

PATHOHISTOLOGICAL CHANGES IN THE LIVER AND KIDNEYS
OF ANIMALS WITH TRANSPLANTED TUMOR AFTER INJECTION
OF THE CORRESPONDING ANTIORGAN SERA

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Translated from *Byulleten' Éksperimental'noi Biologii i Meditsiny*, Vol. 56, No. 7,
pp. 83-86, July, 1963
Original article submitted November 16, 1962

In a work performed earlier [10] it was shown that the injection of organ-specific sera into rabbits with a transplanted Brown-Pearce tumor affected the localization of metastases. Large doses of these sera caused intense development of metastases in the corresponding organs, while small doses reduced the process of metastasis. Thus, with injection of large doses of antikidney serum, larger numbers of metastases were observed in the kidneys than with injection of the same doses of normal serum; with use of small doses of this serum, we observed metastases in the kidneys in smaller numbers than with small doses of normal serum. We obtained the same type of results in the liver with injection of antiliver serum.

According to the opinion of a number of authors, small doses of cytotoxins exert a stimulating action on the tissue metabolism of the corresponding organs, while large doses yield an opposite effect, up to gross structural damage [1-9, 11, 12, 13].

It is possible that this action of the sera sensitizes the tissues of the corresponding organs, and prepares the kidney for seeding with the malignant cells, circulating in the blood and lymph, and thus, for development of metastases.

We considered it of interest to determine which morphological changes in the organs led to increased or decreased metastasis.

EXPERIMENTAL METHOD

Cytotoxic sera were obtained by immunizing sheep with aqueous-saline extracts of tissues from the liver and kidneys of rabbits. Antigens for the immunization were prepared according to the widely accepted method. The antigens were injected into the sheep intravenously in three 3-day cycles, with 4-day intervals between the cycles. The amount of antigen injected was determined from the nitrogen (the method of Conway).

According to the reaction of complement fixation, the titers of the obtained sera were the following: antiliver — 1:40, antikidney — 1:160. With non-homologous antigens, the sera reacted in lower titers (antiliver with kidney antigen — in a dilution of 1:20, antikidney with liver antigen — in a dilution of 1:40).

Thus, the sera used in the experiment were relatively specific. We also used normal sheep serum in the experiment. All three sera were injected separately into 3 groups of male rabbits of the chinchilla family, weighing $2\frac{1}{2}$ -3 kg, with transplanted Brown-Pearce tumor in the testicle (8 animals per group). In 4 rabbits of each group we used one of the sera in a dose of 2 ml (approximately 0.7 ml per kg of weight) 15 times, with intervals between the injections of 1 day. The other 4 rabbits of each group received the corresponding serum in a dose of 0.2 ml (approximately 0.07 ml per kg of weight) 5 times in 3 days.

The animals were sacrificed by air embolism. Fragments of the liver and kidneys were fixed in Bouin's solution. The material was imbedded in paraffin, sections were prepared with a width of 7-8 micra, and staining was carried out with hematoxylin-eosin.

