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Aspects of Comorbid Pathology in Rheumatoid Arthritis

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Abstract The article reveals the problems of comorbid background in patients with rheumatoid arthritis. Comorbid background of such patients is an important aspect of observation and correction in patients with rheumatoid arthritis due to its significant effect on the course of the disease and its outcome. An adequate diagnosis and correction of traditional risk factors are required to improve these indicators.

Keywords Rheumatoid arthritis, Comorbid background, Arterial hypertension, Dyslipidemia, Insulin resistance, Osteopenia, Cardiovascular risks

1. Introduction

Rheumatoid arthritis continues to be one of the most relevant pathologies in modern medical practice: on the one hand, this is facilitated by the prevalence of the disease – up to 2% in the general population; on the other hand, the high social and economic significance of the process, based on high rates of persistent disability in patients and the significant cost of treatment and necessary laboratory control [5]. A high degree of prevalence of the disease implies the presence of concomitant pathologies in such patients and, accordingly, a burdened comorbid background, which has a significant impact on the prognosis, therapy tactics and, as a result, the quality of life of patients with rheumatoid arthritis [23].

Despite the active and timely modern therapy of rheumatoid arthritis with basic anti-inflammatory and genetically engineered drugs, indicators of life expectancy and quality of life in such patients remain insufficient. An important role in this problem is played by a burdened comorbid background [14]. Concomitant diseases (comorbid background) in patients with rheumatoid arthritis, they imply a significant influence on both the course of rheumatoid arthritis and the choice of diagnostic and therapeutic tactics in the management of such patients, and as a result on the long-term prognosis and quality of life. Insufficient assessment of comorbid components makes it impossible to achieve the main goal in the treatment of rheumatoid arthritis – Treat to Target [2]. It should be borne in mind that the comorbid background can be formed in the form of two main variants: concomitant pathology that arose before the onset of rheumatoid arthritis (or arose separately at the time of the disease) and the consequences of the activity of penetration of the systemic disease and its therapy. The National Database of Rheumatic Diseases in the United States has made it possible to systematize data on the relationship between the presence of concomitant pathology and the features of rheumatoid arthritis. The following comorbid pathologies, in descending order of importance, had the maximum effect on increasing the mortality rate of disability, loss or decrease in the functional status of patients and the economic costs of therapy: cardiovascular diseases, diabetes mellitus, osteopenia, respiratory diseases, damage to the digestive tract [20]. The comorbid background of patients with rheumatoid arthritis was assessed in detail in the multicenter prospective study COMORA: arterial hypertension was detected in 18% of the subjects, diabetes mellitus in 3.7%, and a violation of the lipid spectrum in 11% [13].

One of the most relevant aspects of comorbidity in rheumatoid arthritis is the issue of cardiovascular complications. In patients with rheumatoid arthritis, the risk varies from 1.4 to 3.96 and has its own pronounced characteristics from the general population: extensive atherosclerotic lesions of the heart vessels, frequently recurring episodes of coronary syndrome, high mortality, often asymptomatic/low-symptomatic myocardial infarctions, correlation with the activity of the rheumatoid process and the magnitude of inflammatory markers [29]. These features are due to several factors: traditional risk factors (hypertension, diabetes mellitus, smoking, abdominal obesity, etc.), the chronic process of systemic inflammation, adverse events in the treatment of rheumatic diseases (therapy with glucocorticoids, nonsteroidal and basic anti-inflammatory drugs). Do not forget that according to the research of H. Maradit Kremers and co-authors, the risk of cardiovascular complications in patients with rheumatoid arthritis increases even at the stage of absence of clinical signs, and at the onset of articular manifestations, its additional sharp increase occurs [24]. According to the previously mentioned studies, an increase in the probability of developing coronary heart disease occurs already 2 years before the final verification of the diagnosis of rheumatoid

