BLOOD RHEOLOGY AND MICROCIRCULATION IN THE COURSE OF ACUTE EXPERIMENTAL PANCREATITIS

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According to recent data in the literature, the course of acute pancreatitis is one of "circulatory shock" with critical disturbances of the macro- and microhemo-dynamics and with considerable changes in the rheologic properties of the blood [3-5].

The aim of this investigation was to study the sequence of development of circulatory and hemorheologic disturbances in the course of acute experimental pancreatitis.

EXPERIMENTAL METHOD

Altogether 63 experiments were carried out on chinchilla rabbits weighing 2.5-3 kg. Pancreatitis was induced by the method in [2]. Under thiopental anesthesia, autologous bile was injected into Wirsung's duct in a volume of 0.5 ml/kg body weight. The microcirculation in various organs was investigated by means of a "Lyumam K-1" contact bioluminescence microscope with parallel photography and subsequent morphometry. To assess the rheologic properties of the blood the structural viscosity of the blood under a sheer velocity of 1 sec^{-1} (η), the aggregating activity of the erythrocytes (AE) and platelets (AP), the suspension stability of the blood (ESR), the hematocrit (Ht), and the mechanical resistance of the erythrocytes (MR) were investigated. Experiments were carried out on six groups of animals: 1) control group (10 animals) to study the effect of laparotomy: a model of acute pancreatitis was produced in 53 animals of the remaining five groups, with durations of the disease of 1, 3, 6, 24, and 36 h respectively.

The experimental results were subjected to statistical analysis on the PDP 11/34 computer (DEC, USA).

EXPERIMENTAL RESULTS

The first signs of microcirculatory disorders appeared in the pancreas as early as 1 h after creation of the model. The diameter of the arterioles decreased from 16.9-2.7 to 8.1-1.3 μ, that of the precapillaries from 11.4-2.2 to 7.2-0.8 μ, and of the capillaries from 6.3-0.6 to 5.0-0.4 μ ($p < 0.05$). After 3 h of acute pancreatitis microcirculatory disturbances appeared in the mesentery, and those in the pancreas were intensified. On the whole, this stage of the experiment was characterized by a sharp rise of the arteriolovenular coeffient (AVC) from 0.53-0.08 to 0.77-0.7 ($p < 0.01$), indicating predominance of inflow over outflow. The first signs of disturbance of the rheologic properties of the blood of the experimental animals were discovered 6 h after creation of the model (Table 1). They corresponded to a progressive disturbance of the blood flow in the microcirculatory system of the mesentery and pancreas: erythrocytic aggregates and juxtamural pavementing of leukocytes were observed in the capillaries. After 24 h of acute pancreatitis the microcirculatory changes appeared in the liver and kidneys. In the pancreas the vascular pattern was virtually undetectable because of developing edema of the organ. Signs of disturbance of the outflow of blood were found in the mesentery (reduction of AVC from 0.53-0.08 to 0.34-0.03; $p < 0.01$), due to marked dilatation of the venular component of the vascular bed. Accumulation of leukocytes and their adhesion to the wall were observed in the blood vessels of the liver, and sinusoids in spasm alternated with others which were dilated, evidence of a re-

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TABLE 1. Changes in Rheologic Properties of Blood in Rabbits with Acute Experimental Pancreatitis

Parameter studied	Control (n=6)	Stage of disease, h				
		1 (n=6)	3 (n=6)	6 (n=5)	24 (n=5)	36 (n=4)
Structural visc. of blood (cP/sec)	10,9±2,8	14,3±2,4	14,6±3,0	22,9±4,1	37,6±6,4	44,9±4,7
p_1		>0,5	>0,5	<0,05	<0,01	<0,01
p_2			>0,5	>0,5	<0,05	>0,5
AE, %	14,9±3,8	16,0±2,5	20,6±6,1	39,2±5,0	63,4±5,3	68,8±5,6
p_1		>0,5	>0,5	<0,05	<0,01	<0,01
p_2			>0,5	<0,05	<0,01	>0,5
AP, %	17,5±2,1	21,8±1,6	25,6±2,5	43,4±5,1	45,3±4,7	34,4±5,9
p_1		>0,5	<0,05	<0,01	<0,01	<0,05
p_2			>0,5	<0,05	>0,5	>0,5
ESR, mm/h	4,2±0,9	5,0±1,6	9,3±2,9	20,8±5,2	37,1±2,5	33,8±1,7
p_1		>0,5	<0,05	<0,01	<0,01	<0,01
p_2			>0,5	<0,05	<0,05	>0,5
Ht, liter/liter	0,34±0,03	0,39±0,04	0,41±0,03	0,45±0,03	0,48±0,02	0,51±0,04
p_1		>0,5	<0,05	<0,05	<0,05	<0,05
p_2			>0,5	>0,5	>0,5	>0,5
MR, %	16,6±1,8	16,0±1,1	15,8±1,4	24,0±3,0	39,9±2,3	41,8±4,7
p_1		>0,5	>0,5	<0,05	<0,01	<0,01
p_2			>0,5	<0,05	<0,05	>0,5

Legend. p_1) Significance of differences compared with control, p_2) the same compared with previous stage of investigation; n) number of animals.

distribution of the blood flow. In vessels of the renal capsule and the heavy tubular capillaries of the renal cortex, the blood flow was interrupted and slowed.

