Ultrastructural Characteristics of Hepatocytes during Echinococcosis

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We performed an electron microscopy study and histological examination of hepatocytes during hepatic echinococcosis. The type of damage to liver cells depended on intrahepatic localization of hydatid cysts, which determined the development of postoperation complications.

Key Words: *hepatocyte; ultrastructure; hepatic echinococcosis*

Hepatic echinococcosis is a severe chronic endemic disease, whose incidence constantly increased in recent years [2-4]. Changes in the liver vary from mild damage to liver cirrhosis and are related to the mechanical and chemical effect of hydatid cysts and their contents, extrahepatic cholestasis, and autoimmune disorders [1]. Morphofunctional changes in the liver determine the early and delayed consequences of surgical treatment.

In the present work ultrastructural changes in hepatocytes during echinococcosis were studied in different intrahepatic localization of hydatid cysts.

MATERIALS AND METHODS

We examined liver biopsy specimens from 38 patients (13 men and 25 women, 23-68 years) operated for echinococcosis at the Department of General Surgery (Therapeutic Faculty, Tashkent State Medical University, Dushanbe; *n*=28) and A. V. Vishnevskii Institute for Surgery (Moscow, *n*=10). The patients had solitary intrahepatic hydatids. Injuries in the right and left lobes were revealed in 29 and 9 patients, respectively. Suppuration of the hydatid cyst, calcinosis of the fibrous capsule, and dead maternal cyst were observed in 4, 3, and 3 patients, respectively. Hydatid cysts were 2-8 cm in diameter. Surgical treatments included closed echinococcectomy (*n*=12), half-closed echinococcectomy (*n*=6), pericystectomy (*n*=9), hepatectomy (*n*=9), and open drainage of the residual cavity (*n*=2). The patients were divided into 2 groups. In group 1 patients (*n*=17) the thickness of liver tissue above the hydatid cysts surpassed 2 cm, and the size of cysts varied from 2 to 5 cm. In group 2 patients (*n*=21) the liver parenchyma was thinned; its thickness did not surpass 1.5-2.0 cm. Liver tissue to the periphery of the cyst was intact. The size of cysts in group 2 patients was 5-7 cm.

Medical histories and morphological examination indicated that patients had no liver diseases and hepatotropic intoxication in the past years.

Liver biopsy specimens were taken intraoperatively at a distance of 1-8 cm from the focus of echinococcosis. Paraffin sections were prepared routinely and stained with hematoxylin and eosin. Electron microscopy was performed using an EVM-100 BR microscope.

RESULTS

Histological examination revealed zonal changes of liver tissue in group 1 patients. There were 3 zones with different severity of injury. Zone 1 was adjacent to the cyst, zone 2 was intermediate, and zone 3 was distant from the focus of injury.

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Light microscopy of zone 1 showed that at the boundary between the parenchyma and fibrous capsule, connective tissue elements grew into the liver to different depth (Fig. 1, *a*). This zone contained cells that were surrounded by fibrous tissue ("enclosed hepatocytes") and lost their characteristic spatial orientation. The degree of injury was maximum in zone 1.

Electron microscopy revealed signs of damage and atrophy of hepatocytes adjacent to the hydatid. The size of hepatocytes and nuclei decreased. Moreover, we revealed a decrease in the number and destruction of energetic, synthetic, and excretory intracellular organelles. Incorporation of conglomerates of bile and lipofuscin in the cytoplasm was related to compression of bile capillaries.

The intermediate zone underwent considerable structural changes. First, the trabecular composition was impaired, hepatocytes were densely positioned, and sinusoids were practically undetectable. And second, hepatocytes in this zone were characterized by pronounced polymorphism. They had various shapes and sizes. Most hepatocytes were smaller than normal cells. It was probably associated with endogenous intoxication and tissue compression [2].

