MORPHOLOGY AND PATHOMORPHOLOGY

Variants of Cardiomyopathic Heart Pathomorphogenesis. Comparison of Echocardiographic and Endomyocardial Biopsy Findings

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The main variants of cardiomyopathies (undifferentiated, dilatational, hypertrophic, and restrictive) were distinguished using a complex pathomorphological analysis of 600 cardiomyopathic hearts detected in 5000 autopsies after cardiovascular death. The main pathomorphological diagnostic criteria for each variant were defined. High diagnostic value of life-time echocardiographic diagnosis in comparison with myocardial biopsy was shown. The informative value of endomyocardial biopsy in cardiomyopathic heart is higher, if the method is combined with clinical examinations, noninvasive and invasive studies.

Key Words: *cardiomyopathic heart; endomyocardial biopsy; cardioventriculography; histopathology*

Common characteristics of different forms of cardiomyopathies and statistical identity of their classification positions made it possible to introduce the term "cardiomyopathic heart" (CMPH) in cardiopathology [11,13-15]. This definition is used in practical pathology and reflected in special decisions of International Committee for Definition and Classification of Cardiomyopathies [1].

Increasing incidence of cardiomyopathies, absence of reliable clinical pathomorphological criteria for CMPH [12], well-grounded distinguishing of variants of its pathomorphogenesis, and the need in evaluating the efficiency of life-time pathomorphological diagnosis prompted us this study.

We evaluated the incidence and pathognomonic pathomorphological symptoms of the main variants of CMPH and the diagnostic value of endomyocardial biopsy.

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MATERIALS AND METHODS

A total of 600 CMPH detected in 5000 autopsies of patients dead from cardiovascular diseases were examined (386 men, 214 women; mean age 48.4±0.6 years; mean disease duration 6.4±0.2 years). For control, 160 hearts (40 for each CMPH variant) of subjects of similar age without myocardial diseases, dead from accidental causes, were examined.

The status of cardiac ventricles was studied by the method of postmortem cardioventriculography developed by us [6]. Case histories with the Holter monitoring data, findings of ultrasonic and radionuclide scanning of CMPH, exercise echocardiography, and the basic therapy were analyzed. Two to six echocardiographic examinations and endomyocardial biopsy (6 months to 4 years before death) were carried out in each case.

Complex pathomorphological analysis was carried out with consideration for the data of volume/weight and planimetric cardiometry, morphometrical and pathohistological studies [4]. Endomyocardial

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specimens (4-6 life-time biopsies in each case and postmortem studies) were fixed in 10% neutral formalin and embedded in paraffin, sliced on a microtome from four sides in order to evaluate the longitudinal and transverse orientations of muscle fibers and the endocardium in a sufficient number of sections [3,5]. The sections were stained by hematoxylin and eosin, picrofuchsin by van Gieson's method, by HBFP fuchsinorrhagic method, by ferric hematoxylin after Heidenhain and Selye, and by Mallory's original method. The data of autopsies and postmortem studies of the endomyocardium were compared with the findings of life-time echocardiographic and pathomorphological studies. The data were statistically processed using variation statistical methods (Student's *t* test) and alternative variations.

RESULTS

Undifferentiated variant was found to be the most incident; it was registered mainly in male patients (Table 1). A significant increase in the net weight of CMPH (640.0±12.2 g) with predominating left ventricular weight (260.4±4.2 g) and higher values of ventricular volumes and planimetric values characterizing cavitary walls and ventricular septum were noted.

Two types of changes in CMPH were detected by the results of cardioventriculography. One of them was characterized by even hypertrophy of ventricular walls with more or less median position of the ventricular septum. The septum looked wave-like, clearly separating the ventricular cavities of similar volume (Fig. 1, *a*). The other type of changes was characterized by predominant hypertrophy of left ventricular walls, increased volume of the ventricular septum and its shift towards the right ventricle; the septum was wedge-shaped and well visualized in the distal segment (Fig. 1, *b*).

