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DIAGNOSTIC VALUE OF LABORATORY MARKERS OF SYNTROPIC LESIONS OF THE CIRCULATORY SYSTEM ORGANS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Abstract.

Introduction: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that affects almost all internal organs, among which circulatory system organs (CSO) lesions are not only among the most common but also at the top of the list of causes of mortality. The tactics of treatment of patients with SLE without and in combination with CSO lesions are fundamentally different, and therefore, improving diagnostic methods will help to enhance the effectiveness of the management of this category of patients.

The aim of the study: To determine the diagnostic value of laboratory markers of syntropic lesions of the circulatory system organs in patients with systemic lupus erythematosus.

Materials and methods: The research included 125 patients with SLE with CSO lesions, among whom the vast majority were young women. Patients were stratified according to syntropy. Syntropic lesions were those whose frequency significantly increased with increasing severity of SLE: retinal angiopathy, capillaritis, Raynaud's syndrome, livedo reticularis, atherosclerosis, mitral valve insufficiency, mitral valve thickening, pericardial effusion, pulmonary hypertension, myocarditis, endocarditis, symptomatic arterial hypertension, and vein thrombosis. During the study, the diagnostic value of individual laboratory markers and their constellations in terms of sensitivity, specificity, and accuracy in patients with SLE with syntropic lesions of CSO was determined step by step, and the one with the highest diagnostic value for the diagnosis of these lesions was chosen. The difference was considered statistically significant if $p<0.050$. The association coefficient and the contingent coefficient were used to determine the closeness of the relationship between the marker and the syntropic lesion. The relationship was considered confirmed if the association coefficient was ≥ 0.50 or the contingent coefficient was ≥ 0.30.

Results: We studied the diagnostic value of individual laboratory markers and their constellations in terms of sensitivity, specificity, and accuracy in patients with SLE with syntropic CSO lesions. It was found that the best diagnostic value for the diagnosis of retinal angiopathy is the constellation of ↑ LDL + ↑ IA + ↑ anti-ds DNA + ↑ ANA; capillaritis – ↑ β-globulins + ↑ IA + ↑ anti-ds DNA + ↑ antiphospholipid antibodies Ig M + ↑ anti-Sm + ↓ C4; Raynaud's syndrome – a separate marker ↓ C3; livedo reticularis – ↑ ESR + ↑ small CIC + ↑ anti-ds DNA + ↑ anti-Sm; atherosclerosis – ↓ hemoglobin + ↑ LDL + ↑ ANA + ↓ C4; mitral valve insufficiency – ↑ ESR + ↑ anti-ds DNA + ↑ ANA + ↑ antiphospholipid antibodies Ig M; mitral valve stenosis – ↑ ESR+↑ LDL + ↑ small CK + ↑ ANA; pericardial effusion – erythropenia + ↑ C-RP + ↑ lupus anticoagulant; pulmonary hypertension – hypercholesterolemia + ↑ LDL + ↑ anti-ds DNA + ↑ ANA; myocarditis – an individual marker ↓ C4; endocarditis – ↑ ESR + ↑ total fibrinogen + ↑ γ-globulins + hypercholesterolemia + ↑ anti-Sm; symptomatic arterial hypertension – ↑ LDL + ↑ anti-ds DNA + ↑ ANA + ↑ anti-SSA (Ro); vein thrombosis – erythropenia + ↓ hemoglobin + ↑ LDL + ↑ ANA.

Conclusions: For each syntropic lesion in patients with systemic lupus erythematosus, an individual laboratory marker or constellations have been identified that having the best diagnostic value for the diagnosis of these lesions.

Key words. Systemic lupus erythematosus, circulatory system organs lesions, syntropic lesions, comorbidities, laboratory markers, constellations, diagnostic value.

Introduction.

Systemic lupus erythematosus (SLE) is one of the most severe diseases in rheumatology. It is a chronic autoimmune disease with multisystemic lesions of unclear etiology that occurs as a consequence of numerous endogenous and exogenous factors in case of genetic predisposition [1]. SLE is characterized by the hyperproduction of a large number of autoantibodies and immune complexes that cause immunoinflammatory damage to almost all internal organs [2], among which circulatory system organs (CSO) lesions are not only among the most common but also, they are at the top the list of causes of mortality in patients with SLE [3].

The tactics of management of patients with SLE without and in combination with CSO lesions are fundamentally different, and protocol methods for instrumental diagnosis of CSO lesions are rarely available and often costly. Patients with SLE with syntropic lesions of CSO (syntropic lesions are those whose frequency increases significantly with increasing activity of SLE because they have etiologic and/or pathogenetic mechanisms, common with the underlying condition), who have a diagnosis of the underlying condition, verified with protocol laboratory tests of blood and urine [4,5], determining the diagnostic value of these laboratory markers for syntropic lesions of CSO will help to improve the effectiveness of the management of this category of patients.

The aim of the study. To determine the diagnostic value of laboratory markers of syntropic lesions of the circulatory system organs in patients with systemic lupus erythematosus.

Materials and Methods.

