MICROCIRCULATORY DISTURBANCES IN THE EARLY PERIOD OF AUTOTOXIC SHOCK

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In connection with the development of vascular surgery the study of the pathogenesis of early postischemic circulatory disorders assume particular importance. Mortality after vascular operations associated with long-term ischemia of large muscle masses is known to be 20-35% [1].

The condition known as tourniquet shock (TS), arising on restoration of the circulation in a limb after prolonged arrest of the blood flow in it as a result of application of a tourniquet, can be used as an experimental model of the postocclusion syndrome [1]. Although by now the state of the central hemodynamics in TS has been studied in fair detail, the microcirculation in this model remains virtually unstudied.

The aim of this investigation was to characterize the early changes in the microcirculation which may lie at the basis of the pathogenesis of TS.

EXPERIMENTAL METHODS

The states of the microcirculation were studied on one of the most convenient objects, namely the rat mesentery. Experiments were carried out on 36 noninbred male albino rats weighing about 300 g. TS was produced by application of rubber tourniquets for 6 h to the upper third of both hind limbs under open ether anesthesia, after which the tourniquets were removed and the microcirculation studied under conditions of developing shock for 3 h. For the intravital study of the microcirculation, the animals were anesthetized with pentobarbital (4 mg/100 g), laparotomy was performed, and the mesentery of the small intestine in the region of the ileocecal angle was laid on a special stage fixed to a large "Leitz" intravital microscope. The preparation was continuously irrigated with Ringer's solution, containing 1% gelatin (pH 7.4), heated to 37°C. Since long-term exposure of the mesentery under these conditions is accompanied by some features of disturbance of its microcirculation, observations in each series of experiments were limited to 1 h.

A general assessment of the state of the microcirculation was made by counting the number of functioning capilliaries in 1 mm^2 of mesentery. Vasomotor responses were assessed by the change in diameter of the arterioles and venules, and the adhesive properties of the leukocytes were studied by the method in [4]. To study vascular permeability the animals were given an intravenous injection of fluorescein isothiocyanate-labeled albumin in a dose of 25 mg/100 g body weight, and transport of the marker was observed under the luminescence microscope (wavelength of light exciting fluroescence 480 nm, K-530 emission filter).

Material for electron microscopy was taken after prefixation of the tissue in situ with glutaraldehyde solution (2.5%; pH 7.4). Next, areas of mesentery, stretched on pieces of cork, were fixed in the same solutions and postfixed in 1% OsO_4 solution, pH 7.4. To increase the contrast the specimens were kept for 2 h in a 1% solution of splenic acid. After dehydration of the whole segment of mesentery in alcohols of increasing strength and acetone, the required fragments were excised and embedded in Araldite.

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EXPERIMENTAL RESULTS

After removal of the tourniquet and restoration of the blood flow in the hind limbs, edema developed quickly. The blood pressure of the rats remained stable during the first 3 h of TS (fluctuations not exceeding ±10%).

Disturbances at the microcirculatory level took the form of progressive slowing of the blood flow in the arterioles, capilliariess, and venules. Some capillaries became plasmatized under these circumstances: no blood cells flowed in them. Compared with capillaries filled with blood cells, these plasmatized capillaries were almost invisible. This feature was used during microscopy to count the number of normally functioning capillaries during the course of development of TS. A progressive decrease in the number of functioning capillaries was accompanied by other features of disturbance of the microcirculation, which were most demonstrative during observation after 3 h. Aggregation of erythrocytes became appreciable in capillaries and small venules and the number of leukocytes adherent to the luminal surface of the endothelium increased to 4-6 times more than in the control. Loose juxtamural thrombi were observed to be formed in the lumen of the venules of collecting type. In some cases the blood flow in the mesentery became pendulum-like with periodic brief stoppages.

No appreciable change in the diameter of vessels of arteriolar type could be found, although in some cases vasomotor reactions were observed at the venule level. These reactions took the form of local spasm of the vessel wall. Contracted regions of the vessels as a rule were distinguished by increased permeability for protein. Disturbance of vascular permeability at the postcapillary level was manifested by diapedesis of erythrocytes also.

