EFFECT OF HEMOPERFUSION ON HEPATOCYTE ULTRASTRUCTURE IN TOXIC HEPATITIS

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UDC 616.36-018.1-099-02:615.
38.015.2:615.246.2

KEY WORDS: liver; poisoning; hemoperfusion; hepatocyte ultrastructure.

Hemoperfusion methods of detoxication are a powerful weapon in the correction of severe disturbances of hemostasis [3, 4]. How extracorporeal perfusion of blood through activated charcoal affects the structure of the liver is an interesting problem. Few investigations into this subject have been undertaken and the conclusions drawn are contradictory [1, 2, 5]. The aim of this investigation was to study structural changes in the liver accompanying hemoperfusion.

EXPERIMENTAL METHOD

Experiments were carried out on 24 dogs weighing from 16 to 21 kg. Five of the animals formed the control group. The first stage of the experiments was to create a model of obstructive jaundice, complicated by hepatic failure. This was done by ligating the cystic and common bile ducts, followed by retrograde injection of 0.1 mg/kg body weight of a solution of CCl_4 into the biliary passages. In the second stage of the experiment the hepatoprotective effect of charcoal hemoperfusion on structural changes in the parenchyma of the organ was studied. For this purpose, percutaneous liver puncture was carried out on the 6th day after the operation with an I-116-117 C-C needle, after which hemoperfusion was carried out using mark SKN-2K activated charcoal. The liver having thus been placed "under protection," punch biopsy of the liver was repeated on the 1st, 3rd, 7th, and 15th days after extracorporeal detoxication. The value of this method is that it allows the phases of the pathological process to be observed in each concrete case.

The experiments were carried out under ether and oxygen anesthesia with artificial ventilation of the lungs, after premedication with 2% trimeperidine solution. The material obtained was fixed and processed by the usual method for general morphological and electron-microscopic analysis. Ultrathin sections were studied in the Hitachi H-600 electron microscope.

EXPERIMENTAL RESULTS

The experiments showed that in the presence of an established pathological process (after 6 days of cholestasis against the background of CCl_4 poisoning) structural changes connected with biotransformation of static bile by the hepatocytes and inactivation of CCl_4, take place in the liver. In the parenchyma, for instance, focal concentrations of lymphohistiocytic infiltration were found. Liver cells were in a state of cloudy-swelling degeneration, and some in a state of destruction. The hepatocytes contained much bile pigment and the nuclei of some of them were in a state of pycnosis or lysis. Diffuse hemorrhages and thrombosis of the interlobular veins indicated severe microcirculatory disturbances. The glycogen content of the liver tissue was greatly reduced. Examination of the fine structure revealed that the clearest changes occurred in the mitochondria. Under the influence of biliary poisoning the mitochondria, as highly sensitive indicators of cell damage, showed marked inhibition of energy metabolism. Besides deformation of the cristae and disturbance

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Experimental Division, Department of Pathological Anatomy, Tashkent Branch, All-Union Scientific Center for Surgery, Academy of Medical Sciences of the USSR. (Presented by Academician of the Academy of Medical Sciences of the USSR D. S. Sarkisov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 99, No. 3, pp. 368-370, March, 1985. Original article submitted May 5, 1984.

0007-4888/85/9903-0375$09.50

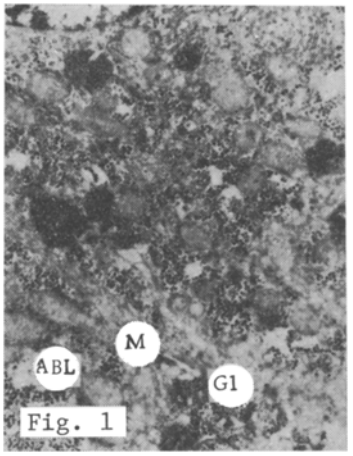

Fig. 1. Ultrastructure of liver after 6 days of cholestasis superposed on CCl_4 poisoning. Deformation of cristae and disturbance of integrity of membranes in mitochondria. Cytoplasmic bodies resembling condensations of bile appear in cytoplasm. Gl) Glycogen granules, M) mitochondria. 10,000×.

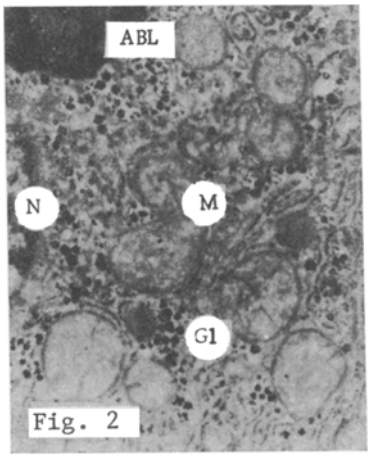

Fig. 2. Ultrastructure of liver 7 days after hemoperfusion. Reduction in number of glycogen granules in cytoplasm of hepatocyte, translucency of matrix in mitochondria. Aggregates of bile and lipofuscin have grown to a considerable size. N) Nucleus, ABL) aggregates of bile and lipofuscin. 18,000×.

of the mitochondrial membranes myeloid degeneration also took place, due to the toxic effect of ammonia. There were few intracellular organelles, and mainly cytoplasmic bodies resembling condensations of bile could be seen (Fig. 1). Bile capillaries were dilated and the microvilli in them were reduced. The perisinusoidal spaces were considerably widened. Integration of the inflammatory and mesenchymal-cell reactions, on the one hand, with microcirculatory disturbances, on the other hand, thus provide the material substrate for hepatic failure.