After signing a voluntary consent to participate, as required by the Helsinki Declaration of Human Rights, the Council of Europe Convention on Human Rights and Biomedicine, in a randomized manner with preliminary stratification based on the presence of SLE and CSO lesions [6-8], the study involved 125 patients, including 110 women (88.00%) and 15 men (12.00%) aged 18 to 74 years (mean age 42.48±1.12 years), including

syntropic lesions: retinal angiopathy (32 patients), capillaritis (4 patients), Raynaud's disease (67 patients), livedo reticularis (35 patients), atherosclerosis (13 patients), mitral valve insufficiency (MVI) (55 patients), MV thickening (47 patients), pericardial effusion (22 patients), pulmonary hypertension (16 patients), myocarditis (29 patients), endocarditis (2 patients), symptomatic arterial hypertension (AH) (43 patients), vein thrombosis (7 patients).

To determine the diagnostic value of laboratory markers of syntropic lesions of CSO in patients with SLE, we analyzed the indicators of complete blood count (erythrocytes, hemoglobin, platelets, leukocytes, leukocyte formula, erythrocyte sedimentation rate (ESR)) and biochemical blood test (creatinine, aspartate aminotransferase (AST), alanine aminotransferase (ALT), C-reactive protein (CRP), antistreptolysin O (ASLO), rheumatoid factor (RF)), coagulogram (prothrombin time, prothrombin index, total fibrinogen, international normalized ratio (INR)), proteinogram (total protein, albumin, α1-globulins, α2-globulins, β-globulins, γ-globulins), lipidograms (total cholesterol, triglycerides, low-density lipoprotein (LDL), high-density lipoprotein (HDL)), atherogenicity index (AI)), the content of circulating immune complexes (CIC) (large, medium, small), specific immunological studies (lupus erythematosus (LE) cells, antibodies to double-stranded deoxyribonucleic acid (anti-dsDNA), antinuclear antibodies (ANA), antiphospholipid antibodies Immunoglobulin M (IgM), antiphospholipid antibodies Immunoglobulin G (IgG), anti-Sjogren's-syndrome-related antigen A autoantibodies (anti-SSA (Ro)) and anti-Smith (anti-Sm) antibodies, complement components C3 and C4), as well as complete urine analysis (protein, components of organized urine sediment)).

For the study, laboratory markers were selected that were statistically significantly different in the number of cases in patients with SLE without the studied syntropic lesion of CSO ($p < 0.050$) and had a positive association with syntropic lesions (association coefficient (CA) greater than 0.00).

The study was conducted in two stages. At *the first stage*, the diagnostic value of individual laboratory markers was determined by sensitivity, specificity, and accuracy in patients with SLE with 12 syntropic lesions of CSO (in patients with endocarditis, separately evaluated laboratory markers did not have statistically significant differences from those in patients with SLE without them) and the one with the best diagnostic value based on the highest value of the sum of sensitivity and specificity was selected (diagnostic accuracy is significantly higher than 50.00% as per one-sided proportion test, $p < 0.050$), at *the second stage* – the diagnostic value of the constellations of these laboratory markers in patients with SLE with 13 syntropic lesions of CSO (all evaluated constellations of laboratory markers in all patients with 13 syntropic lesions of CSO had a statistically significant relationship with the lesion and their diagnostic accuracy was significantly higher than 50.00 % (based on a one-sided proportion test)), and, additionally, the closeness of the relationship between marker constellations and syntropic lesions of CSO and between individual markers and syntropic lesions of CSO in patients with SLE were compared.

The actual material was statistically processed on a personal computer in Excel, 2010 and Statistica 6.0 using descriptive statistics. The diagnostic (sensitivity, specificity, and accuracy) values were calculated based on contingency tables. To determine the constellations of laboratory markers, Newton's binomial coefficient was used applying Solver add-in to MS Excel. The best constellation was the one with the highest sum of sensitivity and specificity among all possible constellations. The difference was considered statistically significant if $p < 0.050$. To determine the closeness of the relationship between the marker and the lesion, the CA, and the contingent coefficient (CC) were used. The relationship was considered confirmed if $CA \geq 0.50$ or $CC \geq 0.30$.

Results and Discussion.

The first stage of the research allowed us to determine that in patients with SLE with retinal angiopathy, the sensitivity of the thrombocytopenia marker (direct correlation, $p = 0.037$) is 40.00%, specificity – 77.63%, accuracy – 66.98%; sensitivity of hypercholesterolemia (direct correlation, $p = 0.017$) reaches 80.65%, specificity – 40.91%, accuracy – 51.26%; sensitivity of hypertriglyceridemia (direct correlation, $p = 0.013$) is 33.33%, specificity – 87.18%, accuracy – 72.22%; sensitivity of ↑ LDL (direct correlation, $p = 0.004$) is 93.10%, specificity – 32.47%, accuracy – 49.06%; sensitivity of ↑ IA (direct correlation, $p = 0.008$) is 75.86%, specificity – 50.65%, accuracy – 57.55%; sensitivity of ↑ anti-dsDNA (direct correlation, $p = 0.009$) is 96.88%, specificity – 21.51%, accuracy – 40.80%. Hypertriglyceridemia has the best diagnostic value for detecting retinal angiopathy in patients with SLE (diagnostic accuracy is significantly higher than 50.00%, $p < 0.001$).

The sensitivity of ↑ ALT (direct correlation, $p = 0.031$) as a marker of capillaritis was 75.00%, specificity – 79.83%, and accuracy – 79.68%. ↑ ALT is a diagnostically valuable marker for the detection of capillaritis (diagnostic accuracy is significantly higher than 50.00%, $p < 0.001$).

