

# Diffuse Toxic Goiter: Features of Surgical Treatment Morphology

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**Abstract** In the course of the study, upon repeated examination of 363 patients hospitalized for rehabilitation, conclusions were obtained on the results of postoperative complications and postoperative morphological data. The reflection of autoimmune aggression in the tissues of the thyroid gland and the spread of lymphoid infiltration were taken into account. One of the reasons for the increase of postoperative hypothyroidism in patients with diffuse toxic goiter was autoimmune processes in the thyroid gland. The degree of manifestation of the thyroid gland lymphoid infiltration was estimated by histological sections in the form of visual half-enlargements, in which individual and small amounts of lymphoid elements were observed. In some samples of preparations, lymphoid follicles of insignificant, and in some impressive sizes were revealed. The formation of branched cell papillae and the abundance of stromal components were also important factors for the development of long-term autoimmune thyroiditis and recurrence of diffuse toxic goiter. When treating patients with diffuse toxic goiter, it was found that the recurrence after subtotal thyroidectomy and the incidence of postoperative hypothyroidism depended on the weight of the remaining gland and its morphological structure. It was found that the recurrence of diffuse toxic goiter and postoperative hypothyroidism in patients did not depend on gender, age, duration and severity of thyrotoxicosis.

**Keywords** Diffuse toxic goiter, Subtotal subfascial stumectomy, Postoperative morphological examination, Follicles, Hypothyroidism

## 1. Introduction

Morphological changes in the tissue of the thyroid gland in patients with diffuse toxic goiter have great variety. It should be especially noted that the histological picture may have significant differences corresponding to the clinical picture of the disease [1]. Distinctive morphological signs of toxic goiter are hyperplastic processes of the thyroid epithelium with transformation of the epithelium and dystrophy of the stroma [2-4]. It is generally accepted to distinguish several variants of the thyroid gland structure depending on the prevalence of various proliferative processes [5-6]. At the colloidal variant the processes of increased proliferation of the thyroid epithelium with the formation of papillary outgrowths prevail.

According to Aristarkhov V.G. et al. (2011), morphological changes in thyroid tissue may correlate with the severity of thyrotoxicosis. So, at a mild severity in micropreparations, the authors revealed moderately pronounced processes of epithelial proliferation with the formation of papillae and follicles of medium size. Pronounced proliferation of the epithelium, papillae, follicles of irregular shape and different sizes, liquid colloid

were typical for moderate and severe forms of the disease.

According to a number of authors, lymphoid and plasmacytic infiltration of the thyroid gland may directly depend on the titer of antithyroid thyroid peroxidase [7-9].

Obviously, the results of researches devoted to the study of morphological changes in the thyroid gland in toxic forms of goiter differ in the diversity of the presented data, although they have much in common. Meanwhile, according to Shin, M.K. (2014), the choice of surgical treatment method of patients with diffuse toxic goiter often depends on the morphological changes in the thyroid gland.

Thus, there is no convincing evidence that the nature and degree of changes in the thyroid gland directly depend on the level of its autoimmune stimulation. At the same time, an incorrect interpretation of the pathomorphological processes occurring in the organ can lead to the development of the disease relapse.

Postoperative hypothyroidism is more common in patients operated on due to diffuse-toxic goiter. Conducted morphological studies indicated a decrease in the amount of epithelial tissue and an increase in the amount of extrafollicular and stromal components. This showed that the age of the patient with a relapse of the disease, the duration of the disease, the intake of thyreostatics, the size of the thyroid gland and the state of the morphological structures of the thyroid gland play an important role.

**Aim** of the research was to study the morphological prognosis of surgical treatment results of diffuse toxic goiter.

## 2. Material and Methods

We analyzed the surgical treatment results of 363 patients with diffuse toxic goiter at the third Surgical Department of the Clinic of Andijan State Medical Institute for the period from 2015 to 2019. In 258 of them a surgery to improve the subtotal subfascial resection of the thyroid gland according to the method of our clinic - with leaving the tissue of the thyroid stump up to 2 g (group I) - was performed. 85 patients were performed subtotal subfascial strumectomy with intraoperative autotransplantation of thyroid tissue with leaving the tissue of the thyroid stump from 0.5 to 1 g and with autotransplantation from 1.5 to 2 g (group II). There were 305 females (88.9%) and 38 (11.1%) males among 343 operated patients. The ratio between men and women was 1: 9. The mean age of the patients made up  $38.6 \pm 12.4$  years. The remaining 20 patients refused surgery and were treated conservatively. Statistical processing was carried out using computer programs of the Microsoft Excel software package.