Pathohistological changes in this CMPH variant were polymorphic, including degenerative necrobiotic and inflammatory manifestations. Disseminated sclerotic changes and irregular hypertrophy of muscle fibers were observed in all cases. These data, together with the volume/weight and planimetric values, indicate peculiar functional characteristics of undifferentiated variant of CMPH; the underlying factor of this condition is increased volume of outflow per unit of myocardial weight together with simultaneous decrease of the reserve volume [8]. Echocardiography detects the undifferentiated variant of CMPH in the majority of cases (63.8%), while life-time endomyocardial biopsy detects this variant in only 30.8% patients.

Dilatational variant of CMPH ranked second by incidence; it was somewhat more incident in male patients (Table 1). Pathomorphological manifestations of this variant were pathognomonic. Net weight of CMPH was 810.0±18.3 g, which was 2.6-fold surpassed the control (312.0±12.5 g). The weights of the left (316.4±4.6 g) and right (228.8±9.2 g) ventricles were more than 3-fold more than the mean weights in

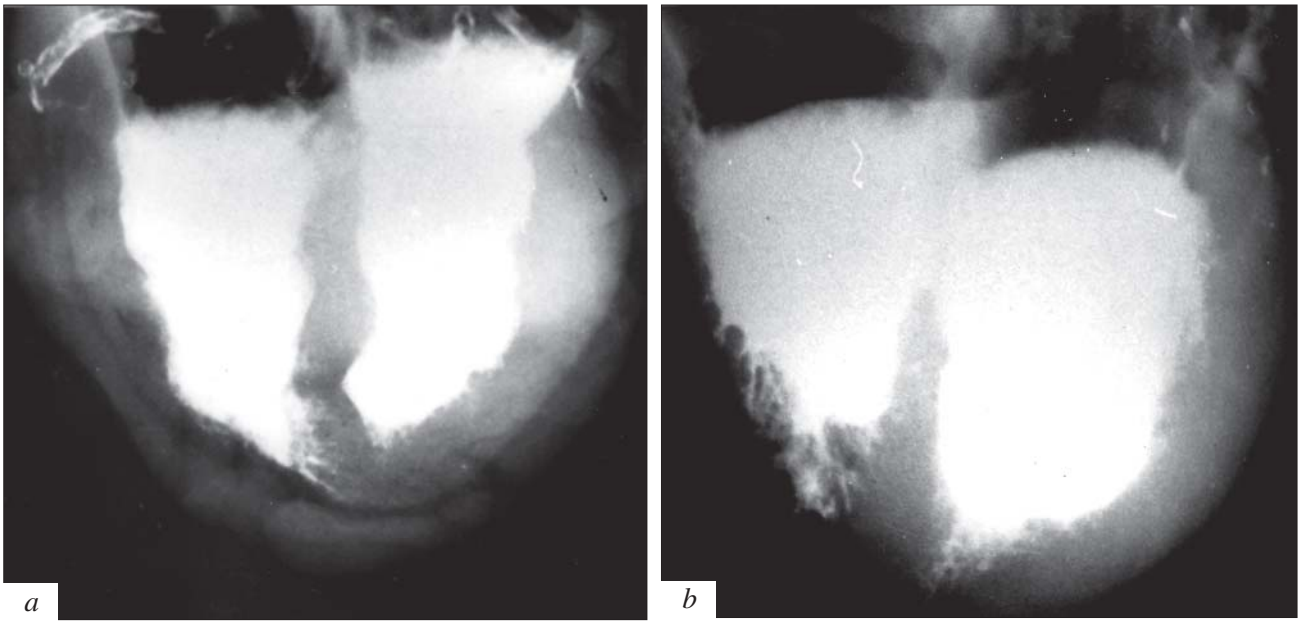

Fig. 1. Cardioventriculographic manifestations of undifferentiated variant of cardiomyopathic heart. *a*) even hypertrophy of ventricular walls with more or less equal volumes of cavities and median position of a "wave-like" ventricular septum in patient (male) V., 48 years; *b*) predominant hypertrophy of left ventricular walls with slight increase of its volume and "wedge-shaped" ventricular septum shifted towards the right ventricle in patient (male) A., 46 years.

