Cardiomyocyte Ultrastructure in Rats with Different Metabolizing Capacities of the Liver during Acute Myocardial Infarction

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Electron microscopy of cardiomyocytes was performed on days 1, 3, and 7 after ligation of the coronary artery in rats previously divided according to liver metabolizing capacities into slowly and rapidly metabolizing animals. In rapidly metabolizing rats cardiomyocyte sarcoplasm contained large number of hyperplastic ribosomes and polysomes at the late stages of experiment, which attested to high activity of protein and RNA synthesis compared to slowly metabolizing rats. In slowly metabolizing animals edema of cardiomyocyte sarcoplasm and mitochondria was usually seen.

Key Words: *rapidly and slowly metabolizing animals; acute myocardial infarction; electron microscopy*

Pathogenesis and pathomorphology (including submicroscopic changes) of myocardial infarction (MI) are still actual aspects of biomedical studies [5,7,8]. Of particular importance is evaluation of individual peculiarities contributing to the mechanisms of ischemic damage to cardiomyocytes (CMC) [1,3,4,6]. Different tolerance to acute oxygen deficiency and different adaptation capacities are determined by peculiarities of biochemical mechanisms. Acute ischemia disturbs various biochemical processes in the myocardium and induces structural changes in all cell systems. Here we examined submicroscopic peculiarities of CMC determining functional and metabolic status of the myocardium during acute ischemia.

MATERIALS AND METHODS

Outbred male rats (n=70) weighing 180-200 g were divided into rapidly and slowly metabolizing animals by the duration of hexanal-induced sleep (100 mg/kg intraperitoneally). Acute myocardial infarction was induced by ligation of the descending coronary artery. Myocardium specimens from ischemic, periischemic, and distant zones were fixed in 2.5% glutaraldehyde on 0.2 M phosphate buffer for 4 h, postfixed in 1% OsO_4 on the same buffer (pH 7.4) for 2 h, dehydrated, and embedded in epon. Ultrathin sections were contrasted with uranyl acetate and lead citrate by the method of Rheinolds and examined under a PEM-100L electron microscope.

RESULTS

Ultrastructure of CMC in intact rapidly and slowly metabolizing rats was similar. Nuclei, nucleoli, mitochondria (MC), endoplasmic reticulum, and sarcolemma had similar electron dense outline. Their shape, number, structure, density, and location in CMC cytoplasm were similar in both groups and did not differ from those described elsewhere [6,8]. However, CMC of rapidly metabolizing rats contained higher number of glycogen and lipid granules. Moreover, in rapidly metabolizing rats, glycogen granules were located between fibrils, while lipids were seen around MC and on the periphery of the cytoplasm. These changes reflect peculiarities of protein synthesis, glycogenolysis,

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and lipid metabolism in rats with different rate of metabolism.

Early postischemic stages were characterized by rearrangement of ultrastructural myocardial elements involved in metabolism in both rapidly and slowly metabolizing rats. Glycogen and lipid granules disappeared in all CMC regions, edema of the cytoplasm and some perinuclear MC was seen in both groups. In rapidly metabolizing rats, enlargement of nuclei and concentration of heterochromatin in the perimembrane zone were observed. Hypertrophy of the nucleoli, hyperplasia of polysomes, endoplasmic reticulum and T-system were noted (Fig. 1). Decomplexation of membrane structures in MC, perimembrane localization of MC, and sometimes their migration into extracellular space were found. Changes in myofibrils (MF) of slowly metabolizing animals were more pronounced: stretching of anisotropic and contraction of isotropic discs sometimes with focal hypercontraction. Structural regions of sarcomeres were not congruent due to MF deformation. M-discs and disappeared from anisotropic and Z-lines in isotropic discs were deformed. Sometimes, loose and swollen anisotropic discs and channels of the T-system were seen (Fig. 1).

