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RELATIONSHIP OF INFLAMMATORY ACTIVITY AND KIDNEY DAMAGES IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Abstract

To solve the problems in the surveyed 45 patients: examination, laboratory complex, immune and instrumental methods. All 45 patients with SLE kidney disease manifested itself in the form of lupus nephritis. Syndrome hypertension met in 35.5% of cases, the syndrome of chronic renal failure in 37.7% of cases. Urinary syndrome characterized by moderate proteinuria (75.5%), hematuria (73.3%) and leukocyturia (73.3%). Positive correlation of tumor necrosis factor α, C-reactive protein level of creatinine, urea, ESR and SLE activity, which confirms the participation of the factors described in the immune process lupus inflammation.

Keywords: systemic lupus erythematosus, kidney disease, tumor necrosis factor α, C-reactive protein.

One of the most severe manifestations of systemic lupus erythematosus is the development of lupus nephritis. Any damage to renal parenchyma cells leads to their production of inflammatory mediators, providing migration of leukocytes and monocytes to the area of damage and formation of inflammatory infiltrate. The works devoted to the role of TNF-α are mostly of experimental nature, and only a few studies are devoted to the assessment of their clinical significance.

Material and methods. To solve the tasks set in the work the patients were examined: examination, a complex of laboratory, immune and instrumental methods. Immunological researches were carried out on the basis of clinical-immunological laboratory. We examined 45 patients. All patients met the given inclusion criteria. The diagnosis of SLE was made according to the criteria of the American College of Rheumatologists (APA, 1990). The degree of disease activity was determined using SLEDAI, SLAM, and ECLAM indices. The mean age of the patients was 36.47±11.42 (16-58 years). Females prevailed (80%). Skin and joint syndromes in various combinations were the most common (77.6%). Patients between 18 and 50 years of age were distributed approximately with equal frequency by age group. General clinical blood and urine tests, biochemical method with determination of total protein, lipoproteins, cholesterol, blood plasma creatinine level, urea were carried out. Additional methods of renal investigation included: Zimnitsky's test with determination of relative urine density, daily diuresis with calculation of diuresis coefficient (volume of daily diuresis divided by volume of night diuresis, estimated norm of coefficient is 1.5); evaluation of glomerular filtration rate using Cockroft-Goult formula. Renal ultrasound was performed with a 5c2 (5MHz) Conventional ultrasound probe. Kidney size, state of cortical and brain layers, thickness of parenchyma and its echogenicity were assessed. Immunological studies included determination of C-reactive protein concentration. To assess the acute phase changes occurring in patients, PSA was used as a laboratory test. Its concentration was determined in human serum by enzyme immunoassay using DACO reagents (Denmark). The results were calculated using a calibration curve and expressed in mg/L. The upper limit of normal value was 5.6 mg/L. Tumor necrosis factor α (TNF-a) was determined by enzyme immunoassay using a Bender MedSystems human serum TNF-α quantification kit, cat. no. BMS223/3-96. Mean 8.19±3.64pg/ml, upper limit 15.47pg/ml. Statistical processing of the data obtained during the study was performed using Statistic 5.9 statistical computer program by StatSoft (USA).

