AUTOIMMUNE THYROID DISEASES: THE STATE OF THE ISSUE

Kodirova Nargizakhon Umarovna
Assistant of department Propaedeutics of internal diseases of Bukhara Medical Institute
giza5552@gmail.com
https://doi.org/10.5281/zenodo.7810278

Annotation
The article is devoted to autoimmune diseases of the thyroid gland: the state of the problem. new approaches to the treatment and management of patients with autoimmune thyroid diseases

Key words: thyroid gland, antibodies, autoimmune diseases, ultrasonography of a thyroid gland, Hashimoto thyroiditis, diabetis mellitus

Thyroid pathology is the most common in the structure of endocrine diseases. It is likely that this trend will continue in subsequent years, since over the past decade there has been a steady increase in the prevalence of thyroid diseases (TD) [1].

The classic organ-specific autoimmune diseases include diffuse toxic goiter (DTG) and autoimmune thyroiditis (AIT) [13]. Immunological disturbances occur in other 1_CG diseases (eg, subacute thyroiditis, nontoxic nodular goiter, and papillary cancer), but in these cases they are secondary. In 1990, R. Wolpe proposed a classification of thyroid diseases with immunological manifestations.

Autoimmune diseases (AID) of the thyroid gland: 1) autoimmune hyperthyroidism (Graves' disease, Graves' disease); 2) AIT: Hashimoto's thyroiditis (lymphomatous struma); fibrous variant; lymphocytic thyroiditis in childhood and adolescence; postpartum "silent" thyroiditis; at least some cases of "silent" thyroiditis; asymptomatic, or "minimal", AIT.Non-immune diseases of the thyroid gland with secondary immune reactions: subacute thyroiditis (De Quervain); papillary thyroid cancer; nodular goiter.

Since the early 1980s, AIT has been diagnosed much more frequently than before. It affects approximately 3-4% of the population. A clear increase in the prevalence of AIT in recent years may partly be a consequence of improved methods of its diagnosis and greater alertness of doctors, but it may also reflect a real increase in its prevalence due to greater iodine consumption [4]. Graves' disease occurs in about 1% of people [26].

Despite the fact that the clinical picture of DTG was first described by Perry in 1825, and AIT-Hashimoto in 1912, interest in these diseases does not weaken. Moreover, in the light of the current environmental situation, which contributes to rapid growth 112], they have become even more important.

It is known that thyroid AIDs are often associated with type 1 diabetes mellitus (DM1), but whether this is the result of specific genetic changes is still unclear.

I. Djilali-Saiah et al. [22| confirm the special role of class II major histocompatibility complex genes in the pathogenesis of thyroid AID in patients with DM1 and suggest that some alleles contribute to the rapid progression of DM in genetically predisposed individuals.

Genetic markers of AID thyroid and T1DM

One of the important discoveries of medicine of the 20th century is the human major histocompatibility complex system HLA. This name Human Leucocyte Antigens (a system of leukocyte antigens) is given due to the fact that HLA antigens are quite fully represented on human peripheral blood leukocytes. The main human histocompatibility complex is located on the short arm of chromosome 6. HLA genes are divided into 4 classes: Class I includes the genes of the A, B, C loci; class II - D-region (D-, DR-, DQ-, DP-subloci); Class III - polymorphic genes that control the synthesis of complement components (C2, C4A, C4B), properdin factor (BT), etc.; Class IV - genes, the relationship of which with HLA is only assumed. The major histocompatibility complex is involved in the implementation of important biological phenomena: it regulates the level and synthesis of steroid hormones, the proteins encoded by it carry out the genetic control of the immune response, HLA antigens are involved in intercellular interaction, control complement activity, and determine the body's resistance and susceptibility to a number of diseases. Currently, it is believed that any disease occurs as a result of the interaction of environmental and genetic factors. Impairments in the immunoregulatory system leading to the development of thyroid AID in combination with T1DM have genetic causes and are associated with environmental influences.

Susceptibility to more than 40 diseases with an autoimmune component in their pathogenesis is associated with HLA-A2, B8, DR3 [9]. These diseases are divided into several groups. The group of organ-specific diseases includes DTG, AIT, etc., and the group of T-cell-mediated diseases includes DM1.

It has been established that histocompatibility antigens are responsible not only for the predisposition to the development of diseases, but also for the timing of occurrence, the nature of the course and the outcome of the pathological process.

