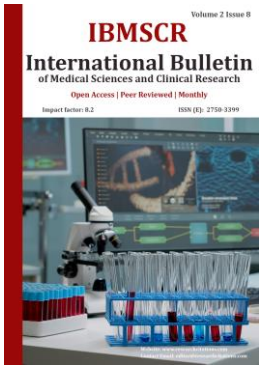

RHEUMATOID ARTHRITIS AND X-RAY PICTURE

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https://doi.org/10.5281/zenodo.8045829

ANNOTATION Purpose of work - determination of the level of radiological imaging and clinical-laboratory indicators in patients with rheumatoid arthritis depending on the haptoglobin system of different phenotypes.The study was conducted on 214 patients diagnosed with rheumatoid arthritis who were treated in the medical association during 2018-2021. The study used general clinical, medico-social, hematological, biochemical, immunological, instrumental and statistical research methods. All patients with RA according to hematological parameters were divided into 2 groups: 50 (23.4%) patients without anemia, who made up our control group; the remaining 164 (76.6%) patients were diagnosed with anemia by hematological parameters, these patients constituted the main group. The type and degree of anemia in RA patients was determined in accordance with the classification recommended by WHO. ACD was observed in 94 (57.3%) patients, IDA in 65 (39.6%) patients, and 5 patients (3.1%) had both ACD and IDA. 76.6% of all RA patients participating in the study were diagnosed with anemia of various forms and degrees, which are characterized by a relationship between the duration, activity and radiographic manifestations of the disease

Keywords: haptoglobin phenotype, rheumatoid arthritis (RA), anemia, ferritin, anemia of chronic disease, iron deficiency anemia

Introduction. Rheumatoid arthritis (RA) is one of the most serious inflammatory diseases of human joints, with a prevalence ranging from 1% to 3% according to various reports [1,2,8]. According to the World Health System (WHO), RA is the third most common disease. The first symptoms of RA are more common between the ages of 35 and 50, but these symptoms can also be seen in other age groups [6,21]. The long-term inflammatory process in the synovial membrane of joints almost always leads to structural and anatomical damage of bone and periarticular tissues and permanent disability of patients [17,20]. People of prime working age are disabled by RA. Economic losses caused by this disease can be compared with cardiovascular disease [9,18]. Even with standard therapy, 60-90% of patients lose their ability to work 20 years after the onset of the disease, and one-third of them become completely disabled [7,25]. In Germany, disability due to rheumatic joint injuries accounts for 24% of the total number of insured persons [4,14,30]. Without effective therapy, life expectancy for RA is reduced by 3 years in women and 7 years in men [5,19,22].

It should be noted that EBV, CMV, HTLV-1 and other viral infections may be one of the etiological causes of RA [16,24,31]. According to the authors, it is likely that the autoimmune transformation of primary (viral-induced) RA is largely determined by factors of antigenic mimicry, but not all patients with RA can identify the association with the above infection, and attempts to identify and localize the virus in the synovial joint are not always successful [22

,28]. Perhaps a long enough time is required from the time of infection to the development of the clinical stage of RA. During this period, the virus is destroyed by itself or by the immune system, causing the disease to become autoimmune in nature. As a proof of this, it can be shown that there is a correlation between the viral load of EVA in blood serum and the amount of anti-EBV autoantibodies and the presence of the HLA-DRB1 allele in patients.

Until recently, the mechanisms of RA development were considered mainly in terms of T-cell immunoregulatory defects. However, at present, the relationship to the V-cell component of immunity as a "secondary" participant in the pathological process in RA is being fundamentally revised. The results of experimental studies show the main role of B-lymphocytes in regulation of T-cell immune response in RA [10,12,9]. Rheumatoid factor (RF) plays an important role in the activation of V-cell immunity. In particular, the autoantibody RF, which reacts with the permanent IgG1 part, is found in the serum of more than 80% of RA patients and may be in a "latent" form in RF seronegative patients. That being said, RF has the ability to repair and activate the complement system. Activated complement components (primarily C3a and C5a anaphylotoxins) are chemical binding agents for leukocytes and accelerate their entry into the joint inflammation. Evidence suggests that increased RA is associated with an increased number of RF-synthesizing cells in the bone marrow and synovial fluid [3,11,13,27]. IgM is synthesized by more than 10% of plasmacytic cells present in the synovial tissue of patients with RA. Introduction of RF into the body does not lead to the development of synovitis, which indicates the low pathogenicity of these autoantibodies. Immune complexes in RF are considered to be of major pathogenetic importance in RA. In addition, RF can be affected not only by the Fc part of IgG1, but also by other antigens and autoantibodies [12,25,26]. According to the results of clinical studies, seropositivity in RF is associated with a further exacerbation of RA and even an increased risk of death. Certain immunochemical differences of the "pathogenic" subtype of RF synthesized in RA have been identified. It turned out that they consist of heterogeneity (for the Fc part of IgG) when compared with the "physiological" RF determined in the sera of patients with various diseases. Although RA-specific clones of B-lymphocytes have not yet been identified, data have been obtained on the maturation of specific B-lymphocyte RFs that cause infiltration of the synovial membrane of patients. Immune complexes in the germinal centers of lymphoid follicles give B-lymphocytes a "positive" signal related to "survival" and clonal selection [15,23, 29].

