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Pathology of the Thyroid Gland in Women Rheumatoid Arthritis

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Abstract
Endocrine disorders are of primary importance in the occurrence and progression of rheumatic diseases. Often, endocrine restructuring that occurs during puberty, menopause, pregnancy, childbirth, and abortion serves as a background for the development of connective tissue diseases. At the same time, the change in neuroendocrine status is an integral component of the progression of rheumatic diseases. Especially distinct hormonal shifts were found on the part of the thyroid gland in rheumatoid arthritis (RA). The prevalence of thyroid pathology in general among patients with rheumatoid arthritis, according to literature data, reaches 34%, and Hashimoto's thyroiditis, according to various authors, from 4 to 13.5%. In addition, the greatest susceptibility to RA in women of reproductive age indicates a certain role of sex hormones in the pathogenesis of the disease. Metabolic and degenerative changes in connective tissue largely determine the pathogenesis and clinical picture of various diseases. Rheumatic diseases, the most common of which is rheumatoid arthritis (RA), make up a significant proportion of the pathology of the joints, musculoskeletal system, and connective tissue. It affects 0.5—1% of the world's population, which is about 63 million patients.

Key words: rheumatoid arthritis, autoimmune thyroiditis, hypothyroidism.

Introduction

The effect of the thyroid condition on the course of rheumatoid arthritis is largely mediated by disorders of the immune system. At the same time, changes in the gland itself may be due to the action of factors that cause rheumatoid inflammation. It is possible that one of the causes of dysfunction thyroid is a vascular pathology in RA, as well as the effect of medications taken.

Currently, RA is considered as a chronic systemic inflammatory disease that leads to damage not only to the joints and periarticular tissues, but also to the autonomic and central nervous systems, the endocrine system, with a possible violation of their relationship, which leads to an additional complication of the course of the underlying disease. Patients with RA are exposed to an increased frequency of development of autoimmune pathology of the thyroid gland. The prevalence of thyroid pathology in general among RA patients, according to data, reaches 28%, and Hashimoto's thyroiditis, according to various authors, ranges from 4 to 13.5%. Based on this, it should be noted that the frequency of autoimmune thyroid pathology in RA significantly exceeds the population level (4-13.5 vs.1-6%), therefore, patients with RA should be oriented to dynamic control of the functional state of the thyroid status. Hereditary predisposition plays an important role the role in the development of both RA and thyroid diseases of an autoimmune nature – diffuse toxic goiter and chronic autoimmune thyroiditis. This is confirmed by the detection of identical haplotypes HLA in patients with RA and autoimmune diseases of the thyroid gland. It can be assumed that the genetic predisposition to the occurrence of pathological autoimmune processes determines the possibility of the development of various cross-syndromes and combinations of systemic and organ -specific autoimmune diseases in the same patient, which is considered a characteristic feature of this pathology. Normal hormonal status is a necessary factor in the normal functioning of the immune system. In RA patients, a close correlation between the TSH content and the indicators of the immune system, the number of B lymphocytes, the concentration of immunoglobulins and a close feedback with the T immune system was revealed. Inverse correlations have been established between the level of T3, T4 and the state of the immune system. In RA, the anterior pituitary lobe is activated against the background of a decrease in the activity of

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the peripheral endocrine glands. A similar type of function the development of the endocrine and immune systems is characteristic of chronic stress.
There is quite little information in the available literature about the processes of antibody formation to thyroid hormones in rheumatic diseases. Therefore, assuming that the determination of antibodies directly to thyroid hormones can be a test for the diagnosis of autoimmune thyroid damage, it became necessary to study the possibility of their determination, as well as their role and effect on thyroid function in RA patients.

Purpose Of The Study: The purpose of this work is to study the functional activity of the thyroid gland in RA and to identify the features of antibody genesis to T3 and T4 in RA patients, depending on the activity and systemic manifestations of the underlying disease.

