Morphological Changes in Myocardium in Rats with Different Resistance to Hypoxia after Ligation of the Coronary Artery

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We studied morphological changes in the myocardium during experimental myocardial infarction in rats with different resistance to hypoxia. Microscopic examination showed that morphological changes in the ischemic zone and adjacent tissues are different in rats with high and low resistance to acute ischemia. In highly resistant rats, necrotic changes in cardiomyocytes included focal contracture and loosening. These changes were followed by the formation of focal necroses with well-defined boundaries, dense demarcation infiltrates, and pronounced hypertrophy of cardiomyocytes in the adjacent tissue. In low resistant rats, pronounced edema in the ischemia zone and numerous hemorrhages in the interstitial tissue developed in the early stage after coronary occlusion. These changes were followed by the formation of more extensive necrotic areas with diffuse boundaries, less pronounced demarcation, and irregular hypertrophy of cardiomyocytes in the surrounding tissue.

Key Words: *hypoxia; high and low resistance to hypoxia; myocardial infarction; microscopy of the myocardium*

Animals highly and low resistant to hypoxic damages differ in the sensitivity of organs and cells to hypoxia [1-3] and the ability to adapt to hypoxic conditions [4,5], which is determined by biochemical mechanisms. The myocardium in rats with different resistance to hypoxia utilizes different energy substrates and metabolic pathways of their oxidation. These peculiarities determine early impairments in the synthesis of macroergic substances and contractile disturbances in the heart of low resistant animals, *i.e.* their low resistance to oxygen deficiency [6]. Acute oxygen deficiency (AOD) leads to disturbances in the major biochemical processes and mechanisms and considerable changes in the energy metabolism. These processes differ in highly and low resistant rats [7]. The existence of morphological differences in cells and tissues (*e.g.*, in the myocardium) in animals with different resistance to hypoxia can be hypothesized.

The aim of he present study was to reveal morphological differences in cells and intercellular structures responsible for the formation of cell resistance to hypoxia and maintenance of the functional and metabolic state of the myocardium during AOD.

MATERIALS AND METHODS

Experiments were performed on male outbred rats weighing 180-200 g. There animals were divided into highly and low resistant to hypoxia depending on the time of the second agonal inspiration at a simulated altitude of 11,000 m (SPT-200 vacuum device, 50 m/sec). Tests were performed 1, 3, and 7 days after ligation of the left descending coronary artery.

Myocardial fragments from the left ventricular wall were fixed in 10% neutral formalin for 48 h, dehydrated in alcohols of increasing concentrations and chloroform, and embedded in paraffin. Sections (5-8 μ) were stained with hematoxylin and eosin and examined under a light microscope.

RESULTS

Microscopic examination of the myocardium in highly and low resistant rats showed similar structure of

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muscle fibers, cardiomyocytes (CM), and their nuclei. Their shape, structure, and density did not differ between these animals, which is consistent with published data. However, in highly resistant rats muscle fibers were characterized by more pronounced transverse striation and the presence of large and hyperchromatic nuclei. In highly resistant animals the myocardial interstitial tissue was more loosened than in low resistant rats and contained well-differentiated vascular and connective tissue fibers and cells. Therefore, initial intensity of staining of structural elements in muscle fibers and myocardial stroma was different in animals with different resistance to hypoxia.

At the early stage after AOD morphological changes in the myocardium of highly and low resistant rats were different. In highly resistant animals we fond insignificant edema of the interstitial tissue, loosening of muscle fibers, focal contracture, and disintegration of myofibrils in the ischemic zone (Fig. 1, *a*). Focal damages included hypercontracture and condensation of muscle fibers, appearance of intensive basophilic strips at their periphery of muscle fibers, and deformation of nuclear structures. Wide areas of loosening and disintegration of CM with irregular intercellular boundaries were found in other ischemic zones. In some regions of muscle fibers myofibrils underwent lysis, while in others they were homogenized and intensively stained. CM nuclei had various shapes and sizes due to karyolysis and karyopyknosis. In low resistant rats, pronounced edema of the interstitial tissue, numerous perivascular hemorrhages, and focal breaks of muscle fibers were found in the zone of acute myocardial ischemia (Fig. 1, *b*). CM were characterized by polymorphic structural changes. Edematous and necrobiotic changes in wide ischemic zones included lysis, disintegration, and homogenization of myofibrils. In some regions we revealed breaks and disintegration of CM.

