ACUTE EXPERIMENTAL STUDY OF THE PATHOMORPHOLOGY OF SLUDGING

Academician A. M. Chernukh*,
I. K. Esipova, O. Ya. Kaufman,
and M. D. Vakar

UDC 616.151.5-06:616.16]-008.6-092.9-091

A disturbance of the rheological properties of the blood (the sludging syndrome) was reproduced by injection of high-polymer dextran. A combination of sludging with administration of the vasoconstrictor agent vasopressin led to ischemic lesions of the myocardium (marked depression of succinate and lactate dehydrogenase activity, disturbance of glycogen utilization) with stasis,and diapedesis of the leukocytes in certain organs, mainly in the lungs.

The term sludging has been proposed to describe a marked disturbance of the rheological properties of the blood, characterized by an increase in its viscosity and simultaneous aggregation of the cells [10]. A disturbance of the capillary circulation is accordingly observed in sludging [1, 3, 7, 8, 9]. To reproduce aggregation of the blood cells and an increase in its viscosity (the sludging syndrome) experimentally, dextran (mol. wt. of the order of 70,000-500,000) is used. Simultaneous administration of a sludging agent (high-polymer dextran) and of vasoactive substances to animals (e. g., albino rats) increases the severity of the microcirculatory disturbances through aggregation of the blood cells. For example, after injection of high-polymer dextran (mol. wt. 500,000) in a dose of 1 g/kg and of vasopressin, focal ischemic changes were found in the myocardium in rabbits [4, 6].

Although a state similar to the sludging syndrome is observed clinically in many diseases (cardiogenic shock, postoperative and post-traumatic states, artificial circulation, injection of x-ray contrast substances, etc. [2, 5, 7, 8, 10-12]) its pathomorphology has not been adequately considered in the literature.

For the above reasons, an acute experiment, the results of which are given below, was carried out to study the pathomorphology of the sludging syndrome.

EXPERIMENTAL METHOD

Noninbred albino rats of both sexes weighing 250-280 g were used. The animals were anesthetized with urethane (20% solution, 0.1 ml/100 g body weight, intramuscularly) and then divided into three groups. The animals of group 1 (8 rats) received an intravenous injection of 10% high-molecular-weight (500,000) dextran in a dose of 100 mg/100 g body weight, the nine rats of group 2 received vasopressin in a dose of one pressor unit/100 g body weight, and the 12 rats of group 3 received high-molecular-weight dextran intravenously followed 1 h later by vasopressin. The animals were decapitated 15-30 min after injection of vasopressin and 1.5 h after injection of dextran. Three intact rats served as the control. Activity of succinate

*Academy of Medical Sciences of the USSR.

Laboratory of General Pathophysiology and Experimental Therapy and Laboratory of Experimental Pathomorphology, Institute of Normal and Pathological Physiology, Academy of Medical Sciences of the USSR, Moscow. Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 73, No. 1, pp. 83-86, January, 1973. Original article submitted July 10, 1972.

