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ANEMIA IN RHEUMATOID ARTHRITIS: PREVALENCE, PATHOGENESIS, CLINICAL AND DIAGNOSTIC SIGNIFICANCE *(literature review)*

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Annotation. Anemia is one of the most common extra-articular manifestations of rheumatoid arthritis (RA) and represents an important clinical and prognostic factor. The prevalence of anemia in patients with RA remains high and varies depending on disease activity, duration, and comorbid conditions. The pathogenesis of anemia in rheumatoid arthritis is multifactorial and includes anemia of chronic inflammation, iron deficiency anemia, and, less frequently, anemia related to medication use or concomitant chronic diseases. Chronic systemic inflammation plays a central role through cytokine-mediated suppression of erythropoiesis, impaired iron metabolism, and reduced erythropoietin response. Clinically, anemia contributes to fatigue, decreased physical function, and reduced quality of life, and it may reflect the severity and activity of the underlying inflammatory process.
Keywords: Rheumatoid arthritis; anemia; chronic inflammation; iron deficiency; anemia of chronic disease; pathogenesis; diagnosis; clinical significance.

Introduction. Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disease of connective tissue characterized by progressive erosive joint damage and systemic extra-articular manifestations. The prevalence of RA in various populations ranges from 0.6 to 1.3%, and the annual incidence is approximately 0.02% [1–5].

Despite significant progress in diagnosis and treatment, RA remains a leading cause of early disability and decreased quality of life for patients. Extra-articular manifestations of the disease, among which anemia occupies a prominent place, play a significant role in determining the unfavorable prognosis [6–9].

Anemia is one of the most common systemic manifestations of rheumatoid arthritis and, according to various authors, is detected in 30–70% of patients [10–13]. The presence of anemic syndrome is associated with higher inflammatory activity, increased ESR and C-reactive protein levels, and high DAS28 index values [14–18].

Decreased hemoglobin concentrations in patients with RA lead to deterioration of tissue oxygenation, the development of chronic hypoxia, and exacerbation of functional impairment of the cardiovascular and respiratory systems. Clinically, this manifests as severe weakness, fatigue, decreased physical performance, and a decline in quality of life [19–23].

Anemia in RA is multifactorial. The most common forms observed in patients include:

- anemia of chronic disease (ACD);
- iron deficiency anemia (IDA);
- mixed variants of anemia.

ACD is diagnosed in 25–64% of cases and is considered one of the systemic manifestations of a chronic inflammatory process. IDA is detected in 36–48% of patients and is typically associated with chronic gastrointestinal bleeding associated with long-term use of nonsteroidal anti-inflammatory drugs and glucocorticosteroids [24–29].

The leading role in the development of anemia in RA is played by proinflammatory cytokines - interleukin-1, interleukin-6, tumor necrosis factor-α, which have an inhibitory effect on erythropoiesis, reduce the production of erythropoietin and disrupt iron metabolism [30–33].

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Chronic inflammation leads to a reduction in the lifespan of erythrocytes, increased destruction in the reticuloendothelial system and a decrease in the sensitivity of erythroid cells to erythropoietin [34–37].

A key regulator of iron metabolism in anemia of chronic inflammation is hepcidin , a liver peptide hormone classified as an acute-phase reactant. Interleukin-6 stimulates increased hepcidin production , leading to blockade of ferroportin , decreased iron absorption in the intestine, and impaired iron release from macrophages [38–42].

hepcidin levels correlate with the activity of rheumatoid arthritis, the severity of the inflammatory syndrome and the degree of hemoglobin reduction, which confirms its important role in the pathogenesis of ACD in RA [43–45].

Differential diagnosis of anemia of chronic disease and iron deficiency anemia presents significant challenges, as serum iron levels may be reduced in both forms. In this regard, determination of ferritin levels, total iron-binding capacity of serum, soluble transferrin receptors, and assessment of inflammatory markers are of particular importance [46–50].

Incorrect interpretation of laboratory data can lead to the unjustified prescription of iron supplements, which increases the risk of its excess accumulation in the body and aggravation of the inflammatory process.

The primary focus of anemia correction in RA is effective control of inflammatory activity. Iron supplementation is indicated only in cases of confirmed absolute iron deficiency or mixed anemia [51–53].

A promising direction in the treatment of anemia of chronic disease is the use of biological drugs, in particular interleukin-6 inhibitors (tocilizumab), which help reduce the level of hepcidin and restore the availability of iron for erythropoiesis [54–58].

Conclusion

Anemia is a common and clinically significant extra-articular manifestation of rheumatoid arthritis, significantly impacting the course of the disease, quality of life, and prognosis of patients. The multifactorial nature of the pathogenesis of anemia in RA requires a comprehensive approach to diagnosis and treatment, taking into account the activity of the inflammatory process and iron metabolism. Modern anti-inflammatory and biological therapies offer new opportunities for the effective treatment of anemia of chronic inflammation in this category of patients.

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