MORPHOLOGY AND PATHOMORPHOLOGY

Pathomorphology of Postinfarction Myocardial Ischemia during Atherosclerotic Obstruction of Coronary Arteries

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Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 139, No. 3, pp. 346-351, March, 2005
Original article submitted December 8, 2004

Pathomorphological criteria of early postinfarction angina included segmentary atherosclerotic obstruction of the upper segments of the coronary artery supplying the infarction area, recurrent acute myocardial infarction, maximum decrease in vascularization of the left posterior ventricular wall; and individual changes in angioarchitectonics of the heart promoting hibernation of the myocardium. Pathognomonic morphological criteria of silent postinfarction myocardial ischemia included diffuse extensive atherosclerotic obstruction of lower segments in the coronary artery supplying the infarction area and total hypervascularization of the myocardium, first acute myocardial infarction of the left ventricular anterior wall, and maximum decrease in vascularization of the anterior and posterior wall in the left ventricle. These coronary-myocardial relationships contribute to stunning of the myocardium. Zones of hypokinesia and akinesia were revealed in the left ventricle, which reflects the phenomenon of resting myocardium associated with isolation of heart angioarchitectonics.

Key Words: *postinfarction myocardial ischemia; postinfarction angina; pathomorphology; coronarography; cardiometry*

Postinfarction myocardial ischemia (PMI) is a complex of symptoms of severe disturbances in coronary circulation characterized by the inadequacy of coronary blood flow to metabolic demands of the myocardium [1,2]. This symptom complex develops 4 h-4 weeks after the incidence of acute myocardial infarction and is divided into early postinfarction angina (EPA) and silent PMI (SPMI) [5,8,11,12].

Coronarography and evaluation of the relationship between clinical and angiographic parameters showed that the development of PMI is associated with residual and hemodynamically important stenosis of the coronary artery supplying the infarct area, deficiency of collateral blood flow in the terminal zone, coronary artery stenosis [10], and severe coronary thrombosis [6]. It remains unclear whether PMI is a form of instable angina or complication of acute myocardial infarction [2,5,11].

Here we evaluated the relationship between the severity of PMI and type of obstructive atherosclerotic injury in main coronary arteries, coronary reserve, left ventricle vascularization, and index of blood supply to the left ventricle.

MATERIALS AND METHODS

We examined 120 hearts of patients with clinical manifestations of EPA who died in the early postinfarction period (86 men and 34 women, average age 52.4±0.2 years). Another series involved 120 hearts of patients dying from SPMI (78 men and 42 women, average age 54.2±0.4 years). Each of the two control groups included 60 hearts from accidentally died subjects.

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0007-4888/05/1393-0363

The hearts from died patients and control subjects were exposed to postmortem contrast multiple-view coronarography. Volume density of the vascular bed in the left ventricle was evaluated [3]. The degree of atherosclerotic obstructions was estimated by combined coronarography and standard anatomical study approved by the World Health Organization. The severity of postinfarction myocardial injury was determined by macroscopic examination of serial transverse sections performed after coronarography. The index of blood supply to the myocardium was estimated by volume-weight and planimetric cardiometry.

Specific forms of left ventricle dysfunction were identified by studying clinical data and results of paraclinical assays (coronary angiography, Holter monitoring, ultrasound and radionuclide scanning of the heart, exercise stress echocardiography, and thrombolytic therapy).

For pathohistological study, the myocardial samples were fixed in 10% neutral formalin and embedded into paraffin. The sections were stained with hematoxylin and eosin, van Gieson's picrofuchsin, and iron hematoxylin (method of Heidenhain and Selye). Treatment also involved Mallory staining. The results were analyzed by the method of variational statistics (pairwise Student's *t* test).

RESULTS

Segmentary atherosclerotic obstruction of the main coronary arteries was accompanied by the development of recurrent acute myocardial infarction mainly involving the posterior wall of the left ventricle (Table 1). EPA prevailed under these conditions. Intermittent and extensive coronary obstruction was also accompanied by recurrent myocardial infarction mainly involving the posterior wall of the left ventricle. SPMI was most typical of these coronary-myocardial relationships.

Diffuse extensive atherosclerotic coronary obstruction most often accompanied the first acute myocardial infarction mainly involving the anterior wall of the left ventricle (Table 1). SPMI was commonly observed under these conditions. Recurrent acute myocardial infarction mainly involving the left ventricular posterior wall was revealed during coronary obstruction. The severity of damage decreased in the following order: left ventricular anterior wall>left ventricular lateral wall>interventricular septum>apex of the heart.

