CHANGES AND SIGNIFICANCE OF CIC, CRP, IMMUNOGLOBULIN AND COMPLEMENT IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

HANWEI WANG[1], XIAOYUE WANG[1], CHENXI LI[1], ZHIXIANG GAO[2,*]
[1]Department of Rheumatology and Immunology, the Third People's Hospital of Bengbu City, Bengbu 233000, Anhui Province, China - [2]Department of Pharmacy, Changhai Hospital, Second Military Medical University, Shanghai 200433, China

ABSTRACT

Objective: *To explore the changes and significance of CIC, CRP, immunoglobulin and complement in patients with systemic lupus erythematosus.*

Methods: *Forty-two patients with systemic lupus erythematosus who were treated in our hospital from June 2018 to April 2020 were randomly selected as the study group. Forty-two healthy subjects who had had physical examinations in our hospital at the same time were selected as the control group. The age, gender, blood pressure and other basic clinical data of the two groups were compared. Enzyme-linked immunosorbent assay (ELISA) was used to measure the serum CIC level of the study group and the control group, and the changes of serum CRP, immunoglobulin, and complement content in the two groups were measured by scattering rate method. Pearson correlation test was used to analyze the correlation among CIC, CRP, immunoglobulin and complement levels in patients with systemic lupus erythematosus.*

Results: *There was no significant difference in age, gender, BMI, blood pressure and heart rate between the two groups (P>0.05). Compared with the control group, the levels of serum CIC, CRP, IgA, IgM and IgG in the study group were significantly increased, while the levels of complement C3 and complement C4 were significantly decreased (P<0.01). Pearson correlation analysis showed that the CIC level was positively correlated with CRP, IgA, IgM and IgG, and negatively correlated with complement C3 and C4 (P<0.05). The sensitivity and specificity of complement C3 and C4 were 71.34, 90.32, 65.01 and 83.77 respectively, and the area under the curve was 0.831 and 0.745 respectively, which were significantly higher than those of CIC, CRP, IgA, IgM and IgG. Complement C3 and C4 have higher value in the diagnosis of systemic lupus erythematosus.*

Conclusion: *CIC, CRP, immunoglobulin and complement levels in patients with systemic lupus erythematosus were significantly abnormal, and the above indicators can be used as important indicators to judge the development of systemic lupus erythematosus.*

Keywords: *Systemic lupus erythematosus, CIC, CRP, immunoglobulin, complement.*

DOI: 10.19193/0393-6384_2022_1_40

Received *March 15, 2020;* ***Accepted*** *October 20, 2020*

Introduction

Autoimmune disease refers to the disease wherein the body's autoimmune reaction is out of control, overreacting, directly or indirectly damaging its own tissue, and resulting in the corresponding organs or clinical symptoms under the joint action of internal and external factors. Systemic lupus erythematosus (SLE) is an autoimmune disease which involves many factors, such as heredity, sex hormones, environment, infection and immune response[(1)]. Systemic lupus erythematosus (SLE) often causes damage or even disability to various organs of patients, which has a serious impact on the quality of life of patients and aggravates the social burden[(2)]. At present, the pathogenesis of systemic lupus erythematosus is not clear. It is considered that the hyperfunction of T helper lymphocytes that stimulates the high activation of B lymphocytes and produces a variety of autoantibodies may be one of

the main reasons for the occurrence and persistence of the disease. The disorder of the immune system is closely related to the occurrence and development of systemic lupus erythematosus[3]. B cell function in patients with systemic lupus erythematosus is in a highly active state. The number of cells producing autoantibodies in bone marrow and peripheral blood increases, producing a large number of immunoglobulin and autoantibodies.

At the same time, serum complement is consumed, forming a large number of immune complex deposition, which causes damage to the organization and organs[4]. In this study, patients with systemic lupus erythematosus who were treated in our hospital from June 2018 to April 2020 were randomly selected, and the changes to and significance of circulating immune complex (CIC), C-reactive protein (CRP), immunoglobulin and complement content were discussed and analyzed.

Materials and methods

General information

All studies in this group were approved by the hospital ethics committee, and all were in line with medical ethics. Forty-two patients with systemic lupus erythematosus who were treated in our hospital from June 2018 to April 2020 were randomly selected as the study group.

Inclusion criteria:

• All SLE patients meet the diagnosis and treatment guidelines of systemic lupus erythematosus proposed by the Chinese Medical Association Rheumatology Branch[5] and are diagnosed with systemic lupus erythematosus;

• The patient has complete medical records and good mental symptoms. Cooperate with treatment;

• Patients and their family members were informed and signed informed consent;

• Have not taken hormones or other immunosuppressive drugs within 2 months before participating in the study.

