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Combined Detection of Mean Platelet Volume and Immunoglobins as a Strategy for the Diagnosis of Systemic Lupus Erythematosus

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ABSTRACT

Objective: To explore the possibility of diagnosing and monitoring patients with systemic lupus erythematosus (SLE) using the combination of mean platelet volume (MPV) and routine immunoglobulin test. **Methods:** 116 patients with SLE were divided into 3 groups according to their clinical characteristics, including 29 patients with renal impairment, 44 cases of active stage and 43 cases of inactive patients. 40 healthy subjects were randomly selected as controls. Subjects were tested for routine blood test and plasma Immunoglobins, such as IgG, IgA, IgM, C3, C4, CH50, CRP. The results were analyzed and the characteristics of each group of subjects were determined, the correlation between test results and diagnosis were studied. **Results:** In comparison to the control group, the serum level of MPV, C3 and C4 were decreased ($P < 0.05$), and C reactive protein level was elevated ($P < 0.001$) in the three groups of SLE patients. The IgG level in active and inactive SLE patients was increased ($P < 0.0001$), CH50 level was decreased in patients with inactive SLE ($P < 0.05$), IgA level of active SLE subjects was found to be elevated ($P < 0.05$), IgM in patients with renal impairment was decreased ($P < 0.05$). Other than that, no other significant characteristic were found. **Conclusion:** The pathogenesis of SLE is a complex process involving multiple factors. The changes of MPV, IgG, IgA, IgM, C3, C4, CH50 and CRP in SLE patients are characteristic parameters. The combination of the above indicators can help to determine the diagnosis and staging of SLE. The timely diagnosis and treatment of SLE patients has important clinical significance in protecting the organ function of SLE patients and improving the prognosis.

1. Introduction

Systemic lupus erythematosus is a recurrent and relapsing autoimmune disorder that invades the skin and multiple organs^[1]. At present, the exact cause

of SLE has not been fully elucidated. SLE patients exhibit numerous aberrations in the immune system. In this study, we examined routine blood test and plasma Immunoglobins, such as IgG, IgA, IgM, C3, C4, CH50, CRP in SLE

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patients and healthy controls, exploring the characteristics of the above results in patients with SLE at different stages, providing a new reference for the diagnosis and treatment of SLE.

2. Materials and Methods

2.1 Subjects

116 SLE patients admitted to the Department of Rheumatology, Nephrology, and Dermatology of Lingnan Hospital from January 2012 to December 2016, were selected for this study. There were 106 females and 10 males, aged between 15 and 73 years, with an average age of 34.0 ± 13.0 years. All subjects met the SLE diagnostic criteria revised by the American College of Rheumatology (ACR) in 1997^[2]. None of the patients received anti-lupus treatment before admission.

Patients with other diseases, such as dyslipidemia, blood system diseases, inflammatory diseases, etc. are excluded. The activity of SLE was evaluated by systemic lupus erythematosus disease activity index (SLE-DAI). SLE-DAI \geq 10 were defined active SLE group, and SLE-DAI $<$ 10 were defined in inactive SLE group. 73 patients were in the active SLE group, including 29 patients with renal impairment (LN) and 44 patients without renal impairment, and there were 43 cases in the non-active period group. 40 healthy controls were randomly selected as controls, including 9 males and

31 females with an average age of (30.2 ± 6.6) years. There were no significant differences in gender, age, BMI, etc. between the active SLE group, SLE active with renal injury group, the inactive SLE group and the control group ($P > 0.05$).

2.2 Methods

6 mL of venous blood sample were collected from each test subjects in fasting state on second morning of admission, or at 9am on the day of the medical examination. Each blood sample was dispensed into 3 tubes, and corresponding pretreatment was performed according to the purpose of the test. IgG, IgA, IgM, C3, C4, CH50 and C-reactive protein (CRP) levels were measured by immunoturbidimetry using a automatic biochemical analyzer (Hitachi 7180, Japan), and the routine blood test was performed using automatic blood cell meter (Sysmex XE-5000, Japan).

All tests and result interpretation were operated in strict accordance with the procedures instructions, all reagents used were within the validity period.

2.3 Statistical Analysis

Statistical analysis was performed using SPSS 13.0 software. Inter-group comparisons of measurement data were performed using unpaired t-test, and Spearman rank correlation analysis were performed.

Table 1. Comparison of different SLE groups and healthy controls

Group	cases(n)	MPV (fL)	IgG (g/L)	IgA (g/L)	IgM (g/L)	C3 (g/L)	C4 (g/L)	CH50 (U/mL)	CRP (mg/L)
in-active SLE	43	9.669 \pm 0.139a	17.85 \pm 1.497a	2.36 \pm 0.155	1.069 \pm 0.084	0.581 \pm 0.039a	0.122 \pm 0.014a	29.16 \pm 2.268a	4.336 \pm 1.041a
active SLE	44	9.824 \pm 0.135a	16.88 \pm 0.943a	2.506 \pm 0.127a	1.037 \pm 0.105	0.713 \pm 0.049a	0.156 \pm 0.018a	33.41 \pm 2.633a	8.676 \pm 2.107a
active SLE plus renal impairment	29	9.558 \pm 0.124a	10.77 \pm 1.149	1.93 \pm 0.169	0.792 \pm 0.095a	0.668 \pm 0.044a	0.156 \pm 0.016a	36.07 \pm 3.003	6.617 \pm 1.414a
Control	40	10.48 \pm 0.144	12.24 \pm 0.337	2.04 \pm 0.075	1.126 \pm 0.063	1.029 \pm 0.027	0.240 \pm 0.009	37.2 \pm 0.999	1.399 \pm 0.273

Notes: a: compared with healthy controls, $P < 0.05$.