To date, numerous data have been obtained on the association of HLA genes with thyroid AID and DM1.

Back in 1976, A. Sveigaard and Z. Ryder proposed a hypothesis to explain the relationship between the HLA system and endocrine diseases, according to which individual HLA molecules are structurally similar to hormones and therefore can compete in the process of physiological interaction with hormone receptors. At the same time, of course, hormones have a significantly higher degree of affinity for specific receptors, and not for HLA alleles. However, receptors are located on target cells, and HLA antigens are present on all cells of the body. This contributes under certain conditions to the pathological binding of hormones to HLA and the development of endocrine disorders.

On the other hand, HLA genes encode the features of immuneabout the response and can determine the predisposition to the occurrence of autoimmune disorders, which also play a significant role in the occurrence of the pathology of the endocrine system.

Immunogenetic factors are important in the development of thyroid pathology. Associations of thyroid AID with HLA-B8, DR3, DR4 have been noted [40].

Chronic AIT (Hashimoto) is based on the formation of autoantibodies to various components of the thyroid gland, which disrupt the synthesis of thyroid hormones and destroy thyroid cells. In the East Slavic population, antigens A19, B40 and haplotypes A2/B15, A9/B16, A9/B27 are significantly more common in this pathology. This may be of practical importance when examining families where autoimmune thyroiditis occurs in more than two family members, i.e. in family forms.

Genetic studies have revealed an increase in the incidence of DQAl*0501-DQBl*0201-ran-type among patients with AIT compared with patients without AID thyroid [23].In the development of DTG, hereditary factors linked to HLA also play a certain role. DTG (or Graves-Basedow's disease) is characterized by hyperplasia and hyperfunction of the thyroid gland and is caused by stimulation of TSH receptors by antibodies, which are now called thyroid-stimulating antibodies.

Data were obtained on the genetically determined heterogeneity of clinical variants of the course of DTG. In patients with endocrine ophthalmopathy, compared with patients without it, the frequency of occurrence of HLA-B5 was significantly increased [6].AID thyroid and T1DM often occur in the same families. At the same time, their penetrance and manifestation depend on such external factors as stress, infections, injuries, drugs, smoking, radiation, nutrition (including iodine intake), pregnancy and aging, all of which affect the immune system [25].

Among the genes associated with T1DM, HLA on chromosome 6p21 is the genetic factor with the strongest predisposition to this disease.Positive associations of DM1 with such alleles of the HLA system as B8, B15, B18 [3], and especially DR3 and DR4, have been established. Negative associations were found for HLA-B7, B12, DR2.If the genotype contains both DR3- and DR4-ajmeneH, the risk of DM1 disease increases many times over. In the population of Western Europe, the risk of developing DM1 in carriers of DR3, DR4 is increased by 5 times [21].

To explain the fact that not all carriers of DR3 and DR4 have DM1, a hypothesis was proposed back in the early 1980s based on the position that each DR phenotype has many antigenic determinants. German scientists have found that the predisposition to DM1 associated with HLA-DR4 increases significantly in the presence of DQ8 in the haplotype [6]. It was found that predisposition to DM1 is associated with HLA-DQ8 (DQBl*0302/DQAl*0301), and resistance is associated with DQ6 (DQBl*0601/DQAl*0103).

Recent studies have found that there is a generalized hereditary factor that leads to thyroid AID in T1DM patients. Yes, haplotype

HLA DQAl*0301-DQBl*0302 was more common in patients with DM1 with antibodies to thyroid peroxidase - TPO (39%) compared with patients with DM1 without antibodies to TPO (23%). Another haplotype DQA1*O5O1-DQB1*O2O1 in patients with DM1 with antibodies to TPO was less common [19].

Summarizing the above data, we can put forward the following main provisions explaining the relationship of HLA antigens with AID thyroid (DTG and AIT) and DM1.Genetically controlled disorders of the immune response determine the development of autoimmune reactions.A certain role in the occurrence of thyroid AID and DM1 belongs to the ability of HLA antigens to compete with specific receptors for interaction with hormones.

The presence of certain antigenic determinants increases the risk of developing thyroid AID in DM1 patients with the DRBl/DQAl/DQBl haplotype, while DR6 is associated with a weak protective effect against thyroid AID in DM1 patients.