The sensitivity of the marker, namely ↓ hemoglobin (direct correlation, $p = 0.016$), for the detection of Raynaud's syndrome in patients with SLE, is 68.66%, specificity – 50.00%, accuracy – 60.00%; sensitivity of lymphopenia (direct correlation, $p = 0.039$) is 34.33%, specificity – 79.31%, accuracy – 55.20%; sensitivity of ↑ ESR (direct correlation, $p = 0.007$) is 82.09%, specificity – 37.93%, accuracy – 61.60%; sensitivity of ↑ small CIC (direct correlation, $p = 0.004$) as a marker reaches 100.00%, specificity – 22.73%, accuracy – 72.13%; the sensitivity of LE cells (direct correlation, $p = 0.014$) is 37.29%, specificity – 82.61%, accuracy – 57.14%; the sensitivity of ↓ C3 (direct correlation, $p = 0.010$) as a marker reaches 72.22%, specificity – 73.33%, accuracy – 72.73%; the sensitivity of ↓ C4 (direct correlation, $p = 0.020$) is 55.56%, specificity – 82.35%, accuracy – 68.57%. The optimal diagnostic value for the detection of Raynaud's syndrome in patients with SLE is ↓ C3 ($p = 0.005$).

The sensitivity of monocytosis (direct correlation, $p = 0.009$) as a marker of livedo reticularis in patients with SLE is 20.00%, specificity – 95.56%, accuracy – 74.40%; sensitivity of ↑ γ-globulins (direct correlation, $p = 0.044$) reaches 50.00%, specificity – 69.01%, accuracy – 63.92%; sensitivity of ↑ ANA (direct correlation, $p = 0.044$) as a marker reaches 91.43%, specificity – 22.22%, accuracy – 41.60%. The best laboratory marker for detecting livedo reticularis in patients with SLE is ↑ γ-globulin ($p = 0.003$).

In patients with SLE with atherosclerosis, the sensitivity of ↑ LDL (direct correlation, p = 0.037) as a marker is 100.00%, specificity – 31.25%, accuracy – 62.07%; sensitivity of LE-cells (direct correlation, p = 0.049) is 54.55%, specificity – 84.62%, accuracy – 70.83%; sensitivity of ↓ C4 (direct correlation, p = 0.044) as a marker is 80.00%, specificity – 85.71%, accuracy – 83.33%. The best diagnostic value for the detection of atherosclerosis in patients with SLE is ↓ C4 (p = 0.010).

Dyslipidemia and its association with atherosclerosis in patients with SLE was described by L. F. Bogmat, et al. [9].

The sensitivity of the marker, namely thrombocytopenia (direct correlation, p = 0.037), for the detection of MVI, is 35.29%, specificity – 80.00%, accuracy – 58.49%; sensitivity of lymphopenia (direct correlation, p = 0.029) is 36.36%, specificity – 78.57%, accuracy – 60.00%; sensitivity of ↑ INR (direct correlation, p = 0.015) is 41.38%, specificity – 90.00%, accuracy – 61.22%; sensitivity of ↑ anti-dsDNA (direct correlation, p = 0.024) is 90.91%, specificity – 22.86%, accuracy – 52.80%; sensitivity of ↑ ANA (direct correlation, p = 0.004) reaches 92.59%, specificity – 26.47%, accuracy – 55.74%; sensitivity of ↑ antiphospholipid antibodies IgG (direct correlation, p = 0.046) is 60.47%, specificity – 57.89%, accuracy – 59.26%. The best laboratory marker for the detection of MVI in patients with SLE is ↑ IgG antiphospholipid antibodies (p = 0.048). Similar results were published in a study by A.G. Mohammed and colleagues [10], who pointed to a significant association between mitral valve regurgitation and positive anti-dsDNA in patients with SLE.

It was found that in patients with SLE with MV thickening, the sensitivity of the thrombocytopenia marker (direct correlation, p = 0.028) was 38.46%, specificity – 79.10%, accuracy – 64.15%; the sensitivity of lymphopenia (direct correlation, p = 0.003) as a marker is 42.55%, specificity – 80.77%, accuracy – 66.40%; sensitivity of ↑ ESR (direct correlation, p = 0.049) is 80.85%, specificity – 32.05%, accuracy – 50.40%; sensitivity of ↑ LDL (direct correlation, p = 0.011) is 86.36%, specificity – 33.87%, accuracy – 55.66%; sensitivity of ↑ IA (direct correlation, p = 0.021) as a marker reaches 68.18%, specificity – 51.61%, accuracy – 58.49%; sensitivity of ↑ ANA (direct correlation, p = 0.018) reaches 91.49%, specificity – 24.00%, accuracy – 50.00%; sensitivity of ↑ urine sediment (direct correlation, p = 0.046) is 48.89%, specificity – 65.38%, accuracy – 59.35%. Lymphopenia has the best diagnostic value for detecting MV thickening in patients with SLE (p < 0.001).

