Morphological Changes in the Lungs during Experimental Acute Ischemia and Reperfusion of the Limb

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The development of 4-h ischemia of the limb was associated with significant disorders in pulmonary microcirculation (increased vascular permeability, capillary plethora, hemorrhages). Pathological changes in the lung tissue progressed during the reperfusion period.

Key Words: *ischemia; reperfusion; lungs*

Lesions caused by ischemia and reperfusion are often observed in the practice of physicians of different profiles [4] and present one of the most serious problems of vascular surgery after reconstructive interventions for chronic critical ischemia of the lower limbs or their acute ischemia [3,4]. The prevalence of this condition and percentage of disability and mortality are permanently increasing [1]. Critical ischemia of the lower limbs annually develops in 150-200 per 1 million subjects [2,5].

The reperfusion syndrome clinically manifests by severe polyorgan insufficiency; its morphological substrate are progressive degenerative disorders in vital organs. The major components of polyorgan failure syndrome, developing after ischemia-reperfusion of the limbs, are respiratory disorders.

We studied the morphological changes in the lungs of animals with ischemia-reperfusion syndrome of the limb.

MATERIALS AND METHODS

The study was carried out on 44 male mongrel dogs (12-15 kg). The animals were divided into 3 groups. Group 1 (reference group: fixation and narcosis) consisted of 14 dogs. In group 2 (n=15) 4-h ischemia was induced; group 3 (n=15) animals after 4-h ischemia were subjected to 72-h reperfusion.

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Acute ischemia-reperfusion was induced by a previously developed method. In brief, a tourniquet was applicated onto exposed vascular bundle of the left hind limb proximally from origination of the deep femoral artery until the moment when the peripheral pulsation in the limbs distally from the site of the tourniquet application was no longer palpated. Reperfusion of the limb was carried out after 4 h by removal of the tourniquet.

Morphological studies were carried out on lung biopsy specimens. The material was fixed in 10% neutral formalin, dehydrated in ascending alcohols, and embedded in paraffin. Morphological changes were evaluated on semithin (0.5-1.0 μ) sections stained with hematoxylin and eosin. Histological preparations were examined under an Olympus trinocular microscope.

Morphometrical analysis was carried out using an ocular grid. Karyo-cytoplasmic index (KCI; marker of degeneration severity) and the percentage of leukocytes in visual fields (LI; marker of free-radical damage to alveolocytes) were estimated for the lungs.

RESULTS

Morphological changes in the lung tissue during acute ischemia of the limbs manifested by dyscirculatory and degenerative processes (plethoric capillaries and diffuse interstitial edema without morphological signs of inflammatory cellular infiltration; Fig. 1).

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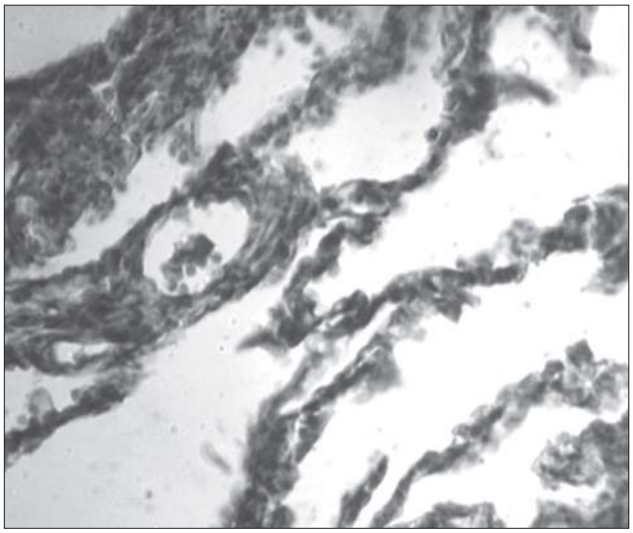

Fig. 1. Thickening of interalveolar septae as a result of vascular plethora and interstitial edema. Hematoxylin and eosin staining, ×56.

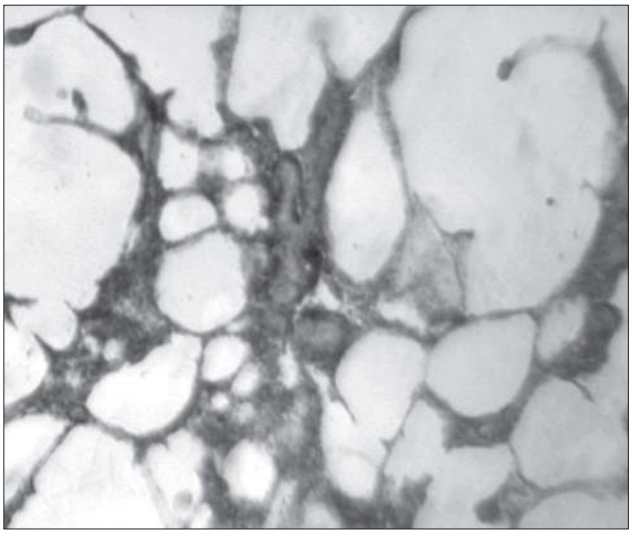

Fig. 2. Congestive hyperemia and alveolar edema. Hematoxylin and eosin staining, ×56.

