ORIGINAL INVESTIGATIONS

Serum calprotectin in vasculitis associated with antineutrophil cytoplasmic antibodies

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Antineutrophil cytoplasmic antibody-associated systemic vasculitis (ANCA-SV) is a group of rare and potentially severe systemic diseases. The search for reliable methods to assess ANCA-SV activity remains relevant. Among the indicators of neutrophil activation that have emerged in clinical practice, the level of serum calprotectin (CLP) stands out, which can be a marker for monitoring vasculitis activity and identifying patients at risk of disease relapse.

Objective: *to determine serum CLP levels in patients with ANCA-SV.*

Material and methods. *The study group comprised 64 patients (37 with granulomatosis with polyangiitis, 11 with eosinophilic granulomatosis with polyangiitis and 16 with microscopic polyangiitis) aged 18 years and older with a confirmed diagnosis of ANCA-SV. The control group consisted of 30 healthy individuals. ANCA-SV activity was determined using the BVAS index; high activity corresponded to a BVAS value of >3. Damage was assessed using the VDI index. Depending on ANCA-SV activity, patients were divided into two groups: high activity group (group 1, n=33) and low activity group (group 2, n=31). In addition to the generally accepted indicators, serum CLP levels were assessed in all patients with ANCA-SV and healthy donors.*

Results and discussion. *Statistically significant differences ($p<0.001$) were found in CLP levels in patients with ANCA-SV in groups 1 and 2. A significant correlation was found between CLP concentration and leukocyte count, neutrophil count, neutrophil-to-lymphocyte ratio (NLR) and systemic inflammatory index (SII). Blood CLP levels in ANCA-SV were associated with creatinine levels and not with glomerular filtration rate and urinary sediment. Although CLP concentration depended on disease activity, it did not correlate with acute phase indicators, including ESR and CRP concentration.*

Conclusion. *Serum CLP concentration is significantly higher in patients with active ANCA-SV and is related to NLR and SII inflammatory indices, so we consider the possibility of using this indicator to assess disease activity.*

Keywords: *vasculitis associated with antineutrophil cytoplasmic antibodies; activity; calprotectin; inflammatory markers; neutrophils.*
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Antineutrophil cytoplasmic antibody (ANCA) associated systemic vasculitides (ANCA-SVs) are a group of rare and potentially severe systemic diseases characterized by necrotizing vasculitis of small vessels with autoantibodies directed against neutrophil cytoplasm components – proteinase 3 (PR3) and myeloperoxidase (MPO) [1, 2]. ANCA-SVs include granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), eosinophilic granulomatosis with polyangiitis (EGPA) [3], which cause multi-organ damage and have a fatal prognosis in the absence of timely and adequate treatment.

Assessment of activity, as well as prediction of relapses and complications in patients with ANCA-SV remains a complex task. The value of ANCA as diagnostic markers is beyond doubt, but their role as a marker of disease activity and relapse remains controversial [4]. ANCAs are detected in the blood even during complete clinical remission and are not necessarily detected during ANCA-SV relapse, despite the high activity of vasculitis [5]. Inflammatory markers such as CRP and ESR, widely used in clinical practice, have low sensitivity for monitoring disease activity [4]. Thus, in connection with the key importance of early diagnosis and timely initiation of adequate treatment, an important task is to find reliable methods for assessing ANCA-SV activity before the development of irreversible organ damage.

Neutrophil hyperactivation is believed to play a major role in the pathogenesis of ANCA-SVs [1, 6]. These diseases can be considered a model of a disease associated with neutrophil dysfunction. Since the time of I.I. Mechnikov, neutrophil reaction has been considered a universal sign of inflammation. In the middle of the last century, a large number of methods for measuring parameters characterizing neutrophil granulocyte function appeared [7]. Among the indicators of neutrophil activation used in clinical practice, we can single out the level of serum calprotectin (CLP). It belongs to the S100 family of proteins (S100A8/A9 and S100A12), released by activated neutrophils and monocytes during inflammation, and plays a key role in innate immunity [8]. CLP is a good systemic indicator of local inflammation in chronic neutrophil-associated inflammatory processes [9, 10]. In ANCA-SV, phagocytes release this protein after their interaction with activated inflamed endothelium [11]. CLP enhances inflammation through activation of Toll-like receptor 4 and Receptor for

