ANNALES
UNIVERSITATIS MARIAE CURIE-SKŁODOWSKA
LUBLIN — POLONIA
VOL. LIII, 20 SECTIO D 1998

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The ultrastructure of thyroid in the course of the experimental diabetes

Ultrastruktura gruczołu tarczowego w przebiegu cukrzycy doświadczalnej

The alloxan-induced diabetes results in the acute hyperglycemia followed by some other symptoms evidencing the presence of diabetes. The condition is due to alloxan which selectively damages the beta-cells of the pancreatic islets of Langerhans. In the alloxan-induced diabetes the lesions are observed in many important organs such as: liver, heart, kidneys and others. The studies performed by many authors showed that diabetes inhibited the hypothalamus-pituitary-thyroid axis (2, 6, 9). This may lead to the impairment of the thyroid activity. The problem which remains unexplained and is a matter for much speculation is a question of the thyroid ultrastructural changes in the course of the experimental diabetes which may also affect the endocrine function of this organ. Thus, the aim of the studies peformed was to determine the changes occurring in the thyroid ultrastructure in the individual stages of the alloxan-induced diabetes in rabbits.

MATERIAL AND METHODS

The studies were carried out in the white New Zealand mature male rabbits weighing about 3 kg. Diabetes was induced by the intravenous injection of 10% solution of alloxan in the dose of 100 mg/kg of body weight. The blood glucose level lower than 11.1 mmol/l (200mg%) was accep-

ted as the criterion of diabetes. The rabbits were divided into the following experimental groups: group 1 – controls, group 2 – the 21 days' diabetes, group 3 – the 42 days' diabetes, group 4 – the 90 days' diabetes, group 5 – the 180 days' diabetes.

The animals classified for the ultrastructural examinations were put to sleep with thiopental and 4% glutaraldehyde in 0.1 M cacodylate buffer was injected to their left ventricles. The thyroid fragments were collected after the several minutes' perfusion and the cardiac arrest. The sections were fixed for 4 h in 4% glutaraldehyde in 0.1 M cacodylate buffer, pH 7.4 at +4°C. Next, the sections were washed out twice (10 minutes each wash) with 0.1 M cacodylate buffer and fixed for 2 hours at +4°C in 1% osmium tetroxide in the same buffer. Having been dehydrated in the series of alcohols and propylene oxide, the specimens were saturated with SPURR Low-Viscosity resin (Polysciences). The ultrathin sections were prepared by means of ultramicrotome, Reichert Om-U3 and then examined and documented in the transmission electron microscope (TEM), BS-500 Tesla type.

RESULTS

The thyroid pictures of the healthy animals in T.E.M. were consistent with the results reported by the other authors (3, 4, 5, 7, 9). The thyroid shows a follicular structure. The thyrocytes lining the follicles presented normal shape and size (Fig. 1). Their basilar part contacted the fine vacuolar reticulum while their apical portion with the numerous cytoplasmic processes faced the follicle lumen. The cellular nuclei present in the thyrocytes were normally shaped with the regular distribution of chromatin which was mostly accumulated in the periphery beneath the nuclear coat (envelope). In the cytoplasm the endoplasmic reticulum mitochondria and numerous secretory granules could be found.

The diabetes of the 21 days' duration has already been reflected in the thyroid ultrastructural image. During that period the flattening of the secretory epithelium and the proliferation of the connective tissue in the interfollicular septa were observed. In the later stage the above mentioned disorders were becoming more intensive.

After 42 days of the experiment the microvilli turned to the follicle lumen were found to be less numerous and shorter. In the epithelial cells the widened endoplasmic reticulum was observed as well as numerous vacuoles and a smaller number of the secretory granules (Fig. 2).

In the diabetes lasting 90 days, further fibrosis of the follicular septa was observed. The epithelial cells were becoming very flat and exfoliative to the follicle lumen (Fig. 3). A large number of vacuoles were present in the colloid which became nonuniform.