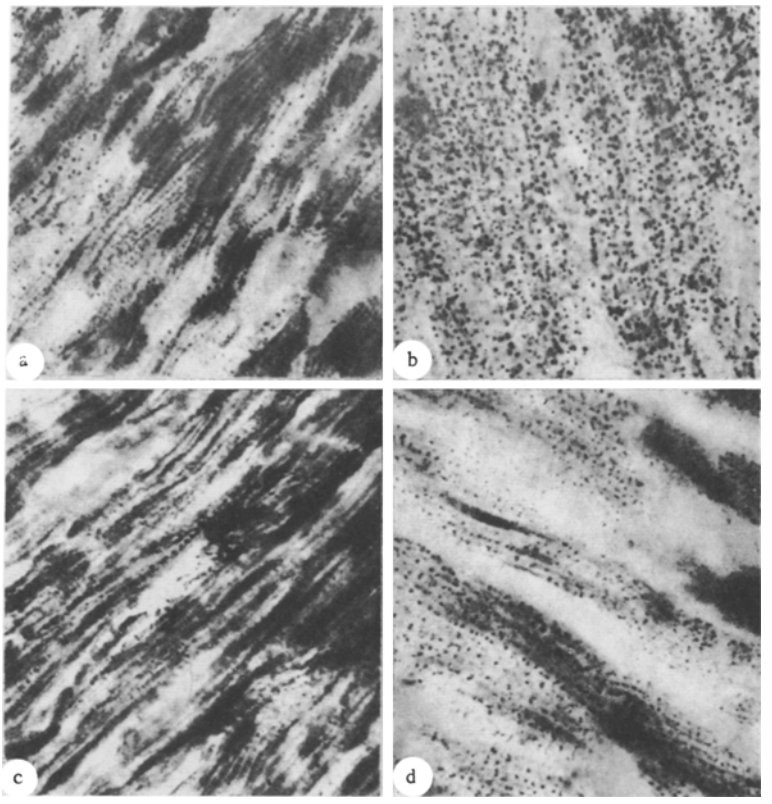

Fig. 1. Deposition of formazan in sections through myocardium of rats showing activity of succinate (C, D) and lactate dehydrogenases (A, B): A, C) linear arrangement of formazan in myocardium of control rats; B, D) deposition of coarsely granular formazan after administration of high-polymer dextran and vasopressin to animals, 900×; immersion.

and lactate dehydrogenases [13] was determined in the myocardium, adrenals, and thyroid gland, and the glycogen content was determined in the myocardium and liver (PAS reaction with diastase control). Survey films were stained with Mallory's azan and by the combined method with fuchselin for elastic tissue and counterstaining by Van Gieson's method. The distribution of the leukocytes was studied by Goldman's method in survey films simultaneously stained to show lipids. The degree of blood filling of the organs was studied by Eros' method [14].

EXPERIMENTAL RESULTS

Investigation of succinate and lactate dehydrogenase activity showed that formazan deposition at the sites of localization of the enzymes in the myocardium of the intact control animals was predominantly linear in form, and only occasionally was finely granular formazan seen (Fig. 1: A, B), in agreement with data in the literature. Foci in which formazan was deposited as large, coarse granules (coarsely granular formazan) were found 1 h after injection of dextran and 15-30 min after injection of vasopressin alone. Determination of lactate dehydrogenase activity showed similar but more marked changes.

After combined administration of dextran and vasopressin, zones with a normal linear distribution of formazan were no longer found in the myocardium, but there were only occasional large coarse granules (Fig. 1: B, D), indicating a sharp decrease in succinate and lactate dehydrogenase activity, i.e., gross damage to the mitochondria.

Combined administration of dextran and vasopressin led to a sharp decrease in the activity of the above enzymes in the adrenals. Side by side with the focal disappearance of activity of these dehydrogenases, deposits of coarsely granular formazan were observed, mainly in the zona fasciculata of the adrenal cortex. No changes were found in succinate or lactate dehydrogenase activity in the thyroid gland.

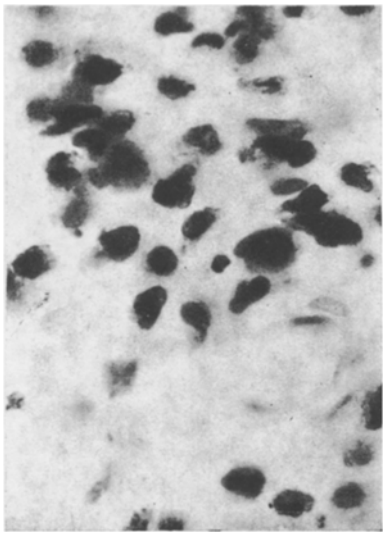

Fig. 2. Accumulation of granulocytes in adventitia of venule in lung of rat with sludging syndrome. Goldman's stain, 900×; immersion.