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arthritis, and the occurrence of myocardial infarction at the time of the first year after diagnosis [24]. When considering issues related to chronic heart failure, the following patterns can be identified: the probability of its development increases after the onset of rheumatoid arthritis, progresses as its activity increases, but significantly decreases with successful treatment of basic anti-inflammatory therapy (in particular, methotrexate, due to a decrease and relief of the activity of the systemic process) [21]. A similar correlation is observed between diastolic dysfunction of the left ventricle and the duration of rheumatoid arthritis [28]. When assessing the thickness of the intima-media complex (a sign of atherosclerosis in the carotid arteries), the progression of this indicator was revealed in patients with rheumatoid arthritis for more than a year, and according to Chung's research, coronary calcification progressively increases every five years [11]. The features of the clinical manifestations of rheumatoid arthritis associated with a high risk of cardiovascular complications have been studied: a large joint score, a significant functional class, systemic manifestations, seropositivity and ADC-positivity, a significant increase in proinflammatory mediators (C-reactive protein, adipokines, ESR) [19]. According to the recommendations of the European Antirheumatic League, the cardiovascular risk in rheumatoid arthritis requires a 1.5 increase on the Score scale, subject to two of the three criteria described above: the duration of rheumatoid arthritis for more than ten years, seropositivity, systemic manifestations [5].

Arterial hypertension is the most common risk factor in rheumatoid arthritis – according to domestic studies, its incidence reaches 70.5% [8]. According to a study by Chung and others, arterial hypertension was detected in almost 40% of patients in the early stages of rheumatoid arthritis, and during a five-year follow-up, the risk increased by 12.8%, while the activity of the systemic process had a direct correlation with a progressive increase in blood pressure figures [11].

It should be noted the important role of the interaction between the degree of systemic inflammation and lipid metabolism in patients with rheumatoid arthritis. A correlation was found between the level of C-reactive protein, proinflammatory cytokines and the likelihood of dyslipidemia development and proagression. In patients, there is an increase in the value of total cholesterol, low-density lipoproteins and triglycerides, as well as a decrease in high-density lipoproteins [6]. 54.8% of patients with documented early stages of rheumatoid arthritis have some kind of lipid metabolism disorder, according to the Georgiadis study [15].

Almost half of patients with rheumatoid arthritis have abdominal obesity, a risk factor for cardiovascular complications, diabetes mellitus and a prognostically negative sign of rheumatoid arthritis. The conducted studies revealed an association between a body mass index of more than 28 kg/m2 and higher DAS28 index values, which reflects the activity of rheumatoid arthritis, as well as a more rare achievement of remission [10].

The smoking factor is also very important in assessing the comorbid background in patients with rheumatoid arthritis, as it is one of the significant traditional cardiovascular risks. According to the data studied, a history of smoking is associated with higher activity and severity of the rheumatoid process and increases the risk of coronary catastrophe up to 3.5 times [17].

Taking into account the importance of the cardiovascular comorbid background in rheumatoid arthritis, recommendations for prevention from the European League Against Rheumatism and the Association of Rheumatologists of Russia have been created [7,24]. These recommendations specify the need to calculate the total coronary risk at intervals of once a year, taking into account adjustments for the duration of rheumatoid arthritis (more than 10 years), positivity for rheumatoid factor and the presence of antibodies to cyclic citrulated peptide, detection of extra-articular lesions, therapy of underlying and comorbid diseases.

Another common comorbid condition in patients with rheumatoid arthritis is diabetes mellitus. According to the Solomon study, in a sample of more than 45 thousand patients with rheumatoid arthritis, the probability of its development is 1.5 times higher than in patients without systemic inflammatory diseases – 8.6 cases to 5.8 cases per thousand examined, respectively [27]. Other studies claim that diabetes mellitus occurs in 15-19% of patients with rheumatoid arthritis, which is a much higher rate than in the general population (up to 8% prevalence) [26]. However, it should be borne in mind that there are studies that refute such a statement and assess the risk of diabetes mellitus in patients with rheumatoid arthritis equally with the general population risk – in particular, similar results are presented in Wasko studies [30]. Given the prevalence of glucocorticoids among patients with inflammatory joint diseases, it is impossible to exclude their effect on the process of gluconeogenesis and, as a result, the relationship with the risk of diabetes mellitus. The interaction of these processes gives contradictory initial data: on the one hand, glucocorticoid therapy sideways increases glucose synthesis and increases the risk of insulin resistance and the development of type 2 diabetes mellitus; on the other hand, a decrease in the level of chronic systemic inflammation, carried out by taking glucocorticoids, improves the process of insulin resistance in tissues [16]. Thus, the comorbid background burdened with diabetes mellitus requires further study.