## 3. Results

The study used the conclusions on the results of postoperative complications and postoperative morphological data of 363 patients who admitted for rehabilitation.

The identified complications after surgery due to diffuse toxic goiter of non-malignant forms in 343 patients were as follows:

From 85 patients who underwent subtotal subfascial strumectomy with intraoperative autotransplantation of thyroid tissue, 20 (23.5%) were diagnosed with hypothyroidism, 6 (7.0%) had a relapse and 59 (69.5%) had a euthyroid state.

From 258 patients who underwent surgery to improve the subtotal subfascial resection of the thyroid gland according to the method of the clinic, 49 (19.0%) were diagnosed with hypothyroidism, 4 (1.5%) - a relapse and 205 (79.5%) - euthyroid state.

The micropreparations in those patients, indicated in the histological examination, were estimated by six parameters, taking into account the classification according to the book "Pathological Anatomy" by A.I. Strukov. (2010), long-term results (5-year) of the thyroid function state were taken into account. The conclusions of postoperative morphological results and late complications in patients underwent surgery due to diffuse toxic goiter are presented in Table 1.

**Table 1.** Long-term predictions of morphological outcomes after surgery

Morphological structure	Total patients
Transition of follicular epithelium from prismatic bodies to cylindrical bodies	76
Formation of branched spurs during proliferation of the follicle inner epithelium	48
Changes and vacuolization of tinctorial properties due to the multiplication of colloid to unsaturation of iodine	150
Lymphoplasmacytic infiltration of the stroma, the formation of lymphatic follicles in the newly formed center	32
Hemorrhage	23
Transformation	14
Total	343
Connective tissue growth	6
Adenoma	12
Cancer, papillary carcinoma	2
Total	20

According to the authors opinion, during the proliferation of the epithelium of the thyroid gland tissues, the formation of branched spurs and the abundance of stromal components are also important factors in the development of long-term autoimmune thyroiditis and the recurrence of diffuse toxic goiter. The postoperative morphological structure of the thyroid gland in patients with diffuse toxic goiter and the outcomes of complications in the future are presented in Table 2.

Thus, on the basis of the future results of diffuse-toxic goiter surgical treatment, it was found that the morphological structure of the thyroid gland left after the surgery was the most important factor in the future.

First of all, the state of functional activity of the existing parenchyma was clarified.

The appearance of the follicular epithelium was carefully observed, since the restoration of the shape of the thyroid tissue depended on the abandonment of the epithelial stump. However, the small height of the follicular epithelium led to the manifestation of moderate severity of fibrosis, as well as to some follicles of the cubic and cylindrical shape of the epithelium which led to stromal dystrophy and sclerosis.

Symptoms such as mildly moderate severity and a clear manifestation of a single papillary proliferation were noted in the morphological structure of the thyroid gland in patients with diffuse toxic goiter.

The presence of large and medium-sized follicles, as well as the presence of a colloid in a dense and semi-liquid state led to the formation of follicular epithelium of various heights filled with a liquid colloid. The presence of medium-sized follicles or the presence of small follicles and sometimes improper differentiation led to the formation of voids in liquid colloids.

**Table 2.** The postoperative morphological structure of the thyroid gland in patients with diffuse toxic goiter and the outcomes of complications in the future

Complication	Subtotal subfacies stumectomy and intraoperative thyroid autotransplantation			Clinical method of subtotal subfascial resection of the thyroid gland			Total patients
	Hypothyroidism	Relapse	Euthyroidism	Hypothyroidism	Relapse	Euthyroidism	
Morphological structure							
Transition of follicular epithelium from prismatic bodies to cylindrical bodies	–	–	7	4	–	65	76
Formation of branched spurs during proliferation of the follicle inner epithelium	5	3	9	3	1	27	48
Changes and vacuolization of tinctorial properties due to the multiplication of colloid to unsaturation of iodine	10	–	38	24	1	77	150
Lymphoplasmacytic infiltration of the stroma, the formation of lymphatic follicles in the newly formed center	2	3	1	8	2	16	32
Hemorrhage	1	–	2	7	–	13	23
Transformation	2	–	2	3	–	7	14
Total	20	6	59	49	4	205	343
Connective tissue growth	–	–	2	–	–	4	6
Adenoma	2	–	5	–	–	5	12
Cancer, papillary carcinoma	–	–	1	–	1	–	2
Total	2	–	8	–	1	9	20