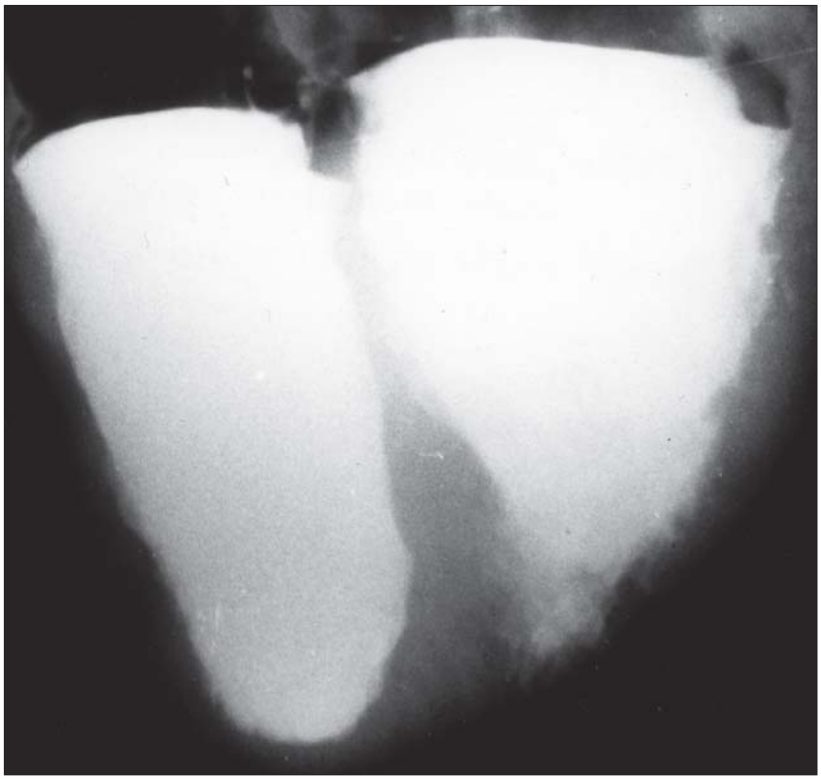

Fig. 2. Cardioventriculographic manifestations of dilatational variant of cardiomyopathic heart. Biventricular form with sharply enlarged volume of triangular (left) and sacculate (right) ventricles with more or less median position of ventricular septum with uneven thickness in patient (male) M., 50 years.

the control. Ventricular volumes were sharply increased, while planimetric parameters of their walls were just slightly shifted.

In dilatational CMPH variant cardioventriculography detected a trend to predominant increase in the volume of one ventricle: left- or right-ventricular forms of the disease were distinguished. Biventricular forms were also detected; they were characterized by equally enlarged volumes of both ventricles. Ventricular septum in this variant was either shifted (in unilateral forms) or its position was more or less median, its thickness being uneven (Fig. 2).

Pathohistological picture of this CMPH variant was close to that of myocarditis, differing by more pronounced degenerative changes in cardiomyocytes, their lumpy degradation, cell reaction, and diffuse polymorphic infiltration. Proliferation of stromal cell elements was as a rule combined with reactive edema and lysis of individual muscle cells. These deep changes in the myocardium caused a significant reduction of contractility and of the force—length isovolumic ratio leading to a drastic decrease in the degree and velocity of fiber contraction during each stage of cardiac cycle with predominant decrease in the CMPH systolic reserve [9].

The values of histopathological index of contractile insufficiency calculated on the basis of endomyocardial biopsy findings confirm this pathophysiological concept. Echocardiography diagnosed the dilatational variant in 90% cases, while endomyocardial biopsy revealed it in 53.3% cases.

