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Modern Aspects of Morphological Features of the Thyroid Gland in Autoimmune Thyroiditis

Khaidarova Nargiza Akhtamovna
Bukhara State Medical Institute

Abstract: Chronic autoimmune thyroiditis is an organ-specific autoimmune disease that leads to progressive death of thyroid cells and is the most common cause of primary hypothyroidism. Morphological diagnosis of Hashimoto's thyroiditis presents significant difficulties due to the variability of histological forms. The article provides a review of the literature on structural changes in the thyroid gland in autoimmune thyroiditis.

Key words: autoimmune thyroiditis, thyroid gland, morphology, disease.

Relevance. Autoimmune thyroiditis (AIT) is a chronic inflammatory disease of the thyroid gland (thyroid gland) with an autoimmune mechanism of development, in which, as a result of long-term progressive lymphoid infiltration, long-term destruction of the thyroid parenchyma occurs with a possible outcome in primary hypothyroidism. The incidence of AIT is currently increasing, which is associated with uncontrolled iodine consumption and is estimated to be 10-15 times more common in middle-aged women aged 30-50 years. AIT occurs in 3-5% of the population [1]. The frequency of manifest forms of the disease is 1% [2]. Women suffer from AIT 4-8 times more often than men [3]. This difference is associated with the presence of a second X chromosome and the hormonal characteristics of women [4]. More often, the disease is detected in women after 60 years of age—the frequency in the population is 6-11% [5].

Morphological diagnosis of Hashimoto's thyroiditis presents significant difficulties due to the variability of histological forms. The thyroid gland in AIT has the following macroscopic structure: it is dense, lumpy, and on section the gland tissue is unevenly lobulated and cream-colored. The lobules are surrounded by dense whitish cords. The gland is often fused with surrounding tissues. Depending on the form of the disease, the mass of the gland varies. Thus, in the hypertrophic form of AIT, the mass of the thyroid gland can reach 250 grams, while in the atrophic form it is about 15 grams [2, 9, 11]. There is numerous information in the literature about histological changes in the thyroid gland in Hashimoto's thyroiditis. Classic microscopic signs of this disease: diffuse or focal cellular infiltration, represented mainly by lymphocytes and plasma cells, with the formation of numerous centers of cell division; atrophy of thyroid follicles and proliferation of connective tissue; pronounced oxyphilic cell metaplasia with the loss of follicles from A-cells and the appearance of follicles, layers, clusters of light large B-cells (Ashkenazi cells). In places, B cells form parts of lobules or entire lobules [12,13]. B cells were first described by Ashkenazi in 1998. The question still remains open: whether the presence of oxyphilic cells is a characteristic sign of AIT. According to a number of researchers, B cells are found in unchanged thyroid tissue, but with pathology the number of these cells increases. According to other authors, oxyphilic cells are never found normally. B cells are formed as a result of metaplasia of the thyroid epithelium. There are typical and atypical B cells. Typical B cells are several times larger than ordinary thyrocytes, have an oval shape and oxyphilic granular cytoplasm. The nuclei of these cells are large, centrally located, and often hyperchromic. Atypical B cells are smaller and less eosinophilic, giving the appearance of a transitional form between typical B cells and the thyroid epithelium. When conducting a histochemical study, high activity of succinate dehydrogenase is observed. The use of electron

microscopic research demonstrates the presence of a large number of mitochondria. The high activity of succinate dehydrogenase also distinguishes them from cells of ordinary thyroid epithelium. It is believed that oxyphilic cells have a common source of development with thyrocytes and represent one of the cell populations of the thyroid gland. According to some authors, B cells appear during autoimmune processes as a sign of a compensatory reaction [3, 4, 8, 9, 11]. Normally, the maturation of the thyroid epithelium occurs in the argyrophilic stroma, which ensures the formation of functionally complete thyroid structures. With AIT, the process of sclerosis of the stroma is activated and the maturation of the epithelium occurs under other conditions. Where hyalinization of the reticular stroma precedes the maturation of the thyroid epithelium, the formation of specialized structures is disrupted and stratified squamous epithelium appears [8, 9]. Diffuse lymphoplasmacytic infiltration with the formation of typical lymphatic follicles is a classic sign of AIT. The formation of lymphoid follicles is associated with prolonged antigenic stimulation and the production of antithyroid antibodies by plasma cells. The severity of infiltration is the same both in the stroma and in the parenchyma of the gland. Some researchers believe that T lymphocytes predominate in the infiltrate, while B lymphocytes and plasma cells are represented by single cells. According to other authors, the cellular composition of the infiltrate directly depends on the stage of development of Hashimoto's thyroiditis. The formation of lymphoid follicles occurs in three stages. The first stage is characterized by the absence of clear boundaries and breeding centers. In the second stage, small reproduction centers are formed, which contain a few blast cells (lymphoblasts and plasmablasts). In the third stage, large follicles appear with clear boundaries and centers containing a large number of lymphoblasts and plasma cells. Due to lymphoplasmacytic infiltration, follicle separation occurs. The remaining large lobules contain follicles with morphological signs of increased functional activity, which is a reflection of the activation of compensation mechanisms. In some areas, small follicles are identified, which are lined with either flattened or hypertrophied epithelial cells transformed into B cells [7, 8, 10]. With AIT, morphofunctional changes in the colloid are detected. The disappearance of the colloid and weakening of its staining are observed during the PAS reaction. This phenomenon is recorded near zones of massive lymphoplasmacytic infiltration, which is evidence of a decrease in the functional activity of thyrocytes. In follicles that have degenerative changes, the colloid is thick or absent. They contain desquamated follicular and giant multinucleated cells, which are formed from the follicular epithelium [4, 6, 8]. Characteristic of AIT is diffuse proliferation of connective tissue. Argyrophilic fibers located between the follicles of the thyroid epithelium thicken, collagenize and transform into dense collagen fibers. Later they are replaced by thick collagen fibers. In the interlobular septa, the stroma of the gland becomes fibrotic; phenomena of pronounced disorganization are detected in the form of metachromasia of the main substance, as well as the accumulation of hemosiderin inside and extracellularly. The development of fibrosis is determined by the large-lobed structure of the gland. Fragmentary disintegration of reticular fibers is demonstrative in sections impregnated with Foute's silver nitrate. In areas where stromal disorganization is pronounced, single giant cells and polymorphonuclear leukocytes are found. Vascular disorders are characterized by the development of plethora, stasis, erythro- and leukodiapedesis, the presence of perivascular hemorrhages, plasma impregnation, metachromasia, and sclerosis of the vascular wall. As a result of Hashimoto's thyroiditis, powerful fibrous cords form, which separate the lobules of the gland into small areas of fibrous hyalinized connective tissue. In these areas, single plasma cells and small lymphoid infiltrates are detected [7, 8, 12]. Many researchers consider focal thyroiditis as a special form of AIT. With this pathology, local lymphoplasmacytic infiltration is observed, occupying small areas of gland tissue (about 25%). In these areas there are lymphoid infiltrates and lymphoid follicles that have reproduction centers that merge with each other. However, even large lesions consisting of clusters of lymphoid follicles do not occupy more than one lobe of the gland. With focal thyroiditis, plasmacytic