Changes in the functional state of the microcirculatory system in different organs corresponded to disturbances of the rheologic properties of the blood, reflected in increased viscosity, Ht, AE, and AP, and a decrease in ESR and MR.

Maximal changes in the state of the microcirculatory bed and blood rheology were discovered after 36 h of acute pancreatitis. Morphological changes in the tissues predominated in the pancreas, with evidence of frank necrosis. The number of diapedetic hemorrhages was increased. In the mesentery the majority of capillaries and postcapillaries were thrombosed; the number of functioning capillaries was reduced from 13-1.1 to 7.0-0.9 ($p < 0.05$). The AVC fell progressively to 0.24-0.01. In the liver there was a decrease in the number of functional terminal venules and sinusoids, with the appearance of "silent zones" and with features of general diapedetic hemorrhages. In the vessels of the renal capsule a dispersed blood flow was observed; the peritubular capillaries of the cortical layer were dilated and filled with erythrocytic aggregates. Corresponding to these changes there was a fourfold increase in viscosity of the blood due to the marked hemoconcentration and to an increase in AE and AP.

The results of these experiments thus indicate that microcirculatory and chemorheologic disturbances in the course of acute pancreatitis develop in definite stages. In the early stages of experimental pancreatitis spastic changes predominate in the microcirulatory bed at the arteriolar level. As a result, foci of local ischemia arise and a process of autolysis is initiated. An important role in the development of the primary microcirculatory and hemorheologic disorders is played by vasoactive substances (serotonin, histamine, kinins), arising from foci of ischemia [1, 6, 7]. These factors are responsible for the biphasic nature of the vascular response in the course of acute pancreatitis. The initial vasoconstriction leads to the appearance of hemorheologic disturbances. The vasoconstriction subsequently gives way to vasodilatation. Against this background the hemorheologic disorders progress still more, become generalized systemic in character, and they are the cause of microthrombosis and of massive diapedetic hemorrhages, accompanying the hemorrhagic stage of pancreonecrosis. In the latter stages of the disease vasodilatation is followed by virtually total paralysis of the vascular wall. Under these conditions the viscosity of the blood assumes fundamental importance in determination of the functional state not only of the regional but also of the systemic hemodynamics.

Thus the creation of a model of acute experimental pancreatitis in rabbits showed that hemorheologic disturbances are one of the most important causes of the circulatory distur-

bance in the microcirculatory system of various organs. In the course of acute pancreatitis the microcirculatory bed of the pancreas itself and the mesentery is first affected; later, at the stage of transition from the edematous form of pancreatic necrosis to the hemorrhagic form the hemorheologic disturbances lead to the development of microcirulatory disorders in the liver and kidneys. It can be concluded from these facts that the degree of the hemorheologic disturbances and of the microcirculatory disorders in different organs corresponds to the severity of the necrotic changes in the pancreas at different stages of the pathological process.

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ELECTRON-AUTORADIOGRAPHIC STUDY OF RNA SYNTHESIS IN DARK AND PALE ADRENAL CELLS

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Dark and pale cells are found in various organs and tissues, including the adrenals. It has been claimed that dark cells possess greater functional capacity and are adapted for long term specific activity, associated with active biosynthesis, whereas pale cells are in a state of exhaustion [1, 2, 5]. Since RNA turnover is an essential characteristic of the cell, it was decided to study this phenomenon by electron-microscopic autoradiography in different structural and functional zones of the adrenals.

EXPERIMENTAL METHOD

The test material consisted of mouse adrenal glands. The animals were given an intraperitoneal injection of the labeled RNA precursor 5-^{3}H-uridine, in a dose of 100 μCi/g. The mice were decapitated 2 and 4 h after injection of uridine under ether anesthesia, and the adrenals were fixed in 2.5% glutaraldehyde solution, washed with phosphate buffer (pH 7.4), post fixed with 1% OsO_4 solution, and embedded in a mixture of Epon and Araldite. Autoradiographs of semithin sections were prepared from each block with the aid of type M emulsion, and on the basis of the results of their analysis, zones for ultramicrotomy were selected. Electron-microscopic autoradiographs were obtained by the method described previously [3, 4]. Semithin sections were stained with toluidine blue. Ultrathin sections were examined in the JEM-100 B electron microscope. The number of grains of silver above the nucleus and cytoplasm of the dark and pale cells and the total number of grains above these cells were counted. The ratio of the number of grains of silver above the nucleus to the number above the cytoplasm was calculated. All the quantitative data were subjected to statistical analysis. The significance changes were calculated by Student's t test. Mean values were obtained from

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