Atherosclerotic obstruction of upper segments in coronary arteries was mainly accompanied by recurrent acute myocardial infarction of the left ventricular anterior wall (Table 1). EPA developed under these conditions. Obstruction of the middle segments in coro-

TABLE 1. Incidence and Type of Obstructive Atherosclerotic Damage to Main Coronary Arteries; and Location and Rate of Acute Myocardial Infarction in Subjects Dying from PMI

Type of atherosclerotic obstruction		Primary location of acute macrofocal transmural myocardial infarction in the left ventricle				Ratio of myocardial infarction		EPA		SPMI	
		anterior wall	posterior wall	lateral wall	septum and apex	first	recurrent	abs.	%	abs.	%
Spread	segmentary	26	32	14	8	36	44	68	56.7	12	10.0
	intermittent and extensive	22	30	12	10	30	44	32	26.7	42	35.0
	diffuse extensive	42	30	8	6	46	40	20	16.7	66	55.0
Location	upper segments	26	22	20	12	38	42	62	51.7	18	15.0
	middle segments	22	40	10	8	34	46	36	30.0	44	36.7
	lower segments	22	32	20	6	28	52	22	18.3	58	48.3

nary arteries was often found during recurrent myocardial infarction mainly involving the posterior wall of the left ventricle and was accompanied by SPMI. Obstruction of the lower segments in coronary arteries was often found during recurrent acute myocardial infarction mainly involving the posterior wall of the left ventricle. These disturbances were mainly accompanied by SPMI.

Angioarchitectonics of the heart during atherosclerotic obstruction significantly differs from the vas-

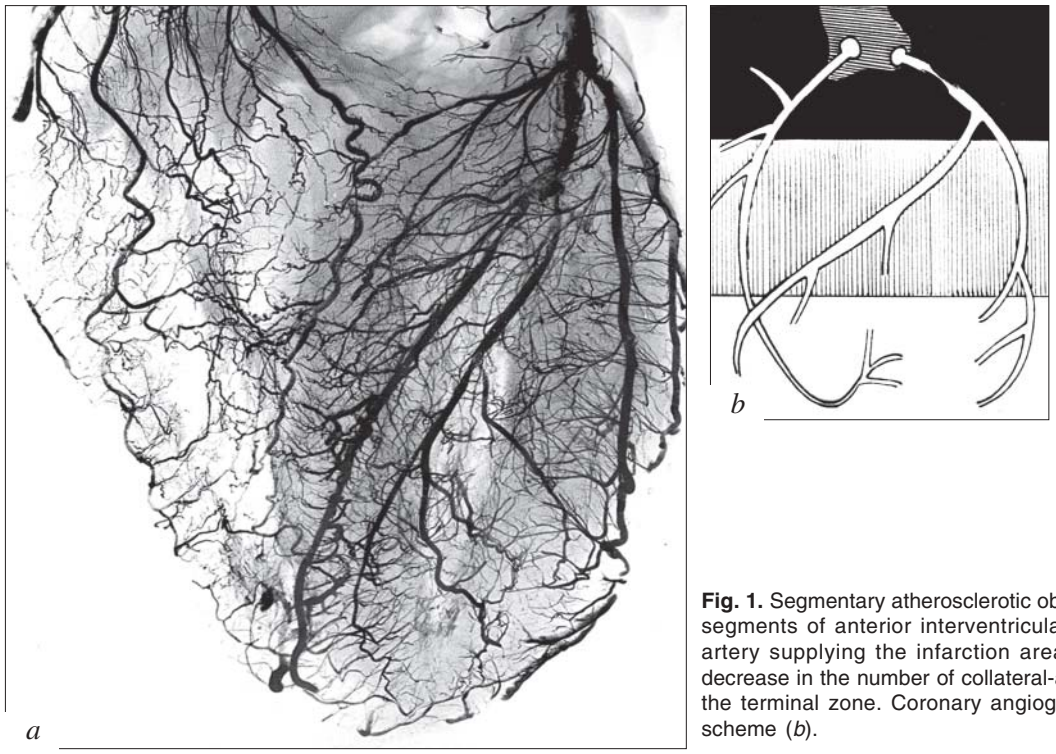

Fig. 1. Segmentary atherosclerotic obstruction of the upper proximal segments of anterior interventricular branch of the left coronary artery supplying the infarction area, collapse of branches, and decrease in the number of collateral-anastomotic vascular plexus in the terminal zone. Coronary angiogram, patient A. (52 years, *a*); scheme (*b*).

