distal direction (segment I in 14.8% cases, segment II in 10.3%, segment III in 7.1%, and segment IV in 5.1% cases). The proximal segments were most often involved in this process (typical location of calcinosis foci in AH). Calcinosis phenomena were the most pronounced in the anterior interventricular branch of the left CA; the circumflex branch of the left CA ranked second and the right CA ranked third.

These data of pathomorphological analysis of atherosclerotic involvement of the main CA in dead patients with AH indicate that the distal segments of these arteries were changed negligibly in an appreciable number of cases (more than in 50%). Some authors studying the distal bed of CA in chronic CHD by clinical pathomorphological comparisons came to similar conclusions [6,15].

Cardioventriculography of AH cavities showed two main variants of its remodeling: dilatation and hypertrophy, both variants are characterized by heart hypertrophy. The weight of AH increased by on average 1.9 times (588.0±16.6 g *vs.* 312.0±12.4 g in the control group), $p<0.001$), the weight of the left ventricle increased by 1.7 times (240.2±4.2 g *vs.* 138.0±6.0 g in the control, $p<0.001$), and the weight of the right ventricle increased 2.3 times (182.4±8.2 g *vs.* 78.8±2.4 g in the control, $p<0.001$). Volume and weight cardiometry of AH showed 9.2 times increased volume of the left ventricle (186.2± 2.6 ml *vs.* 20.2±2.6 ml in control, $p<0.001$). The right ventricle was by 8.9 times larger than in the control (110.6±4.2 *vs.* 12.4±2.4 ml, $p<0.001$). These values are pathognomonic for AH.

The dilatation variant predominated (280 cases, 70%) and was characterized by enlargement of AH ventricular cavities and volumes. Cardioventriculography showed dilated ventricular cavities with enlarged volumes and ventricular septum in the median position (Fig. 2, *a*). "Elongated" hearts were seen in appreciable number of cases with this variant of AH remodeling. Cardioventriculography showed displacement of ventricular septum towards the right ventricle, which acquired a triangular shape; the left ventricle had a characteristic elongated configuration with enlarged volume (Fig. 2, *b*).

Postmortem contrast polypositional coronarography revealed obstructive atherosclerotic involvement of the proximal segments of the main CA and characteristic diffuse dilatation of the left coronary vessels in the dilatation variant of AH (Fig. 2, *c*). Dilated distal segments of the main CA and their