The sensitivity of erythropenia (direct correlation, p = 0.001) for detecting pericardial effusion is 55.56%, specificity – 84.16%, accuracy – 79.83%; the sensitivity of leukocytosis (direct correlation, p = 0.048) is 27.27%, specificity – 88.35%, accuracy – 77.60%; the sensitivity of lymphopenia (direct correlation, p = 0.010) as a marker of pericardial effusion is 50.00%, specificity – 76.70%, accuracy – 72.00%; the sensitivity of ↑ creatinine (direct correlation, p = 0.002) is 45.45%, specificity – 85.29%, accuracy – 78.23%; the sensitivity of ↑ C-RP (direct correlation, p = 0.016) is 78.95%, specificity – 49.00%, accuracy – 53.78%; the sensitivity of ↑ prothrombin time (direct correlation, p = 0.048) is 55.56%, specificity – 66.28%, accuracy – 64.42%; the sensitivity of ↑ medium CIC (direct correlation, p = 0.039) for the detection of pericardial effusion is 66.67%, specificity – 69.23%, accuracy – 68.85%. The best laboratory marker for detecting pericardial effusion in patients with SLE is erythropenia (p < 0.001).

In patients with SLE with pulmonary hypertension, the sensitivity of the marker, namely ↑creatinine (direct correlation, p = 0.015), is 43.7%, specificity – 83.33%, accuracy – 78.23%; the sensitivity of hypercholesterolemia (direct correlation, p = 0.006) as a marker of pulmonary hypertension in patients with SLE is 93.75%, specificity – 39.81%, accuracy – 47.06%; the sensitivity of hypertriglyceridemia (direct correlation, p = 0.018) is 42.86%, specificity – 85.11%, accuracy – 79.63%; the sensitivity of ↑ LDL (direct correlation, p = 0.012) reaches 100.00%, specificity – 29.35%, accuracy – 38.68%; the sensitivity of the marker, namely ↑ IA (direct correlation, p = 0.049) is 78.57%, specificity – 46.74%, accuracy – 50.94%; the sensitivity of the presence of ↑ anti-dsDNA (direct correlation, p = 0.043) is 100.00%, specificity – 19.27%, accuracy – 29.60%. The best diagnostic value for detecting pulmonary hypertension in patients with SLE is hypertriglyceridemia (p < 0.001).

The sensitivity of erythropenia (direct correlation, p = 0.003) for the detection of myocarditis is 44.00%, specificity – 84.04%, accuracy – 75.63%; the sensitivity of ↓ hemoglobin (direct correlation, p = 0.002) reaches 82.76%, specificity – 46.88%, accuracy – 55.20%; sensitivity of monocytopenia (direct correlation, p = 0.037) is 27.59%, specificity – 87.50%, accuracy – 73.60%; sensitivity of ↑ creatinine (direct correlation, p = 0.021) for detection of myocarditis is 34.48%, specificity – 84.21%, accuracy – 72.58%; sensitivity of hypoproteinemia (direct correlation, p = 0.038) is 17.39%, specificity – 96.20%, accuracy – 78.43%; the sensitivity of ↑ AST (direct correlation, p = 0.012) was 34.48%, specificity – 86.17%, accuracy – 73.98%; the sensitivity of ↑ ALT (direct correlation, p = 0.004) was 41.38%, specificity – 84.04%, accuracy – 73.98%; the sensitivity of ↑ C-RP (direct correlation, p = 0.001) as a marker of myocarditis reaches 81.48%, specificity – 52.17%, accuracy – 58.82%; sensitivity of LE cells (direct correlation, p = 0.043) is 43.48%, specificity – 75.61%, accuracy – 68.57%; sensitivity of ↓ C3 (direct correlation, p = 0.002) is 90.91%, specificity – 68.18%, accuracy – 75.76%; sensitivity of ↓ C4 (direct correlation, p < 0.001) as a marker of myocarditis is 83.33%, specificity – 86.96%, accuracy – 85.71%. The best laboratory marker for detecting myocarditis in patients with SLE is ↓ C4 (p < 0.001).

It was found that the sensitivity of erythropenia and lymphopenia (direct correlation, p = 0.027 and p = 0.043, respectively) for detecting symptomatic hypertension was 32.50 and 37.21%, specificity – 83.54 and 76.83%, accuracy – 66.39 and 63.20%, respectively; the sensitivity of hypoproteinemia, ↑ ALT and ↑ C-RP (direct correlation, p < 0.001, p = 0.041 and p = 0.040, respectively) is 20.59, 30.95 and 65.85%, respectively, specificity – 100.00, 82.72 and 50.00%, respectively, accuracy – 73.53, 65.04 and 55.46%, respectively; sensitivity of ↑ LDL and ↑ IA (direct correlation, p = 0.022; p = 0.042, respectively) reaches 86.49 and 67.57%, specificity – 31.88 and 49.28%, accuracy - 50.94 and 55.66%, respectively; sensitivity of ↑ anti-dsDNA, ↑ ANA, ↑ antiphospholipid antibodies IgG, ↑

anti-SSA (Ro) (direct correlation, p = 0.020, 0.017, 0.023, 0.036, respectively) is 93.9 and 94.5 0.036, respectively) is 93.02, 92.68, 66.67, 88.89%, respectively, specificity – 21.95, 23.46, 56.86, 50.00%, respectively, accuracy – 46.40, 46.72, 60.49, 58.54%, respectively; the sensitivity of proteinuria (direct correlation, p = 0.002) as a marker of symptomatic hypertension reaches 48.84%, specificity – 78.05%, accuracy – 68.00%. Proteinuria has the best diagnostic value for detecting symptomatic hypertension in patients with SLE (p < 0.001).

