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The development of compensatory processes in the liver and kidney in conditions of distant tumor growth

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Background

Cancer patients often suffer from fatigue, a complex syndrome associated with loss of muscle mass, weakness and depressed mood. Cancer-related fatigue can be detected during diagnosis, manifest during treatment, and persist for many years after treatment.

Development of malignant tumor accompanied endogenous intoxication of an organism having a mixed nature, in particular due to dysfunction of organs detoxification and excretion damaging effect of tumor metabolism. The active process of moving toxic and biologically active substances formed during tumor progression from the primary focus by blood and lymph flow leads to damage of distant organ.

The aim of this work was to identify structural changes in the liver and kidney under the conditions of distant tumor growth.

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Materials and methods

An experimental study was conducted on cba male mice weighing 18-20 g. In the experiment, 2 groups of animals were used. Group 1 included intact mice (n = 5); group 2 - animals, with the development of the tumor process (n = 20). Hepatocarcinoma-29 cells (G-29) were used to simulate tumor growth. The material for research was collected after 3, 7, 13, and 30 days of the experiment. Fragments of liver and kidney were treated by standard method for electron microscopy. Ultrathin sections with a thickness of 70-100 nm were obtained from the selected material and studied using a JEM 1400 electron microscope morphometric analysis was performed using imagej computer software (wayne rasband, USA). The average value (M) and standard deviation (SD) were calculated using microsoft excel software (microsoft, USA). The significance of differences between the studied parameters was determined using the statistica 6.0 software (statsoft, USA) using the mann-whitney u-test at a confidence level of 95% ($P < 0.05$).

Results

Liver. In the dynamics of tumor growth, a decrease volume density of mitochondria, endoplasmic reticulum, lipid inclusions and an increasing volume density of lysosomal structures were demonstrated in hepatocyte. The development of intracellular autophagic degradation of cytoplasmic organelles was revealed. In autophagosomes, fragments of cytoplasm, glycogen rosette, mitochondria, fragments of the endoplasmic reticulum with ribosomes were observed (Fig.1). The data obtained indicate that in conditions of distant tumor growth in the liver, non-selective autophagy develops to maintain intracellular hepatocyte homeostasis, as well as energy and trophic homeostasis of the body.

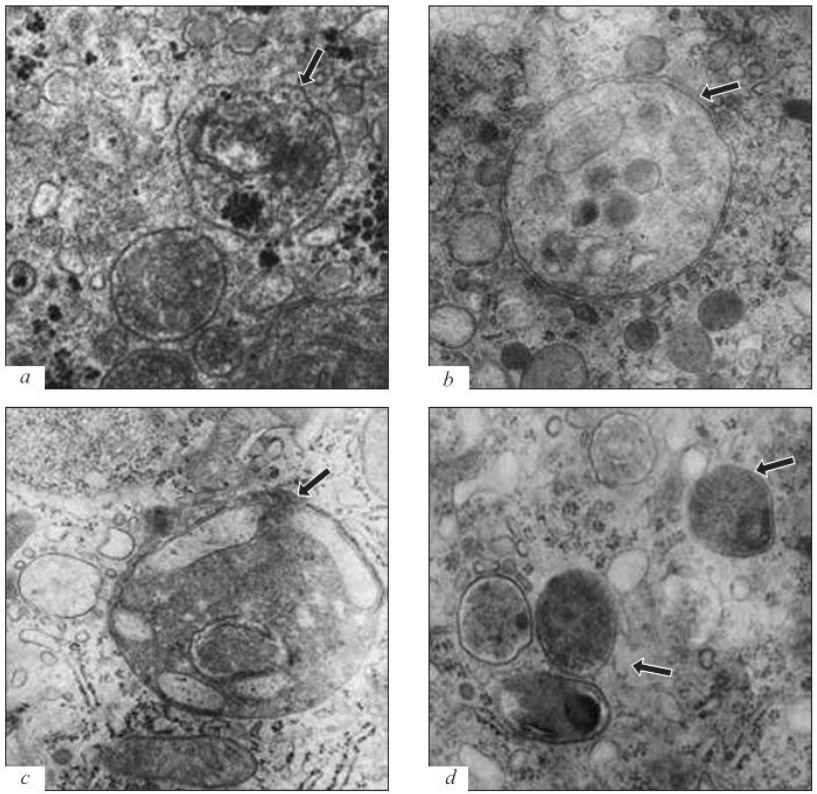

Fig. 1. Autophagy in hepatocytes in conditions of distant tumor growth

(a) Autophagosome with mitochondria and glycogen rosette (arrow), ×20,000;
(b) Autophagosome with organelles in hepatocyte cytoplasm (arrow), ×15,000.
c) Autolysosome in hepatocyte cytoplasm (arrow), ×15,000.
(d) Assembly of secondary lysosomes (arrows), ×15,000.