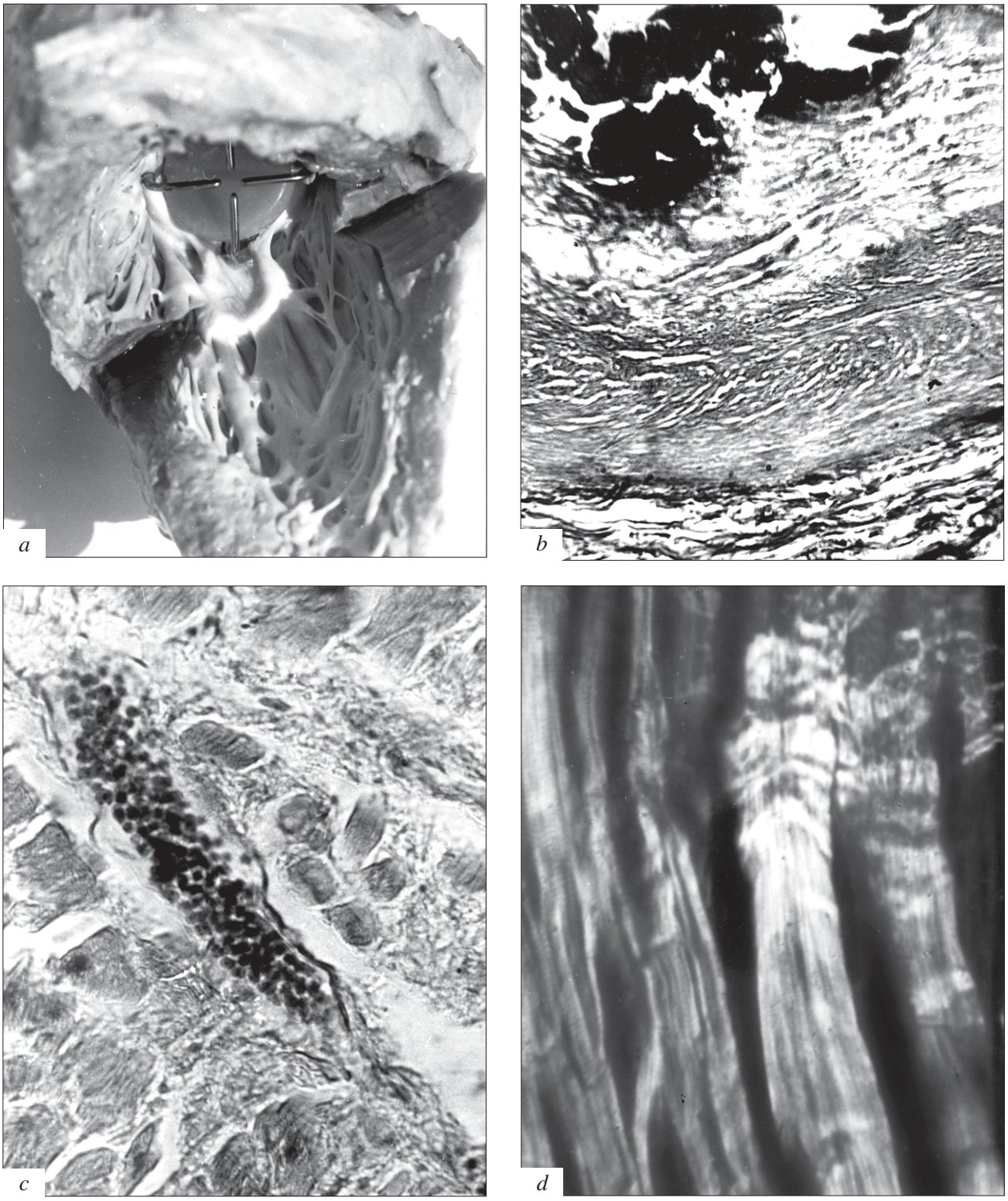


**Fig. 1.** Pathomorphological changes in the myocardium of atherosclerotic heart (AH). *a*) patient (male) G., 60 years: macroscopic changes in left-ventricular myocardium; *b*) calcinosis of circumflex branch of left coronary artery (destruction of atherosclerotic patch and release of calciferous mass into vascular lumen). Staining after Coss, ×140; *c*) patient (female) K., 68 years; degenerative changes in cardiomyocytes against the background of pronounced edema and venous stasis. Hematoxylin, eosin, and light green staining, ×400; *d*) contractures and primary lumpy degradation of myofibrils in polarized light, ×900.

