DYNAMICS OF MORPHOLOGICAL INDICES OF THE JUXTAGLOMERULAR COMPLEX OF THE KIDNEY IN RATS WITH EXPERIMENTAL RENOVASCULAR HYPERTENSION

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Experiments on 188 sexually mature albino rats showed a regular pattern of topographical distribution of the juxtaglomerular complex (JGC) in the different zones of the renal cortex. Renovascular hypertension was shown to intensify granularity of the JGC as early as the third day of the experiment. This was confirmed by an increase in the granularity index and also in the classes of the JGC. The cytomorphometric indices of the macula densa were increased after the second week of the experiment, changes before that time being not significant.

KEY WORDS: juxtaglomerular complex; renovascular hypertension; granulated cells; macula densa.

Many aspects of structural mechanisms of the pathogenesis of essential hypertension still remain inadequately studied. Further studies of the organization of the juxtaglomerular complex (JGC) of the kidney, the granulated cells of which secrete renin, which participates in the formation of the vasopressor substance [5, 7], are promising in this respect.

The components of the JGC have been shown to be: 1) juxtaglomerular cells of the afferent arteriole, 2) Goormaghtigh's cells, 3) mesangiocytes, and 4) the macula densa [6, 9, 11]. Studies of the functional morphology of the JGC have yielded data characterizing the reactive responses of these components of the JGC during experimental renovascular hypertension [4], after transplantation of the kidneys [1] and adrenalectomy [3], and in acute renal failure [13].

No information is yet available on the structural features of the specific granulated cells of the JGC depending on their heterotopic distribution in the renal cortex and the order of morphometric changes in its components during the development of renovascular hypertension. The investigation described below was devoted to the study of these problems.

EXPERIMENTAL METHODS

The microscopic structure of the JGC under normal conditions and at different periods of renovascular hypertension was studied in 188 male albino rats. The disease was produced experimentally by measured constriction of the abdominal aorta below the origin of the renal arteries [8]. Granulated cells were detected by light (with staining by Masson's and Bowie's method) and cytoluminescence microscopy (Fig. 1a, b). The granularity index [10] and morphometric indices of the macula densa [12] were determined.

EXPERIMENTAL RESULTS

The normal range of granularity of the JGC was shown to depend on the level of dislocation of the juxtaglomerular cells in the renal cortex. In its middle zone, for instance, where most renin is produced [2], high granularity of the JGC was observed (classes 2 and 3). Granularity was low, however, in the juxtamedullary and subcapsular zones. The relative proportions of the different classes of JGC were determined, because the numerical value of the granularity index does not give a complete picture of the functional activity of single

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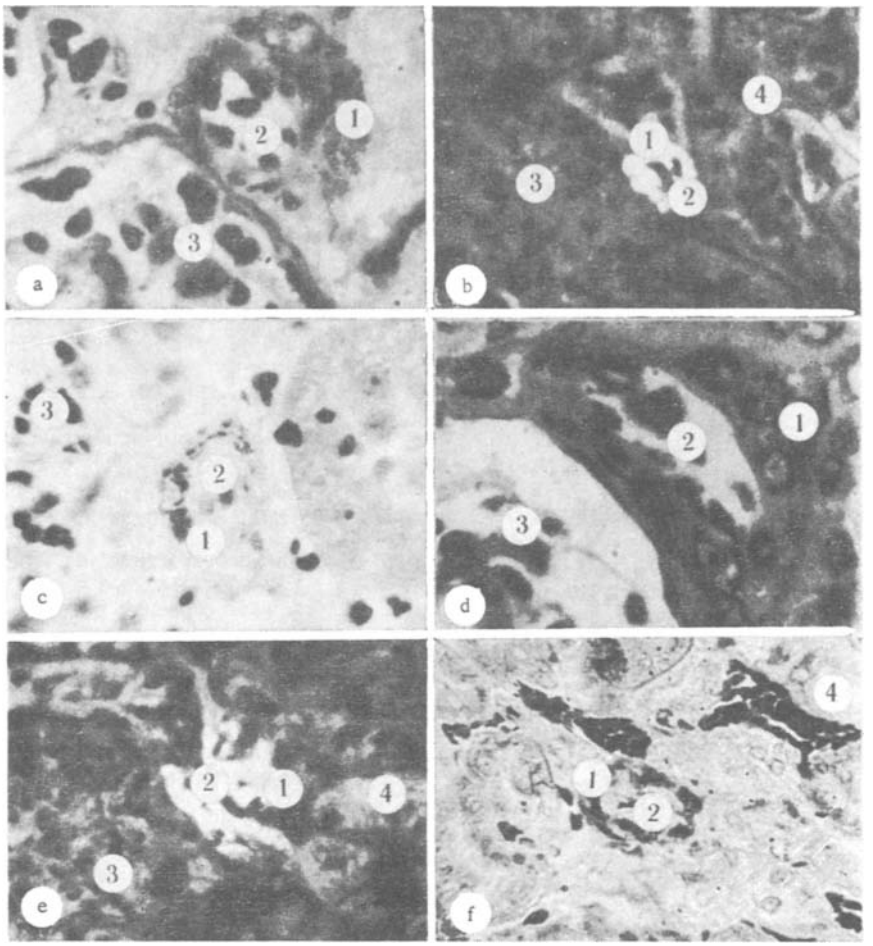