Materials And Methods
75 RA patients (61 (81.4%) women and 14 (18.6%) men) aged 25-78 years who were on inpatient treatment at the Clinical Samarkand were examined. Of these, 35 (46.6%) women and 11 (14.6%) men belonged to the socially active population, i.e. they were in the age groups up to 55 and 60 years, respectively. Thus, a significant (45 (60%)) some of the RA patients) belonged to the working age. The average age of patients was 54.1 ± 11.6 years. The average duration of the disease is 9.47 ± 8.83 years. The control group consisted of 30 practically healthy donors of the regional blood transfusion station aged from 24 to 56 years (22 women and 11 men) who have passed a preliminary medical examination. The diagnosis of RA was made on the basis of a thorough clinical, laboratory and instrumental examination of patients in accordance with the working classification and nomenclature of rheumatic diseases recommended by the III All-Union Congress of Rheumatologists, and according to the diagnostic criteria system of the American Rheumatology Association (1987). The activity of the rheumatic process was evaluated on the basis of clinical data, immunobiochemical indicators and the DAS 28 index (Disease Activity Score).
During the observation, the following were carried out: collection of complaints and anamnesis, examination, physical examination and a set of general laboratory tests, performed immunological tests. The ELISA method was used to determine the amount of TSH, free T4 (sv. T4), total T3 ("Alkor-Bio", St. Petersburg) and free T3 (sv. T3) (CJSC "HVO Immunotech", Moscow), antibodies to TPO and TG (LLC "HEMA-MEDICA", Moscow). According to the indications, instrumental studies were performed: ECG, chest and joint radiography, ultrasound of the heart, abdominal organs and thyroid. The study was conducted in accordance with the principles of the Helsinki Declaration of the International Medical Association and recommendations on the ethics of biomedical research.
The articular form of RA was observed in 45 (60%) people, and 23 (51%) of them had a polysemic form of the disease. Systemic manifestations of RA were noted in 30 (40%) patients. Among RA patients, signs of thyroid pathology were found in 11 (14.6%) cases. Of these, diffuse toxic goiter (DTZ) with thyrotoxicosis was observed in 4 people, primary hypothyroidism (increased TSH level) - in 2, increased level of antibodies to TPO and TG — in 5 patients. When determining the content of antibodies to T3 (anti-T3) and T4 (anti-T4) in blood serum by solid-phase ELISA, immobilized granular antigenic preparations with magnetic properties were used in modification to obtain soluble forms of hormones T3 and T4 (from the preparations "Berlin-Chemie", Germany). The results were expressed in units of optical density (units of optical area) and were considered positive when the extinction values of the control group exceeded by more than 2st.
The obtained data were analyzed using the statistical program "Statistica 6.0"
(StatSoft, USA). The data are presented in the form of mean (M) and standard deviation (st), median (Me) and 25% and 75% percentiles were also calculated if the distribution of the indicator was different from normal. Statistical analysis was carried out using a test for qualitative data, /-Student's criterion and criterion Manna—Whitney. The Spearman correlation coefficient was used to assess the relationship between quantitative characteristics. The critical level of significance of the differences was assumed to be 0.05.

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Results

According to the obtained data for determining the amount of antibodies to thyroid hormones T3 and T4, it was found that most patients with RA had an increased titer compared to the control group: anti-T3 — 0.143 ± 0.03 units of opt. pl (in healthy individuals 0.028 ± 0.008 units of opt. pl.) (Fig. 1) and anti-T4 — 0.146 ± 0.05 units of opt. pl. (in healthy individuals 0.034 ± 0.008 units of opt. pl.). A sufficiently high frequency of detection of anti-T3 (39%) and anti-T4 ((45%) in RA patients prompted us to conduct a detailed study of the processes of autoantibody formation to thyroid hormones, depending on activity and form of WORK. The activity of the pathological process in RA was assessed on the basis of clinical data, immunobiochemical parameters, as well as the combined Disease Activity index Score — DAS 28, recommended by the American Association of Rheumatologists for use in conducting research and clinical trials in RA patients (1987). The values of the DAS28 index, which are 3.2 or less, correspond to I degree of RA activity was detected in 20 (26.7%) people, DAS28 over 3.2 to 5.1 (II degree of activity) - in 42 (41.3%) and DAS 28 over 5.1 (III degree) — in 23 (32%) patients.