Signs of tissue discomplexation presenting as foci of dystelectasis and emphysema appeared by the 4th hour of acute ischemia. Arteriolar slugging of blood cells and increase in vascular permeability for blood cells and liquid plasma fraction were combined with the development of metachromasia of the main substance of the perivascular, peribronchial, and interalveolar connective tissue, edema of the bronchiolar mucosa, and desquamation of the prismatic epithelium.

On the whole, interstitial changes with peribronchial and interalveolar components were observed in the lungs during acute ischemia of the limb. The presence of these changes in the lung tissue could indicate changes in the alveolar gas exchange, resultant from microcirculatory disorders under conditions of acute ischemia.

Morphometrical analysis of degenerative tissues after 4-h ischemia showed a 4-fold drop of KCI ($p<0.005$) for the alveolar epithelial cells and a 36-fold increase of LI in comparison with the reference group ($p<0.001$). Reperfusion was associated with the progress of pathological changes in the lung tissue in comparison with the shifts observed during ischemia.

The development of venous plethora (congestive hyperemia; Fig. 2) and arteriolar microthromboses in the lung tissue indicated microcirculatory changes in the system connected to lung function (pulmonary arteries and veins) and in the system of blood supply to the organ parenchyma. Due to numerous anastomoses between these two systems, these changes confirm the presence of a "shock" block of microcirculation in the lung tissue of animals exposed to 72-h reperfusion.

The type of morphological changes in the interstitial lung tissue in the airways and respiratory compartment of the lungs was changed in group 3 animals after 72-h reperfusion: dyscirculatory changes in the bronchiolar mucosa and impairment of the bronchiolar patency. Persisting plethora and swelling of the bronchiolar mucosa were paralleled by accumulation of serous exudation with an admixture of desquamated prismatic epithelium in the bronchiolar lumen (Fig. 3).

Hemorrhagic impregnation of not only perivascular sites of the lung tissue, but also of the intraalveolar space (alveolar serous hemorrhagic edema) was observed in group 3 animals after 72-h reperfusion; foci of atelectasis and diffuse hemo-

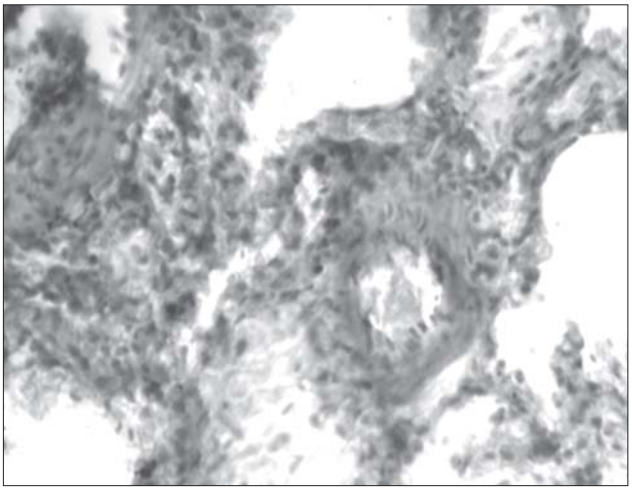

Fig. 3. Accumulation of serous exudation with admixture of desquamated epithelium in bronchiolar lumen. Hematoxylin and eosin staining, ×56.

siderosis were discerned in the lung structure. These morphological changes were an important constituent of the polyorgan failure syndrome.

Morphometric analysis of the lung tissues in animals exposed to 72-h reperfusion of the limb also confirmed augmenting degenerative changes in comparison with the status after 4-h ischemia. Alveolar epitheliocyte KCI in this group decreased by 27% ($p<0.001$) and LI increased 1.5 times in comparison with animals after 4-h ischemia ($p<0.001$).

Hence, 4-h ischemia of the limb was accompanied by significant disorders in microcirculation of the lungs, with dyscirculatory degenerative changes paralleled by tissue discomplexation, leading to disorders in gas exchange without signs of inflammatory reaction. Morphological changes in the lung tissue augmented during the reperfusion period, their picture corresponding to that of the respiratory distress syndrome, a component of polyorgan failure syndrome. These changes indicate that elimination of the cause of ischemia is insufficient: extra measures are needed for the correction of metabolic and structural ischemic damage to the tissues.

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