The most intensified pathological changes in the thyroid gland were found after 180 days of the experiment. Apart from the significant organ fibrosis, further exfoliation of the follicular epithelium cells to the follicle lumen could be observed. The thyrocytes presented an extremely high number of vacuoles which gave the picture of the vacuolar degeneration of the cells (Fig. 4, 5). The widening and disruption of the endoplasmic reticulum, the presence of numerous vacuoles and the changes in the shape and structure of the cellular nucleus resulted in the blurring of the cell internal structure (Fig. 6).

DISCUSSION

The interdependence between the thyroid diseases and diabetes was a matter of interest to many authors. However, the considerations analysing the diabetes effects on the thyroid gland were mainly to the evaluation of the organ function. Only a few reports concern the changes in the thyroid microscopic structure and their results are often inconsistent.

The changes in the thyroid of the diabetic rats were described by Rogoziński et al. (8). On the basis of the microstereometric analysis they found out the most characteristic features were observed in the alloxan-induced diabetes of the 2 weeks' duration. Compared to the controls the changes consisted in the cytoplasm surface decrease and the reduction of the surface and volume of the thyroid epithelial follicle nuclei. The authors explained those changes by the severe disorders of the biochemical reaction balance as well as the cell metabolism as a whole. They rejected the hypothesis of the toxic effects of alloxan on the thyroid as this compound is found to be quickly excreted with urine or may be converted into the non-toxic alloxan acid. The significant reduction of the cytoplasm surface and of the epithelial follicle nucleus diameters occurred in rats after the 4 weeks' duration of diabetes which fact was explained by the authors as the result of the regression of the morphological-functional changes in the pancreatic islet cells.

The studies concerning the changes in the thyroid histological structure in rats with the induced diabetes were also presented by Bestetti et al. (1). One month after the streptozotocin administration the decrease of the epithelial follicle height and the average follicle surface was observed. The cells contained numerous vacuoles but the number of the colloid drops containing thyroglobulin was reduced. In the basilar part of the thyrocytes the cisterns of the rough endoplasmic reticulum were flattened and their contents showed lower electron density.

In the present studies of the above experiment the fact that the most intensive changes were found in the 180 days' diabetes seems to be particularly interesting. The epithelial cells were extremely flat and contained single, short microvilli protruding to the follicle lumen. In the thyrocytes the significantly widened endoplasmic reticulum was observed as well as the presence of numerous vacuoles. These changes resulted in the blurring of the cell internal structures and the image of the vacuolar degeneration. Above all, the exfoliation of the epithelial cells to the follicle lumen was noteworthy. Moreover, the relevant proliferation of the connective tissue causing fibrosis of the whole organ was observed.

The changes presented above prove the significant thyroid damage in the course of the experimental diabetes which may manifest itself in the thyroid function impairment, in particular its endocrine activity.

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Otrz.: 1998.12.06

STRESZCZENIE

Cukrzyca alloxanowa jest często skojarzona z upośledzeniem funkcji osi podwzgórzowo-przysadkowo-tarczycowej. W przedstawionej pracy wywołano chemicznie alloxan – cukrzycę doświadczalną. Ultrastrukturę gruczołu tarczowego badano u dorosłych królików 21, 42, 90, 180 dni po iniekcji alloxanu (100 mg/kg wagi). Do dalszych obserwacji użyto królików, u których stężenie glukozy w surowicy krwi było wyższe niż 11,1 mmol/l. Wyniki badań udokumentowano zdjęciami fotograficznymi.

EXPLANATIONS TO FIGURES

Fig. 1. T. E. M. The control group. The thyroid secretory epithelial cell fragment. Magn. 8000x.

Fig. 2. T. E. M. The 42 days' diabetes. The thyroid follicular epithelium. Magn. 8000x.

Fig. 3. T. E. M. The 90 days' diabetes. The cell exfoliation to the follicle lumen. Magn. 4000x.

Fig. 4. T. E. M. The 180 days' diabetes. The thyroid follicular epithelium fragment. Magn. 6000x.

