EFFECT OF ACTH ON GIANT CELLS IN THE CORTEX OF THE DEVELOPING ADRENAL IN ALBINO RATS

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Giant cells in the cortex of the developing adrenal in rat embryos and young newborn rats were studied. Some females received ACTH injections during pregnancy. It is concluded that the giant cells are a constant cellular component of the developing adrenal and that they are stimulated by ACTH.

Giant cells are often found [1-9] in the cortex of the developing adrenal of animals and man, but their importance has not yet been determined.

In this investigation the functional importance and hormonal activity of the giant cells in the adrenal cortex and the factors regulating their growth were studied.

EXPERIMENTAL METHOD

The investigation was conducted on 215 rat embryos and fetuses aged from 5 to 22 days of intrauterine life. The experiments of series I acted as control. In series II the giant cells were studied against the background of administration of long-acting ACTH (3 units/100 g body weight) to the females during pregnancy. Of the 62 newborn rats used, 30 were controls and the mothers of 32 received ACTH. The material was fixed in formalin or Zenker-formol with acetic acid and embedded in paraffin wax. Sections were stained with hematoxylin-eosin and for lipids, and the ascorbic acid distribution was investigated histochemically (by the method of Giroud and Leblond).

EXPERIMENTAL RESULTS

In the experiments and control the early appearance of giant cells in the anlage of the adrenal cortex was observed (8th-10th day). Their increase in size started with enlargement of the nucleus and nucleoli. The chromatin appeared as large granules or a compact network, or it became homogeneous. The cytoplasm stained as bright pink granules. Sometimes inclusions were found in the cytoplasm and vacuoles, staining palely with eosin, in the nuclei. As a rule the giant cells divided by amitosis, sometimes forming multinuclear cells. In size the giant cells varied from 10 to 100 μ, and in every case after adminstration of ACTH they were 5-10 μ larger than the controls. The inclusions in the cytoplasm and vacuoles in the nuclei also were larger in the experimental series and they were strongly stained with eosin. Parallel with the formation of giant cells, they degenerated more quickly than in the control. By the 14th day these cells could no longer be found, which corresponds to the period of organogenesis.

In the second half of pregnancy (18 days) giant cells were rarely found in the adrenal cortex of the fetuses after adminstration of ACTH, and their number increased toward the end of pregnancy (20 days), especially at birth and during the first 3 days after birth.

Giant cells were observed in the adrenals of the newborn rat (in the experimental series) in the hyperplastic cortex in 15.6% of cases, compared with 6.6% in the control, multiple cells being more common. Just as in the control, these cells were found linked with other systems of cortical cells (Fig. 1), but sometimes they were not so linked and were present as free elements (Fig. 2). These latter were round or oval in shape, with homogeneous pink, hyaline-like cytoplasm and a dense, hyperchromic nucleus. No inclusions were present in the cytoplasm and no nucleoli or vacuoles in the nuclei (Fig. 3). Sometimes these cells showed signs of degeneration, with reduced activity [5]. The increased size of these cells, nuclei, and nucleoli, their more intense staining, and their low content (absence) of lipids and ascorbic acid

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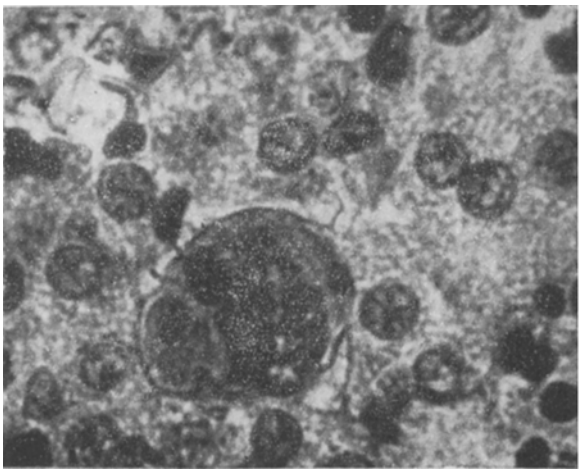

Fig. 1. Giant cells in the adrenal cortex between zona fasciculata and zona reticularis. Hematoxylin-eoxin. Ocular 10 ×, objective 40 ×.

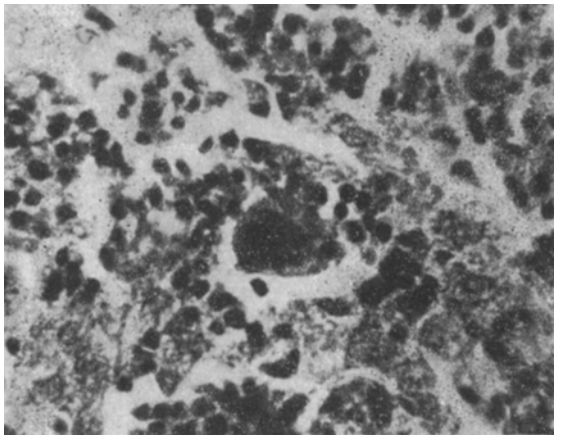

Fig. 3. Multinuclear giant cell with hyaline-like cytoplasm. Hematoxylin-eosin. Ocular 10 ×, objective 20 ×.

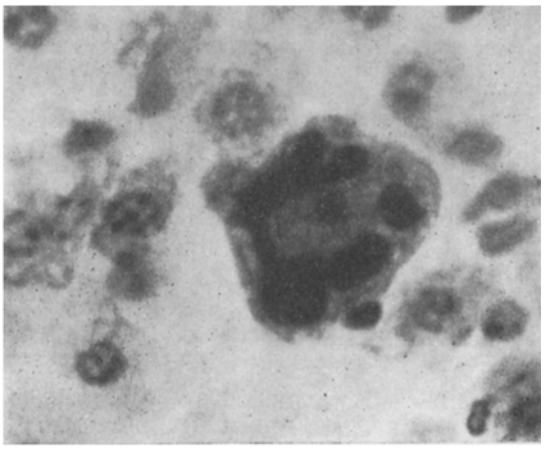

Fig. 2. Multinuclear giant cell partially freed from connections with neighboring cells. Hematoxylin-eosin. Ocular 10 ×, objective 40 ×.

at the height of development of the giant cells are evidence of their high functional activity. Differences in the state of the cytoplasm are collected with different stages of the secretory cycle of these cells.

The results of these experiments cast doubt on the view [7] that the giant cells are preneoplastic elements of the adrenal cortex. The isolated distribution of these cells, the absence of any tendency toward excessive growth, metastasization, or formation of cell nests or nodules, the rarity of amitotic division, the high sensitivity to various unfavorable factors, and their decrease in number and disappearance in the postnatal period are evidence in support of its rejection.

The results showed that the giant cells are a constant cellular component of the developing adrenal gland of embryos, and that they are stimulated by exogenous ACTH, and in fetuses and in newborn animals they are stimulated by the endogenous ACTH of the pituitary. The number of giant cells starts to increase at birth. The adrenal cortex of newborn animals responds to powerful stress by the formation of giant cells, functioning in close connection with ordinary cortical cells with secretion of both merocrine and holocrine type.

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