Table 1. Characteristics of patients with ANCA-SV

Indicators	GPA (n=37)	EGPA (n=11)	MPA (n=16)	Total (n=64)	p
Age, years, Me [25th; 75th percentiles]	52 [36; 60]	53 [42; 66]	57 [43; 65.5]	53 [39.5; 63]	0.3
Gender, male/female, n	13/24	5/6	2/14	20/44	>0.05
Age of onset, years, [25th; 75th percentiles]	49 [33.5; 56]	51 [37; 65]	51 [37.5; 64]	51 [35; 59]	0.6
Duration of disease, months, [25th; 75th percentile]	23.5 [15; 55.5]	22 [15; 50]	43.5 [18.5; 64]	29 [16; 53]	0.45

Note: ANCA-SV – ANCA-associated systemic vasculitis, GPA – granulomatosis with polyangiitis, EGPA – eosinophilic granulomatosis with polyangiitis, MPA – microscopic polyangiitis, p<0.05.

Advanced Glycation Endproducts (RAGE) [12]. Increased levels of circulating CLP and its expression on the surface of neutrophils and monocytes have been shown in ANCA-SV patients with high disease activity [13–17]. In addition, CLP levels do not normalize during remission [12, 16, 18], which may indicate that subclinical inflammation persists. In one study, CLP-positive leukocyte infiltration of the tubules was observed in renal biopsy specimens from patients with active ANCA-SV [13]. The degree of tubular inflammation was closely related to the expression of CLP, confirming its role as a mediator of inflammation in this disease. The results of some studies suggest that serum CLP is a prognostic biomarker of subsequent renal function deterioration and relapse in patients with remission or low activity of ANCA-SV [15, 16]. These characteristics make CLP a potentially important mediator of vascular inflammation and tissue damage in ANCA-SV. Serum CLP is of interest for monitoring vasculitis activity and identifying patients at risk of disease recurrence during maintenance treatment.

Objective: to determine serum CLP levels in patients with ANCA-SV.

Material and methods. *Patient characteristics.* The prospective cross-sectional study included 64 patients (37 with GPA, 11 with EGPA, 16 with MPA) with a reliable diagnosis of ANCA-SV, among whom women predominated (n=44, 69%). The control group consisted of 30 healthy individuals (22 women and 8 men). The median age of the patients was 53 [39.5; 63] years, and that of the control group was 30 [25, 37] years. At the time of inclusion in the study, none of the patients had active infectious diseases, malignant neoplasms, or other autoimmune diseases that could also increase the level of CLP. Written informed voluntary consent was obtained from all participants before inclusion in the study. The study was approved by the local ethical committee of V.A. Nasonova Research Institute of Rheumatology (protocol №11 of 26.09.2023).

The diagnosis of ANCA-SV corresponded to the ACR (American College of Rheumatology) criteria and/or the classification adopted at the Chapel Hill conference in 2012 [3], the classification criteria for GPA and EGPA proposed by the ACR in 1990 [19, 20], and the ACR/EULAR (European Alliance of Associations for Rheumatology) criteria of 2022 [21–23]. The diagnosis was confirmed by morphologic examination in more than one third of patients (37.5%). The internationally accepted Birmingham Vasculitis Activity Score (BVAS, version 3) was used to determine the activity of ANCA-SV [24]. High activity of ANCA-SV corresponded to BVAS score >3 points. Damage was assessed using the Vasculitis Damage Index (VDI) [25]. Demographic and clinical characteristics of patients with ANCA-SV at the time of inclusion in the study are presented in Table 1 and Fig. 1.