Exclusion criteria:

• Patients with infectious diseases;

• Patients with other autoimmune diseases;

• Patients with severe liver and kidney dysfunction, and cardiac dysfunction;

• Patients experiencing pregnancy or lactation;

• Patients who cannot adhere to the study.

Forty-two healthy subjects who underwent physical examination in our hospital during the same period were selected as the control group.

Observation indicators

General data

Compare the general clinical data of all research subjects, including age, gender, body mass index, blood pressure (diastolic blood pressure, systolic blood pressure), heart rate, et cetera. All study subjects collected 5 mL of fasting median cubital venous blood before and after admission. The serum and blood cells were separated using a low-temperature high-speed centrifuge at a speed of 3000 r/min. The supernatant was taken and placed in an ultra-low temperature refrigerator at -80°C for cryopreservation for follow-up research and inspection.

Determination of serum CIC and CRP levels

The enzyme-linked immunosorbent assay was used to determine the serum CIC levels of patients in the study group and the control group; the scatter rate method was used to determine the serum CRP levels of the two groups.

Detection of immunoglobulin and complement levels

The scatter rate method was used to determine the changes in the levels of immunoglobulin and complement in the study group and the control group.

Correlation analysis

Pearson correlation testing was used to analyze the correlation among CIC, CRP, immunoglobulin, and complement levels in patients with systemic lupus erythematosus.

Statistical methods

In this study, sex and other counting data were compared χ^2 inspection. An independent sample t test was used to compare the measurement data of serum CIC, CRP, immunoglobulin and complement. The Pearson correlation test was used for correlation analysis. In this study, SPSS21.0 software was used for statistical data analysis, with statistical results $P<0.05$ as the difference was statistically significant.

Results

Comparison of general data between study group and control group

There was no significant difference in age, gender, BMI, blood pressure and heart rate between the two groups ($P>0.05$). See Table 1.

Group	Study	Control	$\chi 2/t$	*P*
Age (years old)	32.32±8.76	34.79±9.31	1.252	0.214
Gender				
Male	7 (16.67)	5 (11.90)	0.389	0.533
Female	35 (83.33)	37 (88.10)		
BMI (kg/m^2)	22.73±2.24	22.15±3.42	0.919	0.361
Blood pressure (mmHg)				
Diastolic pressure	75.58±7.16	74.52±7.65	0.656	0.514
Systolic pressure	124.26±10.23	123.14±9.62	0.517	0.607
Heart rate (times/min)	73.36±10.32	71.28±10.29	0.925	0.358

Table 1: Comparison of general data between study group and control group.

Comparison of serum CIC, CRP, immunoglobulin and complement levels between study group and control group

Compared with the control group, the levels of serum CIC, CRP, IgA, IgM, IgG and other immunoglobulins in the study group were significantly increased, while the levels of complement C3 and complement C4 were significantly decreased (P<0.01). See Table 2.

Group	CIC (RU/mL)	CRP (mg/L)	IgA (g/L)	IgM (g/L)	IgG (g/L)	C3 (g/L)	C4 (g/L)
Study	83.84± 62.52	13.43± 3.99	4.32± 1.84	2.44± 1.42	22.79± 3.46	0.61± 0.31	0.12± 0.07
Control	31.14± 39.73	4.65± 0.49	1.06± 0.64	1.18± 0.64	12.33± 2.49	1.02± 0.35	0.22± 0.10
t	4.611	14.155	10.845	5.243	15.902	5.683	5.309
P	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Table 2: Comparison of serum CIC, CRP, immunoglobulin and complement levels between study group and control group ($\bar{x}$±s).

Correlation analysis of CIC, CRP, immunoglobulin and complement levels in patients with systemic lupus erythematosus

Pearson correlation test showed that the level of CIC was positively correlated with CRP, IgA, IgM and IgG, and negatively correlated with complement C3 and C4 (P<0.05). See Table 3.

Diagnostic value of CIC, CRP, immunoglobulin and complement in patients with systemic lupus erythematosus

The results showed that the sensitivity and specificity of complement C3 and C4 were 71.34, 90.32, 65.01 and 83.77 respectively, and the area under the curve were 0.831 and 0.745 respectively, which were significantly higher than those of CIC, CRP, IgA, IgM and IgG. Complement C3 and C4 had higher value in the diagnosis of systemic lupus erythematosus. See Table 4.

