



RESULTS OF IMMUNOHISTOCHEMICAL STUDY OF THE THYROID GLAND IN GRAVES' DISEASE

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KEY WORDS

During macroscopic examination in the control group, the dimensions of each lobe of the thyroid gland were: length $6.8 + 0.04$ cm, width $3.87 + 0.03$ cm, thickness - $2.1 + 0.02$ cm. The weight of the gland in the control group was $24.8+0.05$ gr.

ABSTRACT

Diffuse toxic goiter is a genetically determined autoimmune disease with a congenital defect of the immune system. With diffuse toxic goiter, the secretion of the thyroid hormones triiodothyronine (T3) and thyroxine (T4) increases, which often leads to thyrotoxicosis. Thyrotoxicosis is a clinical syndrome characterized by a persistent and prolonged increase in the level of thyroid hormones in the blood, which is caused by hyperstimulation of the thyroid gland by antibodies to the pituitary thyroid-stimulating hormone receptor. A characteristic sign of thyrotoxicosis is a significant increase in the level of basal metabolism with damage to all organs and systems [1,2,3]. The degree of proliferative activity of the follicular epithelium of the thyroid gland is important. Currently, to determine the degree of proliferation of the thyroid epithelium, an immunohistochemical research method is used [4,5]. Purpose of the study: to study the degree of proliferation of the follicular epithelium of the thyroid gland in diffuse toxic goiter.

Relevance of the topic. Diffuse toxic goiter is a genetically determined autoimmune disease with a congenital defect of the immune system. With diffuse toxic goiter, the secretion of the thyroid hormones triiodothyronine (T3) and thyroxine (T4) increases, which often leads to thyrotoxicosis. Thyrotoxicosis is a clinical syndrome characterized by a persistent and prolonged increase in the level of thyroid hormones in the blood, which is caused by hyperstimulation of the thyroid gland by antibodies to the pituitary thyroid-stimulating hormone receptor. A characteristic sign of thyrotoxicosis is a significant increase in the level of basal metabolism with damage to all organs and systems [1,2,3]. The degree of proliferative activity of the follicular epithelium of the thyroid gland is important. Currently, to determine the degree of proliferation of the thyroid epithelium, an immunohistochemical research method is used [4,5]. Purpose of the study: to study the degree of proliferation of the follicular epithelium of the thyroid gland in diffuse toxic goiter.

Material and research methods. The work was performed using surgical material. A histological study was carried out of 74 thyroid glands removed from patients who were treated in 3-surgery and using the puncture biopsy method at the endocrinology department of the ASMI clinic for 20-23 years. The surgical material and biopsy specimen were examined macroscopically and microscopically. During macroscopic examination, the shape, size, weight, consistency, color, appearance from the side of the capsule and on the section were determined. For histological examination, pieces of the gland were taken from the right and left lobes and the isthmus. The pieces were fixed in 10% buffered formalin solution. The pieces were passed through a processor and then embedded in paraffin. Sections 6 microns thick were prepared from paraffin blocks. Sections were stained with hematoxylin and eosin, picrofuchsin according to Van Gieson. For immunohistochemical studies, the peroxidase-antiperoxidase method was used based on standard diagnostic protocols from the manufacturer. Pieces of gland tissue were fixed for 48 hours in 10% buffered formalin. They were passed through a processor and embedded in paraffin. The material was visualized using the indirect immunoperoxidase method. Sections 5 microns thick were prepared from the finished paraffin blocks. Paraffin sections were deparaffinized and dehydrated using standard histological techniques. Antigenic determinants were unmasked by heating in a water bath at 98 degrees for 30 minutes. Biomarkers against Ki-67 and P53 were used for immunohistochemical studies. The specific number of immunopositive cells was assessed.

Research results. The analysis showed that out of 73 patients, 59 (81.1%) were women, 13 (18.9%) were men. Diffuse toxic goiter is more common in women (79.1%) than in men (14.9%), with a ratio of 1:4. Analysis of the table data showed that diffuse toxic goiter occurs in people aged 41-50 years. In people over 50 years of age, the number of patients with diffuse toxic goiter is gradually decreasing.