Fig. 1. Granules in cytoplasm of juxtamedullary cells in wall of afferent arteriole of rat kidney under normal conditions (a, b) and on 7th (c), 14th (d, e), and 90th (f) days of experiment. 1) Granules; 2) lumen of afferent arteriole; 3) glomerulus of renal corpuscle; 4) renal tubules. a, c, d, f) Stained by Bowie's method; b, e) by acridine orange. Magnification: a, c, d) 630×, b, e) 320×, f) 400×.

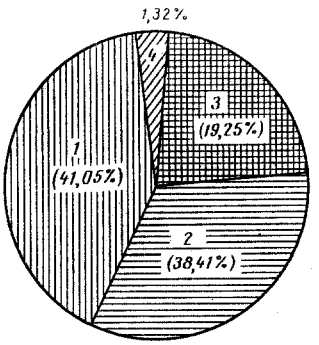

Fig. 2. Relative proportion of granularity classes of normal JGC.

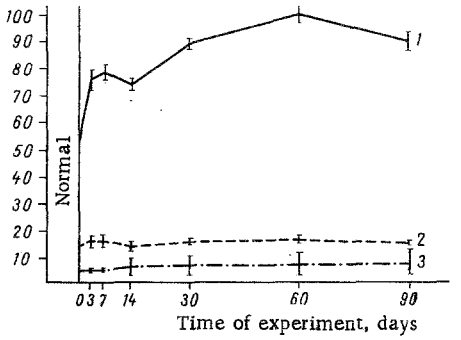

Fig. 3. Cytomorphometric indices of macula densa at different stages of renovascular hypertension. 1) Total number of cells; 2) total number of sections of macula densa; 3) index of macula densa.

nephrons (Fig. 2). A similar relationship also applies to the distribution of sections of the macula densa. These indices were lowest (10.6) in the subcapsular zone of the cortex, they increased in the juxtamedullary zone (11.3), and increased still more in the middle zone (14.1).

Concentration of juxtaglomerular cells and epithelial cells of the macula densa, components of the JGC directly concerned with the control of the microhemodynamics of the vascular glomerulus, is thus observed in those zones of the cortex which are functionally the most active.

On the third and seventh days after constriction of the abdominal aorta the granularity was increased in only a few of the juxtaglomerular cells (Fig. 1c) and the granularity index as a whole was unchanged. This indicates that the secretion of renin into the blood stream exceeded its synthesis.

