EFFECT OF THYROID HORMONE ON REGENERATION OF THE ADRENAL CORTEX

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Thyroid hormone causes hypertrophy of the cortex of the intact adrenal [5, 8] and stimulates regeneration of the cortical layer after enucleation [1, 7]. A fall in the concentration of thyroid hormone under the influence of antithyroid drugs leads to atrophic changes in the adrenal cortex [6, 9, 11].

The object of the present investigation was to study the effect of thyroid hormone on regeneration of the adrenal cortex after partial adrenalectomy.

EXPERIMENTAL METHOD

Experiments were conducted on 58 albino rats of both sexes (weighing from 120 to 160 g), divided into 3 groups: the first group were controls; the animals of the second group received thyroid extract by mouth in a dose of 5 mg/10 g body weight; the animals of the third group received 6-methylthiouracil in a dose of 10 mg.

The right adrenal (in toto) and half the left adrenal were removed from all the animals under ether anesthesia. Material was taken for histological investigation 2, 5, 10, 20, and 30 days after operation. Pieces of tissue were fixed in Bouin's and Carnoy's fluids, 10% neutral formalin and 10% silver nitrate. Paraffin wax sections were cut to a thickness of 6-7 μ and stained with hematoxylin-eosin, for lipids with Sudan IV and Schiff's reagent, and for the presence of ascorbic acid by the method of Giroud and Leblond.

EXPERIMENTAL RESULTS

In normal conditions the adrenal capsule of albino rats is formed by bundles of collagen fibers, between which lie fusiform cells with elongated nuclei, usually arranged in several layers. As the zona glomerulosa is approached the cells become thicker and their nuclei become rounder in shape. The capsule is followed by a thin subcapsular layer, consisting of loose connective tissue, and containing cells morphologically similar to the cells of the inner layer of the capsule [3]. The zona glomerulosa is built up of tortuous bands of cells with round nuclei, relatively rich in chromatin.

Side by side with typical fibroblasts, the internal layer of the capsule and the subcapsular layer contain undifferentiated epithelial cells of mesodermal origin, the "transitional cells" [12]. These cells in certain conditions are transformed into active secretory cortical cells, and together they form the "subcapsular blastema" [2, 4].

In the adrenal of the control animals in the early stages (2-5 days) after the operation areas of parenchyma persisted in the region of injury showing necrotic changes, with pale cells with indistinct outlines, the nuclei of which showed signs of chromatolysis and pycnosis. In the part of the gland left after the operation hyperemia of the capsule, the cortex, and the medulla was observed. In the subcapsular layer and the zona glomerulosa numerous mitoses appeared. Mitoses were also found in the zona fascicularis.

The adrenal capsule was thickened, and this thickening was most marked in the areas of the capsule lying next to the region of injury. In the internal layer of the capsule and the in subcapsular layer many cells with irregularly shaped, translucent nuclei and a small rim of cytoplasm could be seen. Subsequently the nuclei of these cells became rounded and rich in chromatin, small droplets of lipids appeared in the cytoplasm, and they acquired the shape of typical glomerular cells.

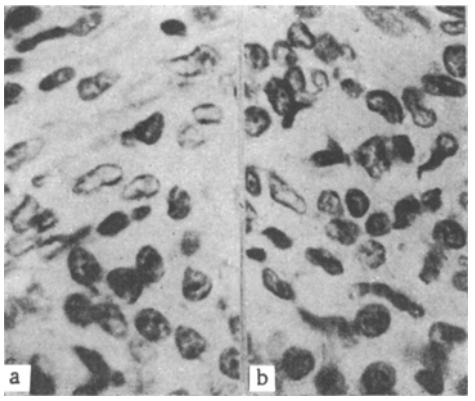

Fig. 1. Stages in the transformation of undifferentiated capsular cells into cells of the zona glomerulosa (5 days after operation). a) Control; b) thyroid. Photomicrograph. Stained with hematoxylin and eosin. Ocular 7, objective 90.

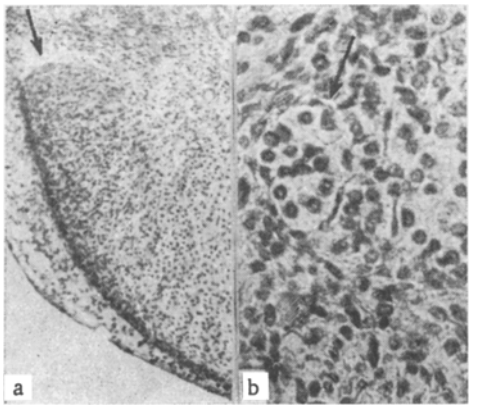

Fig. 2. a) Control: protrusion of cellular material of the zona glomerulosa (arrow) in the region of injury (20 days after operation); b) thyroid: invasion of young connective tissue by bands of cortical cells (20 days after operation). Photomicrograph. Stained with hematoxylin-eosin. a) Ocular 7, objective 8; b) ocular 7, objective 40.

Five days after the operation all stages of the transition from undifferentiated capsular cells to cells of the zona glomerulosa of the cortex could be seen in the internal layer of the capsule and in the subcapsular layer (Fig. 1a).

