ACTA HISTOCHEM. CYTOCHEM. Vol. 5, No. 1, 1972

AN ELECTRON MICROSCOPICAL STUDY OF THE ADRENAL MEDULLA IN SPONTANEOUSLY HYPERTENSIVE RATS, PARTICULARLY ON CATECHOLAMINE-GRANULES IN SECRETING CELLS

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Received for publication February 24, 1972, and in revised form April 13, 1972

Recently it has been stressed that catecholamines play a significant role in the pathogenesis of hypertension in Spontaneously Hypertensive Rats (Okamoto and Aoki) (SHR). In this report electron microscopical observation in male SHR was made on the adrenal medulla through the processes of the hypertension. The mild hyperfunctional state of norepinephrine-secreting cells in the initial stage of hypertension was expected on the feature of increased population of norepinephrine-secreting cells, its prominent Golgi complex and rough-surfaced endoplasmic reticulum and increased degranulation in the cell. Moreover, it may be assumed a certain functional change of epinephrine-secreting cell system on the base of increased population of dark epinephrine-secreting cells which are regarded as premature cells.

Recently it has become apparent that catecholamines play an important role in the pathogenesis of hypertension in Spontaneously Hypertensive Rats (Okamoto and Aoki) (SHR)[13]. However, there are only few reports[8,15,16] on morphological changes of the catecholamine-producing organs in SHR. The present study has been made by electron microscopical observation of the adrenal medulla in SHR and normotensive rats.

MATERIALS AND METHOD

Twenty-four male SHR, raised and maintained in our laboratory, were used for this study at the following stage: (1) 40–50 days after birth and blood pressure of 120–140 mmHg (prehypertensive stage), (2) 4–5 months and 160–180 mmHg (initial stage of hypertension) and (3) 12–16 months and 170–220 mmHg (advanced stage of hypertension). Thirty normotensive Wistar strain rats of the same sex, age and weight were examined as the control. The adrenal glands were fixed in 1% glutaraldehyde with perfusion and were followed by 1% osmium tetroxide. After dehydration in a series of aceton, the material was embedded in Epon 812. Thin sections were stained with uranyl acetate and lead citrate.

RESULTS

Catecholamine-producing cells of the rat[1,3,4,7] were differentiated to norepinephrine-secreting cells (NE cells) (Fig. 1) and epinephrine-secreting cells (E cells) (Fig. 2). These two types of cells can readily be identified[2] in tissue treated

with glutaraldehyde fixation followed by osmication. NE cells were gathered in group and scattered among E cells throughout the medullary tissue. The distribution of two types of the cells in the rat[14] is the same rate and independent of the age. The cytoplasm of both types of cells contained numerous "secretory granules of norepinephrine or epinephrine". Secretory granules of NE cells were intensely electron dense and eccentrically situated within the membrane. Secretory granules of E cells were relatively less electron dense and centrically situated. The nucleus was round or ovoid. The cells had well-developed Golgi complexes which were more prominent in NE cells, dispersed rough-surfaced endoplasmic reticulum, mitochondria and dense bodies. Glycogen granules and free ribosomes were widely distributed throughout the cytoplasm in variable number. The plasm membrane was almost smooth. Among those cells, endothelial cells and myelinated and non-myelinated nerve fibers were seen.

In the initial stage of hypertension aged 4–5 months of SHR, the ratio of NE cells to E cells increased slightly. However, this tendency appeared not so remarkable in the prehypertensive and advanced hypertensive stages. Secretory granules in NE cells of SHR differed a little from that of the control rats in containing form. Some NE cells in SHR were packed with granular substances and others were contained small amount of secretory granules. Moreover, variable degree of degranulation of secretory granules may be a prominent feature in NE cells of SHR (Fig. 3). The Golgi complexes of NE cells were well developed and rough-surfaced endoplasmic reticulum were more prominent in SHR (Fig. 4).