Goal: determination of the level of radiological imaging and clinical-laboratory indicators in patients with rheumatoid arthritis depending on the haptoglobin system of different phenotypes.

Materials and methods. The study was conducted in 214 patients diagnosed with RA during 2018-2021. The average duration of the disease was 8.6±0.7 years.

All RA patients were divided into 2 groups based on hematological parameters: 50 (23.4%) patients without anemia, who constituted our control group; remaining 164 (76.6%) patients were diagnosed with anemia according to hematological indicators, these patients formed the main group. The type and degree of anemia in RA patients was determined according to the classification recommended by WHO. SKA was observed in 94 (57.3%) patients, TTA in 65 (39.6%) patients, and in 5 patients (3.1%) both SKA and TTA occurred.

Examination of patients was carried out using generally accepted clinical, laboratory and instrumental methods. In all patients under follow-up, conventional X-rays were

performed in the right (anterior-posterior) projection of the distal part of the fingers and soles of the feet, and the radiological stage of RA was determined by the modified Steinbrocker method. Progressive destructive processes developed in small joints were measured according to the Larsen method.

Among the laboratory methods, a general blood test, quantitative composition of fibrinogen, biochemical analysis of blood, and a general analysis of urine were performed. Methods such as STsPA (antibody against cyclic citrulline peptide) in blood serum, synovial fluid study, Hp (haptoglobin) phenotype determination by disc electrophoresis on PAGE were also used.

Processing of the obtained data was analyzed using the Microsoft Excel software package of a personal computer and the "STATISTICA 6.0" software package. Descriptive statistics methods included arithmetic mean (M), mean error (m) and mean squared deviation (σ) of markers with normal distribution.

Results: Level I activity of the disease was observed in 48 (22.4%) patients and averaged 2.72±0.16 according to DAS28. Level II activity of RA was observed in 101 (47.2%) patients and averaged 4.29±0.32 according to DAS28. Level III disease activity was detected in 65 patients (30.4%) and averaged 5.24±0.29 according to DAS28. Thus, in the examined patients, RA II and III activity was observed in almost 78% of patients, and the total DAS28 index was 4.77±0.08.

When we describe RA by X-ray appearance, only 12 (5.6%) patients had I degree of joint damage, 118 (55.1%) patients had II degree, 79 (37%) had III degree, and 5 had IV degree. (2.3%) was observed in the patient (Fig. 3.1b). So, in the examined patients, mainly the second and third (92.1%) radiological stages of the disease were detected.

The distribution of patients according to BFB showed the following: grade 0 was observed in only 3 (1.4%) patients, grade I was observed in 17 (7.9%), grade II - 90 (42.1%), grade III - 91 (42.5%) and IV degree - was found in 13 (6.1%) patients. Rheumatoid nodules were found in 49 (22.9%) patients and indicate a persistently severe course of the disease. So, mainly RA II and III levels (84.6%) were detected in our study patients. Among functional disorders, 105 patients (49.1%) had high functional disorders according to the questionnaire, and the number of patients with III-IV class of joint functional insufficiency was also high, making up 104 patients (48.6%).

The duration of the disease in patients in the observation groups was 8.3 ± 0.71 years on average, ranging from 1 to 25 years. Only 74 (34.6%) of RA patients in the study had disease duration up to 5 years, 5 to 10 years - 89 (41.6%), and more than 10 years - 51 (23.8%) patients. Patients with systemic changes were excluded from the study group, patients with only joint form of the disease were observed. In addition to joint syndrome, patients under observation had complaints such as general weakness (88.3%), irritability, sleep and attention disorders (36.9%), agitation (18.7%), fear (6.1%). In our data, anemia was the leading symptom of non-articular RA. Anemia was characteristic of 164 patients under observation (76.6%).