Fig. 5. T. E. M. The 180 days' diabetes. The exfoliation of the cells to the follicle lumen. Magn. 6000x.

Fig. 6. T. E. M. The 180 days' diabetes. The thyrocyte changed. Magn. 6000x.

Fig. 1

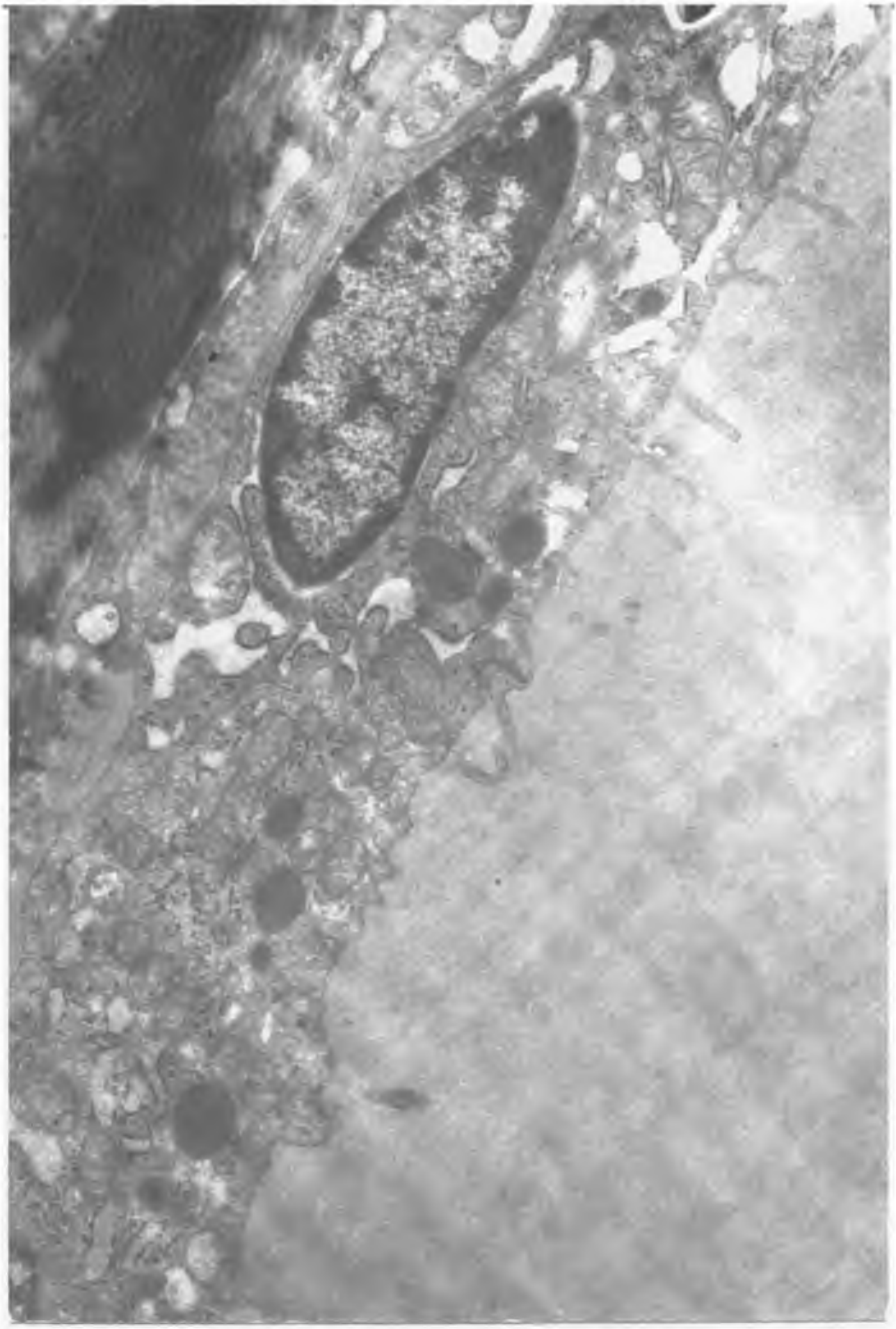

Fig. 2

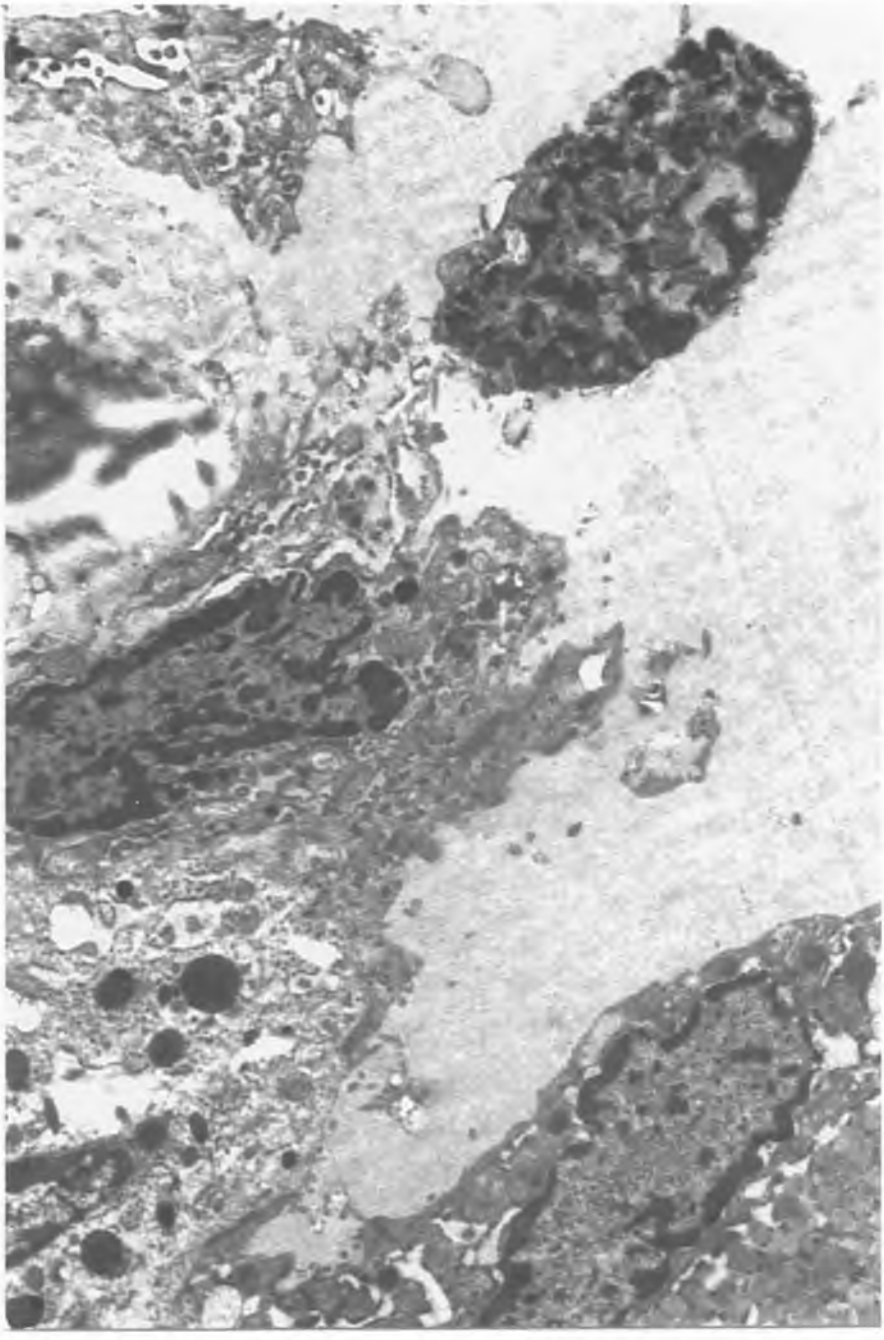

Fig. 3

Fig. 4

