Ultrastructure of STH Cells of the Pars distalis of Castrated Male Mice after Hepatectomy*

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Summary. An electron microscopic study aimed at differentiation between “castration gonadotrophs” and “posthepatectomy STH cells” was performed on the pars distalis of the pituitary of castrated male mice, after partial hepatectomy. The ultrastructural features observed permit the distinction of both cell types. In the present experiments some remarkable ultrastructural changes, other than those described in a previous report, have been found in STH cells of hepatectomized mice with or without previous castration. Most of them contained masses of heterogeneous electron density, suggesting fusion of granules. These masses and some secretion granules were observed close to the plasma membrane, apparently in the process of discharging material into the pericapillary space. Granular extrusion was more frequent than normally. An increased number of lysosomes, probably related to the digestion of overproduced secretion material, was evident. The appearance of concentric lamellar formations might be related to an increase in cell movements. STH cells with severe cytoplasmic damage were also found, indicating an increased rate of cell loss.

Key words: Pars distalis — House — STH cells — Castration — Hepatectomy — Electron microscopy.

In a previous paper we reported important changes in STH cells of the pituitary after partial hepatectomy (Echave Llanos, Gómez Dumm and Nessi, 1971 a). The possibility suggested by M. Herlant (Brussels) that the modified cells, instead of being STH cells, may be gonadotrophs modified in a way similar to that after castration, was tested even though the hormonal imbalance resulting from liver insufficiency and increase in blood estrogens after hepatectomy does not support this interpretation. The results of these experiments are reported in the present paper.

Material and Methods

C3H-S male mice, from the time of weaning to that of the experiment, were kept under the same standard conditions described previously (Echave Llanos, Gómez Dumm and Nessi, 1971 a), except that they were caged in groups of five animals. Six groups were used: 1) 3 intact mice; 2) 3 partially hepatectomized mice; 3) 2 sham operated mice; 4) 3 castrated mice; 5) 7 castrated-partially hepatectomized mice; 6) 2 castrated-sham operated mice. The castrations were performed when mice were 12 weeks old. At age 10 to 12 months they were hepatectomized (Bruce, Drury and Brues, 1946) and sham operated at 14:00 hours. The animals from all groups were sacrificed at midnight (34 hours postoperation for groups 2, 3, 5 and 6) by decapitation and exsanguination. The skull was opened, the brain removed and the pituitary exposed by eliminating the meningeal covers. A drop of cold fixative*

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Milloning, 1962) was placed on the sella turcica. After a few seconds the hypophysis was removed and immersed in fixative. The lateral wings of the pars distalis were separated and sliced into small pieces. The material was then fixed for two hours, dehydrated in increasing concentrations of ethanol and embedded in araldite (Luft, 1961). Sections were cut with glass knives on an LKB Ultratome III, mounted on copper grids and stained with lead citrate (Reynolds, 1963). They were examined with a Siemens Elmiskop I at 60 kV.

Results

The gonadotrophs of the pars distalis of all castrated mice showed the typical ultrastructural change first described by Farquhar and Rinehart (1954). They presented a high degree of endoplasmic reticulum dilatation. Many “signet ring” cells were observed.

The STH cells, also undergoing important changes, could be easily distinguished from gonadotrophs (Fig. 1). These changes occurred in both, the castrated-hepatectomized and the hepatectomized groups (Figs. 1, 2). In some STH cells whorls of concentric smooth lamellae encircled various cytoplasmic components such as secretion granules, lysosomes, endoplasmic reticulum and irregular smooth membranes connected with the inner concentric lamellae (Fig. 3). Such lamellar formations from STH cells could also be seen in the cytoplasm of other cell types. Other cytoplasmic inclusions in modified STH cells were irregular masses of heterogeneous density (Fig. 2) which sometimes, together with single granules, fused with the plasma membrane. In these areas a finely granular material was observed in the pericapillary space (Fig. 6). The extrusion of secretory granules from the STH cells was far more frequent in hepatectomized than in normal mice (Fig. 5). Smooth vacuoles containing finely granular material (Fig. 2) were a common finding.

Most of the modified STH cells contained numerous autophagic vacuoles. In some fields they showed severe alterations, i.e., organelle disruption and formation of large vacuoles (Fig. 4).