A study of the hepatoprotective effect of hemoperfusion on liver morphology showed that reducing the concentration of the toxic factor in the blood as early as on the first day after hemoperfusion improves the microcirculation of the liver. The bile concentration in

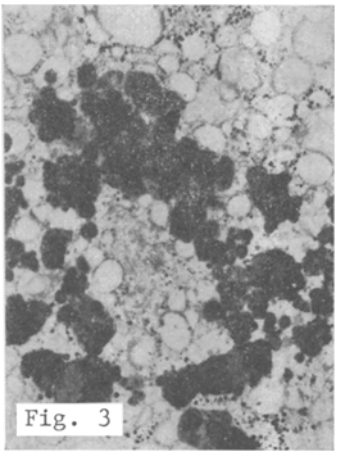

Fig. 3. Ultrastructure of liver 15 days after hemoperfusion. Marked decrease in number of glycogen granules in hepatocyte cytoplasm which contains numerous condensations of bile and lipofuscin granules. Widening of profiles of rough endoplasmic reticulum. 10,000×.

the cytoplasm of the hepatocytes was considerably reduced. The cell boundaries were more clearly outlined and binuclear cells appeared in some areas. The glycogen content in the hepatocytes increased and its granules filled the whole of the cytoplasm.

Activation of intracellular regeneration was found particularly clearly by ultrastructural analysis of liver biopsy material. For instance, the number of cristae in the mitochondria was increased, as also was the electron density of the matrix. A very characteristic finding was an increase in the number of lysosomes, evidence of intensification of intracellular regeneration. In this connection it is logical to suppose that regenerative processes maintaining the specific function of the cells must be regarded as the material basis for all reactions aimed at maintaining homeostasis [6].

These changes remained stable 3 days after hemoperfusion. In some cases, however, in the immediate vicinity of the biliary pole of the hepatocytes, bile structures were concentrated again. The perisinusoidal space was narrowed. Analysis of liver biopsy material 7 days after hemoperfusion showed an increase in the content of bile pigment in the cytoplasm of the hepatocytes, and the portal tracts were dilated. The concentration of pyroninophilic substances was reduced. Mitochondria with fragmented cristae and translucent matrix were found on electron micrographs of the liver. The extent of the endoplasmic reticulum was considerably increased but the number of glycogen granules was sharply reduced (Fig. 2). The bile capillaries were again thrombosed with condensations of bile. In the dilated perisinusoidal spaces microvillus-like outgrowths formed by the plasma membranes of the vascular pole of the hepatocytes were found. During a later observation on the state of the liver on the 15th day after detoxication by hemoperfusion massive foci of lymphohistiocytic infiltration were observed, and the dilated vessels were thrombosed. Mitoses were virtually not found and in some cells there were no pyroninophilic substances. The ultrastructural organization was dominated by cytoplasmic bodies containing condensations of bile and lipofuscin granules (Fig. 3). In other cells the predominant feature was profiles of the rough endoplasmic reticulum and Golgi complex. The perisinusoidal space was greatly widened, edematous, and filled with delicately granular material.

These investigation thus revealed the following structural changes in homeostasis of the liver before and at various times after hemoperfusion. In the early stages (up to 3 days) after detoxication by hemoperfusion regenerative changes in the liver were considerably activated. Later (on the 7th day), however, the unresolved cholestasis led to the development of destructive changes, and these were more advanced still on the 15th day.

Hemoperfusion, while an effective method of detoxication, cannot therefore be the final stage in the treatment of obstruction of the common bile duct complicated by hepatic failure. The results of these investigations indicate that hemoperfusion must be carried out during the 2-3 days before surgical treatment of occlusion of the biliary tract.

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DESTRUCTIVE AND REGENERATIVE CHANGES IN THE ALBINO RAT KIDNEY DURING MERCURIC CHLORIDE NECROTIZING NEPHROSIS

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UDC 616.61-002.4-099-003.9-07

KEY WORDS: mercuric chloride; nephron; necrosis; repair.

Mercuric chloride (corrosive sublimate), which acts as a nucleus for the thiol group, 24 h after introduction into animals gives rise to heterogenous necrotic changes in the epithelial cells of the renal tubules. Despite many histological investigations devoted to the study of regeneration in mercuric chloride necrotizing nephrosis, many disputed and unsolved problems to do with determination of the sources of reparative regeneration of the renal tubular epithelium still remain.

According to some data [5, 6], regeneration of the epithelium of the proximal urinary tubules, damaged by mercuric chloride, takes place by ingrowth of mitotically dividing cells of the uninjured epithelium located distally to the zone of necrosis. According to histological and histoautoradiographic data obtained by other workers [2-4, 8], the source of regeneration of the necrotically changed epithelium of the urinary tubules is solitary cells which remain viable in the zone of necrosis, which resemble epithelial cells of loop segments located below, which later cover the injured areas of the tubule again. On the basis of the results of an extensive study of autopsy material, Permyakov and Zimina [1] postulate that partially injured epithelial cells ("amputant" cells) in the zone of necrosis are able, in the early period of necrosis, to perform the role of primary "patch," protecting the basement membrane of the tubules, and later the set of preserved epithelial cells acts as the source for true proliferation, covering the denuded areas of the basement membrane.

This paper describes the results of a morphological analysis of destructive and regenerative changes observed during a study of serial semithin sections of the kidneys of albino rats with mercuric chloride necrotizing nephrosis.

EXPERIMENTAL METHOD

Experiments were carried out on noninbred male rats weighing 160-220 g. The animals were divided into two groups: Six rats of group 1 served as the control, 18 rats of group 2 received a single subcutaneous injection of mercuric chloride in a dose of 0.6 mg/100 g body weight, dissolved in physiological saline.

Department of Biology, Grodno Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR D. S. Sarkisov.) Translated from Byulletin' Éksperimental'noi Biologii i Meditsiny, Vol. 99, No. 3, pp. 370-373, March, 1985. Original article submitted June 15, 1984.

 0007-4888/85/9903-0378$09.50