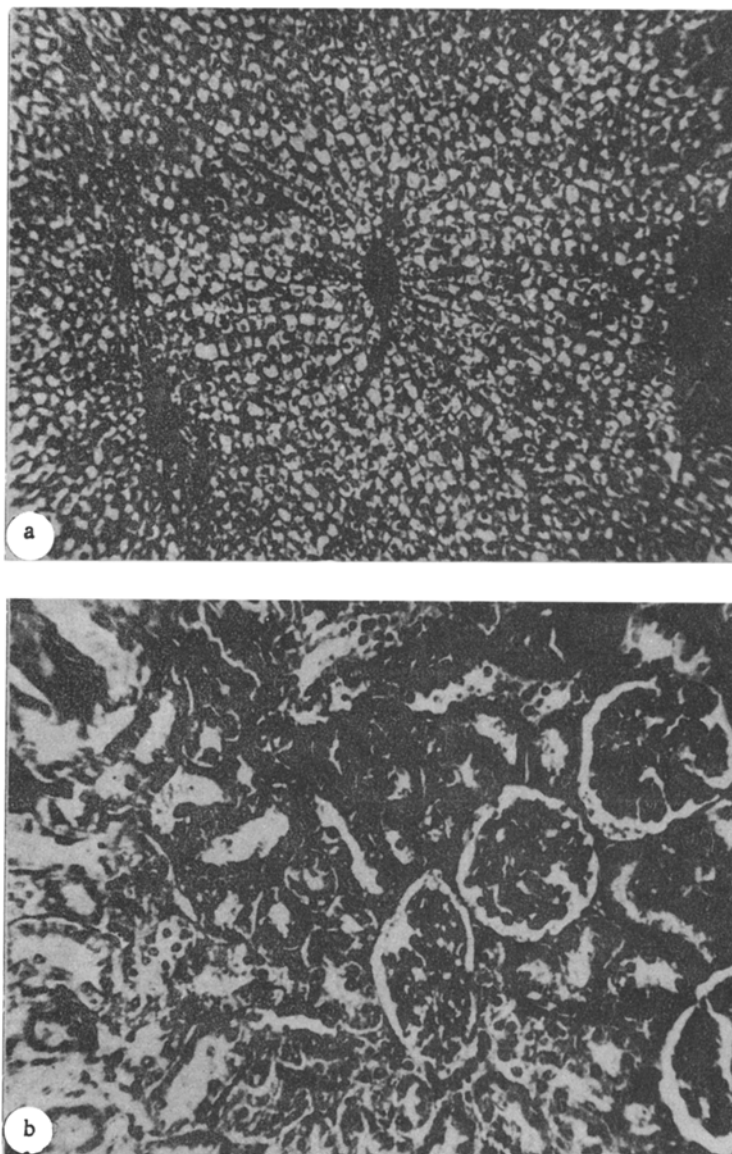


Fig. 1. Absence of visible pathological changes in the liver (a) and kidney (b) following injection of large doses of normal serum.

EXPERIMENTAL RESULTS

Control group (sera not injected): in the liver – hyperemia of all systems of the portal and hepatic veins and sinusoids, and a large number of frothy, light liver cells, apparently rich in glycogen; in the kidneys – hyperemia of the medullary substance, ischemia of the cortex, and the presence of protein exudation in the lumen of the Bowman's capsules.

Normal Serum. Small dose (0.07 ml per kg of weight): the histological structure of the liver and kidneys were the same as in the control rabbits. Large dose (0.7 ml per kg of weight): no essential changes were observed in the organs, with the exception of a small proliferation of histiocytic elements throughout the interstices (Fig. 1a, b).

Antiliver Serum. Small dose: in the liver – small proliferation of stromal cells in the organ; in the kidneys – focal proliferation of the interstitial cells, in the pattern of interstitial nephritis. Large dose: in the liver – intense proliferation of the stromal cellular elements, clear dystrophic changes, scattered sites of protoplasmic fusion of the liver cells, pyknosis of the nuclei, swelling of the Kupfer cells (Fig. 2); in the kidneys – proliferation of the elements in the interstitial tissue.