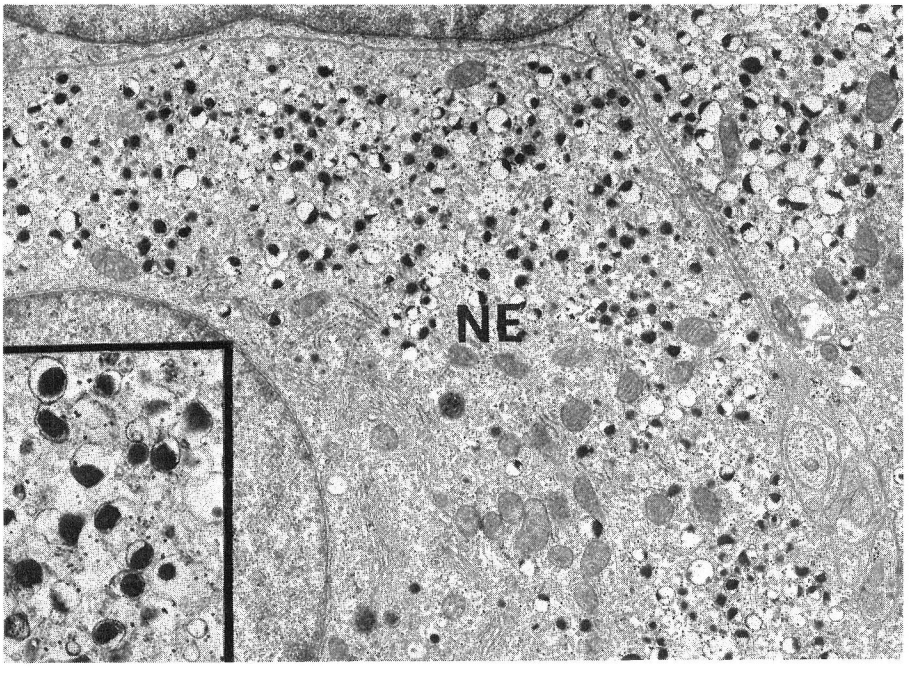

FIG. 1. Norepinephrine-secreting cell (NE cell) with many secretory granules and Golgi complex in the adrenal medulla of Wistar strain rats. × 7,000; inset. × 16,000.

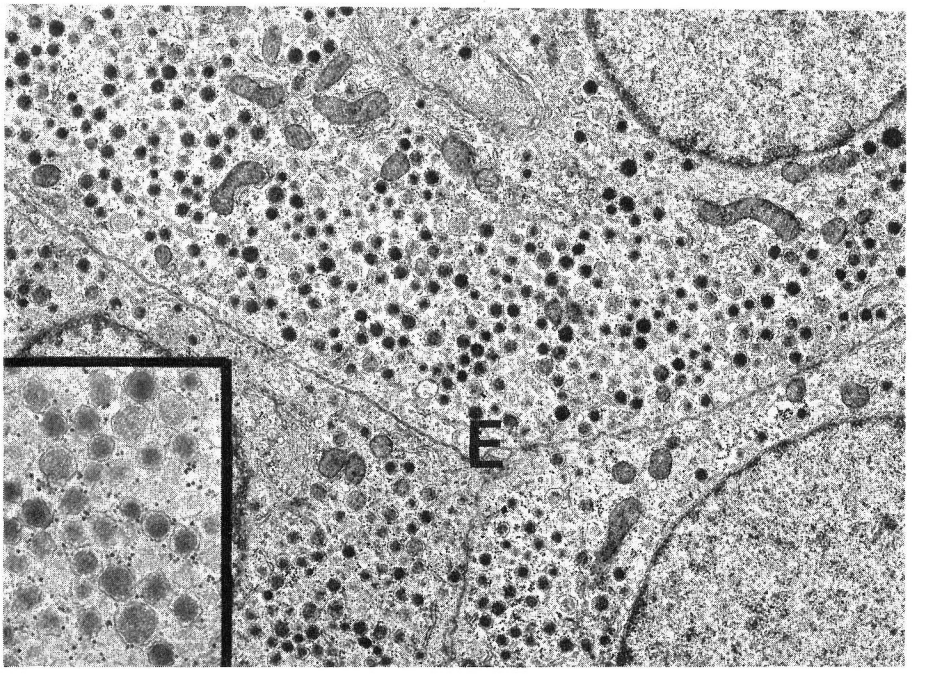

FIG. 2. Epinephrine-secreting cell (E cell) with many secretory granules in the adrenal medulla of Wistar strain rats. × 7,000; inset. × 16,000.