Despite the marked histochemical evidence of myocardial damage of an ischemic character following administration of dextran and vasopressin to the animals, glycogen disappeared from the muscle cells of the myocardium, especially after administration of vasopressin alone. In this same series, the glycogen content of the liver was sharply reduced. After the combined administration of dextran and vasopressin glycogen was detected as small granules, filling the cytoplasm of the muscle cells and hepatocytes uniformly.

In sections stained by Goldman's method the lipid content of the adrenal cortex was reduced, especially after administration of vasopressin, and changes in the concentrations of leukocytes were observed in the tissues. These occurred in the animals of all three groups but were most marked after the combined administration of dextran and vasopressin. A sharp increase in the leukocyte concentration was found in the spleen, and in particular, in the lungs. In the lungs leukocytes were found in the lumen of the capillaries, venules, and veins, as well as in lymphatic capillaries. Neutrophils formed cuffs in the adventitia of the veins, venules, and bronchi. These accumulations of granulocytes reached such an intensity (30 to 40 granulocytes were found in a field of vision of the microscope with a ×40 objective) that in places the picture simulated that of suppuration (Fig. 2). In some places the concentrations of leukocytes plugged the lumen of the venules and lymphatic capillaries, simulating the picture of suppurative thrombophlebitis and lymphangitis. Many leukocytes also were found in the alveolar septa.

Marked diapedesis of the leukocytes occurred in the animals of all groups in the spleen, where the granulocytes accumulated at the periphery of the follicles and in the pulp.

In the liver a few granulocytes (up to 10 per field of vision) were found in the lumen of the sinusoids, mainly in the animals of group 2, but diapedesis and stasis of leukocytes in the liver were not characteristic features of the animals of groups 1 and 3.

Diapedesis of the leukocytes in the brain was ill-defined and granulocytes were found in the substance of the slightly edematous meninges, while in the myocardium there was neither stasis nor diapedesis of the leukocytes.

By the use of elective stains (Mallory's azan, Eros' stain) the redistribution of blood among the organs in the sludging syndrome was revealed. The greatest hemoconcentration was found in the lungs together with marked congestion of the capillaries, with foci of diapedesis of blood into the lumen of the alveoli and into the adventitia of the small veins and arteries. In all the experimental animals the veins of the lungs showed a spastic response, whereas in other organs the blood vessels (small muscular arteries and veins) were mainly in a state of normo- or dystonia.

Marked hemoconcentration was also found in the liver, and congestion was observed in the sinusoids lying beneath the capsule and around the hepatic veins in the interior of the organ.

The results of this investigation thus confirmed those obtained earlier in Professor A. M. Chernukh's laboratory [4]: after injection of a sludging agent together with the vasoconstrictor agent vasopressin, changes characteristics of coronary arterial spasm and hypoxia were found on the ECG. The sharp decrease in succinate and lactate dehydrogenase activity discovered in the present investigation, manifested as replacement of the linear arrangement of the formazan by single large granules, can be interpreted as the result of hypoxic injuries to the myocardial muscle cells.

It is also important to note that the morphological findings confirmed the results of a biochemical study of the myocardium during a combination of sludging and vasopressin administration [4]: a disturbance of the utilization of glycogen in the myocardium also was detected biochemically, despite the hypoxia. A marked decrease in the glycogen content in the myocardium of the animals was found only when vasopressin alone was given. It is interesting to compare the sharp decrease in the lipid content of the adrenal cortex under these conditions with this fact.

The most characteristic features of the morphology of the sludging syndrome in its acute stage were the isolated leukocytosis of specific organs, with stasis and diapedesis of the leukocytes and irregular changes in hemoconcentration. In the animals studied (rats) this process was localized predominantly in the lungs.

These foci of localized leukocytosis can simulate focal suppuration, but the subsequent fate of these foci is not yet understood.

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