On days 3-7 postinfarction, polymorphic structural changes developed both in CMC and extracellular space of the periinfarction zone. In rapidly metabolizing rats, nuclei and nucleoli were hypertrophied with signs of chromatin redistribution; nucleoli with osmiophilic granules appeared. MC in these CMC were hypertrophic, hyperplastic, and differed by shape and size; cristae became osmiophilic, their number increased; accumulation of lipid and osmiophilic inclusions and hyperplasia of glycogen granules, free ribosomes, and polysomes were observed. MF were contracted, most sarcomeres were shortened, and electron density of anisotropic and isotropic discs increased (Fig. 2, *a*). Z-lines in isotropic discs became wide and osmiophilic, transparent zones disappeared. Hypercontracted MF were surrounded by enlarged channels of T-system and hyperplastic ribosomes and polysomes. Edema of peripheral sarcoplasm was associated with migration of some MC and osmiophilic bodies into the extracellular space.

In slowly metabolizing rats, loosening of MF, thin and thick fibrils were observed (Fig. 2, *b*). Sarcoplasm was swollen, glycogen granules and free ribosomes were less abundant. MC had well-developed cristae and electron dense matrix. In other myocardium regions, MF contractures appeared, some discs and lines became undetectable. Other closely located CMC elements were deformed and collected in bundles, sometimes, disruptions of MC membranes and sarcolemma were noted. In hypercontracted MF we observed edema of MC matrix and appearance of homogenous substance

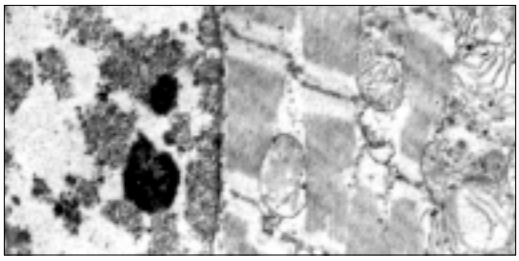

Fig. 1. Periinfarction zone on day 1 after myocardial infarction, ×12,000. Heterochromatin redistribution, hypertrophied nucleolus, deformed sarcomere discs, and enlarged T-system channels.

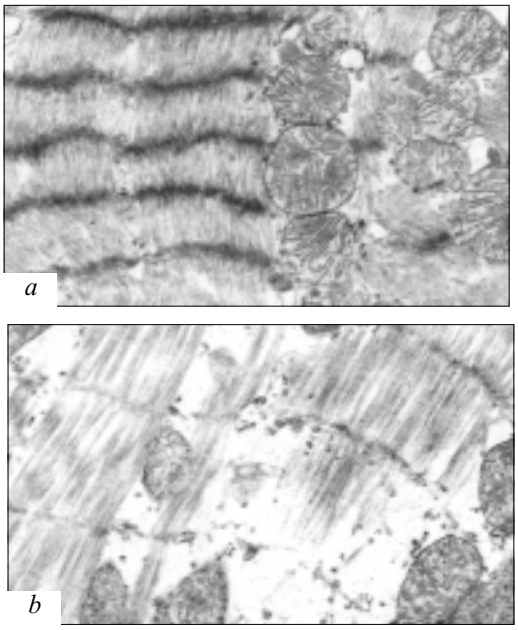

Fig. 2. Periinfarction zone in rapidly (*a*) and slowly (*b*) metabolizing rats on day 7 after acute myocardial infarction, ×12,000. *a*) contracted sarcomeres, disappearance of isotropic discs, thickening of Z-line; *b*) loosening of sarcomere protofibrils, sarcoplasm edema.

(probably, tissue fluid), which was transported to cell periphery and released to the extracellular space.

Thus, activity of protein synthesizing system was higher, while intensity of carbohydrate and lipid oxidation was lower in rapidly metabolizing rats compared to slowly metabolizing animals. In rapidly metabolizing rats, MF contraction and shortening of some sarcomere discs were observed, while in slowly metabolizing rats, loose and hypercontracted MF were found. There are published data that glycogen and lipid stores are used as energy substrates during myocardial ischemia and hypoxia [2,6-8]. The presence of hyperplastic ribosomes and polysomes in CMC of rapidly metabolizing rats at the late stages of the experiment attests to more pronounced activation of protein and RNA synthesis compared to that in slowly metabolizing animals, in whom edema of the sarcoplasm and MC prevailed.

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