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Red blood cell distribution width is a potential index to assess the disease activity of systemic lupus erythematosus

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ABSTRACT

Background: General population-based investigations have revealed that red blood cell distribution width (RDW) is associated with inflammatory indexes such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Chronic inflammation is one of the major components of many autoimmune diseases and RDW may reflect the severity of these autoimmune diseases as well. Therefore, the objective of this study was to investigate the correlation between RDW and disease activity of systemic lupus erythematosus (SLE).
Methods: The medical records of 131 SLE patients were retrospectively analyzed. Correlations between RDW and disease activity or other inflammatory indexes were analyzed. The effect of glucocorticoid treatment for three months on RDW was estimated in 3 newly diagnosed SLE cases.
Results: Increased RDW was observed in SLE patients. RDW was positively correlated with serum IgM, CRP, ESR, and SLE Disease Activity Index 2000 (SLEDAI-2K). Glucocorticoid treatment decreased both SLEDAI-2K and RDW.
Conclusion: RDW may be a useful index to estimate the disease activity of SLE.

1. Introduction

Red blood cell distribution width (RDW) is a parameter routinely tested to describe the heterogeneity of red blood cells [1]. During the past decades, it has been regarded as a useful index to differential diagnosis between thalassemia and megaloblastic anemia, as well as iron deficiency anemia [1]. Recent studies have revealed that RDW is associated with onset of cardiovascular diseases and their prognosis [2,3], however the mechanism is still illusive. One of the many hypotheses to explain the association between RDW and cardiovascular diseases is that increased RDW may represent an inflammatory status in the body [4]. In fact, previous studies have observed that RDW is positively correlated with inflammatory indexes, such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) in a large cohort of unselected outpatients [5], as well as in patients with coronary artery disease (CAD) [6].

Autoimmune diseases usually consist of inflammatory components. The chronic inflammatory process, which is triggered by auto-antigen and maintained by both environmental and genetic factors, is a common characteristic for all autoimmune diseases [7]. Therefore, inflammatory indexes, such as CRP and ESR, may be useful to assess the activity of autoimmune diseases as well. As a novel index for inflammation, RDW may be also useful to estimate the activity of autoimmune diseases. Previous studies have shown that RDW was associated with the severity of inflammatory bowel disease (IBD) [8,9] and rheumatoid arthritis (RA) [10]. A recent study has also shown that RDW was increased in patients with systemic lupus erythematosus (SLE) [11]. However, whether RDW has prognostic value in assessing the disease activity of SLE remains unknown.

In this study, we retrospectively analyzed the medical records of 131 SLE patients. The relationship between RDW and commonly used disease activity markers, including CRP, ESR, and SLE Disease Activity Index 2000 (SLEDAI-2K) [12] was evaluated.

2. Materials and methods

2.1. Participants

All the patients enrolled in this study were identified from the electronic database of Changhai Hospital of Second Military Medical University. SLE patients that were administrated in the hospital between January 2010 and January 2013 were included in this study. Patients were excluded if they had one of the following combined diseases/situations: 1) other autoimmune disease, such as Sjogren Syndrome (SS), RA and IBD; 2) malignant diseases; 3) end stage of

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Table 1
Characteristics of participants.

	SLE patients		Healthy controls		P value
	No	Results	No	Results	
Age (y)	131	35 ± 14	147	37 + 12	NS
Gender (male/female)	131	13/118	147	15/132	NS
Newly diagnosed (yes/no)	131	21/110	–[b]	–	–
Disease duration (month)[a]	131	44 ± 62	–	–	–
C-reactive protein (mg/l)	127	8.3 ± 15.1	–	–	–
Erythrocyte sedimentation rate (mm/h)	128	38 ± 35	–	–	–
Urine protein (g/24 h)	62	1.36 ± 2.37	–	–	–
Creatinine (μmol/l)	131	70 ± 40	147	66 + 13	NS
C3 (g/l)	130	0.66 ± 0.60	–	–	–
C4 (g/l)	126	0.12 ± 0.07	–	–	–
Lymphocyte count ($\times 10^9$/l)	131	1.54 ± 1.77	147	1.74 + 0.69	NS
Serum IgA (g/l)	123	2.60 ± 1.24	–	–	–
Serum IgG (g/l)	127	15.27 ± 7.92	–	–	–
Serum IgM (g/l)	123	1.14 ± 0.86	–	–	–
Anti-dsDNA antibody (IU/ml)	123	229 ± 251	–	–	–
Anti-nucleosome antibody (positive/negative)	112	42/70	–	–	–
Anti-histone antibody (positive/negative)	113	44/69	–	–	–
SLEDAI-2K score	58	9.5 ± 4.6	–	–	–