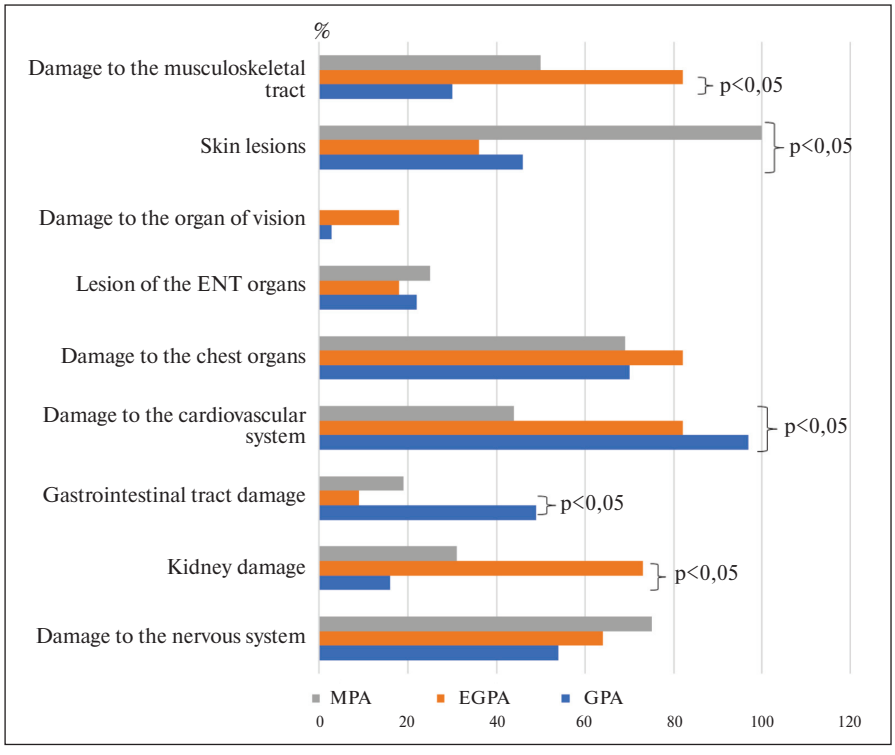

Fig. 1. *Clinical characteristics of patients with ANCA-SV*

Women predominated in all ANCA-SV groups (see Table 1). The patients did not differ in age of onset and duration of the disease. Skin and nervous system involvement was significantly more frequent in EGPA than in GPA. Renal involvement was detected significantly more frequent in MPA (100% of cases) than in GPA (46%) and EGPA (36%). GPA was characterized by visual organ damage, which was observed in almost half of the patients. Upper respiratory tract involvement was present in the vast majority of patients with GPA (97%) and EGPA (82%) and in a much smaller proportion of patients with MPA (44%; see Fig. 1).

Table 2. Laboratory parameters in patients with ANCA-SV

Parameters	GPA (n=37)	EGPA (n=11)	MPA (n=16)	Total (n=64)	p
ANCA-PR3. n, %	25 (68)	1 (9)	4 (25)	30 (47)	p_{1-2}=0.002 p_{1-3}=0.01 p_{2-3}=0.59
ANCA-MPO, n, %	4 (11)	7 (64)	11 (69)	22 (34.4)	p_{1-2}=0.0011 p_{1-3}<0.001 p_{2-3}=0.89
ANCA positive (no specificity), n, %	2 (5)	0	1 (6)	3 (4.6)	p_{1-2}=0.94 p_{1-3}=0.6 p_{2-3}=0.85
ANCA negative, n, %	6 (16)	3 (27)	0 9 (14)		p_{1-2}=0.7 p_{1-3}=0.22 p_{2-3}=0.11
BVAS, Me [25th; 75th percentiles]	5 [0; 7]	3 [0; 9]	3 [0; 8.5]	4 [0; 7.5]	>0.05
VDI, Me [25th; 75th percentiles]	2 [1; 3]	1 [0; 3]	1.5 [0; 3.5]	2 [0; 3]	>0.05

Note: ANCA-SV – ANCA-associated systemic vasculitis, GC – glucocorticoids, n – number of patients, p – reliability, p1 – between GPA and EGPA, p2 – between GPA and MPA, p3 – between MPA and EGPA, p<0.05.

Table 3. Drug therapy in patients with ANCA-SV at enrolment in the study, n (%)

Parameters	GPA (n=37)	EGPA (n=11)	MPA (n=16)	Total (n=64)	p
GC	35 (94.6)	9 (82)	15 (94)	59 (92)	p_{1-2}=0.47 p_{1-3}=0.6 p_{2-3}=0.73
Cyclophosphamide	1 (2.7)	0	2 (12.5)	3 (4.7)	p_{1-2}=0.51 p_{1-3}=0.44 p_{2-3}=0.64
Mycophenolate mofetil	9 (24.3)	1 (9)	4 (25)	14 (22)	p_{1-2}=0.5 p_{1-3}=0.77 p_{2-3}=0.59
Methotrexate	3 (8)	2 (18)	0 5 (7.8)		p_{1-2}=0.69 p_{1-3}=0.6 p_{2-3}=0.37
Azathioprine	3 (8)	3 (27)	2 (12.5)	8 (12.5)	p_{1-2}=0.24 p_{1-3}=0.99 p_{2-3}=0.64
bDMARDs (rituximab)	17 (46)	6 (54.5)	10 (62.5)	33 (52)	p_{1-2}=0.87 p_{1-3}=0.42 p_{2-3}=0.99
No therapy	1 (2.7)	1 (9)	1 (6.25)	3 (4.7)	p_{1-2}=0.94 p_{1-3}=0.87 p_{2-3}=0.64