When we analyzed comorbidities, they were identified in 80.4% of patients, and comorbidities were not identified in 19.6% of patients. 164 (76.6%) RA patients were diagnosed with anemia of various forms and degrees. Therefore, we divided all patients into 2 groups: 50 patients without anemia (control group), 164 patients (main group) with different levels of anemia. In particular, the 1st degree of anemia was observed in 59 (36%) patients,

the 2nd degree in 68 (41.5%), the 3rd degree - 31 (18.9%) and the 4th degree - 6 (3, 7%) was found in patients.

When we analyzed acute inflammatory proteins in blood serum, we observed that their amount increased. Biochemical analysis of blood serum in RA patients showed that all parameters were not different from normal parameters. Reactive hyperenzymemia has been observed in some patients, especially those receiving methotrexate. This was observed in the main group with RA with anemia.

The general analysis of urine showed the presence of protein, leukocytes and epithelial cells in urine in only 18% of 214 patients. These were found mainly in patients with RA+SKA, the frequency of proteinuria was 21.3%. RA was observed in the form of anemia and indicated the presence of kidney pathology.

Based on the obtained results, we analyzed the course of RA in the control and main groups. The results showed that the presence of RF was characteristic of the majority of patients and was observed in the same percentage (75 and 68.3%) in the control and main groups, and there were no significant differences between the groups.

Determining RA activity on DAS28, activity levels 2 and 3 were more common in anemic patients (78.6%), and activity levels 1 and 2 were predominant in patients without anemia (95%). In particular, if the 1st (35%) and 2nd (60%) levels of activity were determined in the comparison group, the 2nd (45.1%) and 3rd (33.5%) levels were observed in the main group. Thus, the observation of anemia in RA patients is characterized by the severity of the disease.

In RA and anemia developed on its basis, hematological indicators change according to their form, the strongest changes are observed in RA+SKA+TTA and RA+SKA. Their main criteria are MCV, MCN and MCNS, as well as the amount of hemoglobin.

It is worth saying that according to the degree of anemia, the changes in hematological parameters deepened. Hemoglobin content is 1.21 (R<0.05) compared to standard indicators; 1.41 (R<0.001); 1.65 (R<0.001) and 2.21 (R<0.001) times, erythrocyte count MCV 1.25 (R<0.05); 1.37 (R<0.001); 1.6 (R<0.001) and 1.88 (R<0.001) times, hematocrit indicator - 1.15 (R<0.05); 1.21 (R<0.05); A statistically significant decrease of 1.35 (R<0.01) and 1.49 (R<0.001) times. MCV indicator 1.14 (R<0.05); 1.20 (R<0.05); 1.3 (R<0.05) and 1.42 (R<0.001) times, MSN – 1.19 (R<0.05); 1.3 (R<0.05); 1.4 (R<0.001) and 1.64 (R<0.001) times, MSNS indicator – 1.17 (R<0.05) (R<0.05); 1.23 (R<0.01); We observed a decrease of 1.34 (R<0.001) and 1.55 (R<0.001) times. although the number of leukocytes did not change, the EC was statistically reliable - 3.04 (R<0.001); 3.81 (R<0.001); 4.37 (R<0.001) and 3.67 (R<0.001) times increase was observed.

The frequency of Hp 1-1, Hp 2-1 and Hp 2-2 phenotypes in RA patients is 19.6; It was 55.4 and 25%, that is, Hp 1-1 and Hp 2-1 phenotypes were slightly predominant, and Hp 2-2 phenotype was less common. In addition, the Hp 1-1 phenotype is more common among female patients (ratio with males - 1: 5.5).

It should be noted that Nr 1-1 phenotype was found in 35% of RA patients without anemia, Nr 2-1 phenotype increased to 65%, and Nr 2-2 phenotype was not found. In patients with anemia, the Nr 1-1 phenotype was 2 times more frequent than in the above group, and the occurrence of the Nr 2-2 phenotype increased to 28%. In RA patients, Nr 1-1 phenotype was found in the lowest percentage (13.8%) of patients with SKA compared to patients without anemia, while the tendency of Nr 2-1 phenotype was found to decrease, the number of patients with Nr 2-2 increased to 31.9%. In the group of patients with TTA, the number of

patients with the Nr 1-1 phenotype increased approximately 2-fold compared to patients with SKA, and the occurrence of the Nr 2-2 phenotype increased to 20%. The highest incidence of this phenotype was observed in the group of RA+SKA+TTA patients (60%).

So, the phenotypic features of the organism of RA patients determine the tendency to develop anemia, and also make it possible to predict what type of anemia may develop.

Conclusions: 76.6% of all RA patients participating in the study were diagnosed with anemia of various forms and degrees, which are characterized by the relationship between the duration, activity, and X-ray appearance of the disease. The phenotypic characteristics of the organism of RA patients determine the predisposition to the development of anemia, and also make it possible to predict the type of anemia that may develop.

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