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Gender Characteristics of the Course of Rheumatoid Arthritis

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Abstract. Rheumatoid arthritis in women is characterized by a more severe course of the pathological process, and the lesion of individual joints depends on the gender of patients (in men, changes in the sacroiliac joints, the development of tendovaginitis, intra-articular Goff bodies are more often noted, and in women — proximal interphalangeal joints of the fingers of the upper and lower extremities, maxillary and knee joints). There is a sexual dimorphism of integral extraarticular (systemic) manifestations of rheumatoid arthritis, while men have more frequent lung and peripheral nervous system damage, and exclusively in the female group — Sjogren's syndrome and changes from the central nervous system. In patients with rheumatoid arthritis, the parameters of bone metabolism in the blood serum change, in addition, in patients with osteoporosis, there are common and gender differences in the concentrations of osteoassociated hormones and chemical elements.

Keywords: rheumatoid arthritis, course, men, women.

Introduction

Female gender is a risk factor for rheumatoid arthritis (RA), and women hospitalized with this disease account for 75-80% of all cases of the disease. It should be noted that RA is accompanied by certain gender-specific features of the course of the pathological process, which are generally characterized by a more severe course of the disease in women. Sexual dimorphism of RA in men and women is manifested by differences in the frequency of metabolic syndrome, venous thrombosis, the development of involvement in the pathological process of sternoclavicular joints, lumbar spine and lungs.

However, the sexual dimorphism of the course of RA is still insufficiently studied, the degree of gender influence on the clinical and radiographic nature of joint damage, the development of osteoporosis and extraarticular (systemic) manifestations of the disease has not been determined, which determined the goals and objectives of this study.

Material and methods

293 RA patients aged 17 to 79 years (on average 45.60 ± 0.68 years) were under observation. Among these patients were 20% of men aged 43.50 ± 1.36 years and 80% of women aged 46.20 ± 0.78years. The duration of clinical manifestation of RA in the male and female groups, respectively, was 7.90 ± 0.91 years and 9.60 ± 0.46 years. The seropositive variant of the disease at the time of examination was established in 3/4 of observations, I degree of activity of the process — in 20%, II — in 46%, III — in 34%; I radiological stage — in 9%, II — in 39%, III — in 34 %, IV — in 19%. The joint score was 20.60 ± 0.51, the Ritchie index was 40.20 ± 1.18 points, the Lansbury index was 156.80 ± 4.19 points, the arthritis progression index (IPA) was 1.50 ± 0.13 oe. Extra-articular (systemic) manifestations of RA were detected in 29% of cases.

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The patients underwent X-ray (MultixCompact-Siemeps, Germany) and ultrasound (Envisor-Philips, the Netherlands) examination of the joints, sacroiliac joints and spine, as well as dual-energy X-ray osteodensitometry of the proximal femur bones (QDR-4500-Delphi-Hologic, USA). The radiological osteoassociated Barnett-Nordin meta—carpal index and bone mineral density indices were evaluated. IPA was evaluated by the formula:

IPA = (S2+∑)/T, where S is the stage of the disease, ∑ is the sum of the radiographic signs, T is the duration of the disease.

Using the BS-200 biochemical analyzer (China), we studied the activity indicators of alkaline phosphatases (alkaline phosphatase) in blood serum. Using the method of atomic emission spectrometry with inductively coupled argon plasma (IRIS-Intepid-IIXDL, UK), the parameters of osteoassociated macronutrients - calcium (Ca), magnesium (Mg) and phosphorus (P) — were determined in the blood, and by atomic absorption spectrometry with an electrographite atomizer (SolAAr-Mk2-MOZe apparatus, UK) — the content of osteoassociated trace elements — copper (Cu), iron (Fe), manganese (Mn), lead (Pb), strontium (Sr) and zinc (Zn).

By enzyme immunoassay (Sanofi reader PR2100 diagnostic Pasteur, France; DRG kits, USA) examined the serum levels of parathyroid hormone (PH), calcitonin (CT) and osteocalcin (OK).

Statistical processing of the obtained research results was carried out using computer variational, correlation, single- (ANOVA) and multifactorial (ANOVA/MANOVA) analysis of variance (Microsoft Excel and Statistica programs StatSoft). The average values (M), standard deviations (SD) and errors, correlation coefficients, variance criteria (D), Student, Wilcoxon—Rao, McNemar—Fisher (∑2) and reliability of statistical indicators (p).

Results

According to one-factor analysis of variance, the gender of patients does not affect the seropositivity of RA, the degree of activity of the pathological process, the stages of the disease, the prevalence of joint syndrome, the Ritchie, Lansbury and IPA indices. At the time of the examination, increased indicators of rheumatoid factor in the blood (> 15 IU/ml) were found in 72% of men and 76% of women. Moderate and high degree of RA activity was found in 72% of men and 82% of women (p = 0.032), and stages III–IV of the disease — respectively in 43 and 55% of cases (p = 0.002). Thus, it is possible to state a more severe course of RA in women, which is confirmed by the literature data. At the same time, according to the average parameters of joint counting, the Ritchie and Lansbury indices, the IPA groups of men and women differed little from each other.

Systemic osteoporosis was found in 43% of men and 49% of women. The metacarpal index in the first group was 0.440 ± 0.007 units, and in the second — 0.430 ± 0.004 units, the T index (according to densitometry) — respectively -1.560 ± 0.178 SD and –1,55 ± 0,089 SD. Average values of markers of bone metabolism (PG, CT, OK, alkaline phosphatase, Ca, Cu, Fe, Mg, Mn, P, Pb, Sr, Zn in blood serum) in men and women did not differ from each other. According to the multivariate analysis of Wilcoxon — Rao, the sex of RA patients has little effect on the integral state of osteoassociated hormones and chemical elements in the blood, whereas a single-factor analysis of variance indicates a significant dependence on the sex of the parameters in the blood of PG and Mn.