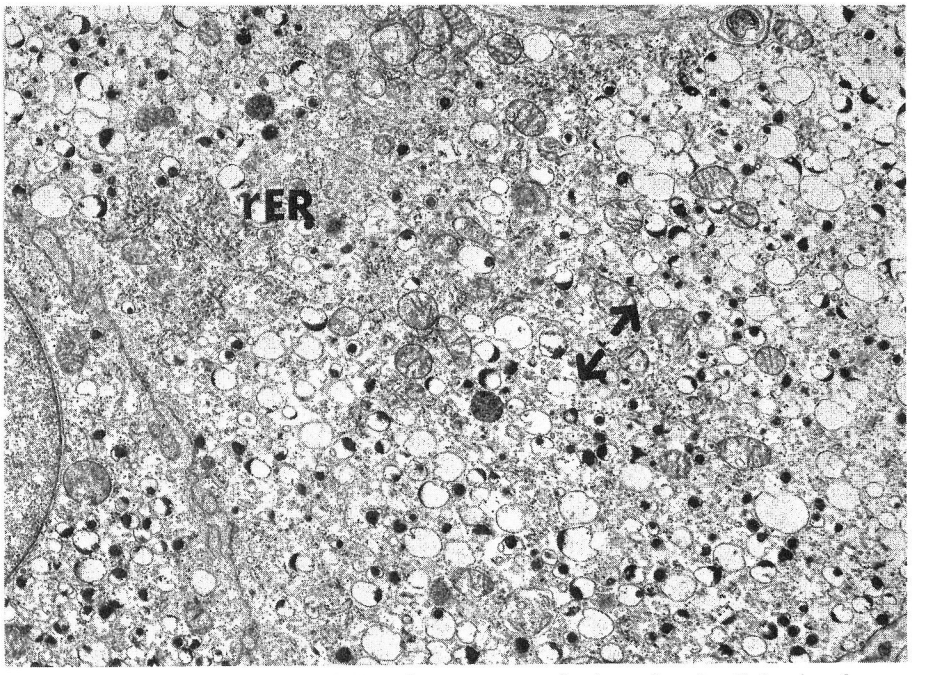

FIG. 3. Prominent degranulation of secretory granules (arrow) and well-developed rough-surfaced endoplasmic reticulum (rER) in NE cell of SHR. × 7,000.

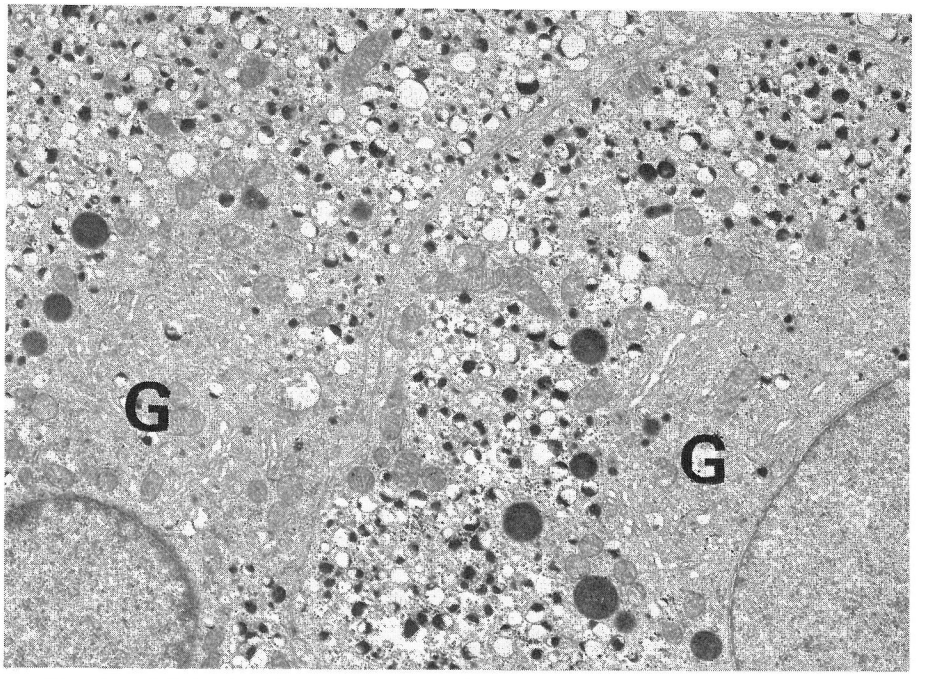

FIG. 4. Well-developed Golgi complexes (G) in two NE cells of SHR. × 7,000.