Electron microscopy showed that hepatocyte nuclei were large. Electron density of chromatin decreased. The matrix of swollen mitochondria was lightened, and cristae were undetectable (Fig. 1, *b*). The granular endoplasmic reticulum was reduced and appeared as fragments around mitochondria. The cytoplasm contained secondary lysosomes and elements of bile and lipofuscin that were localized in the sinusoidal pole of hepatocytes. The perisinusoidal Disse's space was moderately enlarged. Sinusoidal cells had signs of injury.

Changes of the liver parenchyma in zone 3 (8-10 cm) were typical of nonspecific reactive hepatitis. The surrounding liver parenchyma had normal structure. The observed changes depended on the size of hydatid cysts, their localization, and development of complications. Signs of compensatory hypertrophy and regeneration of hepatocytes were revealed in regions distant from the giant hydatid. Severe damage and cell necrosis occurred near the cyst. In group 1 patients the degree of these changes was similar in tissues peripheral and medial to the hydatid cyst.

Electron microscopy and histological examination of the liver in group 2 patients gave interesting results. The patients of this group were selected empirically taking into account unsatisfactory results of organ-preserving surgeries. Typical changes were revealed in liver tissues medial to the hydatid cyst. Damage and necrosis of hepatocytes were found in the peripheral region. These changes were not characterized by zonal distribution (Fig. 2, *a*). Light microscopy revealed impaired trabecular structure, fibrous interlayers inside hepatic acini, fibrosis and lymphohistiocytic infiltration of portal tracts, and sometimes damage to the terminal lamina. Sinusoids were practically undetectable. Sinusoidal cells were swollen. The hepatocyte cytoplasm was vacuolized in perivenular and intermediate zones of hepatic acini. Regions of necrotized cells formed monocellular and perivenular necroses.

Electron microscopy revealed hepatocytes with signs of reversible and irreversible damage (Fig. 2, *b*). Energy-producing mitochondria underwent most pronounced changes. The matrix was characterized by irregular electron density, and cristae were not visualized. Cisternae of the granular endoplasmic reticulum were widened and looked like electron transparent vacuoles with different size and shape, ribosomes were

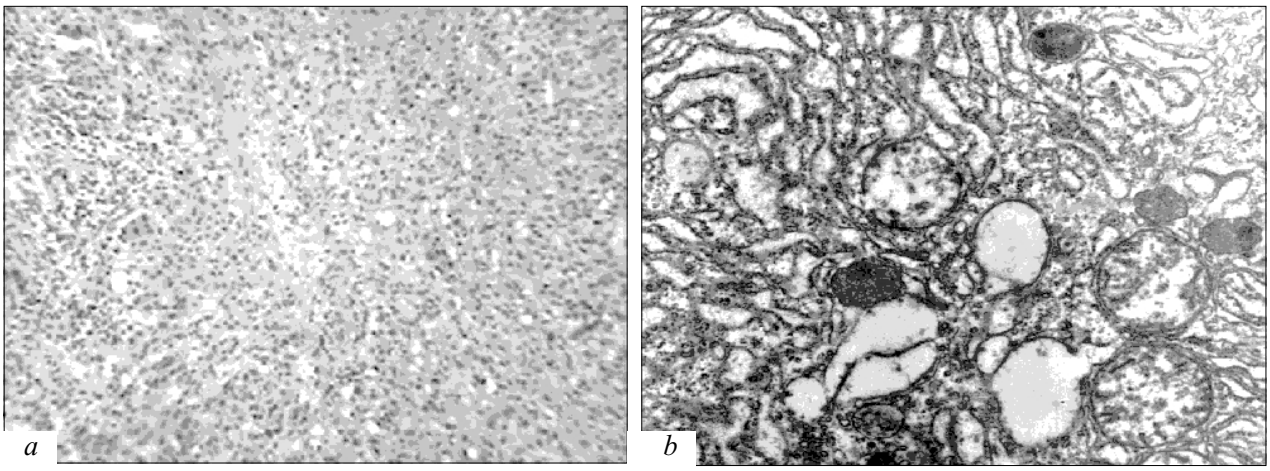

Fig. 1. Morphological changes in the liver in group 1 patients: fibrosis of portal tracts and periportal zone, vacuolization of the cytoplasm, and necrosis of hepatocytes (hematoxylin and eosin, ×60, *a*); swelling of mitochondria, destruction of cristae, widening and fragmentation of cisternae of the granular endoplasmic reticulum in hepatocytes (×36,000, *b*).