With an increase in the activity of the pathological process, there was an increase in sv. T4 and a decrease in sv. T3 in the blood serum of RA patients, i.e. a picture of an imbalance of thyroid hormones was observed. Us there was a significant correlation between the level of St. T4 and the activity of RA (g, = 0.26, p = 0.029) and an inverse correlation between the amount of St. T3 and the activity of the pathological process in rheumatoid arthritis and was (g, = 0.25, p = 0.03). The content of anti-T4 and anti-T3 in patients with RA was significantly higher than in the group of healthy individuals ($p < 0.001$), and progressed with an increase in the degree of disease activity: the correlation coefficient of anti-T4 levels with the activity of the pathological process g, was 0.32 (p = 0.023), and for anti-T3 and RA activity g3 = 0.24 (p = 0.049). With high RA activity, concentrations of free thyroxine were higher than similar indicators with minimal and moderate disease activity, and concentrations of free triiodothyronine were lower. At the maximum activity of RA, a correlation was found between the concentration of free thyroxine and the level of AT to it (rs = 0.6, $p < 0.05$) and the concentration of free triiodothyronine and the level of AT to it (g, = 0.3, $p < 0.05$).

To identify the relationship between the form of the disease, the amount of thyroid hormones and antibodies to them in RA patients, 3 groups were formed: group 1 - healthy individuals, group 2 — patients with articular form of RA and group 3 - patients with systemic form of RA. Patients with systemic RA and thyroid dysfunction (n = 6) were not included in the analysis. The maximum indicators of St.T4) antibodies to T3 and T4 and the minimum level of sv. T3 were observed in group 3 patients with RA, especially with high activity of the pathological process. The euthyroid state noted by us in RA patients without concomitant thyroid pathology is qualitatively different from that in healthy individuals, since with this pathology, a low T3 syndrome develops against the background of eu-thyroidism (1o\y T3). It is believed that T3 occurs as a general response of the body as a compensatory reaction and reflects adaptive metabolic reactions and energy savings in conditions of chronic inflammatory process. In addition, we have noted a shift in the ratio of the levels of St. T3 and St. T4 in RA, which may be associated with changes in the metabolism of thyroid hormones in peripheral tissues, a decrease in the sensitivity of receptors to them in cells and target tissues, as well as a decrease in the activity of T4 deiodases, which leads to a decrease in serum T3 levels, an increase in the content of reversible T3 and is often combined with an increase in the amount of T4. With an increase in the activity of RA, there is an increase in the breakdown of proteins, which leads to a faster accumulation of free forms of hormones in the blood, and, possibly, more intensive formation of autoantibodies to them already in the early stages of the disease.

According to the literature, thyroid hormones are involved in the processes of immunogenesis and antibody formation, therefore, thyroid pathology may be a factor contributing to the chronic course of RA. With the involvement of the thyroid gland during RA, the pathological process increases, weighting its currents. An excess of thyroid hormones leads to a violation of the processes of formation of the general adaptation syndrome, patients become torpid to any therapy. The condition improves with a gradual decrease in the functional activity of the thyroid gland during treatment. On the other hand, this can be explained by the fact that in addition to autoimmune mechanisms, the direct influence of "anti-inflammatory" cytokines plays an important role in thyroid damage, which can enhance immune responses and additionally stimulate the production of thyroid hormones. The thyroid gland expresses interleukins when exposed to circulating immune complexes (which are formed in excess in RA), and cytokines, in turn, stimulate the proliferation of

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fibroblasts, excessive production of collagen and glycosaminoglycans, leading to narrowing of the articular gap, the formation of bone outgrowths and a decrease in the functional activity of the joint.

Conclusions

1. In the blood serum of a significant part of patients Antibodies to thyroid hormones were found in RA (in 45% — anti-T4 and in 39% — anti-T3), the content of which depends on the activity of the pathological process.
2. The revealed significant decrease in the level of T3 and the tendency to increase T4 are proportional to the increase in RA activity, which should be considered as a "low T3" syndrome in this disease.
3. Indicators of antibodies to thyroid hormones They can be used as an additional test to characterize the activity of RA along with traditional clinical and laboratory indicators.

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