



## **PATHOLOGICAL BLOOD CHANGES IN SYSTEMIC LUPUS ERYTHEMATOSUS**

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<b>Received:</b> December 11 <sup>th</sup> 2022 <b>Accepted:</b> January 11 <sup>th</sup> 2023 <b>Published:</b> February 20 <sup>th</sup> 2023	The article describes the features of the course of systemic lupus erythematosus in patients with anemia of chronic diseases, iron deficiency anemia and autoimmune hemolytic anemia. Patients from 18 to 60 years old with varying degrees of disease activity were examined. Various examination methods used to diagnose systemic lupus erythematosus as an autoimmune disease are reviewed, some of these methods include (complete blood count, serum iron, hematocrit, etc.). In addition, the pathological mechanism of anemic syndrome in systemic lupus erythematosus is discussed.

**Keywords:** systemic lupus erythematosus, anemia of chronic diseases, iron, iron-deficiency anemia, hemoglobin.

**INTRODUCTION.** Systemic lupus erythematosus (M32 according to ICD-10) is a systemic autoimmune disease of unknown etiology, which is based on a genetically determined violation of immune regulation, which determines the formation of specific antibodies to antigens of cell nuclei and immune complexes with the development of immune inflammation in the tissues of many organs [1,3 ,5, 6, 7, 10, 14, 16].

Hematological parameters are of great importance in the diagnosis of SLE, especially in determining its activity and the risk of progression. The hematological manifestations observed in SLE can be represented by both true autoimmune phenomena of autoimmune hemolytic anemia (AHA), leukopenia (LP), and thrombocytopenia (TP), as well as cytopenic syndromes associated with the use of immunosuppressive drugs. Currently, it is known that hematological manifestations vary significantly in severity and often do not require specific treatment, with the exception of severe cytopenia, refractory to glucocorticoids (GC) [3,11,15]; at the same time, their significance as possible predictors of the further course of SLE has not been sufficiently studied.

One of the causes of anemia in SLE is anemia of chronic diseases (ACD), the cause of which is considered to be a disorders of iron metabolism in the macrophage system under the influence of inflammatory cytokines [2,4,5,8,9]. This type of anemia in SLE is much less studied, although the frequency of ACD in SLE varies from 11.9% to 37.1%. [1,3,5,6,7]. There is practically no information about the existence of iron deficiency anemia (IDA) in SLE, although this type of anemic syndrome can occur in these patients as well as in the general population. In single studies, it is indicated that changes in the level of serum ferritin and the content of bone marrow sideroblasts are practically not informative in the diagnosis of this type of anemia (Lila A.M., 2017).

Thus, the pathogenetic mechanisms of anemic syndrome in SLE are complex, while there are no clear clinical and laboratory criteria for it, and there are practically no data on the relationship between anemic syndrome and clinical manifestations of SLE [4,5].

**AIM OF STUDY** - to characterize the clinical and hematological signs of SLE in patients of different age groups.

**MATERIALS AND METHODS.** We examined 60 patients (51 women and 9 men) with SLE aged 18 to 60 years who were treated at the TMA Multidisciplinary Clinic in 2020-2023. The diagnosis was established in accordance with the 2012 SLICC (Systemic Lupus International Collaborating Clinics) criteria [1]. A mandatory condition for the inclusion of patients in the study was their signed informed consent. The average age of the examined patients was 48.9±15.6 years.

The average time from the onset of the disease to the establishment of a diagnosis and the start of treatment was 7.3±1.3 months. At the time of the examination, the average duration of SLE in years was 8.7±2.8 (96.6±37.7 in months). All patients underwent a standard examination, which included an assessment of the activity of the disease according to the SLEDAI 2K index (Systemic Lupus Erythematosus Disease Activity Index-2K), immunological parameters: antinuclear factor, rheumatoid factor (RF), linical and biochemical analyzes of blood, urine according to unified methods.

**RESULTS AND DISCUSSION.** Among the examined patients, there were various systemic signs of the disease. All patients had damage to the skin, joints, kidneys, heart, lungs. The frequency of joint damage in the examined patients was 90.0% (n=54). The most common were polyarthrits 60% (n=36), skin lesions in the form of facial erythema 66% (n=41) (Fig. 1.),

discoid lupus 50% (n=30) and photosensitivity 60% (n=36). Lung involvement was determined in 35 (58%) patients with SLE. Most often, X-ray or computed tomography of the lungs revealed infiltrates 25% (n=15), less often cavities in the lungs 10% (n=6). One patient (1.1%) with SLE was diagnosed with hemorrhagic alveolitis. Respiratory system involvement included involvement of various lung regions: airways, parenchyma, vessels, pleura, and diaphragm.

