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PATHOLOGY OF THE THYROID GLAND IN PATIENTS WITH RHEUMATOID ARTHRITIS

Urakov Jamshid Rustamovich

Department of Rehabilitation and Sports Medicine Bukhara State Medical Institute

Abstract: Endocrine disorders are of significant importance in the occurrence and progression of rheumatic diseases. Often, endocrine changes that occur during puberty, menopause, pregnancy, childbirth, and abortion serve as a background for the development of connective tissue diseases [6, 13]. At the same time, changes in neuroendocrine status are an integral component of the progression of rheumatic diseases [2, 5, 14].

Key words: rheumatoid arthritis, autoimmune thyroiditis, hypothyroidism.

Particularly distinct hormonal changes were found in the thyroid gland in rheumatoid arthritis (RA) [3, 9, 12]. The prevalence of thyroid pathology in general among patients with rheumatoid arthritis, according to the literature, reaches 34% [7], 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 [8].

The influence 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 can be caused by the action of factors that cause rheumatoid inflammation [7]. It is possible that one of the causes of thyroid dysfunction is vascular pathology in RA, as well as the influence of medications taken.

Material and methods

A cross-sectional study included 52 women with a definite diagnosis of rheumatoid arthritis, according to the criteria of the American Rheumatological Association (1987). The patients permanently lived in the Orenburg region, which belongs to the region of mild to moderate iodine deficiency [10]. The criteria for inclusion in the study were the age of women under 50 years and voluntary consent to participate in the study. Exclusion criteria from the study included severe somatic pathology, pregnancy, postmenopause, and taking medications that affect the metabolism of thyroid hormones and interfere with their absorption. The age of the women ranged from 20 to 49 years (39 [34.5; 43]), and the duration of the disease was from 4 to 15 years (6 [3.75; 10.5]). All were diagnosed with a high degree of RA, which was assessed by calculating the DAS28 index (2006). Almost every second patient had systemic manifestations of RA (53.18%). In 61.54% of cases, rheumatoid factor was detected.

All were determined by the titer of antibodies to thyroid peroxidase (ATTPO), the content of free thyroxine (fT4), thyroid-stimulating hormone (TSH) using Alkor Bio reagent kits (St. Petersburg), free triiodothyronine (fT3) - DRG diagnostics (USA) by enzyme-linked immunosorbent assay Multiscan apparatus (Finland). Subclinical hypothyroidism was confirmed by a stable increase in TSH levels with normal levels of fT4 and fT3 according to two studies with an interval of 6 months.

Ultrasound of the gland was performed using a Logic 5 pro device with a linear sensor with a frequency of 7–10 MHz. The structure, contours, and echogenicity of the gland were assessed in

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a gray scale mode. In addition, the quantitative characteristics of blood flow in the lower thyroid gland were studied in spectral Doppler mode with measurements of peak systolic blood flow velocity (Vps), maximum end-diastolic blood flow velocity (Ved) and calculation of the peripheral resistance index (sometimes called the resistive index (RI)). A small thyroid volume was diagnosed taking into account the weight of women according to the standards proposed by V.A. Kostyuchenko and S.I. Pimanov [4]. The volume of the thyroid gland, calculated using the Brunn formula, was considered increased if it exceeded 18 ml in women.

When nodes with a diameter of more than 1 cm were detected in the gland, a fine-needle puncture biopsy was performed according to the standard method (Belfiore A., La Rosa G.L., 2001).

The obtained data were subjected to statistical processing using the Statistica 6.0 package (Stat Soft, 2001) and the Biostatistica 4.03 program (S.A. Glantz, McGraw Hill // Translated into Russian - “Practice”, 1998). Quantitative values in the text and tables are given in the form Me [25; 75] (Me – median; 25 and 75 – 1st and 3rd quartiles). To statistically evaluate the results, nonparametric methods were used: Mann–Whitney test and Spearman correlation analysis. Differences were considered statistically significant at $p < 0.05$.

Results and its discussion

Depending on the functional state of the thyroid gland, women were divided into two groups. 11 (18%) women with RA (group 1) were diagnosed with hypothyroidism (8 - manifest, 3 - subclinical), which differs from the general population prevalence of hypothyroidism among women of reproductive age in the region of mild iodine deficiency (2%) [11]. In two patients aged 31 and 47 years, hypothyroidism was diagnosed at the ages of 12 and 35 years, respectively, before the manifestation of RA. Moreover, in the first case, while taking 75 mcg of levothyroxine, the TSH level was 16 mU/l, and in the second case, hypothyroidism was compensated (TSH - 0.3 mU/l) while taking 100 mcg of levothyroxine; in the rest, a decrease in thyroid function was detected for the first time during our examination. The main cause of hypothyroidism in all of them was naturally autoimmune thyroiditis (AIT). No cases of hypertrophic form of AIT were identified according to ultrasound examination.