Predisposition to AID thyroid and T1DM is largely due to immunogenetically controlled heterogeneity of cellular and humoral response to GAD

Similarities in the pathogenesis of thyroid AID and DM1

The pathogenesis of AID thyroid and T1DM is due to a partial genetic defect in immunological surveillance, expressed in the fact that forbidden clones of thymus-dependent lymphocytes

directed against the protein substrate (antigen) of the follicular epithelium of the thyroid gland and [3-cells of the pancreas, develop unhindered and enter into an antigen-antibody reaction, causing destruction of the follicular epithelium and islet cells of the pancreas. In healthy people, the reproduction of forbidden T-lymphocyte clones is prevented by the immunological surveillance system in the form of suppressor T-lymphocytes. A genetic defect in T-suppressor lymphocytes, which manifests itself under the influence of environmental factors, leads to the reproduction of a forbidden clone of T-lymphocytes, followed by their contact with antigens of the thyroid gland and islet B cells and the transmission of information to B lymphocytes and plasma cells. The latter produce organ-specific antibodies, which, cooperating with killer T-lymphocytes on the surface of follicular epithelial cells and pancreatic B-cells, have a cytotoxic effect on hormonally active cells, causing their destruction and changes in function.

As mentioned above, in DTG, the genetic defect is realized through a deficiency of T-suppressors. R. Wolpe noted that an inverse relationship was observed between the number of nonspecific T-suppressors and the concentration of triiodothyronines in serum. As a result of the loss of immunological control over the production of prohibited clones of T-lymphocytes, thyroid-stimulating antibodies are synthesized, which belong to the group of immunoglobulins G. Thyroid-stimulating antibodies, acting on and TSH receptors cause hyperproduction of thyroid hormones and an increase in the thyroid gland.

In AIT, due to pathological immune reactions, autoantibodies are produced, such as antibodies to TPO and thyroglobulin, which disrupt the synthesis of thyroid hormones and destroy thyroid follicles.

R. Wolpe in 1997 proposed a hypothesis for the development of thyroid AID, developed on the basis of the clonal selection theory of Burnet (1959). It consists in the following: the disease is caused by a partial defect in immunological surveillance, which is associated with a specific deficiency of suppressor T-lymphocytes. As a result of exposure to provocative external factors, the suppression of T-lymphocytes is weakened to such an extent that they, in the presence of antigen and antigen-presenting cells (for example, monocytes), go out of control and become activated. N. Watanabe et al. [39] showed that dendrites (outgrowths of nerve cells) are the most effective antigen-presenting cells that initiate and regulate the immune response. To investigate the contribution of dendrites to the pathogenesis of thyroid AID, an animal model of experimental AIT induced in mice by thyroglobulin immunization was created. Thyroglobulinimpulse dendrites have also been transferred to mice to stimulate AIT. The severity of AIT was positively correlated with antibodies to thyroglobulin and γ-interferon, indicating that Thl cells are activated by thyroglobulin impulse dendrites and are involved in the pathogenesis of AIT. Activated T-lymphocytes produce γ-interferon and cytokines (ICAM. CD40, etc.), which leads to damage to the thyroid follicles. Helper T-lymphocytes act accordingly on B-lymphocytes, which turn into plasma cells and form antibodies to thyroglobulin and microsomal protein structures of the follicular epithelium. Circulating antibodies, cooperating on the surface of follicular epithelial cells with killer T-lymphocytes, have a cytotoxic effect on hormonally active thyroid cells, causing their destruction, a gradual decrease in their mass and a decrease in thyroid function. In response to the damaging effect of autoaggression, thyroid hyperplasia is observed, maintaining the state of euthyroidism, and sometimes accompanied by signs of hyperfunction. A long process of autoaggression leads to a gradual decrease in the functional activity of the thyroid gland -

progressive hypothyroidism. According to the feedback principle, TSH production by the pituitary gland increases. Ultimately, this leads to the formation of a goiter. The above mechanism refers to the hypertrophic form of AIT 114].

The atrophic form of AIT is associated with the effect of blocking antibodies to the TSH receptor [15]. Autoantibodies to thyroglobulin and TPO circulating in the blood are not able to have a damaging effect until they cooperate with killer T-lymphocytes, which secrete cytotoxic factors that cause cell destruction. This process is called antibody-dependent cell-mediated cytotoxicity. T-lymphocytes sensitized to specific antigens release lymphokines that are involved in the effect of cytotoxicity and can directly damage target cells. Lymphokines include lymphotoxin, chemotaxis factor, MIF factor, tumor necrosis factor, etc. Thus, cellular and humoral components of the immune response are involved in the pathogenesis of AIT.