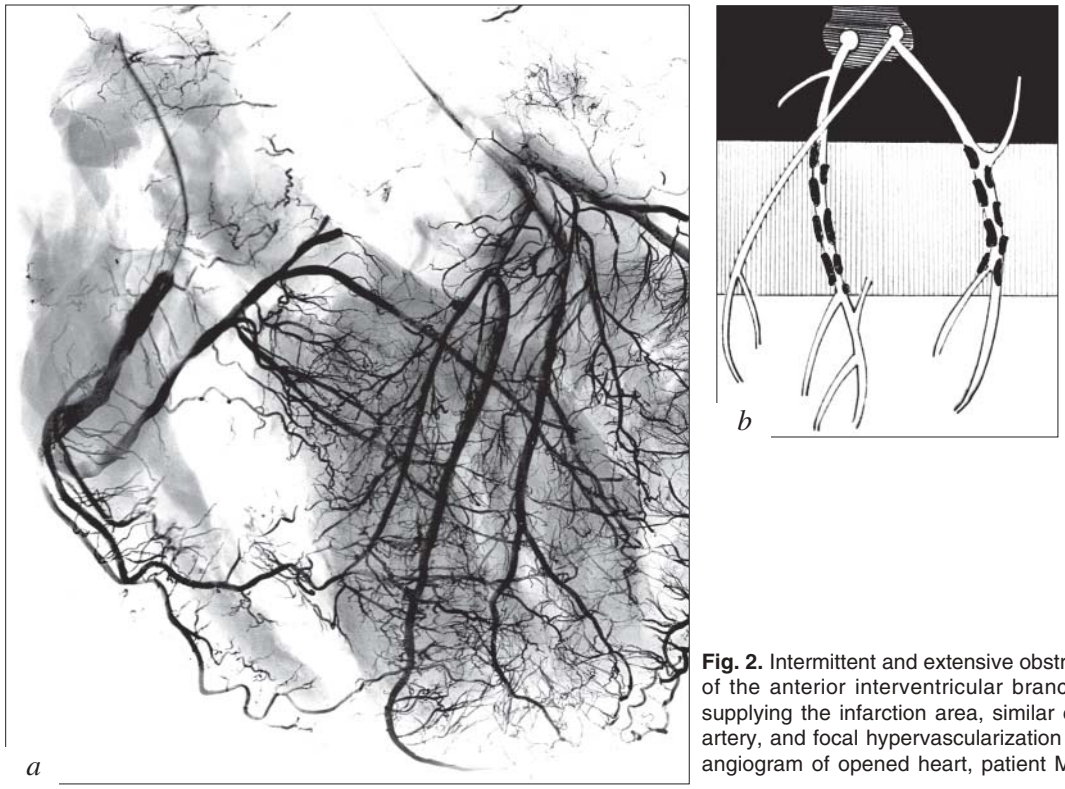

Fig. 2. Intermittent and extensive obstruction of the middle segments of the anterior interventricular branch of the left coronary artery supplying the infarction area, similar changes in the right coronary artery, and focal hypervascularization of the myocardium. Coronary angiogram of opened heart, patient M. (54 years, *a*); scheme (*b*).

TABLE 2. Index of Blood Supply, Vascular Volume Density in the Left Ventricle, and Specific Forms of Dysfunction during PMI (*M±m*)

Type of PMI	*n*	Index of blood supply to the myocardium, g/mm^2	Vascular volume density in the left ventricle, %				Specific forms of left ventricle dysfunction					
			anterior wall	posterior wall	lateral wall	interventricular septum and apex	hibernated myocardium		stunned myocardium		resting myocardium	
							abs.	%	abs.	%	abs.	%
Control-1	60	17.6	48.8±1.4	46.6±1.2	36.2±1.4	38.6±1.4						
EPA	120	22.4	38.2±1.2	34.2±1.4	28.4±1.8	32.6±1.6	42	35.0	28	23.3	14	11.7
Control-2	60	18.0	50.2±1.6	46.6±1.4	38.4±1.2	40.2±1.6						
SPMI	120	24.2	40.6±1.4	36.4±1.2	30.4±1.4	32.2±1.2	24	20.0	26	21.7	18	15.0

cular bed of remodeled postinfarction heart [3]. Focal stenosis of the proximal arterial region was revealed during segmentary obstruction of upper segments of the coronary artery supplying the infarction area. First-order and second-order coronary branches were collapsed. We revealed a small number of collateral anastomoses in the surrounding tissue (Fig. 1). Transcalibration of the left coronary vessels was often followed by focal vascular depletion.