Note: ANCA-SV – ANCA-associated systemic vasculitis, bDMARDs - biological disease-modifying antirheumatic drugs, n – number of patients, p – reliability, p1 – between GPA and EGPA, p2 – between GPA and MPA, p3 – between MPA and EGPA, p<0.05.

ANCA to PR3 was significantly more frequently detected in GPA. Antibodies to MPO were more specific for MPA and EGPA. BVAS and VDI values were not significantly different in these patient groups (Table 2).

ANCA-SV therapy also showed no significant differences (Table 3).

Laboratory Methods. The examination was carried out on the basis of V.A. Nasonova Research Institute. Common methods were used, according to the standards, in addition, neutrophil reactivity (NEUT-RI), neutrophil granularity (NEUT-GI), immature granulocytes (IG) levels were determined in the blood test of patients and control group using an automatic hematological analyzer XN 1000 (Sysmex, Japan). ESR was assessed according to Westergren (normal ≤20 mm/h). Neutrophil to lymphocyte ratio (NLR) was calculated according to the formula: absolute neutrophil count/absolute lymphocyte count. Systemic immune inflammation index (SII) was calculated by the formula: absolute neutrophil count Ч absolute platelet count/absolute lymphocyte count.

For determination of CLP in ANCA-SV patients and control group we used a reagent set Bulhmann Laboratories AG (Switzer-

Table 4. Inflammatory parameters in the study groups, Me [25th; 75th percentile]

Parameters	ANCA-SV, n=64	Control group, n=30	p
Calprotectin, μg/mL	3.66 [2.67; 7.6]	2.9 [2.18; 3.93]	0.078
White blood cells, 10^9/L	9.05 [6.9; 11.8]	5.65 [4.8; 7]	<0.001
Neutrophils, 10^9/L	5.56 [3.5; 7.6]	3.06 [2.7; 3.89]	<0.001
NLR	2.3 [1.5; 3.6]	1.74 [1.41; 2]	0.0078
SII	714.7 [440.4; 1051]	414.97 [293.9; 503.8]	<0.001
NEUT-RI, FI	44.1 [412.3; 45.4]	42.5 [41.3; 44.6]	0.069
NEUT-GI, SI	153.5 [151.8; 156.4]	149.8 [149.1; 152]	<0.001
IG, 10^9/л	0.05 [0.03; 0.11]	0.01 [0.01;0.02]	<0.001

Note: ANCA-SV – ANCA-associated systemic vasculitis, NLR – neutrophil-lymphocyte ratio, SII – systemic immunoinflammatory index, NEUT-RI – neutrophil reactivity, NEUT-GI – neutrophil granularity, IG – immature granulocytes, p<0.05.

land). In patients with ANCA-SV the level of CRP in the serum (normal ≤5 mg/l) was studied using a highly sensitive immunonephelometric method on an automatic analyzer Siemens (Germany). Specificity of ANCA (presence of antibodies to PR3 or MPO) was studied by enzyme immunoassay. All patients underwent a standard study of blood biochemical parameters.

Statistical methods. Statistical data processing was performed on a personal computer using Statistica 10.0 for Windows statistical data analysis package (StatSoft Inc., USA). Numerical data are presented as mean and standard deviation (M±σ; minimum-maximum value) or as median and interquartile range (Me [25th; 75th percentile]) in case of non-normal distribution. Categorical values are expressed as percentages. The Shapiro-Wilk test was used to assess independent groups to determine whether the distribution of variables was normal. Comparison of quantitative data of two groups was performed using Student's T-test or Mann-Whitney's U-test. To compare two or more groups, the Kruskal-Wallis test was used for parameters whose distribution differed from normal. Correlation analysis was performed using Spearman's rank correlation coefficient. The $\chi 2$ criterion with Yates' correction was used to evaluate categorical data. The 95th percentile of the control group (healthy individuals) was used to determine the cutoff value for high levels of CLP. Differences were considered statistically significant at p<0.05.