It was determined that the sensitivity of erythropenia and ↑ γ-globulins (direct correlation, p = 0.005; p = 0.047, respectively) as markers of vein thrombosis reaches 71.43 and 80.00%, specificity – 81.25 and 67.03%, accuracy – 80.67 and 67.71%, respectively. The best laboratory marker for detecting vein thrombosis in patients with SLE is erythropenia (p < 0.001).

The second stage of the study allowed us to determine:

the constellation of laboratory markers deviating from the reference values (CA = 0.67) in patients with SLE with retinal angiopathy (↑ LDL + ↑ IA + ↑ anti-ds DNA + ↑ ANA (sensitivity – 75.00%, specificity – 62.37%, accuracy – 65.60%, p < 0.001,), which has a closer relationship with retinal angiopathy than a single laboratory marker (CA = 0.55) in these patients; the constellation of markers (CC = 0.38) in patients with SLE with capillaritis (↑ β-globulins + ↑ IA + ↑ anti-ds DNA + ↑ antiphospholipid antibodies Ig M + ↑ anti-Sm + ↓ C4 (sensitivity – 100.00%, specificity – 84.30%, accuracy – 84.80%, p = 0.001)), which has a closer relationship with capillaritis than a single laboratory marker (CA = 0.84); the constellation of markers (CA = 0.55) in patients with SLE with Raynaud's syndrome (↑ ESR + ↑ small CIC + ↑ ANA + ↓ C4 (sensitivity – 62.69%, specificity – 67.24%, accuracy – 64.80%, p = 0.001)), which has a weaker association with Raynaud's syndrome than a separate laboratory marker ↓ C3 (CA = 0.75); the constellation of markers (CA = 0.50) in patients with SLE with livedo reticularis(↑ ESR + ↑ small CK+↑ anti ds DNA+↑ anti-Sm (sensitivity – 62.86%, specificity – 62.22%, accuracy – 62.40%, p = 0.007)), which has a closer relationship with syntropic lesions than a single laboratory marker (CA = 0.40); the constellation of markers (CA = 0.94) in patients with SLE with atherosclerosis (↓ hemoglobin + ↑ LDL + ↑ ANA + ↓ C4 (sensitivity – 76.92%, specificity – 93.75%, accuracy – 86.21%, p < 0.001)), which has a closer relationship with atherosclerosis than a single laboratory marker (CA = 0.92); the constellation of markers (CA = 0.53) in patients with SLE with MVI (↑ ESR + ↑ anti-ds DNA + ↑ ANA + ↑ antiphospholipid antibodies Ig M (sensitivity – 56.36%, specificity – 71.43%, accuracy – 64.80%, p = 0.001)), which has a closer association with MVI than a single laboratory marker (CA = 0.40); the constellation of markers (CA = 0.58) in patients with SLE with MV thickening (↑ ESR + ↑ LDL + ↑ small CIC + ↑ ANA (sensitivity – 63.83%, specificity – 67.95%, accuracy – 66.40%, p < 0.001)), which has a closer relationship with syntropic lesions than a single laboratory marker (CA = 0.51); the constellation of markers (CA = 0.86) in patients with SLE with pericardial effusion (erythropenia + ↑ C-RP + ↑ lupus anticoagulant (sensitivity – 59.09%, specificity – 90.29%, accuracy – 84.80%, p = 0.001)), which has a closer relationship with pericardial effusion than a single laboratory marker (CA = 0.74); the constellation of markers (CA = 0.79) in patients with SLE with pulmonary hypertension (hypercholesterolemia + ↑ LDL + ↑ anti-ds DNA + ↑ ANA (sensitivity – 87.50%, specificity – 55.05%, accuracy – 59.20%, p = 0.001)), which has a closer relationship with pulmonary hypertension than a single laboratory marker (CA = 0.62); the constellation of markers (CA = 0.71) in patients with SLE with myocarditis (erythropenia + ↓ C4 (sensitivity – 51.72%, specificity – 84.38%, accuracy – 76.80%, p < 0.001)), which has a weaker association with myocarditis than a separate marker ↓ C4 (CA = 0.94); the constellation of markers (CC = 0.39) in patients with SLE with endocarditis (↑ ESR + ↑ total fibrinogen + ↑ γ-globulins + hypercholesterolemia + ↑ anti-Sm (sensitivity – 100.00%, specificity – 91.87%, accuracy – 92.00%, p = 0.009)) the constellation of markers (CA = 0.78) in patients with SLE with symptomatic hypertension (↑ LDL + ↑ anti-ds DNA + ↑ ANA + ↑ anti-SSA (Ro) (sensitivity – 83.72%, specificity – 60.98%, accuracy – 68.80%, p < 0.001)), which has a closer relationship with syntropic lesions than a single laboratory marker (CA = 0.54); the constellation of markers (CA = 0.90) in patients with SLE with vein thrombosis (erythropenia + ↓ hemoglobin + ↑ LDL + ↑ ANA (sensitivity – 71.43%, specificity – 88.14%, accuracy – 87.20%, p = 0.001)), which has a closer relationship with vein thrombosis than a single laboratory marker (CA = 0.83).

Conclusion.