Stenosis of several segments of the coronary artery supplying the infarction area was observed during intermittent and extensive coronary atherosclerotic obstruction. The same combined damage was often found in other main coronary arteries. These changes were revealed during focal hypervascularization of the myocardium that alternated with zones of vascular depletion (Fig. 2). Obstructive changes in the middle segments were found in most patients dying from PMI. Diffuse extensive atherosclerotic obstruction was manifested in severe stenosis of all segments of the coronary artery supplying the infarction area and often found in lower segments of coronary arteries. These changes accompanied total hypervascularization of the myocardium and presence of numerous collateral-anastomotic microvascular plexuses (Fig. 3).

The index of correlation between various forms of PMI and vascular volume density in the functionally overloaded left ventricle sharply decreased compared to the control (Table 2). For example, during EPA vascular volume density most significantly decreased in the posterior wall of the left ventricle. Vascular volume density decreased in the following order: anterior wall>lateral wall>interventricular septum>apex of the heart. During SPMI vascular volume density significantly decreased in the posterior and anterior wall of the left ventricle.

Obstruction of left coronary vessels and significantly impaired vascularization of the left ventricle contribute to changes in the index of blood supply to the myocardium. We revealed an increase in the pure weight of the heart per 1 mm^2 main coronary artery lumen. The index of blood supply to the myocardium during EPA and SPMI significantly differed from the control. These data indicate that the volume of coronary circulation in patients dead from PMI did not satisfy myocardial demands and could not compensate long-term hypoperfusion of the myocardium, which produced specific dysfunction of the left ventricle during thrombolytic therapy in the acute period of myocardial infarction.

Specific forms of left ventricular dysfunction were found in 84 patients dying from PMI (70%). The incidence of dysfunction decreased in the following order: myocardial hibernation>stunned myocardium> resting myocardium (Table 2). Specific forms of left