Results and discussion. In all 45 patients with SLE, renal damage was manifested as lupus nephritis. Arterial hypertension syndrome occurred in 35.5% of cases, chronic renal failure syndrome in 37.7% of cases. Signs of impaired renal function to varying degrees were registered in all patients with lupus nephritis. Urinary syndrome in the majority of SLE patients was characterized by moderate proteinuria (75.5%), moderate hematuria (73.3%) and leukocyturia (73.3%). Nephrotic syndrome was not registered in any of the examined patients. In 15.5% of cases lupus nephritis manifested as acute nephritic syndrome, in the remaining 38 (84.5%) patients moderate chronic nephritic syndrome. The estimation of urinary syndrome in patients with lupus nephritis depending on the activity degree of lupus process showed significant increase of proteinuria in patients with SLE (I stage - 0,37±0,04; II stage - 0,61±0,08, $p<0,001$). At stage III the proteinuria increase did not reach the level of reliability. There was a similar pattern in hematuria analysis. Significant changes in leukocyturia depending on the degree of activity were not registered. Impaired renal function was assessed by plasma urea level and glomerular filtration rate (GFR) calculated according to Cockroft-Goult formula. The level of decrease in renal function was very moderate. Only a significant increase of urea level in comparison with the control group was noted ($p<0,001$). Reliable increase of urea level in three activity levels was observed in the analysis of urea and GFR changes depending on the process activity, reliable changes of GFR were not observed. This result can probably be explained by the fact that changes in azotemic indices are associated with acute renal process, in which urea reacts more intensively than creatinine. When analyzing the parameters of azotemic metabolism depending on the duration of the disease, there was an increase in urea level in patients in the first 3 years of the disease, with its subsequent increase after 5 years of the disease. Probably, these fluctuations in urea levels reflect the course of lupus nephritis - cyclic alternation of exacerbation and remission. After an active lupus process manifested by impaired kidney function with elevated urea levels (M=9.0+1.08), there comes a remission stage lasting about 2 years, followed by resumption of active lupus process. At the same time glomerular filtration rate reliably decreased only in patients with the disease duration more than 5 years in comparison with the control group. We would like to note quite smooth character of decrease in FFR in patients with lupus nephritis. Correlation analysis of clinical and laboratory indexes in SLE patients was carried out. Reliable negative correlation of patients' age with creatinine level was revealed (r±0,94, $p<0,001$).

In order to assess immune disorders in lupus nephritis the following parameters were investigated: proinflammatory process activity - tumor necrosis factor-α (TNF-α) and C-reactive protein (CRP), the level of which in blood was significantly higher than the control values in SLE. When assessing changes in immune indices depending on the activity of SLE, there was a significant increase in pro-inflammatory and inflammatory activity depending on the degree of lupus process (TNF-α and CRP). Blood levels of CRP were significantly different from the control group in all degrees of activity. The TNF-α index in the blood increased significantly only in degree III of SLE activity. This confirms the participation of these factors in the immune process of lupus inflammation. To estimate the influence of "time factor" on immune process in SLE, we analyzed immune indices depending on disease duration. The values of TNF-α and CRP changed significantly. Thus, their level was the highest when the disease duration was more than 5 years, and in the period from 3 to 5 years it was lower than the values of the control group. This tendency probably reflects the cyclic nature of SLE, with alternating exacerbations and remissions of the lupus process.

Evaluation of TNF-α and CRP indices reflecting proinflammatory activity of the disease in lupus nephritis revealed the following correlations. There was a rather close positive correlation between these parameters and the duration of the disease, especially for TNF-α (r±0.62). We found positive correlations of TNF-α, CRP with SLE activity (r±0.54, r±0.42, respectively) and CRP (r±0.76; r±0.44, respectively), as well as negative relation of TNF-α with hemoglobin level (r±0.62). It's noteworthy that the strongest correlations between the SLE activity and TNF-α values were observed, which probably reflects the acute inflammatory activity in SLE to a greater extent. As for kidney function indices (creatinine and urea), there was a positive, rather strong correlation of TNF-α with creatinine level (r±0.76) and urea level (r±0.77).

Conclusions. During examination of SLE patients, arterial hypertension syndrome occurred in 35.5% of cases, and chronic renal failure syndrome in 37.7% of cases. In the majority of patients, urinary syndrome was characterized by moderate proteinuria (75.5%), moderate hematuria (73.3%) and leukocyturia (73.3%). In 84.5% of cases, patients had moderate chronic nephritic syndrome. The severity of these changes increased depending on the degree of lupus activity ($p<0.01$- 0.001).

Positive correlations of TNF-α and CRP with SLE activity, CRP, as well as the presence of negative correlation of TNF-α with hemoglobin level, positive, rather strong correlation of TNF-α with creatinine and urea level were established, which confirms the participation of the described factors in the immune process of lupus inflammation. Significant negative correlation between the age of patients and creatinine level indicates a more severe course of the disease in young patients.

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