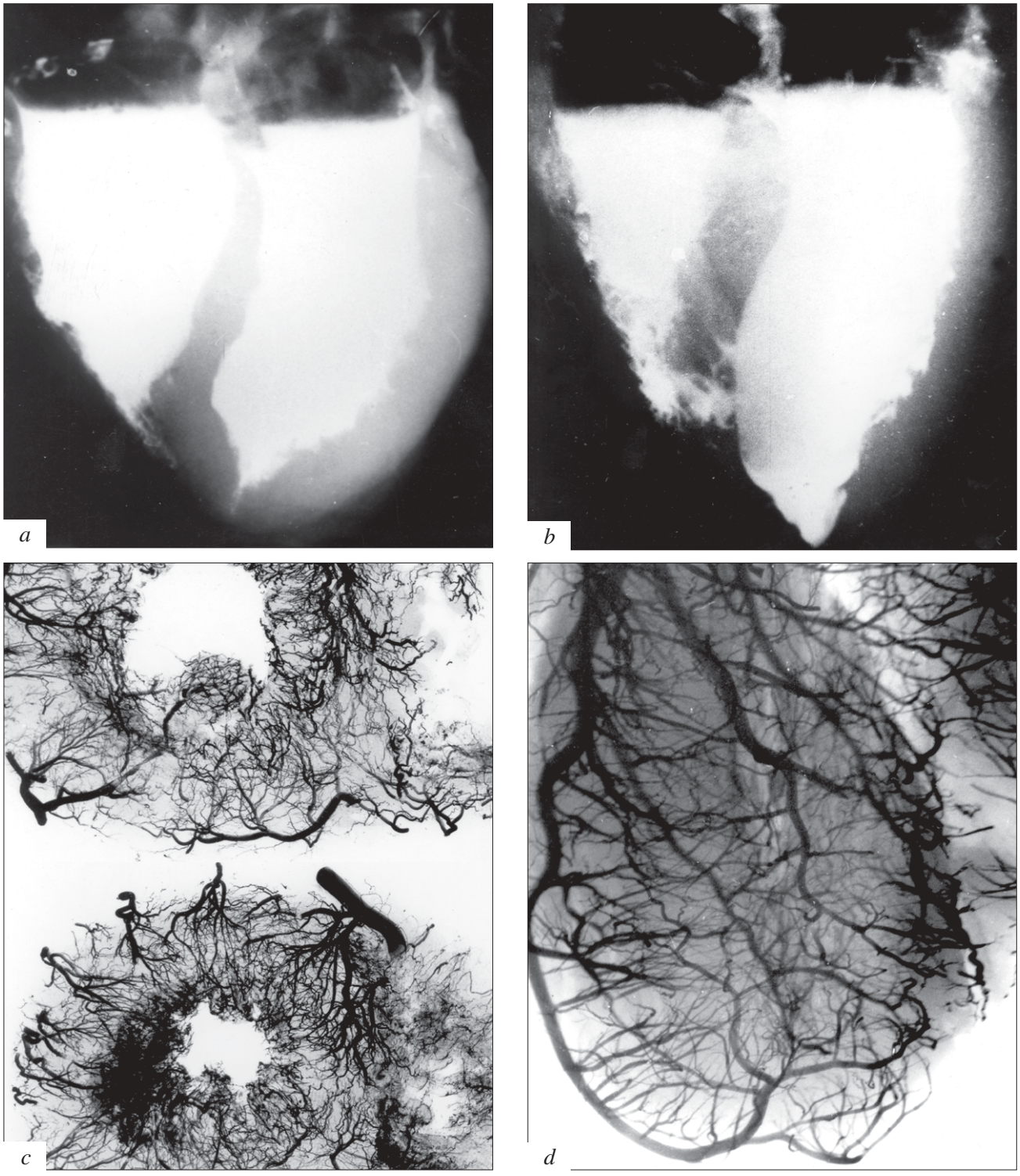


**Fig. 2.** Pathomorphology of dilatation variant of AH. *a*) patient (male) K., 66 years: enlarged ventricular cavities and volumes with median topography of ventricular septum of the heart. Postmortem contrast cardioventriculography; *b*) patient (male) Sh., 62 years: sharply pronounced elongated configuration of enlarged left ventricle with shift of ventricular septum towards the right ventricle, its thickness 2-fold surpassed that of the left-ventricular wall. Postmortem contrast cardioventriculography; *c*) patient (male) G., 68 years: orderly capillary plexuses in subendocardial regions of left ventricle. Fragments of coronarograms; *d*) patient (male) K., 66 years: annular collateral anastomoses. Fragment of unfolded heart coronarogram.