Kidney. In the early stages development of the tumor process, destructive disorders in the kidney were noted, indicating a violation of the renal filter - a decrease in the number of fenestra of glomerular capillary endotheliocytes, an increase in the thickness of the glomerular membrane, fusion of the legs of podocytes. Starting from 13 days of tumor development, compensatory processes were noted in the structure of nephron components. Podocyte hypertrophy was identified: the concentration of organelles in the cytoplasm of podocytes and the number of cytopodia were increased. A decrease in the thickness of the glomerular membrane and hypertrophy of endothelium of glomerular capillaries were observed (Fig. 2).

Conclusions

The development of both destructive and compensatory changes in the liver and kidney in conditions of distant tumor growth was revealed. In the liver, a decrease a size of hepatocytes and concentration of organelles, as well as development of autophagy, as a mechanism for maintaining intracellular homeostasis, were noted. In the kidney at the early stages of the development of tumor growth, structural signs of a disorder of the filtration barrier are shown, subsequent development of compensatory hypertrophy of podocytes and glomerular capillary endothelium were identified.

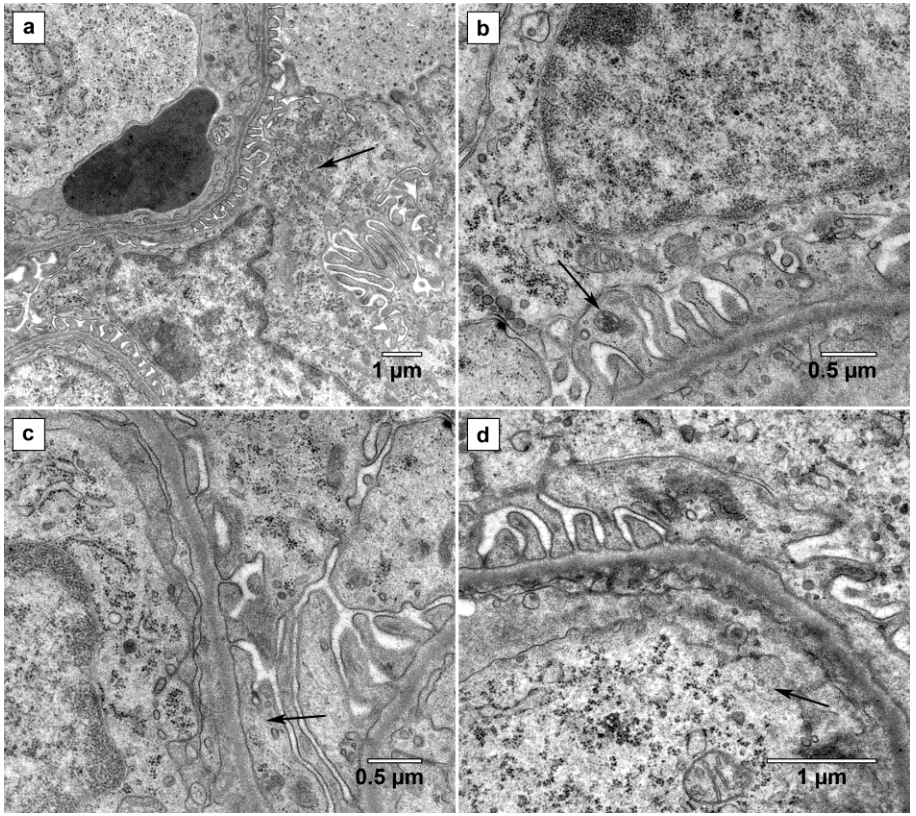

Fig. 2. The structure of kidney filtration barrier after 30 days of distant tumor growth.
(a) Hypertrophy of the cytoplasm of the podocyte (arrow); (b) Multivesicular body in the cytoplasm of the podocyte (arrow); (c) Effacement of podocyte foot processes (arrow); (d) Hypertrophy of endothelium of the glomerular capillary (arrow).