The pars distalis of intact and sham operated mice did not show any abnormal feature. Several ultrastructural modifications of the pars distalis of castrated mice other than the well known “castration cells” will be reported elsewhere.

Fig. 1. Castrated hepatectomized mouse. Gonadotroph (castration cell) in upper part showing dilatation of endoplasmic reticulum and somatotroph with increased number of lysosomes. × 8500

Fig. 2. STH cell from hepatectomized mouse. Note masses of varying electron density (arrow), apparently the result of granular fusion, and vacuole (Va) with fine granular content. × 27000

Fig. 3. STH from castrated-hepatectomized mouse showing concentric lamellar formation (La). × 10000

Fig. 4. STH cell from castrated-hepatectomized animal showing severe regressive changes and large cytoplasmic vacuole (Va). × 15000

Fig. 5. STH cell from castrated-hepatectomized mouse. Extrusion of secretory granule, × 20000

Fig. 6. Finely granular material seems to be released from secretory granules and larger masses into pericapillary space. × 20000
Figs. 1–6
Discussion

The striking changes suggesting growth hormone release in STH cells of the pituitary of hepatectomized mice (Echave Llanos, Gómez Dumm and Nessi, 1971a; Echave Llanos and Gómez Dumm, 1971b) agree well with the results of experiments in which plasma and pituitary extracts, from animals with this ultrastructural appearance, strongly stimulated DNA synthesis in normal intact liver (Echave Llanos, Gómez Dumm and Surur, 1971c; Badrén, Echave Llanos and Surur, 1973). Recently some of these findings have been corroborated, also in hepatectomized mice, but under different experimental conditions (Zotter, 1972).

In older hepatectomized mice of the present experiments, with or without long term castration, similar changes have been found. In the present material STH cells show additional features such as concentric lamellar bodies, granular fusion, signs of exocytosis, increased number of lysosomes and severe regressive changes.

The lamellar bodies described here are similar to those observed in many other cell types (Girod and Dubois, 1971). Clementi and DeVirgiliis (1967) reported them in STH and LTH cells in castrated female rats treated with estrogens and progesterone. Irregular infoldings of the plasma membrane have been seen in STH cells from mice bearing transplanted hepatomas (Badrén, Nash and Echave Llanos, 1971). We interpret the concentric lamellae in our material as formations that segregate diverse cytoplasmic elements.

The irregular masses of heterogenous density observed in STH cells of hepatectomized and castrated-hepatectomized mice of the present experiments seem to result from granular fusion (Fig. 2). Masses of this type as well as individual granules seem to fuse with the plasmalemma in areas in which finely granular material is seen in the pericapillary space (Fig. 6). This appears to be an indication of hormone release. The observation of exocytosis is relevant in view of the extremely rare occurrence of this phenomenon under normal conditions (Gómez Dumm and Echave Llanos, 1972). It adds further support to the suggestion that there is an increase in the synthesis and release of growth hormone after hepatectomy (Echave Llanos, Gómez Dumm and Nessi, 1971a).

Several authors have observed an increased number of different types of lysosomes in somatotroph cells under various conditions, for example in immature rats (Behrens and Martins, 1972). Administrations of hypothalamic extract produces an increase of the number of lysosomes of the lamellar type in STH cells (DeVirgiliis, Meldolesi and Clementi, 1968; Coates, Ashby, Krulich, Darival and McCann, 1970). This kind of lysosome also occurs in the normal mouse pituitary but it is not found in the somatotrophs of a diabetic strain of mice (Yamada, Nakamura and Yamashita, 1967). Furthermore, lysosomes have been implicated in intracellular digestion of excess unutilizable hormone in LTH cells (Smith and Farquhar, 1966). The remarkable increase in lysosomes in our material seems related to the disposal of excess cellular products of STH cells after hepatectomy. Furthermore the severe organelle damage observed in some STH cells (Fig. 4) might be due to an increased activity of the lysosome system (De Duve and Wattiaux, 1966) and could be related to the appearance of agranular cells containing large lysosomes (Echave Llanos, Gómez Dumm and Nessi, 1971a).
References


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