



Changes in the connective tissue element of the thyroid gland in normal and recurrent euthyroid goiter

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Abstract

Goitre recurrence is a common problem following subtotal thyroid gland resection for multinodular goitre disease. The aim of our study was to trace out the ultrastructure of the thyroid gland of man after primary and redo operations for struma nodosa.

We undertook the task to study the fine ultrastructural changes taking place in the stromal part of the gland. For ultrastructural examination we used routine transmission electron microscopy. The electron microscopy has been made on Hitachi H-500 microscope. Our main goal was to compare the ultrastructural characteristics of the thyroid gland in two different groups - patients with primary disease and patients with recurrence.

The results from our research showed that in the first group the stroma was presented by one or two rows of cells in the septum or in small groups in the interfollicular space. Studies by electron microscopically showed that the cells of the stroma had the ultrastructural characteristics of fibroblasts, but there was an increased number cisterne of Granular endoplasmic reticulum, well developed Golgi complex, as well as relatively small amount of vesicles and vacuoles. The examination of the specimens from the second group showed a much thicker stroma between the follicles. There was an increased amount of stromal cells and collagen bundles in the interfollicular space. The proteoglycan complexes in the extracellular matrix were rarely situated.

Our results suggest that the connective tissue of the thyroid gland reacts faster to the changes of the structure of the gland than the epithelial cells of the follicles.

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Introduction

Multinodular goiter is the most common indication for surgery in endemic iodine-deficiency regions. Ever since Theodor Koher proposed surgery for goiter about a century ago there has been a debate about the best surgical resection for the disease. Nowadays the paradigm shift in thyroid surgery away from Kocher's principles of nodal enucleation or subtotal resection to extended thyroidectomy involving at least hemithyroidectomy

(total unilateral lobectomy) is a well-accepted approach for the treatment of multinodular goiter disease. The transition time in surgical practice, in our country from subtotal to total resection offered us a unique opportunity to compare the ultrastructure of the thyroid gland in primary and redo-operation in patients with nodular goiter. The structural particularities of the thyroid gland in various normal and pathological conditions [1-3]

have always been thoroughly studied. In most cases the object of these studies was the epithelial cells of the thyroid gland [4, 5]. Relatively little attention was given to the stroma elements of the thyroid gland, especially to the ultrastructure of the connective tissue elements of the thyroid gland [6]. There have been several studies related to the interaction between the structural elements in a state of hyperfunction and hypofunction of the gland [7, 8]. The aim of our study was to trace out the ultrastructure of the thyroid gland of man after primary and redo operations for struma nodosa.

Material and methods

For the purpose of this study we used operative material from patients from 20 to 69 years of age with euthyroid nodular goiter. The material derived from two groups –from patients with primary operations (50 patients) and patients with reoperation (50 patients). The tissues were prepared in accordance to the protocols for light microscopy examination and they were stained with Hematoxylin eosin and Masson technique [9]. For ultrastructural examination we used conventional transmission electron microscopy. The electron microscopy was carried out using Hitachi H-500 microscope. For the immunohistochemical examination we used Safranin O staining [9].

Results

The results of our study showed that there are differences in the quantity and in the structure of the stroma of the thyroid gland before and after the operation. In the material from the first group we found that the stroma is represented by one or two rows of cells in the septum or in little group of cells in the space between the follicles. Examined under electron microscope the cells of the

stroma had ultrastructural characteristics of fibroblasts - they had very well developed endoplasmic reticulum, Goldgy complex and a small number of vesicles and vacuoles. The proteoglycan complexes were situated mainly in the territorial matrix (Fig. 1).

The examination of the material from the second group showed a significant thickening of the intrafollicular septum. We found an increase in the quantity of the cells and collagen bundles in the interfollicular space. The cells had smaller volume and less developed intracellular organs. The volume of the endoplasmic reticulum was decreased. The Goldgy complex was rarely found (Fig. 2). The formation of the collagen bundles is accompanied by the expansion of the cytoplasmic appendages of the fibroblasts. That is how they encircle an exact number of collagen filaments. There was a decrease in the number of proteoglycan complexes in the intracellular matrix. At the same time there was an increase in the capillary network of the stroma. In this group we found an increased number of fenestrated capillary. A great number of pinocytic vesicles in the luminal surface of the endothelial cells were detected. Pericytes were also observed.

Discussion

Our studies showed that the connective tissue of the thyroid gland plays an important role in the formation of the tumors and in the processes of postoperative recovery of the gland. The changes in the connective tissue elements are more significant and occur earlier than in the epithelial cells [10]. This gives us a reason why surgery needs to be more extensive - the changes induced by the tumor are not limited by the thyroid parenchyma. Its main action in the recovery process was the growth of the intracellular matrix. There was a thickening of the intercellular septums, an increase of the number of cells and formation of thicker collagen bundles. The cells

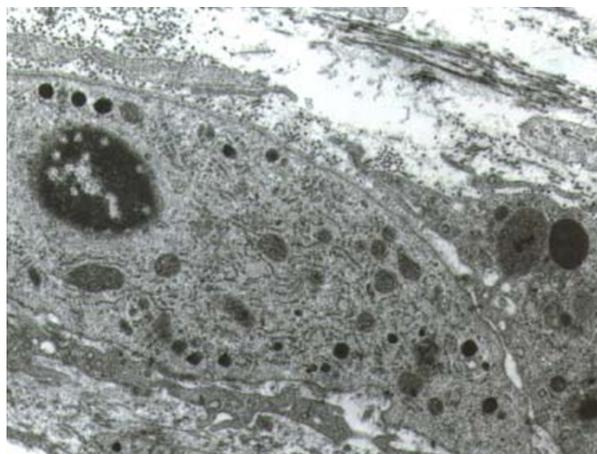


Figure 1. Cells from stroma of thyroid gland with primary operation.

