HISTOAUTORADIOGRAPHIC STUDY OF [^{3}H]THYMIDINE UPTAKE INTO PARENCHYMAL NUCLEI OF THE KIDNEY AND OTHER ORGANS IN RATS WITH NEPHROTOXIC NEPHRITIS

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Data were obtained to show how changes in the [^{3}H]thymidine uptake by parenchymal nuclei of the kidney compare with those in other organs in rats with nephrotoxic nephritis. The labeling index in the kidneys increased: by 7.5 times in the epithelial cells of the renal cortex and by 15 times in the epithelium of the medulla. The number of labeled cells in the glomeruli increased by 2.5 times. The labeling index in the epithelium of the adrenals, liver, thymus, and small intestine fell to between 80 and 70% of normal.

KEY WORDS: nephritis; [^{3}H]thymidine labeling index.

Organ-selective absorption of antibodies of nephrotoxic serum in the kidneys is now a firmly established fact. It has been clearly demonstrated in experimental studies with labeled antibodies [10, 11] and by the immunofluorescence method [2, 3]. At the electron-microscopic level Ortega [8], using an immunoferritin technique, observed absorption of renal antibodies along the basement membranes of the renal glomeruli.

The antigen–antibody reaction in the renal glomeruli is a very important pathogenetic component in the development of nephrotoxic nephritis, a characteristic morphological feature of whose development is proliferation of the endothelial and mesangial cells of the renal glomeruli and thickening and loosening of the fibers of the basement membranes. Subsequently the tubular system of the nephron becomes involved in the pathological process [5, 6, 9]. However, renal antibodies are also absorbed to a certain extent by other organs (the liver, lungs, placenta, etc.) [10-12].

It was accordingly interesting to compare the reaction of the kidneys and of other organs to nephrotoxic serum.

EXPERIMENTAL METHOD

Experiments were carried out on two groups of noninbred male rats weighing 220-230 g: group 1 consisted of 10 rats with nephrotoxic nephritis (experimental), group 2 of 10 healthy rats (control). Nephrotoxic nephritis was produced in the rats by Masugi's method [5]. The animals were decapitated on the 10th day of the experiment, i.e., at the height of the disease. Histologically a picture of diffuse proliferative-membranous glomerulonephritis was identified in the kidneys. Besides the kidneys, other organs in whose parenchyma more or less well marked structural changes were found histologically (staining with hematoxylin and eosin) also were studied: the liver, adrenals, thymus, and small intestine. The technique used was that of Merkulov [1]. [^{3}H]Thymidine was injected intraperitoneally in a dose of 1 μCi/g into the animals 2 h before sacrifice. The number of labeled cells was counted. The number of labeled nuclei in the renal glomeruli (in 100 glomeruli per animal) and the percentage of labeled nuclei in the parenchymal cells of other organs in the sections were determined. The labeling index was calculated for 50,000 cells of each animal (in the epithelium of the renal tubules, epithelium of the thymus, hepatocytes, cells of the adrenal cortex and medulla) and for 5000 cells of each animal (in the epithelium of the small intestine).

The results of the counting were subjected to statistical analysis by Student's t test.

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TABLE 1. Changes in [^{3}H]Thymidine Labeling Index of Cell Nuclei in Various Parts of the Kidney, Liver, Adrenals, Thymus, and Intestine in Healthy Rats and in Rats with Glomerulonephritis (M ± m)

Group of animals	Kidneys			Adrenal		Thymus		Liver	Intestine
	cortical epithelium	medullary epithelium	No. of labeled cells per 100 glomeruli	cortical epithelium	cells of medullary epithelium	cortical epithelium	medullary epithelium	hepatocytes	epithelium of small intestine
Healthy rats	0,230±0,049	0,073±0,013	13,9±*	0,560±0,190	0,230±0,034	1,213±0,0112	1,275±0,105	0,480±0,140	36,190±0,950
Rats with glomerulonephritis	1,810±0,460	1,030±0,201	52,5±*	0,160±0,020	0,180±0,029	0,856±0,043	1,102±0,072	0,380±0,950	28,960±1,120
P	<0,05	<0,01	—	>0,05	>0,05	<0,02	<0,1	<0,05	>0,01
Comparative intensity of labeling, % of control	787	1471 (15-fold increase)	241	28,6	78,3	70,6	86,4	79,3	80,0

*As in Russian Original – Consultants Bureau.

EXPERIMENTAL RESULTS

The changes observed in the DNA-synthesizing power of the nuclei of the parenchymal cells of the various organs of rats with nephrotoxic nephritis and of healthy rats are shown in Table 1. Clearly in healthy rats the DNA-synthesizing power varied in different organs. It was highest in the epithelium of the small intestine, evidently in connection with the continuous physiological regeneration of the intestinal epithelium during digestion. Of all the organs studied, the kidneys occupied the last place for intensity of incorporation of the radioactive label; the [^{3}H]thymidine labeling index of the nuclei of the convoluted tubules, moreover, was higher than that of the nuclei of the glomerular cells, where only solitary nuclei were labeled.

In nephrotoxic nephritis the DNA-synthesizing power of the nuclei of the parenchymal cells of the organs differed from that in the healthy animals. The response of the kidneys differed from that of other organs as regards both the intensity and the direction of the changes: In the kidneys DNA-synthesizing power was sharply increased in glomerulonephritis, whereas in all the other organs studied it was reduced. During the period of marked edema and proteinuria the number of cell nuclei in the renal glomeruli labeled with [^{3}H]thymidine increased by 2.5 times (241%); the DNA-synthesizing power of the epithelial nuclei of the renal tubules, located in the cortex, was increased by 7.5 times (787%) and in the medullary layer by 15 times in nephritis. The DNA-synthesizing power of the parenchymal cell nuclei of the other organs studied fell to between 80 and 30% of normal.

Comparison of the [^{3}H]thymidine labeling indices of the nuclei of the parenchymal cells of all the organs studied in rats with glomerulonephritis showed that the kidney cells exceeded the epithelial cells of all other organs in this respect. The results showing an increase in the [^{3}H]thymidine labeling index of the cell nuclei of the renal glomeruli in Masugi's nephritis agree with the observations of Noltenius et al. [7], who observed an increase in the labeling index of the endothelial nuclei of the renal glomeruli in rabbits with nephritis parallel with an increase in the number of mitoses and in cell proliferation.

The much greater intensity of the response of the kidneys than of other organs in nephritis, demonstrated by the present experiments, can be regarded as evidence of preferential absorption of renal antibodies of nephrotoxic serum in the kidneys; this is connected with the specific functional and structural features of the kidney antigens and their complementary behavior toward the antibodies. The similarity in the response of different parts of the nephron (the glomeruli and the tubular system) to nephrotoxic serum (activation of cell proliferation) suggests the possibility of crossed absorption of heterogeneous antibodies not only on the basement membranes of the renal glomeruli, but also on the basement membranes of the tubules. Consequently, in nephrotoxic nephritis the tubular system can be damaged not only as a result of the disturbance of glomerular function, but also as a result of primary immunologic injury due to the common nature of the antigenic components. The opposite changes in DNA-synthesizing activity (inhibition) in the epithelial cells of the other organs studied may evidently be connected with biochemical changes in homeostasis caused by the development of nephritis in the animal.

The facts discovered are not confined to nephrotoxic nephritis but may also arise in other cytotoxic pathological states.

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