Ultrasonography

The main echographic sign of thyroid AID is a diffuse decrease in echogenicity. The sensitivity of this sign is 80-85%, which is a convincing argument in favor of the widespread use of ultrasound for the diagnosis of AID thyroid.

Before the introduction of ultrasound, the diagnosis of AIT was extremely difficult. This disease is characterized, as a rule, by an increase in the organ (width and thickness, as well as the expansion of the isthmus). Due to this, the iron acquires a rounded-smoothed appearance. Typical ultrasound findings are varying degrees of decreased echogenicity; diffuse heterogeneity, spreading throughout the gland, from fine-grained to coarse.

In the atrophic form of AIT, ultrasound determines a very small volume of the thyroid gland (less than 3 ml).

It should be noted typical ultrasonic variants of AIT.Diffuse form, when there is an enlarged gland of the usual form with clear contours and ultrasound signs characteristic of AIT.Focal form, when typical ultrasound signs of AIT are located locally.Against the background of AIT, nodes of various echogenicity and structure are determined.Focal and diffuse forms of AIT are manifestations of the same disease, and possibly stages of the same process in the thyroid gland [17].

Ultrasound of the thyroid gland of patients with DTG reveals 2 groups of ultrasound signs: 1) a decrease in echogenicity of a diffuse nature, the degree of which can reach the level of acoustic muscle density; 2) change in the volume of the body. The echograms show swelling of the anterior surfaces of the organ, displacement of the vascular bundle laterally and posteriorly, the esophagus is not visualized, the thickness of the isthmus increases by 2-7 times. DTG is characterized by a uniform increase in all parts of the thyroid gland [18].

References:

1. Algorithms for the diagnosis, prevention and treatment of thyroid diseases / Dedov I. I., Gerasimov G. A., Aleksandrova G. F. et al. - M., 1994.
2. Aleksandrov Yu.K. Puncture methods in the diagnosis and treatment of thyroid diseases. - Yaroslavl, 1996.
3. Balabolkin M. I. Endocrinology. - M., 1989.
4. Diseases of the thyroid gland / Ed. L. I. Braverman. - M., 2000.
5. Bomash N. Yu. Morphological diagnosis of thyroid diseases. - M., 1981.