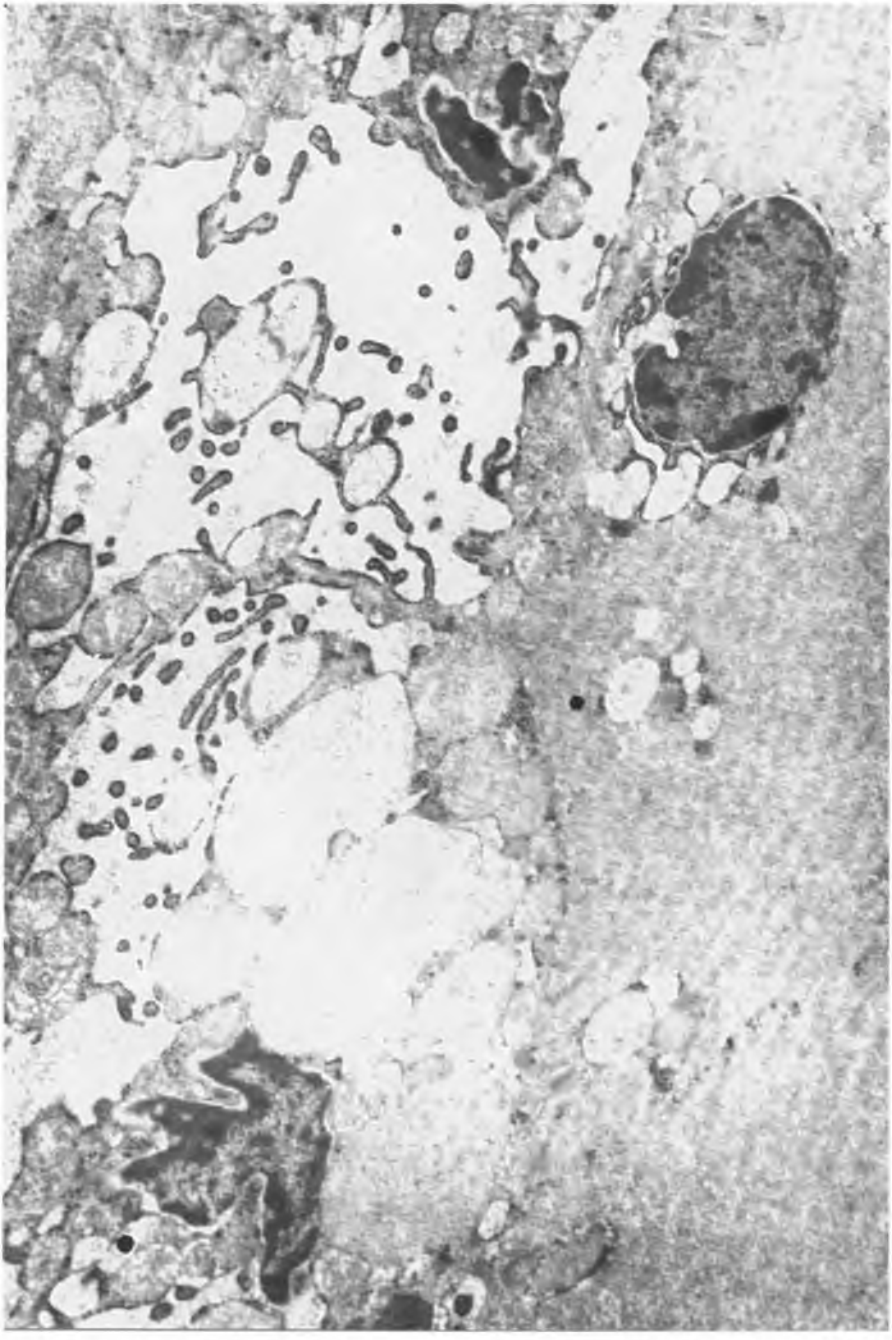

Fig. 5

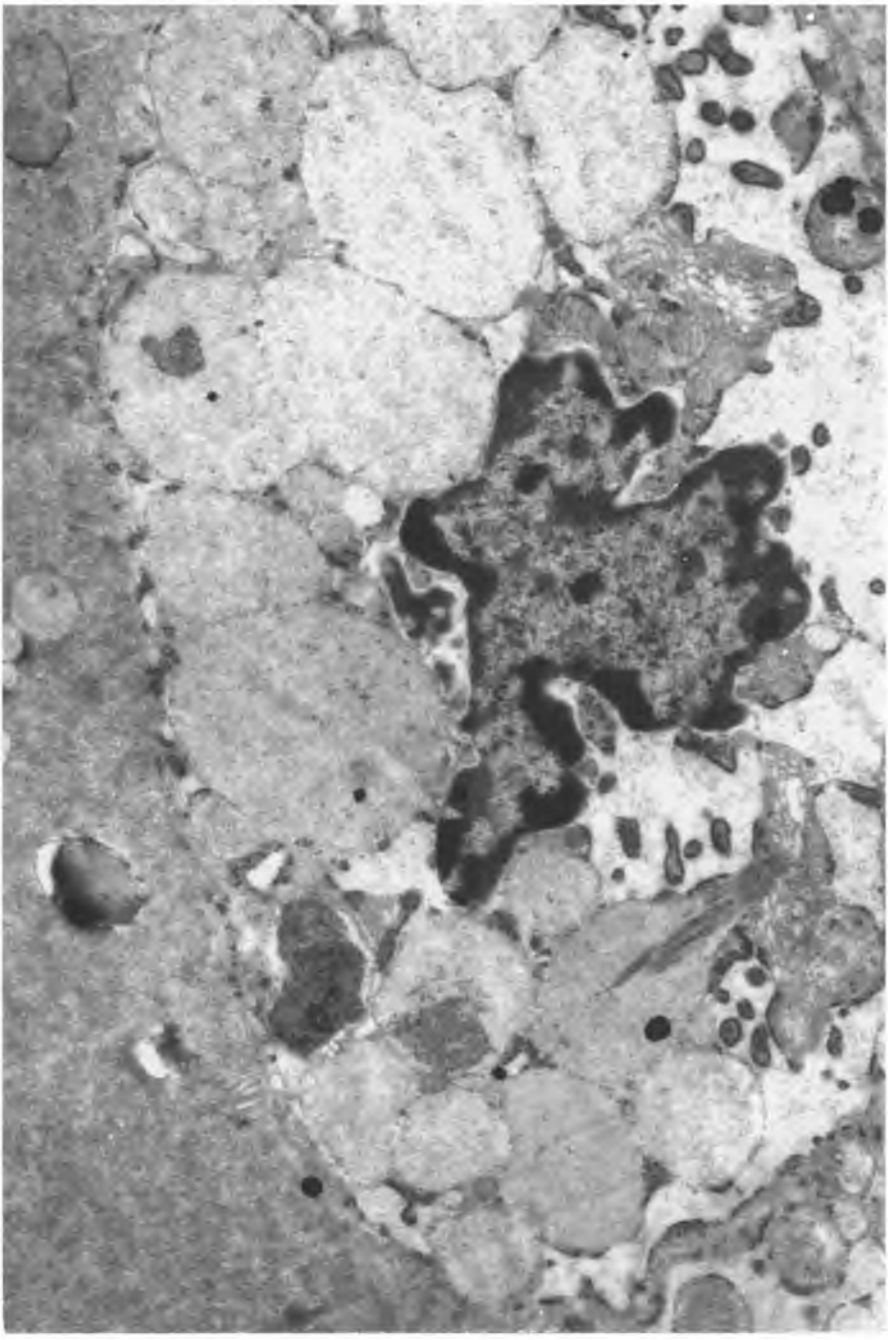

Fig. 6