INTERSTITIAL CELLS OF THE RENAL MEDULLA IN RATS WITH GENETIC SPONTANEOUS HYPERTENSION

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The content of lipid granules in the interstitial cells (IC) of the renal medulla of rats with genetic spontaneous hypertension (rats of the SHR strain) was studied by electron-microscopic morphometry. At the age of 1.5 months no difference was found in the volume of the lipid granules in SHR and Wistar (control) rats. At the age of 1 year the total volume of lipid granules in hypertensive SHR rats exceeded their volume in the control. At the same time, features of hypertrophy and hyperplasia of the rough and smooth endoplasmic reticulum and Golgi complex were found in the SHR rats, especially in the period of formation of hypertension. It is evidently not the degree of reduction in the volume of lipid granules, as was hitherto considered, but the state of the organelles of synthesis and secretion that must be used as the morphological criterion of IC function in arterial hypertension.

KEY WORDS: interstitial cells of the kidney; lipid granules; hypertension; electron-microscopic morphometry.

Investigations [4, 6, 10, 13, 14] have shown that the interstitial cells (IC) of the medulla are the most probable site of prostaglandin synthesis in the kidneys. Since this group of fatty acids has an antihypertensive action, the content of lipid granules in the IC has been investigated in different types of hypertension [1, 11-13, 16, 17] and an attempt made to regard the decrease in the number of granules observed under these circumstances as a manifestation of the depressed antihypertensive function of the kidney. Meanwhile, Postnov and Orlov [2, 3] found no decrease in the granule content of the IC (DOCA-hypertension in rats) or they found an increase (ischemic cerebral hypertension in rabbits). Because of the contradictory nature of views regarding the degree of lipid granulation as indicators of the antihypertensive function of the IC, a further investigation was made of these cells in different forms of hypertension. In this paper the results are given for genetic spontaneous hypertension in rats, as the most adequate model of essential hypertension in man.

EXPERIMENTAL METHOD

Inbred male SHR rats were investigated at two ages: 1.5 months (three animals in the early hypertensive stage and three in the prehypertensive stage) and 1 year (three rats with high arterial pressure and three rats in which a small, transient rise of pressure had been observed previously, but had remained normotensive at least for the last 7 months). Normotensive inbred male Wistar rats (NW) of the same age (from the Stolbovaya Nursery) were used as the control. After separation from the mother, all animals were kept under identical conditions. The cystolic blood pressure was measured in the caudal artery by a plethismographic method (MPP-3S "Nihon Kohden" transducer) in young animals once a week, and thereafter once every 2 weeks. At the age of 1.5 months the arterial pressure of the hypertensive SHR rats was 140 ± 4 mm Hg, in the SHR rats in the prehypertensive stage 95 ± 2 mm Hg, and in the NW rats 86 ± 9 mm Hg; at the age of 1 year the corresponding values were 145 ± 8, 100 ± 3, and 85 ± 4 mm Hg. The kidneys were fixed by intraaortic perfusion *in vivo* with 1% solution of

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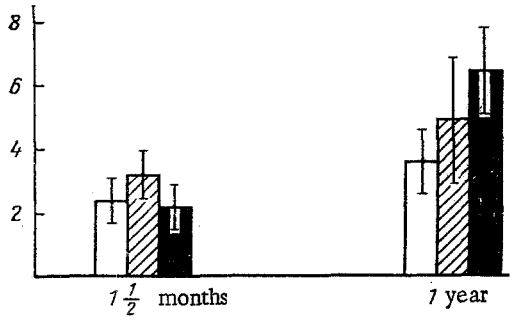

Fig. 1. Total volume of lipid granules in interstitial cells of the renal medulla. Abscissa, age of animals; ordinate, volume of granules (in %). Unshaded columns) normotensive inbred Wistar rats; obliquely shaded columns) normotensive SHR rats; black columns) hypertensive SHR rats. Confidence limits with 95% level of probability shown.

glutaraldehyde in 0.1 M phosphate buffer, pH 7.4, for 3 min after preliminary rinsing of the blood vessels of the kidney with 0.05% procaine solution containing heparin and sucrose. After perfusion pieces were excised from the inner zone of the medulla, fixed in glutaraldehyde and osmium tetroxide, dehydrated in alcohols, and embedded in a mixture of Epon and Araldite. Before final sharpening of the pyramids, a section 1 μ thick was cut from each block, stained with a mixture of methylene blue and azure II, and examined in the light microscope to obtain better orientation in the sample. After staining, the ultrathin sections were photographed in the HU-11-ES electron microscope with an accelerating voltage of 50 kV. To judge the content of material of the lipid granules in IC, the number of granules itself was not counted but their total volume was determined, for this is a more informative parameter and correlation between the number of granules and their volume, as the results showed, is weak. To calculate the volume of the lipid granules in each animal, 30 fields of vision of the cytoplasm of different IC were chosen at random and photographed under a direct magnification of 8600. All 540 objects (30 cells from each of 18 animals) were measured morphometrically [18] using photographic prints with a final magnification of 27,000, using a grid with a 1-cm pitch.