A particularly important place in the structure of comorbid pathology in rheumatoid arthritis is assigned to the lesion of the digestive tract. The relevance of this issue can be considered using the example of the previously mentioned COMORA study: when considering the clinical situation of 3920 patients with rheumatoid arthritis, 11% with signs of ulcerative lesions of the gastrointestinal tract, 5% with signs of damage to the hepatobiliary system were identified [13]. Many studies have also found that in patients with rheumatoid arthritis, digestive tract pathology is much more common: up to 15.4 and 9.5%, depending on gender, the probability of developing gallstone disease is higher

against 5.2 and 3.8% in the population, respectively; a 60% increase in the risk of pancreatitis. In these studies, the association with the side effect of glucorticoid and basic anti-inflammatory therapy was excluded [12]. It should be borne in mind that patients with rheumatoid arthritis have a high probability of death due to damage to the gastrointestinal tract, which clearly reflects the negative relationship between rheumatological and gastroenterological pathology: according to Kuo and co-authors, the comorbid background burdened with digestive pathology in patients with rheumatoid arthritis increased mortality up to 2.49 times [18]. Thus, the lesion of the digestive tract is an urgent issue of comorbidity in rheumatoid arthritis: it affects the level of quality of life and its duration, as well as the effectiveness of the therapy.

Another factor aggravating the concomitant condition in rheumatoid arthritis is infection. The frequency of their occurrence depends not only on the active use of immunosuppressants during therapy, but also largely on the duration of the systemic process for more than ten years [4]. Extra–articular manifestations of the disease, high activity of the process, high rates of erythrocyte sedimentation, anamnesis of hormone therapy are the main factors that increase the risk of developing comorbid infectious pathology. According to domestic studies, 32.8% of patients with rheumatoid arthritis faced this problem: the main infectious agents are Klebsiella bacteria and fungi of the genus Candida, provoking 17.1% of urinary tract infections, 7.1% of respiratory infections [3].

The relevance of concomitant respiratory pathology is obvious, given that among patients with rheumatoid arthritis, mortality from pneumonia reaches 22%, Legionella spp., S. Aureus., K. Pneumoniae were especially common etiological flora [1]. According to the research of the Research Institute of Rheumatology of the Russian Academy of Medical Sciences, the main risk factors for pulmonary comorbid lesions in patients with rheumatoid arthritis are: a high inflammatory component, a history of chronic lung diseases, lack of basic anti-inflammatory therapy, monotherapy with glucocorticoids; the combination of several factors increases the risk to 19.3% [1].

Rheumatoid arthritis is a common background for the development of renal pathology. From 57 to 84.7% of patients with systemic rheumatological lesions have some kind of kidney lesion [9]. The mechanism of the relationship between rheumatoid arthritis and renal pathology has the following features: immuno-inflammatory factors, side effects of drug therapy. The main cause of secondary amyloidosis is rheumatoid arthritis [9].

Osteoporosis is another factor that significantly aggravates the comorbid background of patients with rheumatoid arthritis. Its prevalence in such patients reaches 67% [22]. The main problem of osteoporosis in rheumatoid arthritis is its clinical asymptomacy and high risk of pathological fractures, which significantly reduces the standard of living of patients and causes disability and an increased risk of mortality. The incidence of pathological fractures in patients with rheumatoid arthritis is twice as high as in others, and when treating the underlying disease with glucocorticoids (even in minimal doses), the risk is doubled [25].

2. Conclusions

The comorbid background is an important aspect of observation and correction in patients with rheumatoid arthritis, due to its significant effect on the prosthetics of the disease and its outcome. To improve these indicators, an adequate and timely assessment and correction of traditional risk factors is required.

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