On day 7 we found small focal necrosis surrounded by dense inflammatory and granulation infiltrate in the zone of myocardial infarction in highly resistant rats. This area was localized in the subepicardial zone and separated from normal myocardial tissue by diffuse infiltrates (Fig. 2, *a*). The inflammatory and granulation tissue surrounding this necrotic zone included thin-wall vessels, monocytes, macrophages, and newly formed fibers. This infiltration penetrated the intercellular space of surrounding myocardial tissues re-

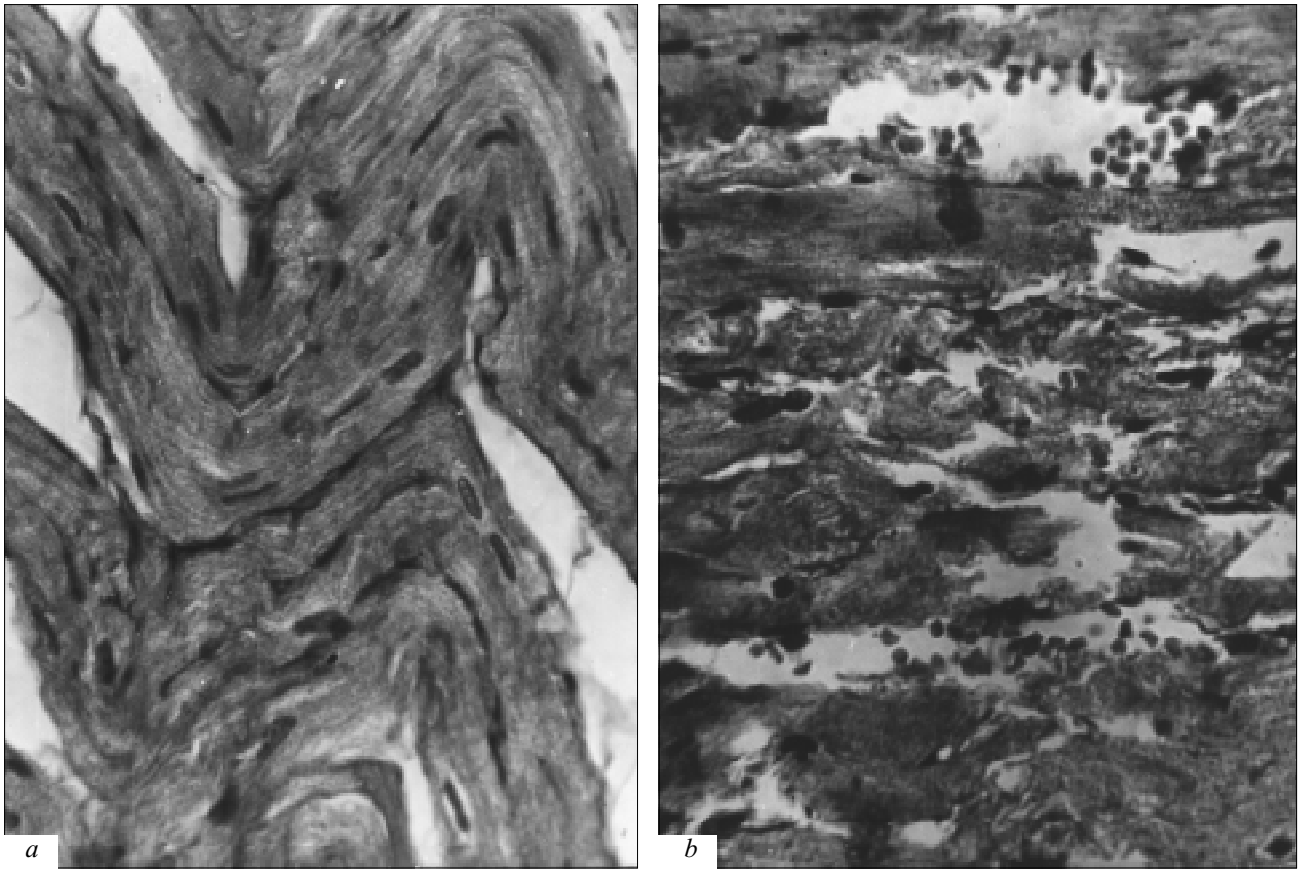

Fig. 1. Early damages to the myocardium in highly (*a*) and low resistant rats (*b*, ×400): *a*) focal contracture of muscle fibers and edema of the interstitial tissue, *b*) disintegration and lysis of cardiomyocytes, hemorrhage in the interstitial tissue. Here and in Fig. 2: staining with hematoxylin and eosin.