Results. *Blood CLP levels in patients with ANCA-SV.* The 95th percentile CLP level in 30 healthy donors was 7.17 μg/mL, a higher concentration was considered elevated. Depending on the value obtained, patients with ANCA-SV were divided into two groups. Group 1 included 19 patients with CLP levels >7.17 μg/mL; group 2 included 45 patients with CLP levels <7.17 μg/mL. Elevated CLP levels (>7.17 μg/ml) were detected in 12 patients with GPA (32%), in 2 patients with EGPA (18%), and in 5 patients with MPA (31%). When comparing ANCA-SV phenotypes, no statistically significant differences in CLP levels were found. This suggests that neutrophil activation occurs at similar levels. Laboratory parameters and clinical manifestations in patients with normal and elevated levels of CLP were almost identical.

Table 5. Characteristics of patients and drug therapy depending on ANCA-SV activity

Parameters	Active form of ANCA-SV, n=33	Inactive form of ANCA-SV, n=31	p
Age, years, Me [25th; 75th percentiles]	54 [36; 63]	52 [41; 63]	0.95
Gender, male/female, n	14/19	6/25	0.085
Age of onset, years, [25th; 75th percentiles]	51.5 [34.5; 61.5]	50 [36; 57]	0.83
Duration of disease, months, [25th; 75th percentile]	18 [5.5; 50.5]	42 [10; 63]	0.012
ANCA-PR3, n (%)	18 (55)	12 (39)	0.3
ANCA-MPO, n (%)	11 (33)	11 (35)	0.9
ANCA positive (no specificity), n (%)	2 (6)	1 (3)	0.96
ANCA negative, n (%)	2 (6)	7 (23)	0.12
BVAS, Me [25th; 75th percentiles]	7 [6; 12]	0 [0; 1]	<0.001
VDI, Me [25th; 75th percentiles]	1 [0; 3]	3 [1; 4]	0.0036
Current drug therapy at the time of inclusion, n (%):			
GC	29 (88)	30 (97)	0.39
Cyclophosphamide	3 (9)	0	0.26
Mycophenolate mofetil	4 (12)	10 (32)	0.1
Methotrexate	3 (9)	2 (6.5)	0.94
Azathioprine	4 (12)	4 (13)	0.9
bDMARDs (rituximab)	7 (21)	26 (84)	<0.001
No therapy	2 (6)	1 (3)	0.96

Note: ANCA-SV – ANCA systemic vasculitis, GC – glucocorticoids, bDMARDs – biological disease-modifying antirheumatic drugs, p<0.05.

The level of CLP in the blood of patients with ANCA-SV and healthy donors did not differ significantly (p=0.078) and did not depend on gender and age (p=0.4. r=0.107), disease duration (p=0.8. r=0.03) and ANCA specificity (p=0.63). Statistically significantly higher levels of leukocytes, neutrophils, IG, NLR, SII, NEUT-GI were observed in ANCA-SV compared to those in the control group (Table 4).

There was a correlation between the blood CLP level and the total number of leukocytes (p=0.006, r=0.34), neutrophils (p=0.004, r=0.36), NLR (p=0.004, r=0.35), SII (p=0.007, r=0.33). The blood CLP level in ANCA-SV also correlated with creatinine concentration (p=0.026, r=0.28), but there was no association with glomerular filtration rate – GFR (p=0.51, r=-0.085), urinary sediment and acute-phase indices including ESR and CRP (p=0.17, r=0.17 and p=0.056, r=0.254 respectively).

Blood CLP level, activity and damage index. The activity and damage indices in the groups of patients with ANCA-SV are presented in Table 2. The active form of ANCA-SV (BVAS >3) was registered in 33 (52%) patients (Table 5). Patients with high and low ANCA-SV activity were comparable in age and gender. Patients with active course had a significantly shorter duration of the disease. Clinical manifestations throughout the disease were comparable in the two groups. The damage index (VDI) was significantly higher in the group with low disease activity. Patients with the "inactive" form of ANCA-SV received RTM significantly more often (see Table 5).