The diagnostic value of individual laboratory markers and their constellations in terms of sensitivity, specificity and accuracy in patients with SLE with syntropic lesions of CSO was determined, and it was stated that ↑ LDL + ↑ IA + ↑ anti-ds DNA + ↑ ANA have the highest diagnostic value for the diagnosis of retinal angiopathy; capillaritis - ↑β-globulins + ↑ IA + ↑ anti-ds DNA + ↑ antiphospholipid antibodies Ig M + ↑ anti-Sm + ↓ C4; Raynaud's syndrome – an individual marker ↓ C3; livedo reticularis – ↑ ESR + ↑ small CIC+↑ anti-ds DNA + ↑ anti-Sm; atherosclerosis – ↓ hemoglobin + ↑ LDL + ↑ ANA + ↓ C4; MVI – ↑ ESR + ↑ anti-ds DNA + ↑ ANA + ↑ antiphospholipid antibodies Ig M; MV thickening – ↑ ESR + ↑ LDL + ↑ small CIC + ↑ ANA; pericardial effusion – erythropenia + ↑ C-RP + ↑ lupus anticoagulant; pulmonary hypertension – hypercholesterolemia + ↑ LDL + ↑ anti-ds DNA + ↑ ANA; myocarditis – an individual marker ↓C4; endocarditis – ↑ ESR + ↑ total fibrinogen + ↑ γ-globulins + hypercholesterolemia + ↑ anti-Sm; symptomatic hypertension – ↑ LDL + ↑ anti-ds DNA + ↑ ANA + ↑ anti-SSA (Ro); vein thrombosis – erythropenia + ↓ hemoglobin + ↑ LDL + ↑ ANA.

REFERENCES

1. Smith PP, Gordon C. Systemic lupus erythematosus: clinical presentations. Autoimmun Rev. 2010;10:43-45.
2. Bengtsson AA, Rönnblom L. Systemic lupus erythematosus: still a challenge for physicians. J Intern Med. 2017;281:52-64.
3. Stojan G, Petri M. Epidemiology of systemic lupus erythematosus: an update. Curr Opin Rheumatol. 2018;30:144-150.
4. Kobak L, Abrahamovych O, Abrahamovych U, et al. The nature and frequency of comorbid heart lesions in patients with systemic lupus erythematosus diagnosed by echocardiography, detection, and characteristics of their syntropic variants. Lviv Clinical Bulletin. 2023;2:36-43.

5. Viunitska LV, Gavrilenko TI, Pidgaina OA, et al. Features of laboratory diagnostics of collagen diseases. Ukrainian Journal of Rheumatology. 2022;88:25-33.
6. Order of the Ministry of Health of Ukraine No. 436 dated 03.07.2006 "On the approval of protocols for the providing medical care in the specialty "Cardiology" with changes introduced in accordance with Order of the Ministry of Health of Ukraine No. 455 dated 02.07.2014.
7. Order of the Ministry of Health of Ukraine No. 676 dated 12.10.2006 "On the approval of protocols for the provision of medical care in the specialty "Rheumatology" with changes introduced in accordance with orders No. 263 dated 11.04.2014, No. 762 dated 20.11.2015.
8. Recommendations of the American College of Rheumatology (ACR), 2010, 2012, taking into account the diagnostic criteria of ACR (1997) in the presence of 4 of 11 criteria.
9. Bogmat LF, Shevchenko NS, Bessonova IM, et al. Specific features of the blood lipid spectrum in children with systemic lupus erythematosus. Ukrainian Journal of Rheumatology. 2020;4:62-67.
10. Mohammed AG, Alghamdi AA, ALjahlan MA, et al. Echocardiographic findings in asymptomatic systemic lupus erythematosus patients. Clin Rheumatol. 2017;36:563-568.