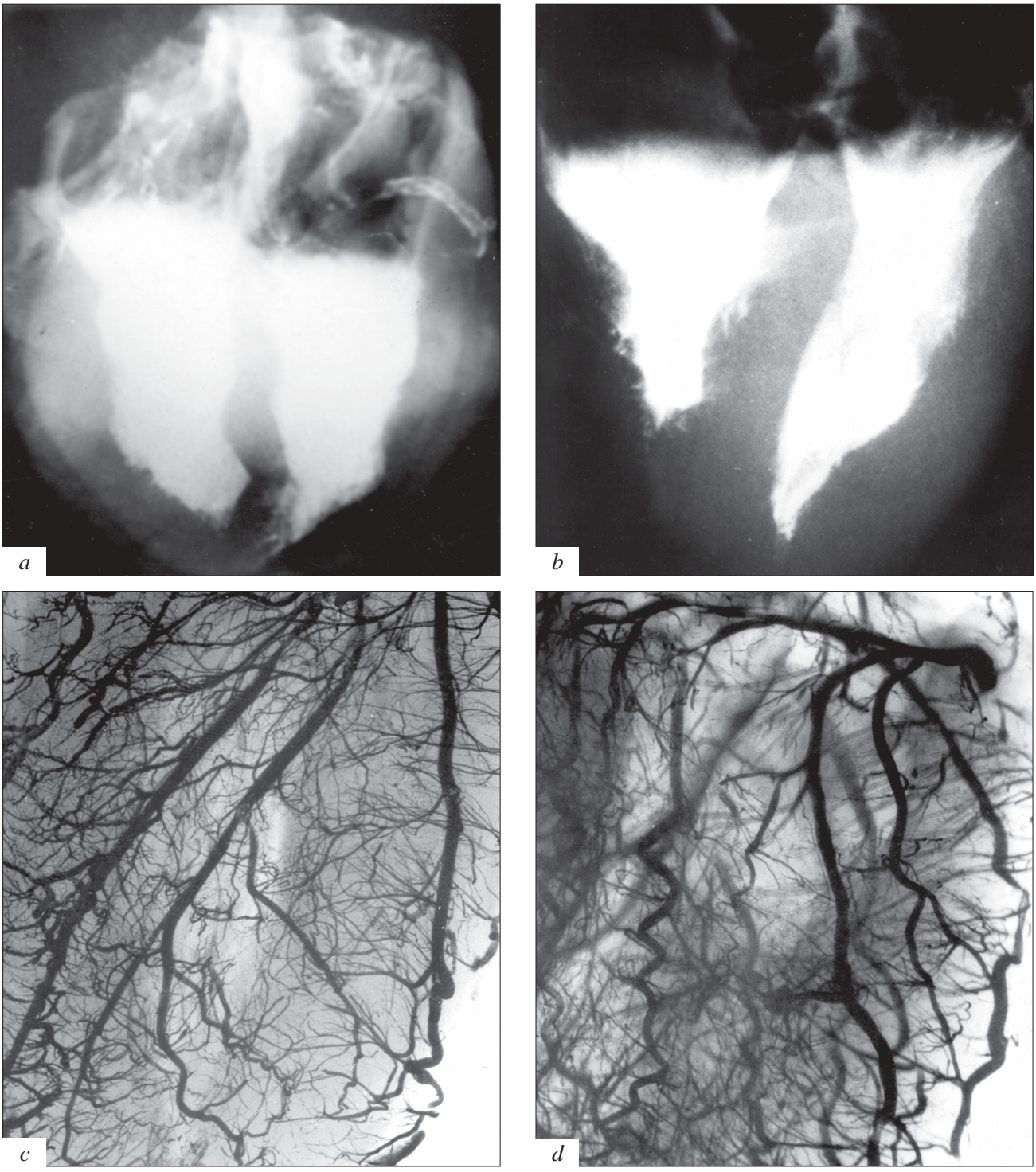


**Fig. 3.** Pathomorphology of AH hypertrophic variant. *a*) patient (male) A., 70 years: drastic changes in the geometrical construction of ventricles with their almost equal volumes and more or less median position of twisted ventricular septum. Postmortem contrast cardioventriculography; *b*) patient (male) Z., 66 years: shrinkage of ventricular volumes; the ventricles are somewhat funnel-shaped with markedly hypertrophic walls. Postmortem contrast cardioventriculography; *c*) patient (male) V., 66 years: intermittent lengthy obstruction of the descending branch of the left coronary artery in the presence of manifest hypervascularization of myocardium. Fragment of coronarogram of unfolded heart; *d*) patient (male) K., 70 years: focal obstruction of proximal segments of the main coronary arteries. Dilatation of vessels of a vast collateral anastomotic network. Fragment of coronarogram of unfolded heart.

branches formed peculiar annular collateral anastomoses (Fig. 2, *d*).