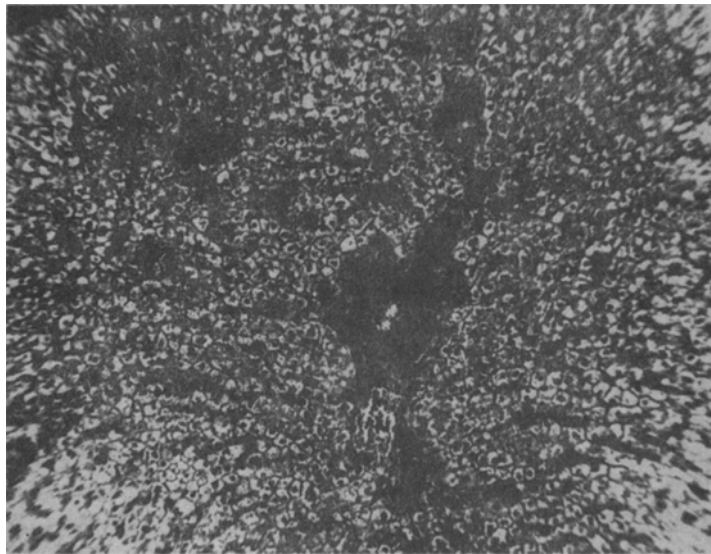


Fig. 2. Intense proliferation of the stromal cells and dystrophic changes in individual hepatic cells following the injection of large doses of antiliver serum.

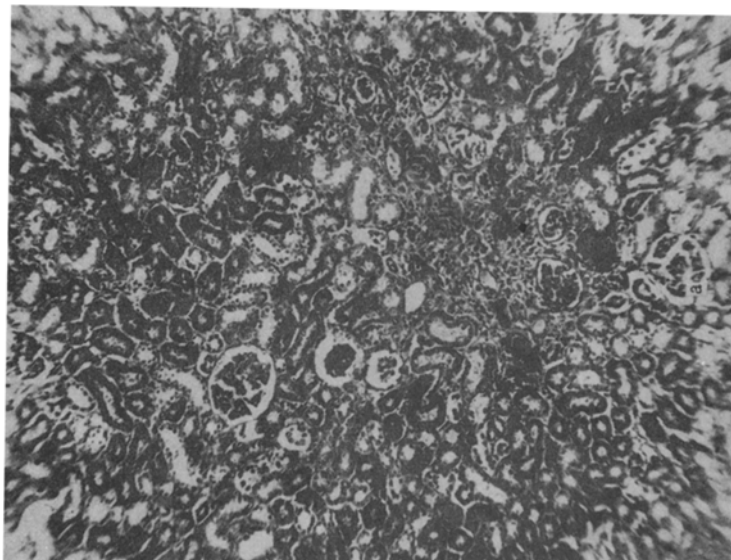


Fig. 3. Proliferation of the interstitial connective tissue, partial "glomerulonephritis", and focal hemorrhages in the kidney following injection of large doses of antikidney serum.

Antikidney Serum. Small dose: in the liver – intense proliferation of the lymphoid and reticular elements throughout Glisson's capsule; in the kidneys – no deviation from the norm. Large dose: in the liver – markedly manifested proliferation of the lymphoid and reticular elements in the organ; in the kidneys – increase in their size, disintegration of the glomeruli, exudate in the cavities of the Bowman's capsules (manifest glomerulonephritis), proliferation of the interstitial connective tissue, small amount of diapedesis of erythrocytes, occasional hemorrhages, edema and deformation of the capillary walls • (Fig. 3).

Thus, following injection of large doses of normal serum and small doses of antiliver serum, we obtained mildly demonstrated interstitial "hepatitis" and "nephritis". With injection of a large dose of antiliver serum and small and

• The histological preparations were examined by Prof. I. K. Esipova, Prof. P. A. Gindin, and Docent V. N. Dobrokhotoy.

large doses of antikidney serum, we observed intensely manifested interstitial "hepatitis". The use of large doses of antiliver serum also caused interstitial "nephritis", and large doses of antikidney serum caused more profound injury to the organ: glomerulonephritis, combined with interstitial "nephritis". The small dose of antikidney serum did not cause any pathological changes in the kidneys. In the animals of the control group, and with injection of small doses of normal serum, we did not observe interstitial "nephritis" or "hepatitis".

It is completely logical to assume that the indicated pathological changes in the organs, caused by the action of the cytotoxic sera and large doses of normal serum, also cause the localization of tumor metastases which we observed earlier [10].

SUMMARY

Interstitial "hepatitis" and "nephritis", induced in rabbits by injection of sheep nephrotoxic and antihepatic sera, and glomerulonephritis observed after inoculation of large doses of nephrotoxic serum evidently cause definite metastasis localization of the transplanted Brown-Pearce tumor.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