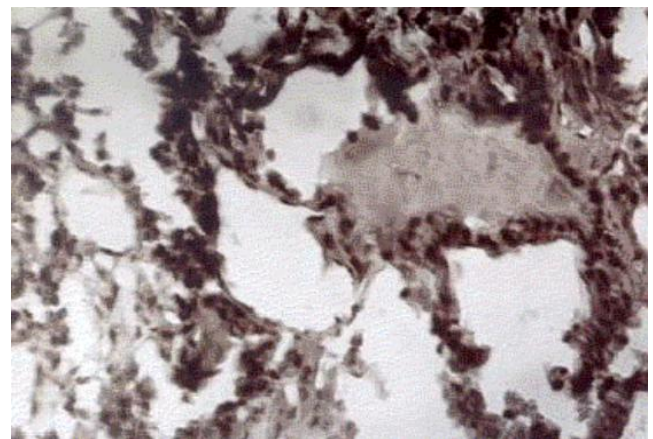
The reflection of autoimmune aggression in the tissues of the thyroid gland and the spread of lymphoid infiltration were taken into account. One of the reasons for the increase in postoperative hypothyroidism in patients with diffuse toxic goiter was the autoimmune processes in the thyroid gland. The higher the degree of autoimmune processes, the more significant is the development of hypothyroidism. The degree of manifestation of lymphoid infiltration of the thyroid gland was estimated in histological sections with optical magnification which were determined by a small number of lymphoid elements. In other preparations follicles were found in some areas of the accumulation of lymphoid elements. Otherwise, lymphoid follicles were visible in the focus of each area.

The severity of lymphoid infiltration of the thyroid gland was assessed in histological sections in the zone of optical magnifications.

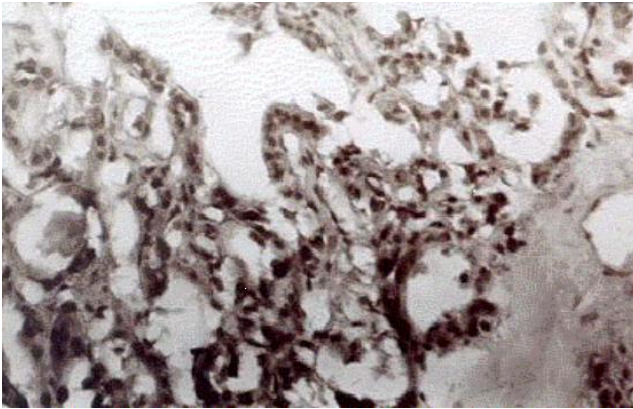
The analysis shows the importance of the functional activity of the morphological structures of the thyroid gland in the development of the disease in the future. Examples of these screening methods include postoperative histology of patients. The studied morphological samples of the structures of the thyroid gland of our patients are presented below:

*Patient M.C., 1963, (History case № 2573-80).* The follicles are different, irregular and large in size. The inner surface of the alveoli is uneven, there are tumor-like nipples in some of them. The appearance of the nucleus is in the form of an oval or circle, with a hyperchromic shade. The number

of colloids decreases sharply; in some places the follicles are saturated reddish in the form of a fusion of several follicles. Epithelium in some places is desquamated with observation in the stroma of edema with the presence of focal lymphoid infiltration and sclerosis (Figure 1).

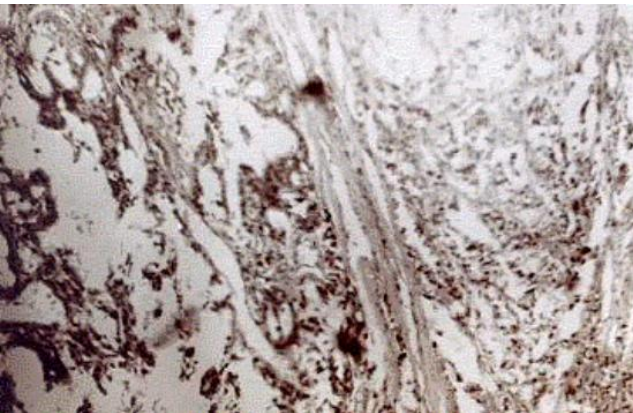
**Figure 1.** Magnification – 7 x 20

*Patient E.T., 1964, (History case № 369-374).* Follicles of varying degrees, shapes and sizes were noted. The inner surface of the alveoli is uneven. The nuclei are oval or round in shape. In some follicles, the number of colloids is sharply reduced, and in some places it is deep reddish or in the form of combinations of several follicles. Epithelium in some places is desquamated. Edema with focal lymphoid infiltration is observed in the stroma (Figure 2).