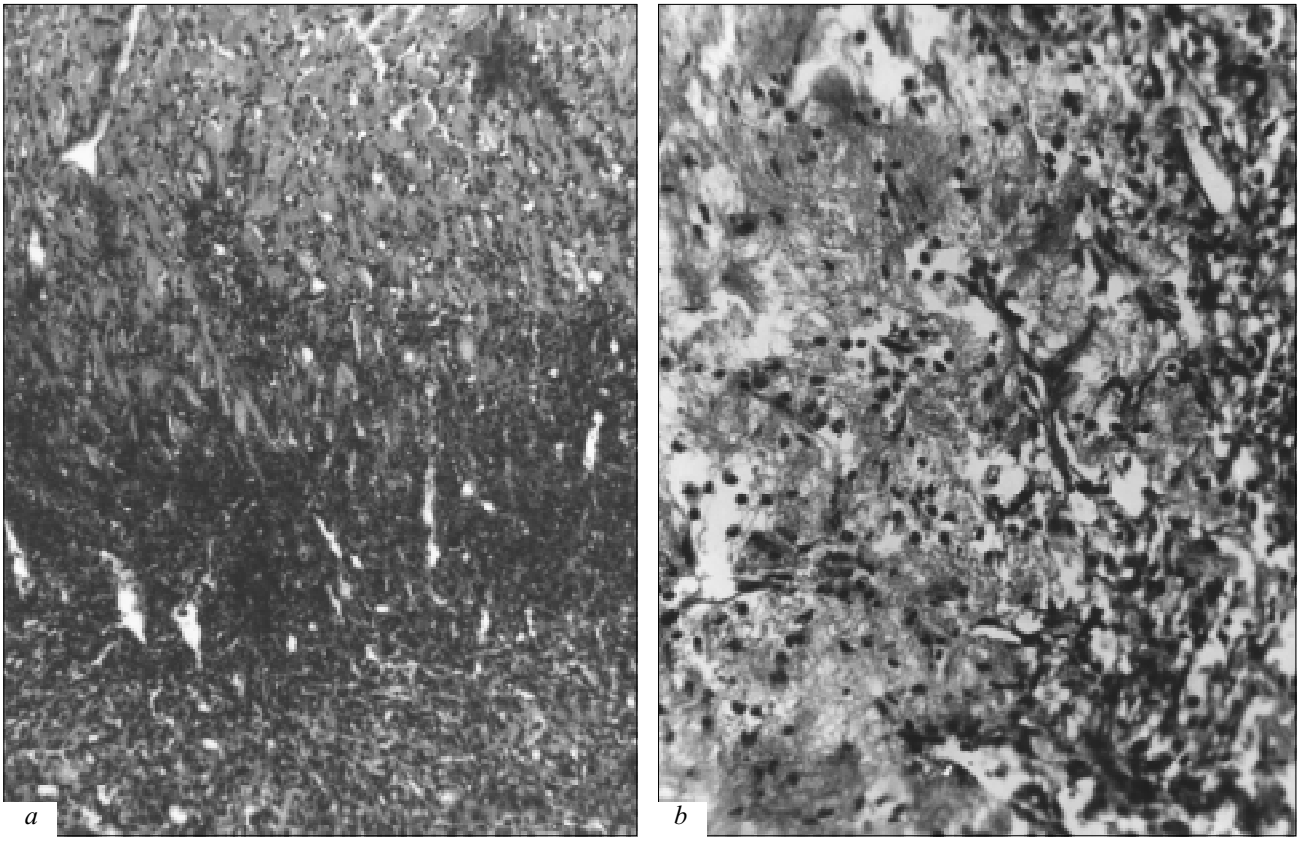

Fig. 2. Zone of damage and surrounding tissues in rats highly (*a*) and low resistant to hypoxia (*b*) on day 7 (×200): *a*) dense cell infiltrate around necrosis focus, *b*) loosened inflammatory and granulation infiltrate around necrosis focus.

sulting in thickening of the stroma and vascular walls; muscle fibers were enlarged due to compensatory hypertrophy of CM. In low resistant rats, necrotic focus in the ischemic zone was more extensive and had diffuse boundaries and less pronounced demarcation structures presented by loosened inflammatory and granulation tissue with low number of vessels, mononuclear cells, and fibers (Fig. 2, *b*). In these animals edema and focal hemorrhages were more pronounced than in highly resistant rats. Loosening of muscle fibers in the surrounding tissue due to edema, cell infiltration, and perivascular hemorrhages was noted. Muscle fibers were irregularly thickened due to hypertrophy of some CM.

Our results demonstrate differences in transverse striation and staining of myofibrils and nuclear structures in rats with different resistance to hypoxia. In highly resistant rats stromal elements are more densely arranged than in low resistant animals. These morphological differences probably determine higher myocardial resistance to hypoxia in these animals.

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