The concentration of CLP in the active course of ANCA-SV was significantly higher than in low activity (p<0.001; Fig. 2). At the same time, 40% of patients with high vasculitis activity had a high level of CLP (>7.17 μg/mL). The concentration of CLP in patients with low ANCA-SV activity and healthy donors was comparable (see Fig. 2).

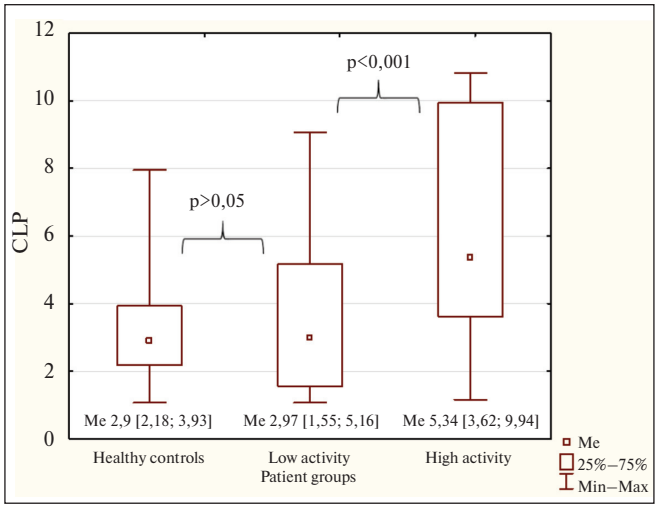

Fig. 2. *CLP levels in patients with ANCA-SV and in the control group. High activity of ANCA-SV – BVAS >3, low activity – BVAS ≤3*

Patients with active ANCA-SV showed statistically significantly higher levels of IG, ESR and CRP than patients with low activity (Table 6).

Discussion. Neutrophils play a key role in vascular endothelial damage in ANCA-SV [6]. ANCA are directed against neutrophil autoantigens, causing degranulation and release of cytokines and molecules that damage the endothelium [16, 26]. CLP released from neutrophils has shown promise as a biomarker for several autoimmune diseases [9, 10], including ANCA-SV [13–17, 27]. Failure to suppress serum CLP activity was a predictor of disease relapse in a cohort of patients with acute ANCA-SV, positive for antibodies to PR3. receiving RTM [27]. The aim of our study was

Table 6. Laboratory parameters in relation to ANCA-SV activity

Parameters	Active form of ANCA-SV, n=33	Inactive form of ANCA-SV, n=31	p
Calprotectin, μg/mL, Me [25th; 75th percentile]	5.34 [3.62;9.94]	2.97 [1.55;5.16]	<0.001
White blood cells, 10^9/L, Me [25th; 75th percentile]	10.2 [6.9;12.1]	8.5 [7.1;9.9]	0.12
Neutrophils, 10^9/L, Me [25th; 75th percentile]	6.2 [3.98;7.72]	5.08 [3.42;6.9]	0.22
Lymphocytes, 10^9/L, Me [25th; 75th percentile]	2.06 [1.45;2.63]	2.4 [1.9;3.01]	0.18
NLR, Me [25th; 75th percentile]	2.6 [1.8;3.6]	1.8 [1.5;3.3]	0.18
SII, Me [25th; 75th percentile]	852.8 [548.1;1144.3]	625.3 [399.6;934.3]	0.97
NEUT-RI, FI, M±	45.04±3.2	43.1±2.2	0.1
NEUT-GI, SI, M±	154.9±3.5	153±4.7	0.28
IG, 10^9/L, Me [25th; 75th percentile]	0.11 [0.025;0.195]	0.04 [0.03;0.05]	0.0445
CRP, μg/L, Me [25th; 75th percentile]	4.1 [1.6;29.4]	1.85 [1.0;5.1]	0.025
ESR, mm/h, Me [25th; 75th percentile]	30 [16;48]	16 [6;20]	<0.001
Creatinine, μmol/L, Me [25th; 75th percentile]	85 [71;113]	81.4 [74;99]	0.46
GFR, Me [25th; 75th percentile]	78 [53;95]	70.5 [60.5;99.5]	0.95