Table 2. Comparison of inactive SLE group, active SLE plus renal impairment group, and active SLE group

Group	cases (n)	MPV (fL)	IgG (g/L)	IgA (g/L)	IgM (g/L)	C3 (g/L)	C4 (g/L)	CH50 (U/mL)	CRP (mg/L)
inactive SLE	43	9.669 \pm 0.139	17.85 \pm 1.497	2.36 \pm 0.155	1.069 \pm 0.084	0.581 \pm 0.039a	0.122 \pm 0.014	29.16 \pm 2.268	4.336 \pm 1.041
active SLE	44	9.824 \pm 0.135	16.88 \pm 0.943	2.506 \pm 0.127	1.037 \pm 0.105	0.713 \pm 0.049	0.156 \pm 0.018	33.41 \pm 2.633	8.676 \pm 2.107
active SLE plus renal impairment	29	9.558 \pm 0.124	10.77 \pm 1.149a	1.93 \pm 0.169a	0.792 \pm 0.095	0.668 \pm 0.044	0.156 \pm 0.016	36.07 \pm 3.003	6.617 \pm 1.414

Notes: a: compared with the active SLE group, $P < 0.05$.

3. Results

3.1 Comparison of Different SLE Groups and Healthy Controls

MPV, C3 and C4 were decreased ($P < 0.05$), and CRP was increased ($P < 0.001$) in the in-active SLE group, active SLE group, active SLE plus renal impairment group. The IgG level in active and inactive SLE patients was increased ($P < 0.0001$), CH50 level was decreased in patients with inactive SLE ($P < 0.05$), IgA level of active SLE subjects was found to be elevated ($P < 0.05$), IgM in patients with renal impairment was decreased ($P < 0.05$). See the table below.

3.2 Comparison between Different SLE Groups

As shown in the table below, C3 were increased in the inactive SLE group ($P < 0.05$), compared with the active SLE group, both IgG and IgA were decreased in the active SLE subjects but not in the active SLE plus renal impairment group ($P < 0.01$; $P < 0.05$).

4. Discussion

At present, the etiology of SLE is still unclear. It is an immune disease characterized by multiple system damage and accompanied by a variety of autoantibodies. The main clinical symptoms of SLE include joint pain, fever, skin erythema, etc^[3]. Hematological damage also is a common manifestation. Studies have shown that SLE may develop immune-mediated leukopenia, thrombocytopenia and anemia^[4], among which thrombocytopenia is the most common, accounting for about 7% to 30% of all cases. In SLE patients, it is an important cause of death. A careful observation of peripheral blood cells parameters is necessary for early detection and a proper assessment of SLE progression and prognosis^[5]. The reduction of platelet count in patients with SLE has become a consensus^[6]. In this study, we found that platelet mean volume decreased in patients with SLE. Size and volume are closely related to the ultrastructure, enzyme activity and functional status of platelets. Bulk platelets contain more glycogen, adenine, nucleotides and orthophosphate, are also more active. A decrease in platelet volume indicates a decrease in tangible substances, activity, and function. In this study, the MPV of SLE patients were significantly reduced compared with the control group, indicating that the reduction of the number and volume of platelets in SLE patients may cause platelet dysfunction.

The serum markers for clinical diagnosis of SLE are mainly autoantibodies and inflammatory factors. Autoantibodies are specific for the diagnosis of SLE. It is generally

believed that when used to diagnose SLE, anti-nuclear antibody (ANA) is more sensitive, but has lower specificity. If it is tested alone, it can only be used as a screening test. Anti-Smith(Sm) antibody, anti-double strand DNA(dsDNA) antibody, anti-nucleosome antibody(AnuA) and anti-ribosomal P protein antibody were some specific indicator for the diagnosis of SLE. However, the positive rates of Anti-Smith(Sm) antibody, anti-double strand DNA(dsDNA) antibody are 37.9% and 32.7%, respectively^[7], so that even though the diagnosis of SLE with both of them has greater specificity, but the diagnostic sensitivity is low, easy to miss, and the project is difficult for primary clinics to practice.

Our study found that the serum levels of C3 and C4 in the three groups of SLE patients were decreased. This may be because a large number of circulating immune complexes were formed in the patient, complement system were activated and thus consumed a large amount of complement C3, C4, which is consistent with other studies^[8,9]. The increase in CRP also reflects the state of immune dysfunction. We have found that IgG and IgA produced by B cells from patients with SLE increased to varying degrees, indicating that the humoral immune system is hyperactive. In the inactive group, IgG was increased, while IgA was increased in active SLE patients, and IgM was decreased in active plus renal injury group, suggesting that there is a certain correlation between immunoglobulin levels and disease activity. Dynamic observation of changes in serum immunoglobulin levels may be helpful in analyzing disease progression^[10].

5. Conclusion

In summary, this study found that levels of C3 and C4 were reduced in different subgroups of SLE patients with a different but characteristic immunoglobulin change. If supported by a larger sample of clinic data, these specific changes, combined with other examinations and clinic symptoms and signs, may have a significant value for the diagnosis and staging of SLE, thereby improving the prognosis of this complicated disease.

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