6. Bondarenko A. L. HLA and diseases. - Kirov, 1999.
7. Bronstein M. E. // Probl. endocrinol. - 1997. - No. 3. - S. 30-37.
8. Gerasimov G. A. // Klin. lab. diag. - 1998. - No. 6. - S. 25-34.
9. Gerasimov G. A., Troshina E. A. // Ibid. - No. 5. - S. 35-41.
10. Goncharov V.P. // Ibid. - 1995. - No. 3. - S. 31.
11. Zefirova G.S. Diseases of the thyroid gland. - M., 1999.
12. Clinical Endocrinology / Ed. N. T. Starkova. - M., 1991.
13. Clinical Guide to Ultrasound Diagnostics / Ed. V. V. Mitkova, M. V. Medvedeva. - M., 1996.
14. Petunina N.A., Gerasimov G.A. // Probl. endocrinol. - No. 4. - S. 30-35.
15. Potemkin VV Endocrinology. - M., 1986.
16. Sviridenko N. Yu., Kryukova I. V., Keda Yu. M. et al. // Probl. endocrinol. - 1998. - No. 1. - S. 21-24.
17. Smetanina 77. I. // Lechash. doctor. - 1998. - No. 2. - S. 18-19.
18. Tsyb A. F., Parshin V. S. et al. Ultrasound diagnosis of thyroid diseases. - M., 1997.
19. Abrams R., De Leeuw I. et al. // Diabetes. Med. - 1996. - Vol. 13, No. 5. - P. 415-419.
20. Chang C. C., Huang C. N., Chuang L. M. // Eur. J. Endocrinol. - 1998. - Vol. 139, No. 1. - P. 44-48. Mironova, E. A. Collection of psychological tests. Part 1, 2002. - 64 p.
21. Kodirova, Nargizakhon Umarovna (2022). MODERN METHODS OF TREATMENT OF CHRONIC LUNG DISEASES. Oriental renaissance: Innovative, educational, natural and social sciences, 2 (Special Issue 4-2), 983-988.
22. Умаровна, К. Н. (2022). Современные Методы Лечения Хронических Заболеваний Легких. Central Asian Journal of Medical and Natural Science, 3(4), 179-182.
23. Kodirova, N. U. . (2022). MORPHOLOGICAL CHANGES OF THE LUNGS UNDER THE EXPOSURE TO NASVAY. EUROPEAN JOURNAL OF MODERN MEDICINE AND PRACTICE, 2(9), 16–20.
24. Kodirova , N. . (2022). THE EFFECT OF TOBACCO SMOKING ON THE THYROID GLAND. Евразийский журнал медицинских и естественных наук, 2(12), 214–216.
25. Jalilovna, K. D., & Umarovna, K. N. (2021). Actual Problems of Internal Diseases (Therapy). CENTRAL ASIAN JOURNAL OF MEDICAL AND NATURAL SCIENCES, 2(6), 456-459.
26. Jalilovna, K. D., & Umarovna, K. N. (2021). In Folk Medicine, New Reforms of the Application of Avicenna Teachings, Suggestions and Analyses. CENTRAL ASIAN JOURNAL OF MEDICAL AND NATURAL SCIENCES, 2(6), 464-467.
27. Khalimova Dilrabo Jalilovna, & Kodirova Nargizakhon Umarovna. (2022). DIAGNOSIS OF ACUTE AND CHRONIC HEART FAILURE. World Bulletin of Public Health, 9, 208-211.
28. Халимова Дильрабо Джалиловна; Кодирова Наргизахан Умаровна. ЛЕЧЕНИЕ АБУ АЛИ ИБН СИНЫ ОТ ТОКСИЧНЫХ ВЕЩЕСТВ В ОРГАНИЗМЕ ЧЕЛОВЕКА. Журнал NX 2022 , 8 , 232-237
29. ХАЛИМОВА , Д. ., УМАРОВА , М. ., & КОДИРОВА , Н. . (2022). ВЛИЯНИЕ ТАБАЧНЫХ ИЗДЕЛИЙ НА НЕРВНУЮ СИСТЕМУ. Eurasian Journal of Academic Research, 2(8), 72–76.
30. ХАЛИМОВА ДИЛРАБО ДЖАЛИЛОВНА, УМАРОВА МАКСФУЗА УСМОНОВНА, КОДИРОВА НАРГИЗАХОН УМАРОВНА. (2022, 29 июля). ПЛОХОЕ ВОЗДЕЙСТВИЕ ТАБАЧНЫХ ИЗДЕЛИЙ НА ОРГАНИЗМ. https://doi.org/10.5281/zenodo.6939407
31. ХАЛИМОВА ДИЛРАБО ДЖАЛИЛОВНА, УМАРОВА МАКСФУЗА УСМОНОВНА, КОДИРОВА НАРГИЗАКСОН УМАРОВНА. (2022). ВЛИЯНИЕ ТАБАЧНЫХ ИЗДЕЛИЙ НА

ВНУТРЕННИЕ ОРГАНЫ ЧЕЛОВЕКА. ПРОБЛЕМЫ И НАУЧНЫЕ РЕШЕНИЯ, Австралия, Мельбурн. https://doi.org/10.5281/zenodo.6941354

32. Jalilovna , K. D., Umarovna, K. N., & Usmanovna , U. M. (2022). The Negative Impact of the Nasvai on the Body of a Teenager. CENTRAL ASIAN JOURNAL OF MEDICAL AND NATURAL SCIENCES, 3(4), 351-355.

33. Xalimova Dilrabo, & Kodirova Nargizakhon. (2022). STANDARDS FOR THE DIAGNOSIS AND TREATMENT OF PATIENTS WITH PATHOLOGY OF THE SPINAL CORD AND SPINE. Innovations in Technology and Science Education, 1(3), 40–46.

34. Xalimova Dilrabo, & Kodirova Nargizakhon. (2022). BACK PAIN: DEVELOPMENT OF ALGORITHMS FOR DIAGNOSIS AND TREATMENT AT THE LEVEL OF PRIMARY HEALTH CARE IN THE REPUBLIC OF UZBEKISTAN. Innovations in Technology and Science Education, 1(3), 33–39.