At the time of hospitalization, 2 (18.18%) patients of group 1 received methotrexate at a dose of 7.5 mg/week for at least 6 months as a basic therapy. Prednisolone was taken by 3 (27.27%), of which one was at a dose of 5 mg/day and two were at a dose of 10 mg/day. The remaining patients did not receive basic therapy and took only non-steroidal anti-inflammatory drugs.

Group 2 included 41 women without thyroid dysfunction. The average age and duration of the disease were not statistically significantly different from similar indicators in group I. Three patients of group 2 had thyroid nodules, one of whom had an enlarged gland. A puncture biopsy revealed colloid goiter in all cases.

Among patients in group 2, 13 (31.7%) patients received basic therapy with methotrexate for at least 6 months before admission to the clinic at a dose of 7.5 mg/week. 15 (36.58%) patients were treated with synthetic glucocorticoids (prednisolone, metypred, diprospan injections) for at least 6 months before hospitalization. The daily dose of prednisolone ranged from 5 to 15 mg, metipred - from 4 to 8 mg. The remaining patients took non-steroidal anti-inflammatory drugs.

In group 1, the number of patients with systemic manifestations of RA was statistically significantly greater than in group 2. A detailed analysis of the main systemic manifestations of

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RA and its complications revealed statistically significant differences between groups only in the incidence of myocardial dystrophy and anemia.

The study showed that RA patients with hypothyroidism (group 1) had higher clinical and laboratory activity of the disease. In this group, ESR, DAS28, and the number of swollen joints were statistically significantly higher compared to women without thyroid dysfunction.

It should be noted the high frequency of detection of ATTPO in both groups. There were no statistical differences in this indicator between the groups. This fact is probably due not only to thyroid pathology, but also to the manifestation of extrathyroid pathology, that is, RA. According to V.V. Fadeeva (2005), the prevalence of ATTPO carriage in random samples of young women and elderly people ranges from 15.8 to 16.9%, and with autoimmune pathology, including RA, this figure is likely to increase, which was the case noted by us.

An analysis of the effect of the main RA therapy on thyroid status indicators was carried out. The TSH level was statistically significantly lower (0.9 [0.7; 1.6] mU/ml) in patients receiving synthetic glucocorticoids (duration of use for at least 6 months) at a dose of 5 to 15 mg in terms of prednisolone than in patients who did not take them (2.3 [1.8, 3.3] mU/ml; p = 0.032; T = 337). There were no statistically significant changes in the level of thyroid hormones and TSH while taking methotrexate.

Noteworthy is the high frequency of detection of the so-called small thyroid volume, which was diagnosed taking into account the weight of women [4]. Of the 52 examined (weight – 66 kg [60.5; 73.5], height – 1.63 m [1.57; 1.66]), a decrease in the size of the thyroid gland (4.6 ml [4.32; 5.13]]) was found in 12 (23.07%): 3 (weight – 75 kg [70; 80], height – 1.64 m [1.55; 1.65]) – from group 1 and 9 – from the 2nd (weight – 62 kg [60; 70], height – 1.62 m [1.58; 1.67]). Thus, the decrease in gland volumes in the subjects is due not only to autoimmune thyroiditis. According to the literature, a small thyroid volume occurs in 6.2% of cases under the age of 50 years according to the results of autopsy studies [11]. No statistically significant differences were found between the groups in terms of ultrasound parameters of blood flow in the gland.

The frequency of detection and the level of ATTPO in patients with a decrease in the size of the thyroid gland did not differ significantly from those with a normal volume of the thyroid gland. Similar data were obtained regarding thyroid function. However, when measuring the speed parameters of blood flow with ultrasound of the thyroid gland, a significant increase in the peripheral resistance index was revealed with reduced organ sizes (0.79 [0.55; 0.8]; 0.59 [0.56; 0.66]; p = 0.028 ; T = 351).

Considering all of the above, it can be assumed that thyroid hypoplasia is not always associated with autoimmune thyroiditis. Chronic ischemia of the organ against the background of immune complex vasculitis and early atherosclerotic vascular damage characteristic of this disease plays an important role in the genesis of atrophic changes in the thyroid gland [1]. Of course, this issue requires further study.

Conclusions.

Our data indicate a high incidence of hypothyroidism and ATTPO carriage in RA. A small volume of the thyroid gland in RA is observed both in patients with and without autoimmune thyroiditis. A decrease in the size of the gland is not associated with the carriage of ATTPO and is combined with an increase in the peripheral resistance index in its arteries, which may be due to chronic ischemia of the organ. The TSH level in patients with RA is determined not only by thyroid pathology, but also by glucocorticoid therapy. In patients with RA in combination with

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hypothyroidism, systemic manifestations and high activity of the articular process are more often observed.

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