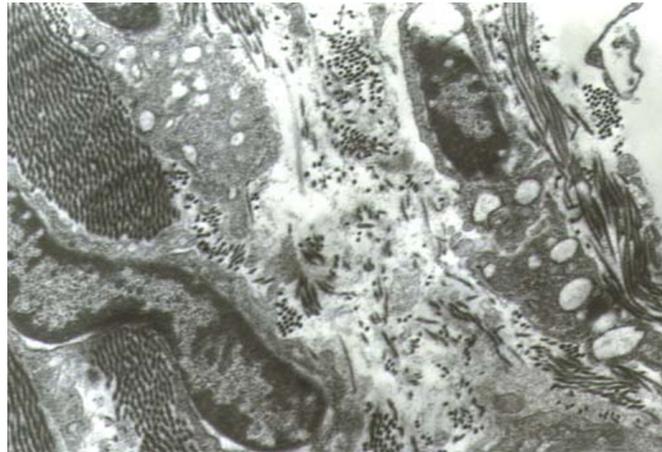


Figure 2. Cells from stroma of thyroid gland after reoperation.

showed increased collagen synthesis and diminished proteoglycan synthesis [11]. As a result the fibroblast had an increased number of their cytoplasmic appendages. The newly formed collagen filaments are encircled and group in-to bundles. This reaction is not common in other types of connective tissue [7, 11]. Our studies show a clear morphological proof for the decrease in the function of the gland. This can be determined in the parenchyma of the gland, as well as in the stroma. The decrease is more vivid in the thyroid parenchyma. The most viable explanation for this is that the ultrastructural changes in the stroma induce a major disruption in the metabolism of the thyroid parenchyma [12-13]. The

increase in the capillary network is due to the decrease in the exchange of substances [12-16].

Conclusions

The connective tissue of the thyroid gland reacts faster to the changes of the structure of the gland than the epithelial cells of the follicles. The main sign of the reaction is the intensification of the collagen production of the fibroblasts and the reduction of the proteoglycan complexes. These changes are pathological in nature and are the main cause for the decrease in thyroid function. This fact justifies a more extensive surgery.

References

- Brooks JR, Starnes HF, Brooks DC, Pelkey JN. Surgical therapy for thyroid carcinoma: a review of 1249 solitary thyroid nodules. *Surgery* 1988; **104**: 940-946.
- Eberle F, Grun R. Multiple endocrine meoplasia, Type I. *Ergeb Inn Med Kinderheilkd* 1981; **46**: 76-149
- Feldman PS, Horvath E, Kovacs K. Ultrastructure of three Hürthle cell tumors of the thyroid. *Cancer* 1972; **30**: 1279-1285.
- Guo SS & Sawicki MP. Molecular and genetic mechanisms of tumorigenesis in multiple endocrine neoplasia type 1. *Mol Endocrinol* 2001; **15**: 1653-1664.
- Shaha AR, Loree TR, Shah JP. Prognostic factors and risk group analysis in follicular carcinoma of the thyroid. *Surgery* 1995; **118**: 1131-1136.
- Carcangiu ML, Bianchi S, Savino D, Voynick IM, Rosai J. Follicular Hürthle cell tumors of the thyroid gland. *Cancer* 1991; **68**: 1944-1953.
- Harness JK, Thompson NW, McLeod MK, Eckhauser FE, Lloyd RV. Follicular carcinoma of the thyroid gland: trends and treatment. *Surgery* 1984; **96**: 972-980.
- Miller RH, Estrada R, Sneed WF, Mace ML. Hürthle cell tumors of the thyroid gland. *Laryngoscope* 1983; **93**: 884-888.
- Prophet E, Mills B, Arrington J, Sobin L. Laboratory methods in histotechnology. *American Registry of Pathology*, 1992.
- Worthington BS, Enwonwu CO. Functional variations in the ultrastructure of the thyroid gland in malnourished infant monkeys. *Am J Clin Nutr* 1975; **28**: 66-75.
- Tissell L, Hansson G, Jansson S. Reoperation in the treatment of asymptomatic metastasizing medullary thyroid carcinoma. *Surgery* 1986; **99**: 60-66.
- Watson RG, Brennan MD, Goellner JR, van Heerden JA, McConahey WM, Taylor WF. Invasive Hürthle cell carcinoma of the thyroid: natural history and management. *Mayo Clin Proc* 1984; **59**: 851-855.
- Harrer P, Bröcker M, Zint A, Derwahl M, Barbera L, Zumbobel V. The clonality of nodules in recurrent goiters at second surgery. *Langenbecks Arch Surg* 1998; **383**: 453-455.
- Studer H, Gerber H, Zbaeren J, Peter HJ. Histomorphological and immunohistochemical evidence that human nodular goiters grow by episodic replication of multiple clusters of thyroid follicular cells. *J Clin Endocrinol Metab* 1992; **75**: 1151-1158.
- Böttcher Y, Eszlinger M, Tönjes A, Paschke R. The genetics of euthyroid familial goiter. *Trends in Endocrinology & Metabolism* 2005; **16**: 314-319.
- Brix TH, Hegedüs L. Genetic and environmental factors in the aetiology of simple goiter. *Annals of Medicine* 2000; **32**: 153-156.