TABLE 1. Incidence of Variants, Distribution by Sex, and Reliability of Ultrasonic Examination and Biopsy in the Diagnosis of Cardiomyopathic Heart

Variant of cardiomyopathic heart	Number of cases		Sex				Echocardiography				Myocardial biopsy			
			male		female		detects		not detects		detects		not detects	
	abs.	%	abs.	%	abs.	%	abs.	%	abs.	%	abs.	%	abs.	%
Undifferentiated	260	43.3	180	69.2	80	30.8	166	63.8	94	36.2	80	30.8	180	69.2
Dilatational	180	30.0	94	52.2	86	47.8	162	90.0	18	10.0	96	53.3	84	46.7
Hypertrophic	100	16.7	76	76.0	24	24.0	82	82.0	18	18.0	55	55.0	45	45.0
Restrictive	60	10.0	36	60.0	24	40.0	40	66.7	20	33.3	20	33.3	40	66.7
TOTAL	600	100	386	64.3	214	35.7	450	75.0	150	25.0	251	41.8	349	58.2

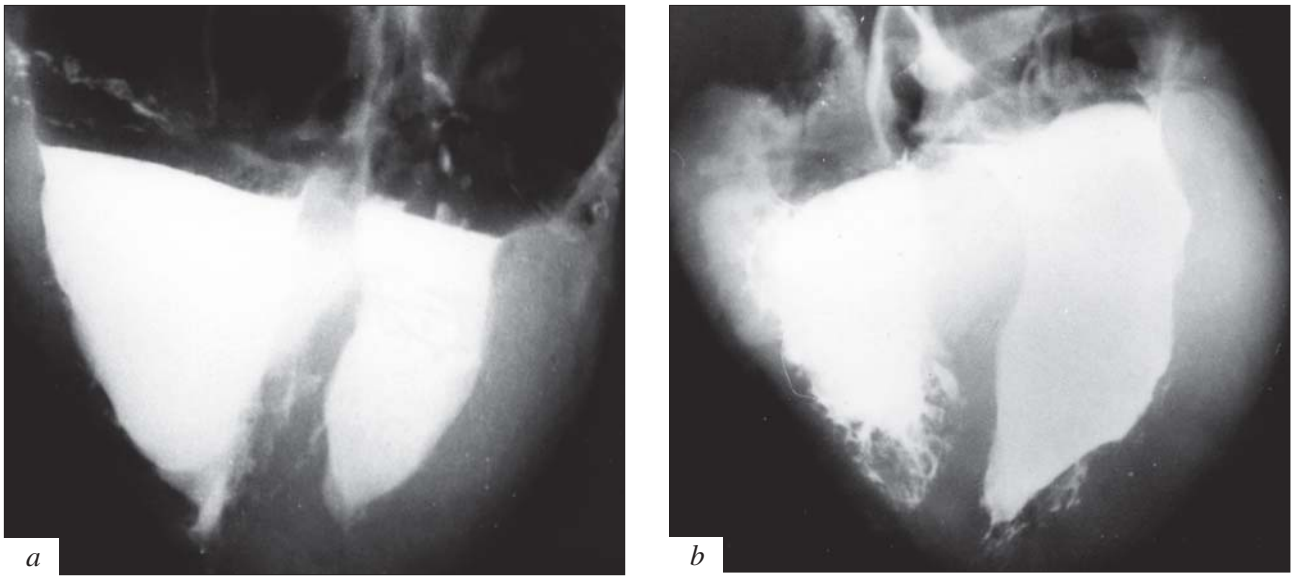

Fig. 3. Cardioventriculographic manifestations of hypertrophic (*a*) and restrictive (*b*) variants of cardiomyopathic heart. *a*) pronounced hypertrophy of left ventricular walls with elimination of its cavity at the expense of symmetrical hypertrophy of ventricular septum in the distal (apical) segment in patient (male) K., 44 years; *b*) sharp hypertrophy of left ventricular walls with decrease in its volume, modification of geometrical construction, and wave-like contour in patient (male) N., 38 years.