In the cells of the zona glomerulosa at this period a few lipid droplets and ascorbic acid granules could be seen. The latter were also present in the cells of the zona fasciculata and zona reticularis, which did not contain lipids. In the region of injury, among the proliferating connective tissue, cells of the fibroblast type, neutrophils, lymphocytes, and also macrophages containing hemosiderin granules in their cytoplasm could be seen.

Twenty days after operation, in the regions of the gland next to the site of injury, small bands of epithelial cells from the zona glomerulosa were seen to be invading the young connective tissue. In the region of injury, in some cases protrusion of cell material of the zona glomerulosa occurred (Fig. 2a) as a result of the proliferation of its own cells and of differentiation of the cells of the capsule and subcapsular layer. Lipids and ascorbic acid were accumulating in the cells of the zona glomerulosa and zona fasciculata at this period.

Thirty days after the operation the adrenal capsule was normal in structure throughout its length. As a rule no hyperemia was observed in the residual part of the gland. In the region of injury a connective-tissue scar was formed.

Proliferation in the adrenal cortex was much more active in the animals receiving thyroid than in the controls. Soon after operation (2-5 days) the residual part of the gland was markedly hyperemic, and hypertrophy of the capsule had attained a considerable degree. The internal layer of the capsule and the subcapsular layer were richer in "transitional cells," among which mature forms with round nuclei were predominant (Fig. 1b). In the cells of zona glomerulosa and external layer of the zona fasciculata numerous lipid droplets appeared. Fewer ascorbic acid granules were present in the cells of the zona glomerulosa than in the controls. In the region of injury numerous large fibroblasts, neutrophils, lymphocytes, and actively phagocytic macrophages were found.

Twenty days after operation, in the region of injury intensive invasion of the newly formed connective tissue by bands of epithelial cells was taking place (Fig. 2b). Between 20 and 30 days after the operation lipids were found in all three zones—z. glomerulosa, z. fasciculata, and z. reticularis. The amount of ascorbic acid in these zones increased. In the region of injury newly formed areas of the zona glomerulosa could be seen, distinguished by the more marked development of its connective-tissue stroma.

After administration of 6-methylthiouracil the regenerative processes in the cortex were depressed. In the early periods after operation the residual part of the gland showed less intensive hyperemia than in the controls, and hypertrophy of the capsule was also less marked. In the capsule and subcapsular layer less highly differentiated "transitional" cells with pale, elongated nuclei were predominant; very few intermediate cell forms were present. A few neutrophils, lymphocytes, and macrophages had migrated into the region of injury; proliferation of small fibroblasts was observed, rapidly filling the region of the defect. In the zona glomerulosa very few lipid droplets could be seen. Ascorbic acid granules in the cells of the zona glomerulosa were much more numerous at this period than in the controls.

Between 20 and 30 days after the operation signs of proliferation were absent in the adrenal cortex. Lipids were seen only in the zona glomerulosa. As a rule no invasion of the connective tissue by bands of cortical cells occurred. Thrity days after the operation a dense scar was visible at the site of the defect; no new areas of parenchyma were formed in the region of the injury.

After resection of one half of one adrenal and total resection of the other, slight hypertrophy of the residual part of the gland was observed. However, along with hypertrophy of the residual portion of the gland, new tissue was formed in the region of injury, in the form of protrusion of the material of the zona glomerulosa as a result of proliferation of its cells and also of transformation of the undifferentiated cells of the capsule and subcapsular layer into cells of the zona glomerulosa.

An experimental increase in the concentration of thyroid hormone caused stimulation of regeneration in the parenchyma of the adrenal cortex, accelerated the differentiation of the cells of the capsule and subcapsular layer, and facilitated an increase in cortical function, as shown by the accumulation of lipid droplets in its cells. Under the influence of thyroid hormone activation of the connective-tissue cells took place, thus ensuring the nutrition of the new epithelial tissue formed in the region of the injury, and constituting a factor favoring the course of regeneration.

A marked fall in the concentration of thyroid hormone caused depression of the proliferation of the epithelial cells of the cortex, slowing of the differentiation of the cells of the capsule and subcapsular layer, and weakening of the function of the cortical cells (as shown by the low lipid content of the cortical layer). In experimental hypothyroidism the development of new epithelial tissue at the site of injury was depressed. A dense connective-tissue scar was formed soon after the operation at the site of injury.

Hence, thyroid hormone has an important influence on regeneration of the adrenal cortex after partial adrenalectomy. Changes in the concentration of thyroid hormone in the body lead to corresponding changes in the regenerative power, structure, and function of the adrenal cortex.

SUMMARY

Albino rats, weighing 120-160 g were used. The first group of the animals served as control; the second group received thyroid per os in a dose of 5 mg/10 g body weight; the third group—6 methylthiouracil in a dose of 10 mg. Total excision of the right adrenal gland and extraction of half of the left one was performed in all animals. The animals were killed 2, 5, 10, 20 and 30 days after the operation. With high concentration of the thyroid hormone there was an increase of proliferation of the cortical epithelial cells and acceleration of transformation of the differentiated capsular cells into cortical cells. At the same time an increase of the function of the residual gland and activation of the connective tissue cells occurred. Lowering of the thyroid hormone level depressed rengeneration of the cortical parenchyma delayed transformation of the undifferentiated cells and inhibited proliferation of the connective tissue cells; a solid scar was formed in the area of the defect.

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