OCCURRENCE OF A KIND OF CASTRATION CELL IN THE ANTERIOR LOBE OF PITUITARY IN RATS WITH THE LONG-TERM ADMINISTRATION OF GLUCAGON

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It has been generally considered that the a-cell in pancreatic islet is a possible site of glucagon production. But the histological effects of chronic administration of glucagon on islets vary with the species of used animals, the dosage of the compound and the duration of injection. The changes in islets due to the exogenous administration of glucagon are so complicated that it has not been established whether or not a-cells are selectively inhibited or degenerated. On the other hand, stronger changes were noted in b-cells (Salter et al., 1956 and 1957; Lazarus and Volk, 1958; Logothetopoules et al., 1959; Lacy 1959). Concerning the action of glucagon to the other endocrine organs, negative data have been accumulated. Recently Lepkosky et al. (1964) pointed out that in depancretized chickens growth of ovary and oviduct in female and comb growth in male is delayed. The present report deals with the extreme hypertrophy and proliferation of gonadotroph-typed basophile cells, identifiable to the castration cells, in the anterior lobe of pituitary in male rats with the chronic administration of glucagon, and the origination of this change was investigated.

MATERIALS AND METHODS

Sixteen male rats of Donryu strain, 30 days of age, were divided into control and experimental groups in equal number. Experimental 8 animals were administered daily with glucagon* 100 ìg in 0.2 ml physiologic saline solution per rat for 3 months (4 animals) and 8 months (4 animals, 2 of whom were imposed to be survived for 2 months after withdrawal of the administration of glucagon), the control 8 rats were done daily 0.2 ml saline solution per rat for 3 and 8 months respectively. All animals were fed on CE-2 standard diet supplied by Central Labora-
tory for Experimental Animals and decapitated at the end of experiments corresponding to the
120th, 270th and 330th day respectively. The pancreas, hypophysis, ventral prostata, seminal
vesicle, adrenal and thyroid were fixed, immediately after the removal, with Bouin solution and
Levi’s liquid. Paraffine sections were stained with hematoxylin eosin. The pancreas was stained
with Gomori’s chromalum hematoxylin, the hypophysis done with periodic acid Schiff’s (PAS)
reaction with the counterstain of iron hematoxylin. The blood sugar was determined by the
method of Somogyi-Nelson on venous blood specimens from the tail vein.

RESULTS

The growth of body-weight of experimental animals was much or less retarded
below the increasing gradient of control rats, with the reduction of 10 to 40 g
at the respective days of age. The average of body-weight at the 270th day was
480 g in control, and 350 g in experimental groups. After 3 months the fasting
blood sugar level was 62 to 110 mg% in administered animals and 60 to 70 mg%
in the control, but after 8 months, it was equivalent in normal and experimental
groups, amounting to 60 to 90 mg%. Histologically, the changes did not appear
in pancreatic islets following the chronic administration of glucagon (Fig. 2): The
development and distribution of the syncytium of α-cell sheet (arrow) surrounding
the islets was not affected, and likewise the stainability of phloxin was not altered,
showing the normal pattern (Figs. 1 and 2); the number and size of CH-positive
granules were kept in the normal state. While in hypophysis, the subsequent
evident hypertrophy and proliferation of spherical gonadotroph-typed basophile
cells (PAS-positive) were worthy of notice (Fig. 4). This became progressive after
3 months administration, and most profound after 8 months. These active cells
which may be identifiable to the castration cells became 1.5 to 2 times, in diameter,
of the normal gonadotrophs (Figs. 3 and 4). They contained the enlarged Golgi-
rings, suggesting an acceleration in cell-function. While thyrotroph-typed polygonal
basophile cells (PAS-positive) almost disappeared. After 8 months administration,
among the castration cells there were scattered the signet ring cells occupied by
the huge colloid mass. This is analogous to the change in the anterior lobe of
spayed rats over 3 months after the castration. Thus the long-term glucagon
administration resulted in strong response of basophile cells, the suppression of
Ledig cells of testis is, therefore, naturally suspected. But any inhibitory pictures
were fail to be found in them. Consequently it is required for us to examine
whether the exogenous secretion of androgen is slightly inhibited or not, in refer-
ence to the cell-height of prostata and seminal vesicle. In Figures 5 and 6, the
central area of ventral prostata consists of numerous follicle-like glands (Figs. 5
and 6). The epithelium of the administered rats appeared to be lower in height
than the control; this reduction was, however, too delicate in degree to be a sub-
stantial change. In addition, the height of epithelium of seminal vesicle of ex-
perimental rats was utterly identical with that of the control (Figs. 7 and 8). In
spite of the negligible changes on the secondary male sex glands, the gonadotroph-
typed cells were thus virtually stimulated.
DISCUSSION

The dosage of glucagon used in the present experimental rats was less than that employed by the previous investigators (Root 1954; Salter et al., 1956 and 1957; Lacy, 1959; Peterson and Hellmann, 1963). This would become a possible cause of no sign of alterations in islets and of no marked elevation in fasting
blood sugar level. Nevertheless, the hyperactivity of gonadotroph-typed cells in hypophysis became progressive. When the duration of administration was prolonged over 8 months, the changes reached to the level corresponding to that in castrated 3 months rats. In reference to the height of prostat and seminal vesicle, it was substantiated that the hyperfunction of gonadotroph-typed cells was not due to the deficiency of endogenous androgen. As the thyroids and adrenals did not undergo the marked atrophy, nor pattern of dysfunction, an assumption could be tenable that glucagon directly stimulates the basophile cells.

**SUMMARY**

The long-term administration of glucagon did not cause the marked histo-
logical changes in pancreatic islets of rats, but induced the obvious picture showing the acceleration in the basophile cells in the anterior lobe of pituitary, resembling the castration cells. This strong response may not be resulted from the deficiency of endogenous androgen, because the cell-height of prostata and seminal vesicle remained unchanged.

REFERENCES