Values are the mean ± SD, where appropriate.
[a] No data available.
[b] Newly diagnosed patients were regarded as 0.

renal disease; 4) liver disease such as hepatitis and liver cirrhosis, since our previous work has shown that RDW can be greatly affected by liver disease [13]; 5) hematology disease or received blood transfusion during the past 4 months. The diagnosis of SLE was based on the criteria established by the American College of Rheumatology (ACR) [14]. The control group included 147 healthy individuals that visited the hospital for routine checkup.

2.2. Data extraction

Clinical characteristics and laboratory test results of all enrolled subjects were extracted from the medical records. In addition, SLE Disease Activity Index 2000 (SLEDAI-2K) [12], a global index based on the symptoms and laboratory findings, was calculated according to medical records for each patient. To exclude the effect of SLE-related treatment on RDW, a subgroup consisting of 20 newly diagnosed patients that had not received any SLE-related treatment on admission were analyzed separately.

2.3. Statistical analysis

Continuous variables were displayed as mean ± standard deviation and compared by Student's *t* test or Mann–Whitney *U* test when appropriate. The Spearman approach was used to analyze the correlation between 2 continuous variables. All the statistical analyses were performed in SPSS 17.0 and Sigmaplot 11.0; $P < 0.05$ was determined as significant.

2.4. Ethics

This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Board of the Changhai Hospital of Second Military Medical University. This study had no influence on the subsequent management of patients.

3. Results

3.1. Characteristics of participants

Characteristics of the 131 SLE patients used in this study are shown in Table 1. SLEDAI-2K was calculated in only 58 patients because some of the clinical variables were not available for all of the patients.

3.2. SLE patients have increased RDW compared with healthy individuals

Increased RDW was observed in SLE patients that received medical intervention, as well as the 20 newly diagnosed SLE patients that did not receive any form of treatment (Fig. 1, $P < 0.01$ for both groups of patients).

3.3. Correlations between RDW and clinical characteristics in patients with SLE

RDW was positively correlated with serum IgM ($n = 123$), CRP ($n = 127$), ESR ($n = 128$), and SLEDAI-2K ($n = 58$) scores (Fig. 2, $P < 0.05$ for all). However, the correlation between RDW and age, disease duration time, serum IgA and IgG, serum creatinine, urine protein, lymphocyte count, C3, C4, anti-dsDNA antibody, anti-nucleosome antibody and anti-histone antibody was not statistically significant (data not shown).

3.4. The effect of glucocorticoid treatment on RDW

Among the newly diagnosed SLE patients, three had medical records for follow-up visits. All of them received glucocorticoid therapy for four months after the diagnosis was confirmed. Their RDW and SLEDAI-2K

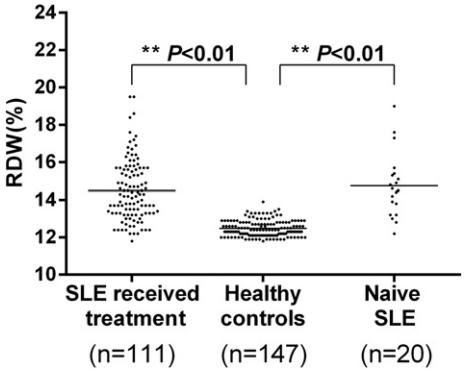

Fig. 1. SLE patients showed increased RDW. Increased RDW was observed in both newly diagnosed SLE patients ($n = 20$) and the patients who had received SLE-related treatment ($n = 111$). The healthy controls consisted of 147 subjects. Horizontal lines represent the mean values.