Note: ANCA-SV – ANCA systemic vasculitis, NLR – neutrophil-lymphocyte ratio, SII – systemic immune-inflammatory index, NEUT-RI – neutrophil reactivity, NEUT-GI – neutrophil granularity, IG – immature granulocytes, CRP – C-reactive protein, ESR – erythrocyte sedimentation rate, GFR – glomerular filtration rate (according to the CKD-EPI formula, ml/min/1.73m^2), p<0.05.

to evaluate serum CLP levels in ANCA-SV and its association with neutrophil parameters and inflammatory markers. The results of the analysis confirmed the feasibility of neutrophilic parameters of inflammation in ANCA-SV, in which significantly higher levels of leukocytes, neutrophils, IG, NLR, SII, NEUT-GI were observed compared to those in the control group, which is consistent with the literature data [28, 29]. This emphasizes the key role of the neutrophil link in the pathogenesis of ANCA-SV.

In the present study, the relationship between CLP and neutrophil granulocyte indices was investigated for the first time. A significant correlation with the parameters of inflammation, such as the number of leukocytes, neutrophils, NLR, SII was revealed. Indeed, the results of an earlier study [30] show that in ANCA-MPO-associated vasculitis, CLP in the area of tissue damage attracts more ANCA-activated neutrophils, thereby enhancing the inflammatory response. CLP can increase neutrophil chemotaxis and migration, which also increases the severity of the disease. However, since ANCA are neutrophil activators, it can be assumed that ANCA-activated neutrophils serve as important sources of CLP and can account for its increased serum levels in ANCA-SV. In vitro experiments have demonstrated that ANCA MPO-containing IgG is able to mediate dose-dependent stimulation of CLP release by neutrophils [30].

Several studies have evaluated the serum level of CLP as a promising biomarker of activity in ANCA-SV and found it to be elevated in the acute phase of the disease [13–17, 30]. A pronounced expression of this protein by neutrophils and macrophages was observed in areas of necrotizing extracapillary damage [13]. On the contrary, no CLP expression was observed in chronic inflammatory lesions (i.e., in sclerotic glomeruli) or in normal renal glomeruli [13]. In the present study, the level of CLP was also higher in patients with high disease activity than in those with low disease activity ($p<0.001$). Elevated CLP levels were observed in 40% of patients with high vasculitis activity. Some studies have shown that in patients in clinical remission the level of CLP remained elevated [13, 16, 18], which may be due to the persistence of subclinical disease activity and latent (low-intensity) vascular inflammation in systemic vasculitis. We did not detect such a relationship, in contrast to X. Bai et al. [30]. This may be explained by the fact that our patients received immunosuppressive therapy, which could affect the result of CLP detection. We believe that further monitoring of this indicator in dynamics may be promising.

In contrast to CRP, a classical acute-phase protein produced by the liver, CLP is released locally in the focus of inflammation, so it is a good systemic indicator of local inflammation in chronic inflammatory processes associated with neutrophils [9, 10]. Our data are in agreement with the results of L. Martinez Valenzuela et al [16], who showed the association of this marker with disease activity, but not with the level of CRP and ESR. The lack of correlation with inflammatory markers may be due to the non-specificity of these parameters.

In addition, CLP is of interest as a biomarker of organ-specific damage in patients with ANCA-SV. In some studies, serum CLP was considered a potential biomarker of renal prognosis in ANCA-SV [15, 16]. It is important to note that in our study, the CLP level in ANCA-SV correlated with creatinine concentration, but was not associated with GFR and urinary sediment, which was also noted by other authors [16, 18]. This allows to use this biomarker in ANCA-SV patients with impaired renal function. An increase in the level of CLP in the blood of patients with ANCA-SV during the first 6 months after the start of maintenance therapy is associated with a high risk of renal function decline [15].

In addition, it has been shown that a change in CLP levels after diagnosis is a prognostic factor for relapse [27]. Elevated serum CLP levels at 2 or 6 months compared to baseline in patients with active PR3-ANCA receiving induction therapy with CYP or RTM were associated with a higher risk of relapse during 18 months of follow-up, whereas baseline CLP values did not indicate the possibility of subsequent relapse [27].

Conclusion. The results of the study of serum CLP in ANCA-SV indicate that its concentration was significantly higher in patients with active ANCA-SV and correlated with the NLR and SII inflammation indices indicating the possibility of using CLP to assess disease activity. Therefore, further study of the dynamics of CLP levels in the blood and urine in patients with ANCA-SV seems relevant.

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