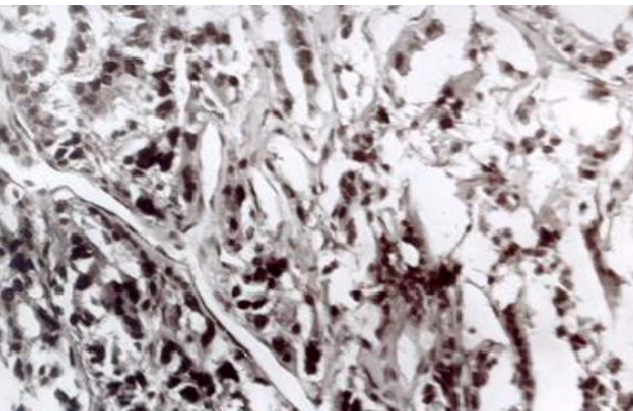


**Figure 2.** Magnification – 7 x 20

*Patient I.M., 1981, (History case №2534-2541).* Follicles are of different sizes, irregular shape, with a predominance of smaller follicles. Instead of connective tissue, glandular elements were formed in some places. The inner surface of the alveoli is uneven, there are tumor-like nipples in some places. There are oval-shaped nuclei with mitosis. The amount of colloid is drastically reduced. Some follicles look like a saturated colloid and some look like a thread. Swelling with full blood flow with focal infiltration was observed in the stroma (Figure 3).



**Figure 3.** Magnification – 7 x 8



**Figure 4.** Magnification – 7 x 20

*Patient Kh.A., 1959, (History case №1183-1188).* Follicles are of different sizes, irregular shape; in some

places the glandular elements have a small oval shape; the inner surface of the alveoli is uneven; there are swollen nipples in some of them. The nuclei are enlarged, hyperchromatic, mitoses were observed in some of them. The amount of colloid is sharply reduced, in some places a visible thread remains, the epithelium is desquamated. There is edema in the stroma with focal lymphoid infiltrates (Figure 4).

## 4. Discussion

Microscopic examination of the thyroid tissue revealed diffuse toxic goiter and the development of autoimmune thyroiditis against its background. The classical histological appearance of diffuse toxic goiter is as follows: signs of autoimmune thyroiditis were revealed against the background of diffuse-toxic goiter (and lymphoid infiltration, stromal edema, proliferation of new follicles were reflected in some of them). The progression of diffuse-toxic goiter was observed in other preparations: with the presence of squamous cell tumor-like icicle in colloids at the apex of the columnar epithelium, irregular stellate follicles, as well as cubic and cylindrical follicles, stromal dystrophy and sclerosis.

In patients with diffuse-toxic goiter we found the following: the size of those follicles was significantly reduced, the Brown's index was also reduced and the size of the nuclei and the height of thyrocytes were increased. Extrafollicular epithelium, nuclear, cytoplasmic and stromal-parenchymal relationships were violated.

In addition, according to a number of authors, the presence of epithelium and stromal components in the glandular tissue is an important factor in the recurrence of diffuse toxic goiter in the future.

## 5. Conclusions

In all 363 patients who were performed resection of the thyroid gland, morphological studies revealed factors leading to recurrence of diffuse toxic goiter and postoperative hypothyroidism: the presence of interfollicular and extrafollicular epithelium of the stromal components, moderate proliferation papillae with lymphoid infiltration. The formation of branched cell papillae and the abundance of stromal components are also important factors in the development of long-term autoimmune thyroiditis and recurrence of diffuse toxic goiter. Morphological changes in thyroid tissue directly depended on the level of autoimmune stimulation of the thyroid gland. At a low level of autoimmune stimulation of the thyroid gland, proliferative changes were not pronounced, the processes of sclerosis and replacement of the thyroid epithelium prevailed. Proliferative and hyperplastic processes prevailed at an increased level of autoimmune stimulation of the thyroid gland. Autoimmune processes were formed in the form of

visual semi-enlargements of the lymphoid infiltration of the thyroid gland. It was found that the recurrence of diffuse toxic goiter after subtotal thyroidectomy and the incidence of postoperative hypothyroidism depended on the weight of the remaining gland and its morphological structure. It was found that the recurrence of diffuse-toxic goiter and postoperative hypothyroidism did not depend on the sex, age, duration of the disease and the severity of thyrotoxicosis of the patient.

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