Indexes	CIC	CRP	IgA	IgM	IgG	C3	C4
CIC	-	0.169	0.061	0.036	0.277	-0.023	-0.002
CRP	0.169	-	0.385	0.231	0.591	-0.046	-0.015
IgA	0.061	0.385	-	0.558	0.227	-0.140	-0.047
IgM	0.036	0.231	0.558	-	0.109	-0.246	-0.082
IgG	0.277	0.591	0.227	0.109	-	-0.027	-0.009
C3	-0.023	-0.046	-0.140	-0.246	-0.027	-	-0.197
C4	-0.002	-0.015	-0.047	-0.082	-0.009	-0.197	-

Table 3: Correlation analysis.

Indexes	Area under the curve	Sensitivity(%)	Specificity(%)
CIC	0.311	67.26	61.13
CRP	0.362	83.45	41.27
IgA	0.213	52.59	59.27
IgM	0.156	62.52	43.58
IgG	0.105	57.85	58.64
C3	0.831	81.34	90.32
C4	0.745	75.01	83.77

Table 4: Diagnostic value of CIC, CRP, immunoglobulin and complement in patients with systemic lupus erythematosus.

Discussion

Systemic lupus erythematosus (SLE) is a common inflammatory connective tissue disease, which is characterized by the activation of polyclonal B cells and the production of a variety of autoantibodies. Due to the interaction of genetic, hormonal and environmental factors, a variety of autoantibodies are produced, which are mainly antinuclear antibodies, resulting in immune inflammatory response characterized by immune complex. Eventually, SLE will cause damage to multiple systems and organs, such as the skin, heart, central nervous system and blood system[6]. According to statistics, the incidence rate of systemic lupus erythematosus is 70/100 000 in China, and the incidence rate among female is higher than that among male. Under the action of unknown internal and external factors, the body's normal immune regulation mechanism is destroyed, so that lymphocytes cannot correctly recognize their own tissues, resulting in autoimmune reaction[7].

Immune abnormalities in patients with systemic lupus erythematosus include dysfunction of antigen-presenting cells, loss of immune tolerance, disorder of T and B cell function regulation, complement deficiency, and immune complex clearance obstacles, which cover almost the entire immune system. According to reports, B cell hyperfunction and expression is one of the most prominent features of systemic lupus erythematosus[8]. The appearance of autoantibodies in the nucleus and various nuclear components, cell membranes, cytoplasm, and various tissue components is not only the result of antibody immune dysfunction, but also the cause of pathological changes. Under physiological conditions, the formation of CIC helps to eliminate foreign antigens. When patients' systemic lupus erythematosus occurs, a variety of autoantibodies produced by the body can form CICs with autoantigens and deposit on the capillary basement membrane, joints and kidneys activating complement, causing inflammation, and further causing the release of autoantibodies. This makes the condition linger and continue to worsen[9]. The results of this study show that the CIC level can reflect the severity of systemic lupus erythematosus to a certain extent, and is one of the important indicators for the diagnosis of the disease. Systemic lupus erythematosus (SLE) is an autoimmune disease. Studies have found that the activation of the complement system by CIC and the consumption of complement components are important manifestations of the disease in the active stage. When SLE is in the active stage of the disease, a large number of CIC are formed in the serum of patients to activate complement, and a large number of complement C3 and C4 are consumed, which significantly reduces the levels of complement C3 and C4[10]. The results are the same as that of this study, which indicates that complement C3 and complement C4 can be used as effective indicators to judge the development of disease.

CRP is an acute phase reaction protein mainly synthesized by the liver, which is an important immune regulatory protein. Its level is significantly increased in infection, tissue injury, tumor and other diseases[11]. In recent years, studies have shown that CRP is not only an inflammatory marker, but is also directly involved in the development of atherosclerosis and other cardiovascular diseases. In addition, CRP can also combine with nuclear debris and apoptotic bodies to play an autoimmune role[12-13]. The results showed that the level of CRP in patients with systemic lupus erythematosus was significantly increased, which was closely related to the patient's condition.

IgA, IgM and IgG are the most commonly used indicators of humoral immune function. They mainly exist in plasma and tissues and are animal proteins with antibody activity. IgG is the only immunoglobulin synthesized and secreted by spleen and lymph nodes, which can pass through placenta and play an important role in natural passive immunity. According to related literature reports, some patients with normal IgG levels due to decreased complement may be caused by a large amount of IgG antibodies deposited in the tissues, resulting in low serum concentrations, but in fact the tissue damage is very serious, which may be due to a large number of immune complexes.