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შესავალი**.** სისტემური წითელი მგლურა (SLE) არის ქრონიკული აუტოიმუნური დაავადება, რომელიც აზიანებს თითქმის ყველა შინაგან ორგანოს, რომელთა შორის სისხლის მიმოქცევის სისტემის (CS) ორგანოების დაზიანება არა მხოლოდ ერთ-ერთი ყველაზე გავრცელებულია, არამედ პირველ ადგილზეა სიკვდილიანობის მიზეზების სტრუქტურაში. სისტემური წითელი მგლურით (SLE) დაავადებული პაციენტების მკურნალობის ტაქტიკა სისხლის მიმოქცევის სისტემის (CS) ორგანოების დაზიანების გარეშე და მათი დაზიანებით კოორდინალურად განსხვავებულია და, შესაბამისად, დიაგნოსტიკური მეთოდების გაუმჯობესება ხელს შეუწყობს აღნიშნული კატეგორიის პაციენტების კურაციის ეფექტურობის გაზრდას.
კვლევის მიზანი. სისხლის მიმოქცევის სისტემის სინტროპული დაზიანებების ლაბორატორიული მარკერების დიაგნოსტიკური ღირებულების განსაზღვრა სისტემური წითელი მგლურას მქონე პაციენტებში.
მასალები და მეთოდები. კვლევაში იყო ჩართული სისტემური წითელი მგლურის (SLE) მქონე 125 პაციენტი სისხლის მიმოქცევის სისტემის (CS) ორგანოების დაზიანებით, რომელთა შორის დიდი უმრავლესობა იყო ახალგაზრდა ასაკის ქალები. პაციენტების სტრატიფიცირება ხორციელდებოდა სინტროპიის არსებობის მიხედვით. სინტროპულ დაზიანებებად მიიჩნევდნენ იმგვარ დაზიანებებს, რომელთა სიხშირე უტყუვრად იზრდებოდა სისტემური წითელი მგლურის (SLE) აქტიურობის საფეხურის გაზრდით - ეს არის ბადურის ანგიოპათია, კაპილარიტი, ა. გ. მ. რეინოს სინდრომი, რეტიკულური ლივედო, ათეროსკლეროზი, მიტრალური სარქვლის ნაკლოვანება, მიტრალური სარქვლის პროლაფსი, პერიკარდიული გამონაჟონი, ფილტვის ჰიპერტენზია, მიოკარდიტი, ენდოკარდიტი, სიმპტომური არტერიული ჰიპერტენზია, ვენური თრომბოზი. კვლევის მსვლელობისას ეტაპობრივად მიმდინარეობდა ცალკეული ლაბორატორიული მარკერებისა და მათი კონსტელაციების დიაგნოსტიკური მნიშვნელობის განსაზღვრა მგრძნობელობის, სპეციფიკისა და სიზუსტის თვალსაზრისით სისტემური წითელი მგლურის (SLE) მქონე პაციენტებში სისხლის მიმოქცევის სისტემის (CS) ორგანოების სინტროპული დაზიანებით და არჩეულ იქნა ერთ-ერთი მათგანი, ამგვარი დაზიანებების დიაგნოსტიკისთვის უტყუვრად უმაღლესი დიაგნოსტიკური ღირებულების მქონე. სტატისტიკურად უტყუვრად ჩაითვალა განსხვავება, თუ < 0,050. მარკერსა და სინტროპულ დაზიანებას შორის კავშირის სიმჭიდროვის დასადგენად. გამოყენებულ იქნა ასოციაციის კოეფიციენტი და კონტინგენციის კოეფიციენტი. კავშირი ითვლებოდა დადასტურებულად, თუ ასოციაციის კოეფიციენტი ≥ 0,50 ან კონტინგენციის კოეფიციენტი ≥ 0,30.
შედეგები. მიმდინარეობდა ცალკეული ლაბორატორიული მარკერებისა და მათი კონსტელაციების დიაგნოსტიკური მნიშვნელობის შესწავლა მგრძნობელობის, სპეციფიკისა და სიზუსტის თვალსაზრისით სისტემური წითელი მგლურის (SLE) მქონე პაციენტებში სისხლის მიმოქცევის სისტემის (CS) ორგანოების სინტროპული დაზიანებით. დადასტურდა, რომ ბადურის ანგიოპათიის დიაგნოსტიკისთვის ყველაზე დიდი დიაგნოსტიკური მნიშვნელობა აქვს ლაბორატორიული მარკერების კონსტელაცია ↑ დაბალი სიმკვრივის ლიპოპროტეიდები + ↑ ათეროგენურობის ინდექსი + ↑ anti-ds DNA + ↑ ANA; კაპილარიტის – ↑ β-გლობულინები + ↑ ათეროგენურობის ინდექსი + ↑ anti-ds DNA + ↑ ანტიფოსფოლიპიდური ანტისხეულები Ig M + ↑ ანტი-Sm + ↓ C4; ა. გ. მ. რეინოს სინდრომის – ცალკეული მარკერი ↓ C3; რეტიკულური ლივედოს - ↑ ერითროციტების დალექვის სიჩქარე + ↑ მცირე მოცირკულირე იმუნური კომპლექსები + ↑ anti-ds DNA + ↑ anti-Sm; ათეროსკლეროზის – ↓ ჰემოგლობინი + ↑ დაბალი სიმკვრივის ლიპოპროტეიდები + ↑ ANA + ↓ C4; მიტრალური სარქვლის ნაკლოვანების - ↑ ერითროციტების დალექვის სიჩქარე + ↑ anti-ds DNA + ↑ ANA + ↑ ანტიფოსფოლიპიდური ანტისხეულები Ig M; მიტრალური სარქვლის პროლაფსის – ↑ ერითროციტების დალექვის სიჩქარე + ↑ დაბალი სიმკვრივის ლიპოპროტეიდები + ↑ მცირე მოცირკულირე იმუნური კომპლექსები + ↑ ANA; პერიკარდიული გამონაჟონის – ერითროპენია + ↑ C-რეაქტიული

პროტეინი + ↑ მგლურას ანტიკოაგულანტი; ფილტვის ჰიპერტენზიის – ჰიპერქოლესტერინემია + ↑ დაბალი სიმკვრივის ლიპოპროტეიდები + ↑ anti-ds DNA + ↑ ANA; მიოკარდიტი – ცალკეული მარკერი ↓ C4; ენდოკარდიტი – ↑ ერითროციტების დალექვის სიჩქარე + ↑ ზოგადი ფიბრინოგენი + ↑ γ-გლობულინები + ჰიპერქოლესტეროლემია + ↑ anti-Sm; სიმპტომური არტერიული ჰიპერტენზია - ↑ დაბალი სიმკვრივის ლიპოპროტეიდები + ↑ anti-ds DNA + ↑ ANA + ↑ anti-SSA (Ro); ვენური თრომბოზი – ერითროპენია + ↓ ჰემოგლობინი + ↑ დაბალი სიმკვრივის ლიპოპროტეინები + ↑ ANA.