During macroscopic examination in the control group, the dimensions of each lobe of the thyroid gland were: length 6.8 ± 0.04 cm, width 3.87 ± 0.03 cm, thickness - 2.1 ± 0.02 cm. The weight of the gland in the control group was 24.8 ± 0.05 gr. The thyroid gland is covered on top with a connective tissue capsule; on a section, the gland tissue is light brown in color and uniform in appearance. Microscopic examination of the surgical material revealed an increase in the size and weight of the gland. The average length of each lobe was 12.7 ± 0.04 cm, width 7.2 ± 0.03 cm, thickness 5.0 ± 0.03 cm. The weight of the gland was from 180.0 to 200.0 ± 0.04 g. In this case, the configuration of the organ is preserved, and deformation of the gland does not occur. Histological examination showed that the lobular structure of the gland was preserved, but the lobules were significantly increased in size due to hyperplastic processes in the thyroid epithelium. There is papillary proliferation of the epithelium with the formation of outgrowths into the lumen of the follicles. Papillary processes are different: short and wide or long and narrow, which branch like a tree. The papillae are covered with follicular epithelium. The basis of the papillae is connective tissue with the presence of a blood capillary. Hyperplastic processes in the thyroid gland are also manifested by the formation of new follicles. Proliferation of extrafollicular epithelium with the formation of epithelial islands between the follicles was detected. From these cells, new small follicles are formed with subsequent accumulation of colloid. Newly formed follicles are pressed into the lumen of the "old" follicles and form cushion-like protrusions (Sanderson's pads). Sanderson's pads are covered with tall prismatic epithelium. With diffuse toxic goiter, metaplasia of the cuboidal

epithelium of the follicles occurs into the prismatic epithelium. The cells of the prismatic epithelium are cylindrical in shape, the nucleus is round, the cytoplasm is light granular. Metaplasia of follicular cells into B cells (Ashkinasi cells) is observed. These cells are large with eosinophilic granular cytoplasm. The follicles are surrounded by a wide network of capillaries. The colloid is liquid, weakly eosinophilic, vacuolated. In the stroma of the gland, focal lymphocytic infiltrates are detected with the formation of lymphoid follicles. Thus, a histological examination of the thyroid glands in diffuse toxic goiter revealed the following signs: hyperplasia of the gland lobules, proliferation of follicular and extrafollicular epithelium, metaplasia of the cuboidal epithelium of the follicles into prismatic or oxyphilic (Ashkinazi cells), vacuolization and liquefaction of the colloid. The presence of lymphoid infiltrates or lymphoid follicles. The immunohistochemical study used the Ki-67 biomarker. It is a marker of proliferation at all stages of mitosis. Positive expression with brown staining of the nuclei is detected. The Ki-67 proliferation index in the control group was up to 10%; 10-15% (I degree of proliferation). In the experimental group, the Ki-67 proliferation index was 15-20% (II degree of proliferation), the proliferation index was 20-35% (III degree of proliferation). In our material, grade III proliferation was detected in 87% of cases, which indicates the presence of grade III dysplasia, which is a precancerous condition. In 10% of cases, the proliferation index was 15-20% (grade II), which indicates a possible recurrence of goiter in the long-term postoperative period. In 3% of cases, the Ki-67 proliferation index was 10-15% (I degree of proliferation). The P53 protein is involved in one of the main signaling pathways regulating programmed cell death - apoptosis. Positive brown staining of the nuclei is noted. Yellow or pale brown staining of nuclei with the P53 biomarker indicates weak expression of the P-53 protein and amounts to 15-20% (control 6-8%). Dark brown staining of cell nuclei indicates moderate expression of the P53 protein (20-25%). More intense brown staining of the nuclei indicates a high degree of protein expression (25-30%). In 73% of cases, a high degree of expression of the P53 protein was detected, which indicates increased apoptosis. Moderate expression of the P53 protein was observed in 18% of cases, weak expression was observed in 1-9% of cases. Thus, in diffuse toxic goiter, 87% of cases show a high degree of epithelial proliferation (Ki-67 35%), and in 73% of cases high expression of the P53 protein (30%) was detected. The results of an immunohistochemical study revealed a high degree of expression of the Ki-67 protein and P53 protein in diffuse toxic goiter. Summary. Analysis of the results of the study showed that diffuse toxic goiter has certain histological signs: hyperplasia of the thyroid lobules, proliferation of follicular and extrafollicular epithelium with the formation of follicular structures and Sanderson's pads. The transition of the cuboidal epithelium of the follicles to the prismatic one, metaplasia of A-cells into B-cells (Ashkinazi cells), liquefaction and vacuolization of the colloid, the formation of lymphocytic infiltrates and lymphoid follicles. Immunohistochemical studies can reliably determine the degree of proliferative activity of cells, predict the risk of goiter relapse, and identify the presence of dysplasia in the thyroid gland.

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