Fluorescent microscopy revealed many fluorescent granules of macula densa in the cytoplasm of the granulated cells by the third and seventh days of the experiment. In the second week of the experiment the total area of their luminescence was increased to 0.5 ± 0.12, as a result of hyperplasia of the juxtaglomerular cells. These values correlated positively with the increase in the granularity index, which rose to 43 ± 4.1 on the 14th day of the experiment compared with 26 ± 4.3 in the control ($P < 0.001$; Fig. 1d, e). On the 30th day of the experiment the granularity index was 46 ± 1.12 ($P < 0.001$). The area of fluorescence of the granules by this time was 0.63 ± 0.17 ($P < 0.001$).

By the end of the third month of experimental renovascular hypertension the absolute majority of components of the JGC contained granules that were densely distributed around the whole perimeter of the tunica media of the afferent vessel (Fig. 1f).

Meanwhile, after the first day of limitation of the arterial blood flow to the kidney the number of JGC of granularity class 1 was significantly reduced, with a corresponding increase in the number of those of classes 2 and 3. It was at that time, it may be supposed, that the synthesis of renin and of its precursors which are present in the juxtaglomerular cells of the afferent vessel began to be activated, for the cumulative type of JGC hyperfunction predominated.

During the development of renovascular hypertension definite correlation was found between the degree of granularity of the JGC and hyperplasia of the macula densa. Positive correlation was found between their morphometric indices ($P < 0.001$); the increase in the index of the macula densa was due to general enlargement of its cells in the sections.

Definite hyperplasia of cells of the macula densa did not take place until the 14th day of experimental renovascular hypertension, when the index reached 6.2 ± 0.33 (Fig. 3). The number of cells of the macula densa rose steadily during the subsequent course of the disease, to reach 6.4 ± 0.3 by the end of the second month ($P < 0.001$), and showed little change 90 days after the beginning of the experiment (6.5 ± 0.58).

The results indicate clear correlation between the process of granule formation in the JGC and their distribution in the renal cortex. The differential study of the state of the JGC belonging to different classes showed that structural changes in its components begin to appear early in experimental renovascular hypertension – by the third day of the development of the disease. In the second week of the experiment statistically significant changes were found in the structure of the granulated cells and of the macula densa.

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CHANGES IN THE ULTRASTRUCTURE OF COMPONENTS OF THE BLOOD – TESTIS BARRIER IN CIRCULATORY HYPOXIA

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Changes in the ultrastructure of the blood–testis barrier in rats 30 and 60 min and 1 and 30 days after ligation of the testicular artery were studied by electron microscopy. The results showed that blocking of the blood flow to the testis causes rapidly progressive changes in all components of the blood–testis barrier. Micropinocytosis and destructive changes increase in the cytoplasm of the endotheliocytes of the capillaries, ending in microclasmatosis. The tunica propria of the seminiferous tubules is highly sensitive to ischemia. It becomes thickened, the nuclei and cytoplasmic organoids of its cellular components are deformed, and folding and infiltration of the basement membrane increase. Vacuolation of the cytoplasm of the sustentocytes is accompanied by destruction of the cell membrane and by separation of the sustentocytes from the tunica propria of the tubules.

KEY WORDS: blood–testis barrier; ischemia; ultrastructure.

The blood–testis barrier is formed by the wall of the blood and lymphatic capillaries, the tunica propria of the seminiferous tubules, sustentocytes, and interstitial tissue [1, 2, 5, 6, 11]. It was shown previously [4, 10, 11, 14] that this endothelial lining of the blood capillaries of the testis is continuous and contains microvilli. According to some observations [7-9, 12, 13], the tunica propria of the seminiferous tubules in rats consists of two cellular (myoid cells and fibroblasts) and two noncellular (inner and outer) layers of complex construction. Sustentocytes, which form specialized connections by their cell membranes [14], are organ-specific components of this barrier.

Light-optical data on the harmful influence of ischemia of the testis on the state of its generative components [5] are present in the special literature, but ultrastructural changes in the components of the blood–testis barrier after disturbance of the blood supply to the testis have been inadequately studied.

The object of this investigation was to study the character of the submicroscopic changes in the components of this barrier in the testes of rats under conditions of circulatory hypoxia produced by ligation of the testicular artery at the point where it arises from the abdominal aorta.

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