The study of the ultrastructure of the wall of the microvessels showed that the most marked changes were at the level of the venules. The surface of the endotheliocytes of the venules was uneven and contained numerous outgrowths and folds predominantly in the zones around the junctions between them. The latter often merged to form branched associations in the cell cytoplasm, sometimes connected with its surfaces. Fusion of the vesicles in the thinner areas led to the formation of transendothelial channels, formed by one or two vesicles. The basement membrane and adjacent areas of connective tissue appeared loosened and edematous over a certain extent, and loss of continuity of the basement membrane was observed. Myelin-like formations were frequently seen between the pericytes and the basement membrane.

The morphological and functional changes observed in the microcirculation in the mesentery can be characterized as nonspecific phenomena, observed in disturbances of the nutritive blood flow of varied genesis [3]. However, the degree of intensity of the various processes evidently varied depending on the character of the acting factor. Microcirculatory disorders arising during shock can be conventionally divided into three groups: 1) vasomotor disorders manifested by a change in vascular tone; 2) hemorheologic disorders connected with disturbance of viscosity of the blood and of hemostasis (sludging syndrome, syndrome of disseminated intravascular blood clotting); 3) disturbance of the transport function of the vessel wall, i.e, of its permeability.

In TS changes in the microcirculation, signs of which were observed virtually at once after the beginning of reperfusion of the limbs, were evidently connected with the appearance of metabolites from the ischemic tissues in the blood stream. The most active of these metabolites are free oxygen radicals [8]. Data in the literature [7] and the results of the authors' previous experiments [2] show that these radicals can cause an increase in vascular permeability both through their direct action and also indirectly, by activating leukocytes [5, 6].

Disturbance of the permeability of the walls of the metabolic microvessels for blood plasma proteins thus evidently plays the decisive role in the pathogenesis of TS. The hemoconcentration arising under these circumstances is expressed as disturbances of the blood rheology, observed in the early period of shock. The progressive decrease in normal perfusion of the capillaries, becoming generalized in character, must lead to irreversible aftereffects, arising in the later periods of development of shock.

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RHEOLOGIC AND MORPHOMETRIC PARAMETERS OF THE MICROCIRCULATORY BED OF THE RABBIT EAR AFTER LOCAL ISCHEMIA

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The study of the adequate level of the blood supply at the microcriculatory levels requires evaluation not only of pathogenetic factors, but also of their correlations with one another, maintaining tissue homeostasis. Much remains uncertain about the role of blood viscosity in the microcirculation [9, 11], although negative correlation has been demonstrated between viscosity and velocity of the blood flow in the microcirculatory bed of the brain, both intact and ischemic [11]. Viscosity does depend on the hematocrit value, but in clinical practice this relationship is not always observed [5] and, in addition, the hematocrit index is not always the dominant factor responsible for the change in blood flow in the microvessles [1]. Positive correlation has been found between the viscosity of arterial blood and the diameter of microvessels [8], and this may evidently be taken as a manifestation of autoregulatory processes. Much attention is being paid to blood cells as a factor controlling the blood flow in microvessels. Some workers consider that the main role in microcirculatory disturbances in pathological states is played by changes in the rheologic properties of the blood and vessel wall [3, 6]. Postischemic disturbances at the microcirculatory level have mainly been studied when the blood flow is restricted in either the arterial or the venous section. A model of ischemia due to simultaneous occlusion of artery and vein has rarely been used. When the arterial blood flow is restricted, myogenic and metabolic mechanisms of autoregulation have been shown to act in the same direction, but when the venous outflow is limited, these mechanisms act in opposite directions [7, 10] and reactive hyperemia is depressed or absent altogether. The effects of simultaneous occlusion of artery and vein will therefore evidently depend on relations between these mechanisms in the region concerned.

The aim of the present investigation was to study correlations between rheologic and morphometric parameters of the microcirculatory bed in the rabbit ear during and after local ischemia.

EXPERIMENTAL METHODS

Experiments were carried out on 10 chinchilla rabbits weighing 2-2.5 kg, by a method using a transparent chamber [4] 7 weeks after implantation. Ischemia was produced by folding the pinna at the junction between its upper and middle thirds. Along the line of folding

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