infiltration is observed, but it is less pronounced than with Hashimoto's thyroiditis. The development of fibrous tissue in this form of thyroiditis was not noted. Scientific opinions differ regarding the metaplasia of thyroid epithelium to B cells. Some researchers believe that in the area of lymphoplasmacytic infiltration, the thyroid epithelium consists of B cells, while other authors argue that with focal thyroiditis, oncocytic cell transformation does not occur. Focal thyroiditis is determined either in an unchanged gland, or against the background of diffuse or nodular goiter, adenoma, cancer, lympho- and reticulosarcoma. In nodular goiter, infiltrates are located both in the tissue of the nodes themselves and beyond in the surrounding thyroid tissue [9, 11]. The atrophic form of AIT is characterized by a decrease in the mass of the gland, the replacement of a significant part of its parenchyma with hyalinized connective tissue containing lymphoid elements with an admixture of plasma cells. The lobules are reduced in size, the follicles are small, the follicular epithelium is flattened. In surviving follicles, transformation of thyrocytes into Ashkenazi cells or squamous metaplasia is detected. B cells line the follicles or form solid structures. There is diffuse plasma cell infiltration of the stroma and focal lymphocytic infiltration with the formation of lymphatic follicles. According to a number of researchers, with this form of AIT, morphofunctional changes are detected in the form of phenomena of deformation, destruction, collapsing, atrophy of follicles, fiber disintegration and destruction of basement membranes. The absence of colloid in the follicles is characteristic [2, 3, 4, 5]. Thus, the classic histological signs of AIT include: diffuse or focal cellular infiltration, which is predominantly represented by lymphocytes and plasma cells with the formation of lymphoid follicles; oxyphilic cell metaplasia of the thyroid epithelium with the loss of typical follicles of A cells and the appearance of follicles, clusters of B cells (Ashkenazi cells); proliferation of fibrous tissue of varying degrees [12]. Diagnosis of many thyroid diseases includes the study of argyrophilic proteins in the area of nucleolar organizers. The number of granules in the thyroid epithelium demonstrates its proliferative activity. In AIT, examination of the nucleolar region in material stained with silver nitrate showed an increase in the number of granules (on average 3-4 granules per nucleus), while in normal thyroid epithelium about 2 granules are detected. This is evidence of a moderate increase in proliferative activity resulting from autoimmune damage to the thyroid epithelium. A moderate increase in granules in the region of nucleolar organizers is also observed in other thyroid diseases - colloid goiter, adenomatous goiter, Graves' disease, and therefore the use of this method as a differential diagnostic method is limited [1, 3, 6]. Currently used preoperative methods for morphological examination of the thyroid gland include puncture biopsy and trepanobiopsy. However, each of these methods has its drawbacks. Thus, in the diffuse form of AIT, it is not recommended to perform a puncture biopsy for diagnostic purposes, since interpretation of the cytological picture is difficult. This is due, first of all, to the scarcity of cellular material obtained during the study. In addition, certain skills are required both for analyzing the cytogram and for collecting material. According to a number of researchers, it is more justified to perform trepanobiopsy of the thyroid gland, since this method allows one to obtain more informative material. But the undoubted advantage of fine-needle puncture biopsy can be considered the perfect safety of the method and the possibility of repeated research. A puncture biopsy is quite informative for nodular formations, and therefore, this diagnostic method is recommended when combining AIT with thyroid nodules. The morphological sign of the autoimmune process is lymphoid infiltration of the gland stroma. These infiltrates are represented by lymphocytes, single plasma cells and macrophages. Combinations of lymphoid cells of varying degrees of maturity are identified (light blast elements mark reproduction centers), plasmacytes. The presence of a “motley” chronic lymphoid infiltrate is characteristic: macrophages, histiocytes, and less commonly neutrophils. Ashkenazi cells, single cells of follicular epithelium, felt-like structures, elements of fibrous tissue are detected [1, 2, 4, 7]. Lymphocytic infiltrates in the background and within clusters of thyrocytes, the presence of altered Hurthle cells are

pathognomonic signs of AIT. In the presence of a combination of a large amount of colloid, anisonucleosis and numerous Hürthl-Ashkenazi cells on cytological smears, the diagnosis should be interpreted carefully in order to reduce the risk of diagnostic errors and not to miss other thyroid diseases.

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