Kidney damage was detected in 70% of SLE patients (n=42). Of 28 (64%) SLE patients with kidney

damage in the form of nephritis, glomerular filtration rate was reduced by more than 50% (mean creatinine  $3.21 \pm 1.12$  mg/dl, mean GFR  $29.8 \pm 9.9$  ml/min/1.73 m<sup>2</sup>). Of 34 (71%) patients with kidney damage, proteinuria was detected, while proteinuria more than 0.5 g/day was determined in 15 (16.7%) patients, hematuria - in 12 (20.0%) patients.

Heart damage was observed in 24 (40.0%) patients with SLE. In 22 (36.7%) patients, according to ECHO-CG, atherosclerotic changes in the aortic valve were determined.



Fig. 1. Patient K. Skin manifestations of SLE. (Case report No. 1494/181).

Myocarditis and chronic heart failure were detected in 10 (16%) patients with SLE. Pericarditis and endocarditis were diagnosed in 3 (5.0%) and 6 (10%) patients, respectively. In 45% of patients, rheumatoid factor was determined in the blood serum, antinuclear antibodies were detected in 1/3 of the patients. Among all patients, IDA was detected in 68% of cases.

To compare ACD and IDA, patients were divided into 2 groups. Group 1 consisted of patients with ACD, group 2 patients with IDA (Tabl.1). Of these, mild anemia was in 82% of patients, moderate - in 12%, severe - in 6%.

There were no signs of overt or covert bleeding. The groups were matched for sex, age, and disease activity. In group 1 with ACD, a significant decrease in reticulocytes was observed (possibly associated with hemolysis), high or normal ferritin levels, and anemia was hypochromic in nature with a normal level of serum iron. These data correlate with the data of other authors [3,6].

In the group with iron deficiency anemia (Group 2), there were mainly signs of a decrease in iron stores, a low level of ferritin, an increase in the total iron-binding capacity of serum with a low level of serum iron. Among patients of group 1, thrombocytopenia was significantly higher. Leukopenia occurred in both groups, but especially low rates were observed in patients of group 1. Some researchers regard leukopenia as a manifestation of an autoimmune process as a result of the production of antibodies to peripheral blood leukocytes, which correlates with the degree of SLE activity [4,5].

Other authors associate leukopenia with increased apoptosis of peripheral blood lymphocytes, morphological and genetic changes in neutrophils [8]. It is noteworthy that patients with severe leukopenia had a statistically significant prevalence of chronic SLE. A decrease in hematocrit was typical for patients in both groups, but significantly reduced in patients of group 2. This was possibly accompanied by hypoxia of



various organs, since it is the red blood cells that normally carry oxygen throughout the body, which worsened the condition of the patients. Polyarthrit

is and nephritis occurred in both groups, but significantly more often in patients with ACD in the form of active nephritis [10, 11, 15].

Laboratory indicator	1group (n=18) ACD	2group (n=20) IDA	P
Hemoglobin	95±5,1	85±2,6	<0,05
Hematocrit	35±3,3	28±2,5	<0,05
Eritrocites	2,1±1,02	4,2±1,3	<0,05
CI	0,8±0,16	0,8±0,04	
Ferritin	50±3.1	38±2,6	<0,01
Total iron binding capacity	45±7,2	60±9,1	<0,05
Serum iron	18±3,5	7±2,6	<0,05
Reticulocytes	11±2,4	7±1,04	<0,05
Leukocytes	4±0,7	9±1,3	0,01
Platelets	98±8,2	235±21,3	0,001

Tabl.1. Hematological manifestations of SLE

The examined groups were dominated by patients with chronic SLE (75.4% and 67.9%, respectively). Among the manifestations of SLE, lesions of the lungs (52.3%), kidneys (50.8%) and the nervous system (52.3%), occupied the central place in frequency, while lesions of the gastrointestinal tract (7%) were much less common. Kidney damage developed early (after 2.5 ± 2.3 months from the onset of general and/or local symptoms) and mainly in patients with ACD. Arthritis had a mono-oligoarticular character with a predominant lesion of the hand, large joints, sometimes it resembled the debut of RA. A decrease in hemoglobin level (110 g/l ≤ Hb < 120 g/l) was determined in 57% of patients, and a decrease in serum iron levels with normal hemoglobin levels in 18%.

Thus, a total iron deficiency state, including developed IDA, was observed in 93% of SLE patients. Among the clinical manifestations of SLE, polyarthrit, facial erythema, nephritis, alopecia, myocarditis, Raynaud's syndrome were more common in patients with ACD. (Fig.1) ACD was characterized by a moderate decrease in hemoglobin (95±5.1 g/l versus 85±2.6 g/l), normocytosis, normo- or moderate hypochromia of erythrocytes, and a moderate increase in the number of reticulocytes.