In the group of men, there is no influence of the degree of activity of the pathological process on the integral indicators of bone metabolism, although there are reliable direct correlations of RA activity with serum levels of Cu and Sr, as well as an inverse correlation with Zn concentration. In addition, the stage of the disease is positively correlated with the content of Mn, and the IPA is inversely correlated with Fe and directly with Sr. In women suffering from RA, there is a significant effect of the activity of the disease on the integral state of bone metabolism, although the parameters of the degree of activity correlate only with the level of Cu in the blood. Taking into account the existing direct connection, we found that, regardless of the gender of patients, the indicators in serum Cu > 1200 mcg/l (> M + SD of patients) indicate a high degree of RA activity.

In men, the defeat of the elbow and shoulder joints significantly affects the integral state of bone metabolism. In turn, the latter in women is associated with the severity of changes in the proximal interphalangeal joints of the hands and feet, the presence of severe osteousures, aseptic osteonecrosis, digital arteritis and osteoporosis. In the group of men with osteoporosis, the PG values were significantly higher than in the rest of the examined, 2.2 times and the OK was 37% higher. In women, PG values increase significantly ($p < 0.001$) by 80%, OK — by 40%, SCHF — by 31% with a decrease CT content by 42% and Mg content by 8%. Taking into account the data obtained, the following conclusions of practical significance were made: in men with RA, PG values > 80 pg/ml, and in women > 70 pn/ml at a level of OK > 20 ng/ml (> M + SD of patients with osteoporosis), regardless of gender, indicate the presence of systemic osteodeficiency.

Discussion

According to ANOVA/MANOVA, the gender of RA patients has a significant effect ($p = 0.005$) on the frequency of damage to individual joints (the so-called articular landscape). The results of the performed ANOVA demonstrate a reliable dependence on the gender of patients of the frequency of lesions of the proximal interphalangeal joints of the hands and feet, knee and sacroiliac joints. At men are 2.2 times more likely to develop rheumatoid sacroiliitis, but 85% less likely to develop damage to the maxillary joints, 15% — proximal interphalangeal fingers, 25% — toes, 12% — knee. Therefore, it can be concluded that the male sex refers to the risk factors of sacroiliac joint damage, and the female — maxillary and knee.

One-factor analysis of variance demonstrates a significant effect of the gender of RA patients on development of tendovaginitis and intra-articular Goff bodies. Men are 36% more likely than women to have tendovaginitis and 4.6 times more likely to have Goff's bodies. Thus, the male sex can be attributed to the predictors of the occurrence of tendovaginitis and intraarticular Goff bodies in RA.

According to the results of the Wilcoxon—Rao analysis, the gender of RA patients significantly affects integral extraarticular (systemic) signs of the disease. At the same time, a single-factor analysis of variance shows the dependence on the gender of lung pathology (interstitial pneumonitis, fibrosing alveolitis, rheumatoid nodes) and the peripheral nervous system (polyneuropathy, radiculopathy), as well as the risk of developing Sjogren's syndrome. Men are 2.8 times more likely than women to have pulmonary pathology and 2.5 times more likely to have changes in the peripheral nervous system. Thus, the male sex of RA patients becomes a risk factor for these extraarticular signs of the disease. The severity of joint damage in men, estimated by the Ritchie and Lansbury indices, determines the level of Mn in the blood, the presence of sacroiliitis, changes in the menisci of the joints and nephropathy (mesangioproliferative and mesangiocapillary glomerulonephritis, AA-amyloidosis) — the content of OK, Baker's cysts and digital arteritis — Cu concentration, osteosuration — Mg, Sjogren's syndrome and peripheral polyneuropathy — Mn, Pellagri — Steidy— Sr intraarticular bodies, major osteocystic and intraarticular Goff bodies — Zn. In women, the content of PG is significantly affected by aseptic osteonecrosis, Pellagri — Steidi bodies, lung and central nervous system damage (dyscirculatory encephalopathy), the presence of pronounced osteousures, OK — enthesopathy, the activity of SCHP — osteocystic fibrosis, calcemia parameters — osteousures, aseptic osteonecrosis, digital arteritis and meniscal changes, for cupremia — only changes in the horns of the menisci, for Mg blood counts — the development of tendovaginitis

Conclusions

1. RA in women is characterized by a more severe course of the pathological process, and the integral lesion of the joints (articular landscape) depends on the gender of the patients; in men, the sacroiliac joints are more often affected, the development of tendovaginitis and intra-articular Goff bodies, and in women, the disease is characterized by a greater degree of damage to the proximal interphalangeal joints of the fingers of the upper and lower extremities, maxillary and knee joints.

2. There is a sexual dimorphism of integral extraarticular (systemic) manifestations of RA, when at the same time, men have a more frequent lesion of the lungs and peripheral nervous system, and

exclusively in the female group — Sjogren's syndrome and changes from the central nervous system, which reflects additional gender features of the course of the pathological process.

3. In patients with RA, the indicators of bone metabolism in the blood serum change, in addition, in patients with osteoporosis has a commonality and gender differences in the concentrations of osteoassociated hormones and chemical elements, which requires consideration by practitioners in the context of the diagnosis of the pathological process in men and women, as well as monitoring the effectiveness of therapeutic measures.

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