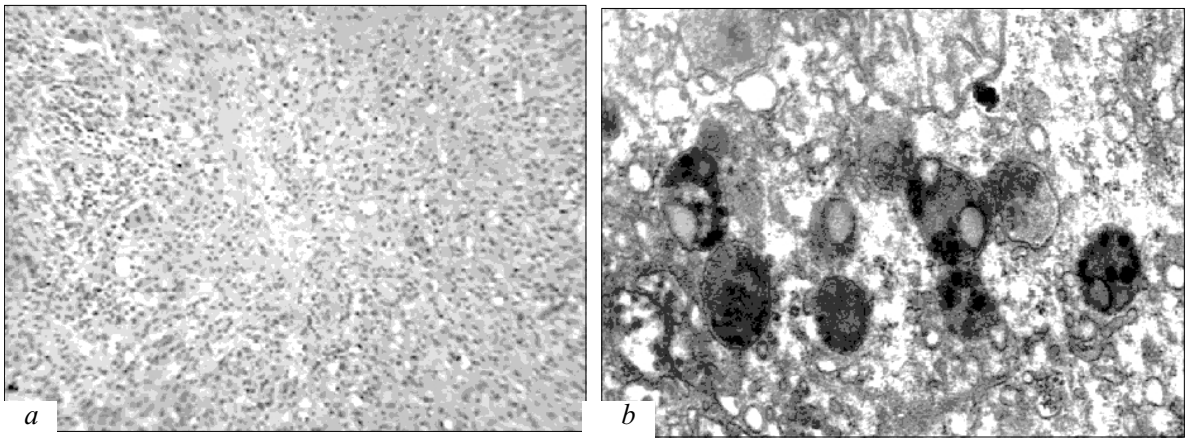

Fig. 2. Morphological changes in the liver in group 2 patients: fibrosis and lymphohistiocytic infiltration of portal tracts and periportal zones, injury and necrosis of hepatocytes (hematoxylin and eosin, ×60, *a*); swelling of the cytoplasm, destruction of mitochondria and endoplasmic reticulum, and considerable number of secondary lysosomes in hepatocytes (×40,000, *b*).

scanty. In most liver cells the Golgi complex was reduced and appeared as smooth membranes surrounded by large and small electron transparent vacuoles. The count of glycogen granules sharply decreased. We found a considerable number of phagosomes filled with destructed fragments of membranes and organelles.

Hepatic echinococcosis is accompanied by the development of parenchymal fibrosis. Bundles of collagen fibers in the perisinusoidal space were revealed in electronograms, which reflected capillarization of sinusoids. These regions contained hepatocytes with zonal distribution of glycogen, which is often observed during this disease and plays a role in the nutrition of the parasite.

Our results show that morphological changes in liver cells depend on the size and localization of hydatid cysts small hydatid cysts localized within the liver parenchyma produces no specific ultrastructural changes in hepatocytes. Irreversible changes and necrosis of hepatocytes, nonspecific reactive hepatitis, and fibrosis are observed in regions peripheral to large intrahepatic hydatid cysts. In this instance the thickness of the liver parenchyma above the hydatid cysts does not surpass 1.5-2.0 cm. These irreversible changes probably contribute to the development of purulen and inflammatory complications after organ-preserving echinococcectomy. Postoperative purulent complications do not develop after radical hepatectomy in patients with these characteristics of intrahepatic hydatids. The presence of these hydatid cysts can be considered as an indication for hepatectomy. The favorable outcome of surgery is determined by removal of the fibrous capsule of the hydatid cysts and resection of the liver tissue with serious atrophic changes. The patients with another intrahepatic localization of cysts should be treated with organ-preserving surgeries.

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