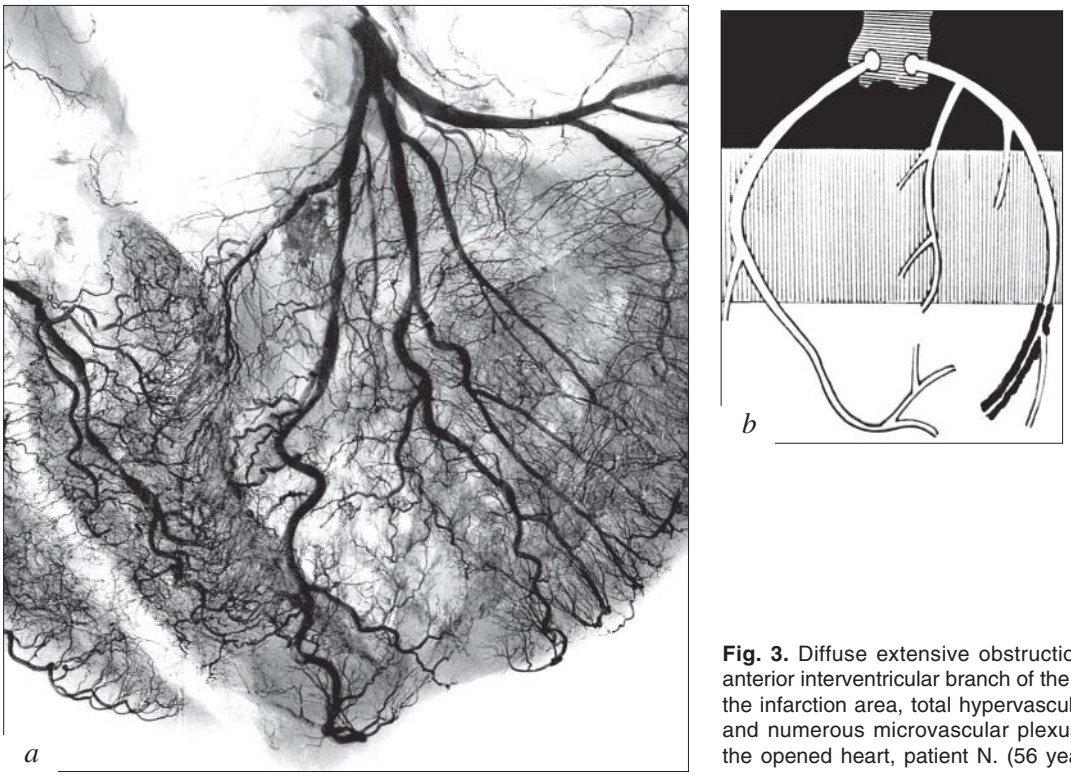

Fig. 3. Diffuse extensive obstruction of lower segments of the anterior interventricular branch of the left coronary artery supplying the infarction area, total hypervascularization of the myocardium, and numerous microvascular plexuses. Coronary angiogram of the opened heart, patient N. (56 years, *a*); scheme (*b*).

ventricular dysfunction developed in 68 patients dying from SPMI (56.7%). The number of subjects with stunned or hibernated myocardium was highest. The phenomenon of resting myocardium was rarely observed. Specific forms of left ventricular dysfunction were revealed in 152 PMI subjects receiving thrombolytic therapy (63.3%).

Hibernation of the myocardium in zones of the coronary artery supplying the infarction area and surrounding tissue reflects a multifactor nature of this process. On the one hand, these changes constitute the compensatory and adaptive reaction of damaged myocardium. On the other hand, they reflect the development of profound structural changes in response to long-term hypoperfusion [4]. Spontaneous or drug-induced recirculation of the coronary artery supplying the infarction area is usually followed by stunning of the myocardium. The diagnostics of stunned myocardium is based on complex reconstruction of left coronary vessels, vascularization of the myocardium, and index of blood supply to the myocardium. Zones of hypokinesia and akinesia in the left ventricular wall are characteristic of stunned myocardium. Our assumption is confirmed by typical changes in angioarchitectonics of the heart, which sharply decreases the degree of perfusion in these zones [9].

These results indicate that segmentary atherosclerotic obstruction of upper segments in coronary arteries and recurrent acute myocardial infarction of the left ventricular posterior wall are pathognomonic signs of EPA. Focal stenotic changes were found in the proximal segments of the coronary artery supplying the infarction area. The degree of vascularization most significantly decreased in the posterior wall of the left ventricle. Changes in angioarchitectonics of the heart and associated disturbances in coronary hemodynamics contribute to hibernation of the myocardium.

Pathognomonic morphological criteria of SPMI include diffuse extensive obstruction of the lower segments in coronary arteries and first acute infarction of the left ventricular anterior wall. Stenotic atherosclerotic damage to various segments of the coronary artery supplying the infarction area was accompanied by hypervascularization of the myocardium. The decrease in vascularization was most pronounced in the anterior and posterior wall of the left ventricle. These coronary-myocardial relationships contribute to stunning of the myocardium.

Our findings indicate show that PMI should be considered as the early complication of acute myocardial infarction.

REFERENCES

1. N. V. Anastasova, *Ukr. Kardiol. Zh.*, No. 4, 13-15 (1998).
2. V. A. Bobrov and M. N. Dolzhenko, *Ibid.*, No. 3, 73-78 (1999).
3. V. D. Rozenberg and L. M. Nepomnyashchikh, *Byull. Eksp. Biol. Med.*, **135**, No. 5, 590-596 (2003).

4. B. A. Sidorenko and D. V. Preobrazhenskii, *Kardiologiya*, No. 2, 98-101 (1997).
5. L. Bentivoglio, K. Detre, W. Yeh, *et al*., *J. Am. Coll. Cardiol*., **24**, 1195-1206 (1994).
6. B. Bertolet, J. Dinerman, R. Hartke, and C. Conti, *Clin. Cardiol*., **16**, 116-122 (1993).
7. R. Bolli, *Dialogues Cardiovasc. Med*., **1**, 5-26 (1996).
8. C. Jespersen, *Clin. Cardiol*., **20**, 623-626 (1997).
9. Y. Kobayashi, S. Miyazaki, A. Itoh, *et al*., *Am. J. Cardiol*., **81**, 117-122 (1994).
10. K. Mizuno, T. Arai, K. Satamur, *et al*., *Lancet*, **337**, 809-812 (1991).
11. H. Nakajima, H. Goto, H. Mateulara, *et al*., *Circulation*, **40**, 1115-1121 (1992).
12. W. Zgu, C. Ni, and C. Wu, *Clin. J. Ant. Med*., **33**, 513-515 (1994).