The deposition of IgG is involved in the immune complex reaction, which may be related to the consumption of IgG[14]. IgA is the main component of the human mucosal defense system and an important defense barrier. IgM is the first antibody synthesized and secreted in the process of ontogeny, and it is also the first antibody to appear in the initial immune response. It has the effects of sterilization, lysis and phagocytosis, and plays an important role in the early defense of the body[15]. The results of this study found that patients with systemic lupus erythematosus have varying degrees of immune dysfunction. This may be related to the B function hyperactivity in patients with systemic lupus erythematosus, which secretes a large amount of immunoglobulin, which promotes the development of the disease[16].

In conclusion, the levels of CIC, CRP, immunoglobulin and complement in patients with systemic lupus erythematosus are significantly abnormal, and the above indicators can be used as important indicators to judge the development of systemic lupus erythematosus.

References

1) Tsokos GC. Systemic lupus erythematosus. N Engl J Med 2011; 365(22): 2110-21.
2) Fors Nieves CE, Izmirly PM. Mortality in Systemic Lupus Erythematosus: an Updated Review. Curr Rheumatol Rep 2016; 18(4): 21.
3) Moulton VR, Suarez-Fueyo A, Meidan E, Li H, Mizui M, et al. Pathogenesis of Human Systemic Lupus Erythematosus: A Cellular Perspective. Trends Mol Med 2017; 23(7): 615-635.

4) Janoff AS, Carpenter-Green S, Weiner AL, Seibold J, Weissmann G, et al. Novel liposome composition for a rapid colorimetric test for systemic lupus erythematosus. Clin Chem 1983; 29(9): 1587-92.
5) Kuhn A, Bonsmann G, Anders HJ, Herzer P, Tenbrock K, et al. The Diagnosis and Treatment of Systemic Lupus Erythematosus. Dtsch Arztebl Int 2015; 112(25): 423-32.
6) Joob B, Wiwanitkit V. Prolactin and systemic lupus erythematosus. Immunol Res 2017; 65(4): 975.
7) Tsokos GC, Lo MS, Costa Reis P, Sullivan KE. New insights into the immunopathogenesis of systemic lupus erythematosus. Nat Rev Rheumatol 2016; 12(12): 716-730.
8) Morawski PA, Bolland S. Expanding the B Cell-Centric View of Systemic Lupus Erythematosus. Trends Immunol 2017; 38(5): 373-382.
9) Magro-Checa C, Schaarenburg RA, Beaart HJ, Huizinga TW, Steup-Beekman GM, et al. Complement levels and anti-C1q autoantibodies in patients with neuropsychiatric systemic lupus erythematosus. Lupus 2016; 25(8): 878-88.
10) Garabet L, Gilboe IM, Mowinckel MC, Jacobsen AF, Mollnes TE, et al. Antiphospholipid Antibodies are Associated with Low Levels of Complement C3 and C4 in Patients with Systemic Lupus Erythematosus. Scand J Immunol 2016; 84(2): 95-9.
11) Sahebkar A, Rathouska J, Derosa G, Maffioli P, Nachtigal P. Statin impact on disease activity and C-reactive protein concentrations in systemic lupus erythematosus patients: A systematic review and meta-analysis of controlled trials. Autoimmun Rev 2016; 15(4): 344-53.
12) Broca-Garcia BE, Saavedra MA, Martínez-Bencomo MA, Montes-Cortes DH, Jara LJ, et al. Utility of neutrophil-to-lymphocyte ratio plus C-reactive protein for infection in systemic lupus erythematosus. Lupus 2019; 28(2): 217-222.
13) Ho C H, Leung A. FRI0273 Role of procalcitonin and c-reactive protein in screening of infection in patients with systemic lupus erythematosus. Ann Rheum Dis 2017, 76(Suppl 2): 589-.
14) Lim DH, Kim YG, Lee D, Min Ahn S, Hong S, et al. Immunoglobulin G Levels as a Prognostic Factor for Autoimmune Hepatitis Combined With Systemic Lupus Erythematosus. Arthritis Care Res (Hoboken) 2016; 68(7): 995-1002.
15) Tsai KL, Liao CC, Chang YS, Huang CW, Huang YC, et al. Low Levels of IgM and IgA Recognizing Acetylated C1-Inhibitor Peptides Are Associated with Systemic Lupus Erythematosus in Taiwanese Women. Molecules 2019; 24(9): 1645.
16) Liu S, Hou XL, Sui WG, Lu QJ, Hu YL, et al. Direct measurement of B-cell receptor repertoire's composition and variation in systemic lupus erythematosus. Genes Immun 2017; 18(1): 22-27.

Corresponding Author:
Zhixiang Gao
No. 168 Changhai Road, Yangpu District, Shanghai City, China
Email: zj7ewp@163.com
(China)