The hypertrophic variant of AH ventricles remodeling was detected in 120 (30%) cases and was characterized by intricate geometrical construction of the ventricles and ventricular septum (Fig. 3, *a*). As the construction of ventricular cavities grew more complex, their volume shrank (Fig. 3, *b*). The most frequent finding was AH with hypertrophic ventricular walls and more or less median position of twisted ventricular septum, 2-fold thinner than the walls of the left and right ventricles.

Postmortem contrast polypositional coronarography in hypertrophic variant of AH revealed persistent obstructive atherosclerotic involvement in various segments of the main CA (Fig. 3, *c*). It usually presented as intermittent lengthy coronary obstruction combined with compensatory collateral network of capillaries in the left ventricular walls (Fig. 3, *d*).

Histological study revealed manifest degenerative changes in cardiomyocytes (CMC) observed in both variants of remodeling and rather often seen in the presence of manifest edema and venous stasis (Fig. 1, *c*). The degenerative changes were caused by different processes: in some cells contracture lesions predominated, the progress of which led to coagulation necrosis, in others focal myocytolysis was observed, which, progressing, transformed into colliquation necrosis; primary lumpy degeneration of myofibrils was also observed (Fig. 1, *d*): an irreversible damage of CMC [1,3].

Histological studies always detected more pronounced sclerotic changes than macroscopic analysis. Diffuse reticular cardiosclerosis was observed, multiple small foci of cardiosclerosis were detected. In some cases with disease of long standing diffuse myofibrosis was so severe, that AH myocardium was characterized by peculiar compactness ("rubber" type) and was whitish.

The pathogenesis of small focal cardiosclerosis is polymorphic and intricate. Disorders in myocardial vascularization and innervation, metabolic changes, immunoaggressive factors, and hyperfunction of overloaded myocardial compartments contribute to its development. However, macro- and microhemocirculatory disorders, caused by manifest atherosclerotic process, acquire the priority pathogenetic significance in AH. Significant changes in the argirophilic backbone favor the development of small focal cardiosclerosis, while collagenization of argirophilic fibers usually precedes diffuse myofibrosis.

Clinical pathomorphological analysis of the direct causes of death in AH showed that patients most often died from chronic heart failure (31.5%), men dying 1.9 times more often than women. Chronic coronary insufficiency ranked second (22.5%); other causes were acute coronary failure (15.5%), arrhythmic and cardiogenic collapse (9.5% each), thrombosis and thromboembolism (6.5%), cardioventricular fibrillation (5.5%).

Hence, manifest degenerative changes in CMC with their subsequent necrosis or apoptosis play a key role in the development of diffuse cardiosclerosis [2,4] of AH and subsequent chronic cardiac insufficiency. The leading role of pronounced degenerative changes in CMC necessitated detailed morphological analysis of their type and outcomes and comparison of these changes with changes in small and large vessels in experimental studies.

Modeling of AH [4] showed that atherogenic factors disordered intracellular regeneration in CMC, thus causing progressive atrophy and predominantly apoptotic death of myocardial cells, the structural markers of regeneratory plastic insufficiency of AH [2]. Importantly that involvement of the capillary bed and CMC are earlier events in the morphogenesis of AH at the early stages of atherosclerotic process, than the formation of atherosclerotic patches in CA [2,4]. These data radically alter our concept on the pathomorphogenesis of heart failure in atherosclerosis.

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