**CONCLUSION.** Reduced serum iron levels and transferrin saturation are noted in both anemias, but the cause is different. If in IDA these changes are associated with absolute iron deficiency, then in ACD iron reserves are sufficient, but they cannot be utilized from the reticuloendothelial system.

An indicator of the state of the iron depot is the level of serum ferritin, which had normal or elevated values in ACD, while it was reduced in IDA. The severity of anemia correlated to some extent with the severity of the disease. Thus, IDA occurred in all children with stage III SLE activity. At the same time, it was of a severe and moderate nature, while with a lesser severity of the disease, mild anemia was more often observed.

Changes in peripheral blood in SLE are usually polyvalent - anemia, leukopenia, thrombocytopenia - and may be the cause of the development of hematological "masks" during the course of the disease. Therefore, the main goal of SLE therapy should be not only the suppression of inflammatory changes in the affected organ and the autoimmune response, but also the fight against anemic syndrome.

**LITERATURE**

1. Alekseeva E.I., Dvoryakovskaya T.M., Nikishina I.P., Denisova R.V., Podchernyaeva



- N.S., Sukhorukikh O.A., Shubina L.S. Systemic lupus erythematosus: clinical guidelines. Part 1. Clinical guidelines.
2. Bugrova O.V., Uvarova E.A. To the question of the peculiarities of the pathogenesis of anemic syndrome in SLE.Zh. Vestnik OGU.2004(2). pp.138-143.
  3. Iskanova G.Kh., Suleimanov A.S., Egamova S.Sh. Systemic vasculitis in children. J. Scientific discussion: questions of medicine, 2016. No. 12. P. 5-9.
  4. Kuchma G. B., Bugrova O. V. Changes in the level of leukocytes of the leukocyte formula in patients with systemic lupus erythematosus depending on the course of the disease and the nature of the therapy. J. Vestnik VolIGMU.2/34. 2010.S.100-103.
  5. Petrov A.V., Beloglazov V.A., Shaduro D.V., Gaffarova A.R., Petrov A.A. Hematological manifestations of systemic lupus erythematosus in the early stage: association with other symptoms of the disease and possible prognostic significance. J. Scientific and practical rheumatology. 2019;57(2):166–170
  6. Uvarova E. A. Features of anemic syndrome in patients with systemic lupus erythematosus. Abstract of diss.c.m.s. 2012.
  7. Barr S, Zonana-Nacach A, Magder L, Petri M. Patterns of disease activity in systemic lupus erythematosus. Arthritis Rheum.1999 Dec;42(12):2682-8. doi: 10.1002/1529-0131(199912)42:12<2682::AID-ANR26>3.0.CO;2-6.
  8. Bastian H, Roseman J, Mcgwin G, et al. Systemic lupus erythematosus in three ethnic groups. XII. Risk factors for lupus nephritis after diagnosis, Lupus. 2002; 11(3): 152-60. doi: 10.1191/ 0961203302 lu158oa.
  9. Bernatsky S, Boivin J, Joseph L, et al. Mortality in systemic lupus erythematosus. Arthritis Care Res (Hoboken). 2012 Feb;64(2):159-68. doi: 10.1002/acr.20683.
  10. Faurshou M, Starklint H, Halberg P, Jacobsen S. Prognostic factors in lupus nephritis: diagnostic and therapeutic delay increases the risk of terminal renal failure. J Rheumatol. 2006 Aug;33(8):1563-9.
  11. Karimdzhanov IA, Iskanova GH, Israilova NA, et al. Juvenile Idiopathic Arthritis: Etiopathogenesis. Therapy And Outcomes. Journal of Pharmaceutical Negative Results. 2022,13(8): 498-506. doi: 10.47750/pnr.2022.13.S08.65
  12. Bruce I, Isenberg D, Wallace D, et al. Anti-C1q antibodies in systemic lupus erythematosus. Lupus. 2015 Jan;24(1):42-9. doi: 10.1177/0961203314547791. Epub 2014 Aug 14.
  13. Hu W, Chen Y, Wang S, et al. Clinical. Morphological Features and Outcomes of Lupus Podocytopathy. Clin J Am Soc Nephrol.2016 Apr 7;11(4):585-92. doi: 10.2215/CJN.06720615. Epub 2016 Mar 16.
  14. Petri M, Orbai A, Alarcon G, et al. Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. Arthritis Rheum. 2012 Aug;64(8):2677-86. doi: 10.1002/art.34473.
  15. Gladman DD, Ibanez D, Urowitz MB. Systemic lupus erythematosus disease activity index 2000. J. Rheumatol. February 2002; 29(2):288-91.
  16. Gladman DD, Ginzler E, Goldsmith C, et al. The development and initial validation of the systemic lupus international collaborating clinics/American college of rheumatology damage index for systemic lupus erythematosus. Arthritis Rheum. 1996 Mar;39(3):363-9.doi:10.1002/art.1780390303.