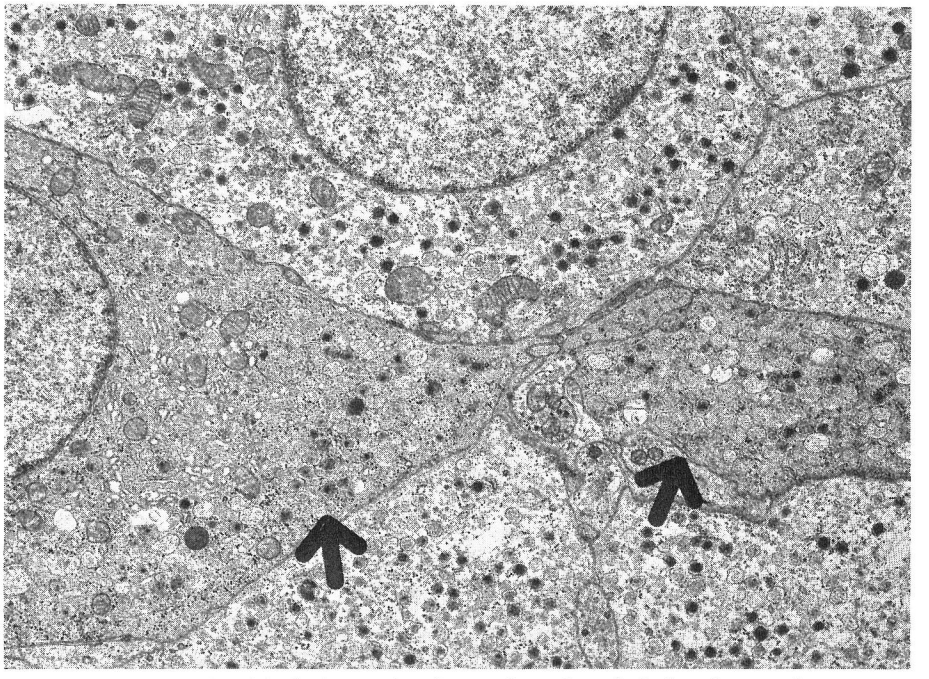

FIG. 5. E cells with dark cytoplasmic matrix and packed, less-electron dense epinephrine granules (arrow) of SHR. × 7,000.

The detail of these findings of NE cells were chiefly observed in SHR in the initial stage of hypertension. Among E cells of SHR, there were intermingled the ones featuring a dark cytoplasmic matrix and containing abundant granules which were larger and less-electron dense (Fig. 5). Although the number of E cells of dark type increased slightly in SHR, there was no apparent evidence of the morphologic differences in the secretory granules or other organelles of E cell itself in any stage of hypertension.

Neoplastic and degenerative changes were not found in the adrenal medulla of SHR.

DISCUSSION

In the present study on SHR, particularly in the initial stage of hypertension, it was certified that an increase in population of NE cells containing well-developed Golgi complex and rough-surfaced endoplasmic reticulum is a characteristic appearance of the adrenal medulla in SHR. These organelles are thought to represent synthetic apparatus of protein-binding hormonal granules in some tissue, such as the pancreatic islet[5,6,9,11] and the catecholamine-secreting cells. Therefore, development of these organelles seemed to be closely related to the functional state of the cells. We also observed an increased number of degranulation in NE cells of SHR. This phenomenon may suggest an active secretory form in the hormone-producing cells.

Increased population of dark E cells were occasionally observed in SHR. These cells showed apparent morphological differences from the usual NE and E cells in the form of secretory granules. The maturation of secretory granules is reflected morphologically by their compact feature and increasing density. Therefore, these less-electron dense granules in dark E cells may represent an immature secretory form in the earlier stage. Fine structure of the cell similar to dark E cells has been described by Misugi *et al.* in the pancreatic islet cells of infant with severe hypoglycemia[10].

Many studies on the pathogenesis of hypertension have been accumulated in SHR[12]. It has been shown in these literatures that functional changes of sympathetic nervous system including hypothalamus and adrenal medulla is intimately related to the development and maintenance of hypertension in SHR. In the present study, we could point out that there exists mild hyperfunctional state of the adrenal medulla in SHR from the ultrastructural alterations. Further investigation on the fine structure in the extramedullary sympathetic ganglia may lead to a better understanding of relationship between catecholamines and development of hypertension.

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