The hypertrophic variant of CMPH ranked third by incidence and was recorded predominantly in male patients (Table 1). Volume/weight and planimetric cardiometry showed a significant (1.9 times) increase in CMPH net weight (632.1±12.2 g) in comparison with the control. However, this value was 1.3 times below the corresponding parameter in patients dead with the dilatational variant. The weight of ventricular septum (142.3±3.0 g) was 2.7 times greater than in the control (52.9±2.3 g), while the volume of the left ventricle (52.8±2.6 ml) was 5.4 times lower than in dilatational CMPH (286.4±3.6 ml). Planimetric cardiometry showed a significant thickening of the ventricular septum (2.40±0.02 cm) in comparison with the control (1.00±0.07 cm).

According to cardioventriculography, the ventricular septum was thicker than the left ventricular wall, this promoting an appreciable decrease in left ventricular cavity. Acquiring different geometrical shapes (catenoids, *etc.*), the ventricular septum caused the development of symmetrical and asymmetrical forms of pathology. Elimination of the ventricular cavity resulted from significant hypertrophy (often segmented) of left ventricular wall. In symmetrical hypertrophy the changes in ventricular septum were located in its distal (apical) segment (Fig. 3, *a*).

Histopathology of the hypertrophic variant of CMPH was often characterized by disorganization of short hypertrophic cardiomyocytes oriented in different directions; hypertrophy and deformation of the nuclei were often observed [2]. These changes, together with remodeling of CMPH cavities (predominantly of the left ventricle, and also of ventricular septum and valvular apparatus) determine pressure gradient significantly modulating the main pathophysiological constants. With time deep shifts in the systolic and diastolic functions of the heart develop with irreversible cardio- and hemodynamic disorders. Echocardiography confirmed the diagnosis at different stages of development of this CMPH variant in the majority of cases (82%), while endomyocardial biopsy detects this condition in 55% of all cases.

The restrictive variant of CMPH was detected in 10% cases (somewhat more frequently in men, Table 1). CMPH net weight (582.3±17.1 g) slightly surpassed the control, but was far lower than in other forms of CMPH. The mean volume of the left ventricle (48.1±2.3 ml) was 2.2 times more than in the control (21.6±1.4 ml) and 5.9 times less than in the dilatational variant of CMPH. Planimetric values were changed in similar ratios.

Cardioventriculography detected pronounced hypertrophy of mainly left ventricular walls and ventricular septum. Annular obliteration of CMPH ventricles led to modification of their geometrical construction, decrease in their volume, and emergence of "wave-like" contour (Fig. 3, *b*). Left-, right-, and biventricular forms were observed.

Pathohistological changes in the myocardium in restrictive CMPH variant were characterized by pronounced degeneration of cardiomyocytes, manifesting by their focal fuchsinophilia and low content of glycogen, DNA, and RNA. Calcinated foci, fibrin depositions, and accumulations of eosinophils were seen in

the presence of diffuse interstitial fibrosis. Activated eosinophils and protein eosinophilic granules were detected. Together with pathoanatomical picture, these changes caused pronounced diastolic dysfunction with decreased pumping capacity of CMPH. Diastolic restriction manifested by significant elevation of the diastolic pressure in one of ventricles [10]. Echocardiographic method detects the restrictive variant of CMPH in 66.7% cases, endomyocardial biopsy in only 33.3% cases.

Hence, echocardiography ensures a sufficiently high level of objective life-time diagnosis of all variants of CMPH (450 cases, 75%) with the best detection rate for the dilatational variant (90%). Life-time pathomorphological diagnosis of these variants is less effective (251 case, 41.8%). Endomyocardial biopsy did not confirm or detect one of CMPH varians in 58.2% of all cases.

High incidence of undifferentiated CMPH variant (43.3%) and low rate of CMPH detection by life-time ultrasonic method and biopsy (150 and 349 cases) persuasively indicate the need in thorough differential diagnosis [7].

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