EXPERIMENTAL RESULTS

As Fig. 1 shows, genetic spontaneous hypertension is not accompanied by any reduction in the volume of granules in IC. Moreover, in the animals aged 1 year the total volume of granules in the hypertensive animals was greater than in the controls.

The results of this investigation thus do not confirm the conclusion [12] that the content of lipid granules in IC is reduced in rats with genetic spontaneous hypertension. At the same time they show that the quantity of lipid material in granules of IC, just as in ischemic renal hypertension, cannot serve as a morphological indicator of the reduction in antihypertensive function of the renal medulla.

So far as the increase in volume of the granules in the animals aged 1 year is concerned, it was evidently due to a disturbance of the balance between synthesis (accumulation) and utilization of the material of the granules, possibly in connection with reduced utilization on account of sclerosis of the medulla, which developed by this time.

By contrast with the lipid granules, the other organoids of IC of the experimental and control animals aged 1.5 months revealed significant differences (Fig. 2): in both hypertensive and normotensive SHR rats an increase in the number of profiles of the granular and smooth endoplasmic reticulum and the Golgi complex was found. The number of ribosomes on membranes of the rough endoplasmic reticulum was increased and electron-dense contents were located in the lumen. The number of polysomes scattered over the cytoplasm was increased. Since one of the most important functions of IC is the production of prostaglandins, with antihypertensive properties, this suggests that these features of increased synthetic activity of IC largely reflect that function. This hypothesis is likely to be correct for the smooth endoplasmic reticulum and Golgi complex are known to be directly concerned with the synthesis of lipids and their liberation from the cell [7, 8].

On the basis of this investigation increased protein synthesis in IC can also be postulated. Evidence in support of this view is given by hypertrophy and hyperplasia of the structures responsible for protein synthesis "for export" (the granular endoplasmic reticulum) and for protein synthesis for the structural needs of the cell itself (polysomes). No reliable evidence of the specific protein-synthesizing function of IC could be found in the literature. Perhaps these cells participate in the production of protein components of the medullary interstitial tissue. If this is so, the activation of the granular reticulum found in the SHR rats

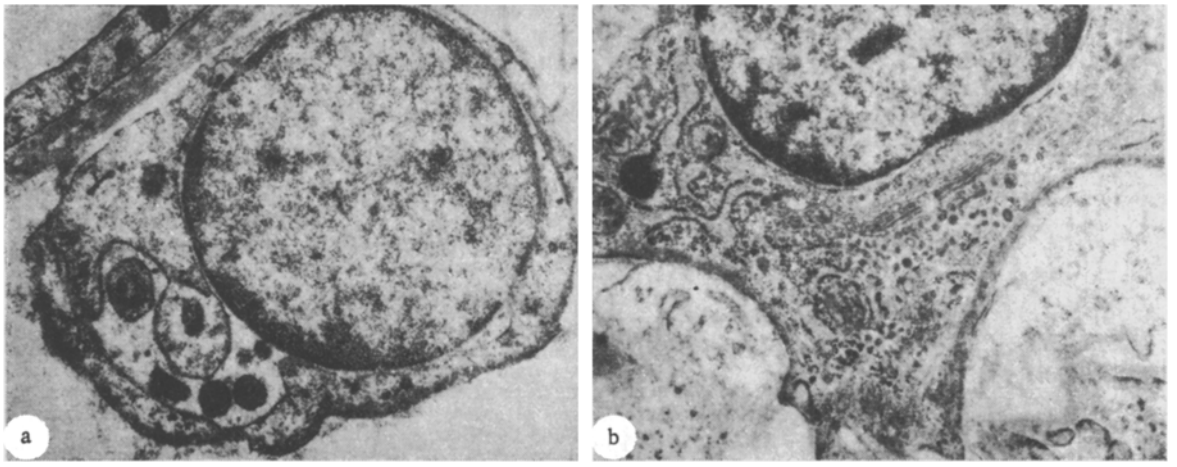

Fig. 2. Ultrastructure of interstitial cells of renal medulla of normotensive control rats (a) and rats with spontaneous hypertension (b). Hyperplasia of profiles of rough endoplasmic reticulum and Golgi complex; increase in number of ribosomes in IC of SHR rats (b).

must be interpreted as a manifestation of hyperproduction of these components. Among them, in particular, tropocollagen might be considered, for hypertension is accompanied by increased sclerosis of the renal medulla [4, 9], and the IC, with several common ultrastructural features with fibroblasts, are essentially the only type of cells in the interstitial tissue of the renal medulla.

Electron-microscopic investigation of IC in rats with genetic spontaneous hypertension thus revealed no decrease in the total volume (quantity of material) of the lipid granules in hypertensive and normotensive animals. Meanwhile, hypertrophy and hyperplasia of elements of the rough and smooth endoplasmic reticulum and Golgi complex were found in the SHR rats, indicating that during formation of hypertension the function of synthesis of protein and lipid substances and their liberation from IC is intensified. These findings, similar to those obtained previously in ischemic renal hypertension, show that the state of the ultrastructures for synthesis and secretion and not the degree of lipid granulation must be used as the morphological criterion for the evaluation of IC function, at least in arterial hypertension.

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