დასკვნა. სისტემური წითელი მგლურას მქონე პაციენტებში თითოეული სინტროპული დაზიანებისთვის დადგენილია ცალკეული ლაბორატორიული მარკერი ან მათი კონსტელაცია, რომლებსაც გააჩნია უდიდესი დიაგნოსტიკური ღირებულება ამგვარი დაზიანებების დიაგნოსტიკისთვის.

საკვანძო სიტყვები: სისტემური წითელი მგლურა, სისხლის მიმოქცევის სისტემის ორგანოების დაზიანებები, სინტროპული დაზიანებები, კომორბიდული დაზიანებები, ლაბორატორიული მარკერები, კონსტელაციები, დიაგნოსტიკური ღირებულება.

ДИАГНОСТИЧЕСКАЯ ЦЕННОСТЬ ЛАБОРАТОРНЫХ МАРКЕРОВ СИНТРОПИЧЕСКИХ ПОРАЖЕНИЙ ОРГАНОВ СИСТЕМЫ КРОВООБРАЩЕНИЯ У БОЛЬНЫХ СИСТЕМНОЙ КРАСНОЙ ВОЛЧАНКОЙ

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Актуальность. Системная красная волчанка (СКВ) – хронический автоиммунный недуг, при котором поражаются почти все внутренние органы, среди которых поражения органов системы кровообращения (ОСК) не только являются одними из самых распространенных, но и занимают первые позиции в структуре причин смертности. Тактика лечения больных СКВ без и в сочетании с поражением ОСК кардинально отличается, а потому усовершенствование методов диагностики поможет повысить эффективность курации этой категории больных.

Цель исследования. Выяснить диагностическую ценность лабораторных маркеров синтропических поражений органов системы кровообращения у больных системной красной волчанкой.

Материалы, методология исследования. В исследование включены 125 больных СКВ с наличием поражений ОСК, среди которых подавляющее большинство женщин молодого возраста. Больных стратифицировали при наличии синтропии. Синтропическими поражениями считали те, частота которых достоверно нарастала с повышением степени активности СКВ – это ангиопатия сетчатки, капиллярит, синдром А. Г. М. Рейно, ретикулярное ливедо, атеросклероз, недостаточность митрального клапана, уплотнение митрального клапана, эндокардит, симптоматическая артериальная гипертензия, тромбоз вен. В ходе исследования поэтапно определяли диагностическую ценность отдельных лабораторных маркеров и их констелляций по чувствительности, специфичности и точности у больных СКВ с синтропическими поражениями ОСК и выбирали один из них с достоверно наибольшей диагностической ценностью для диагностики этих поражений. Статистически достоверной считали разницу, если $p<0{,}050$. Для определения тесноты связи между маркером и синтропическим поражением использовали коэффициент ассоциации и коэффициент контингенции. Связь считали подтвержденной, если коэффициент ассоциации $\geq 0{,}50$ или коэффициент контингенции $\geq 0{,}30$.

Результаты. Изучали диагностическую ценность отдельных лабораторных маркеров и их констелляций по чувствительности, специфичности и точности у больных СКВ с синтропическими поражениями ОСК. Выяснили, что наибольшую диагностическую ценность для диагностики ангиопатии сетчатки имеет констелляция с ↑ ЛПНП + ↑ ИА + ↑ anti-ds DNA + ↑ ANA; капиллярита – ↑ β-глобулинов + ↑ ИА + ↑ anti-ds DNA + ↑ антифосфолипидных антител Ig M + ↑ anti-Sm + ↓ C4; синдрома А. Г. М. Рейно – отдельный маркер ↓ C3; ретикулярного ливедо – ↑ СОЭ + ↑ малых ЦИК + ↑ anti-ds DNA + ↑ anti-Sm; атеросклероза – ↓ гемоглобина + ↑ ЛПНП + ↑ ANA + ↓ C4; недостаточности митрального клапана – ↑ СОЭ + ↑ anti-ds DNA + ↑ ANA + ↑ антифосфолипидных антител Ig M; уплотнение митрального клапана – ↑ СОЭ + ↑ ЛПНП + ↑ малых ЦИК + ↑ ANA; перикардиального выпота – эритропения + ↑ С-РП + ↑ волчаночный антикоагулянт; легочной гипертензии – гиперхолестеролемия + ↑ ЛПНП + ↑ anti-ds DNA + ↑ ANA; миокардита – отдельный маркер ↓ C4; эндокардита – ↑ СОЭ + ↑ общего фибриногена + ↑ γ-глобулинов + гиперхолестеролемия + ↑ anti-Sm; симптоматической артериальной гипертензии – ↑ ЛПНП + ↑ anti-ds DNA + ↑ ANA + ↑ anti-SSA (Ro); тромбоза вен – эритропения + ↓ гемоглобина + ↑ ЛПНП + ↑ ANA.

Выводы. Для каждого синтропического поражения у больных системной красной волчанкой определен отдельный лабораторный маркер или их констелляция, имеющая наибольшую диагностическую ценность для диагностики этих поражений.

Ключевые слова: системная красная волчанка, поражение органов системы кровообращения, синтропические поражения, коморбидные поражения, лабораторные маркеры, констелляции, диагностическая ценность.