The changes and clinical significance of anti CCP antibodies, complement and immunoglobulin in the pathological process of rheumatoid arthritis

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ABSTRACT

Objective: To detect the serum levels of anti-Cyclic Citrullinated Peptide (CCP) antibodies, complement (C3 and C4) and immunoglobulin (IgG, IgA and IgM) in patients with rheumatoid arthritis (RA). Methods: A total of 100 patients with RA were selected as the observation group, and 60 healthy people were selected as the control group. The RA patients were divided into the high disease active group (25 cases), moderate disease active group (30 cases), low disease active group (24 cases) and remission group (21 cases) according to the disease activity score in 28 joints (DAS28 score). The levels of anti-CCP antibodies, C3, C4, IgG, IgA and IgM of each research object were detected. Difference of all the serum indexes between the observation group and control group were compared, as well as that between the RA patients in different disease activity states. Finally, the correlation of anti-CCP antibodies with C3, C4, IgG, IgA and IgM were analyzed. Results: (1) The levels of anti-CCP antibodies, C3, C4, IgG, IgA and IgM in the observation group were obviously higher than that in the control group. (2) Compared with RA in remission, the levels of anti-CCP antibodies, C3, C4, IgG, IgA and IgM of RA in activity were significant higher. Compared with the low disease active group, the levels of anti-CCP antibodies, C3, C4, IgG, IgA and IgM in the moderate and high disease active groups were obviously higher. And the anti-CCP antibodies levels in the high disease active group were significantly higher than that in the moderate ones. The anti-CCP antibodies in RA patients had significant positive correlation with C3, C4, IgG, IgA and IgM. Conclusion: The levels of anti-CCP antibodies, C3, C4, IgG, IgA and IgM in RA patients were increased obviously, and they were correlated with the disease activity of RA. They could be important indexes for the diagnosis and illness monitoring of RA.

1. Introduction

Rheumatoid arthritis (RA) is a common autoimmune disease, the specific etiology is not yet clear, may be related to genetic, infection, endocrine and immune disorders and other factors[1]. RA early diagnosis and timely treatment is critical to control the development of the disease[2]. The laboratory examination of RA was mainly based on autoantibody immunological test, a large number of studies have shown that the autoantibodies anti-cyclic citrullinated peptide (CCP) has a high sensitivity and specificity on the RA[3-5]. In addition, the RA pathological process is also associated with humoral immune responses, in addition, this study detect the expression of serum anti-CCP antibody in RA, and the serum complement and immunoglobulin levels, then analyzed the pathology changes and clinical significance of which in RA.

2. Materials and methods

2.1 General information
A total of 100 cases of RA patients treated in our hospital from January 2016 to October 2016 were selected, including male 42 cases, female 58 cases, age 27-65 years old, RA history of 1-5 years. All patients were in accordance with the 1987 American College of Rheumatism (ARA) revision of the RA diagnostic classification criteria[6]. RA patients with non-autoimmune diseases excluded; joint deformity and other arthritis patients; anti-RA related treatment before detection; patients with severe cardiopulmonary, hepatorenal insufficiency, hematopoietic system diseases and other long-term chronic diseases; Severe disturbance of consciousness or mental illness; pregnant and lactating women. According to the DAS28 score, RA patients were divided into four different disease activity groups: highly active group (25 cases), moderate activity group (30 cases), low activity group (24 cases) and remission group (21 cases). 60 healthy people in the hospital health examination center over the same period were selected as control group, 25 males, 35 females; age 25-70; There was no history of rheumatism or other autoimmune diseases. There was no significant difference in age and sex between the observation group and the control group ($P>0.05$).

2.2 Detection methods

RA patients were hospitalized before the elbow vein blood extraction, the control group of healthy persons admitted to the hospital examination during the extraction of elbow vein blood, 3000 rpm/min centrifugation 15 min, serum was collected, stored in the -20°C, rapid thawing in 37°C before detection. The anti-CCP antibody was detected by latex-enhanced immunoturbidimetric assay. The detection instrument was Beckman AU680. The anti-CCP antibody was Ningbo Ruiyuan Biotechnology Co., Ltd. The levels of C3, C4, IgG, IgA and IgM were detected by immunoturbidimetry. The kit is Beckman AU680. Complement C3, C4 diagnostic kit and IgG, IgA and IgM diagnostic kit is provided by Zhejiang Illikang Biotechnology Co., Ltd.; the specific operation steps refer to the instruction manual of the kit.

2.3 DAS28 score standard

DAS28 > 5.1, for a high degree of activity; 3.2-5.1 DAS28, for moderate activity; 2.6-3.2 DAS28, for low activity; DAS28 < 2.6 for ease.

2.4 Statistical analysis

SPSS 17.0 statistical software was used to analyze the data. The data were expressed as mean ± SD, the two groups were compared using t test; multi-group comparison between the use of single factor analysis of variance, the two comparison using LSD-t test; correlation using Pearson correlation analysis Test; $P<0.05$ that the difference was statistically significant.

3. Results

3.1 Comparison of serum immune index level in observation group and control group

The serum anti-CCP, complement C3 and C4, IgG, IgA and IgM levels of 100 patients in the observation group and 60 healthy persons in the control group are shown in Table 1. The levels of serum anti-CCP, C3, C4, IgG, IgA and IgM in the observation group were $[67.75 \pm 21.28]$ U/mL, $[1.95 \pm 1.14]$ g/L and $[0.63 \pm 0.22]$ L, $[18.77 \pm 4.83]$ g/L, $[4.74 \pm 1.06]$ g/L and $[4.02 \pm 0.98]$ g/L respectively, which were significantly higher than those in the control group, the difference was statistically significant ($P<0.05$).

3.2. Analysis of serum immune indicators levels between different RA disease activities

Among 100 RA patients, there were 79 patients in the active stage and 21 in remission stage. The serum anti CCP antibody, complement C3, C4, IgG, IgA and IgM of the active group were significantly higher than those in remission stage ($P<0.05$). 79 cases of RA patients in high, medium and low activity were 25 cases, 30 cases, 24 cases; Among them, medium and high activity group of serum anti CCP antibody, complement C3 and C4, IgG, IgA and IgM levels were significantly higher than that in low activity group ($P<0.05$); The level of serum anti-CCP in patients with high activity group was significantly higher than that in moderate activity group ($P<0.05$).
group, while the serum C3, C4, IgG, IgA and IgM levels were not significantly different between the two groups (P > 0.05). See Table 2.

### 3.3. Correlation of anti CCP antibody with complement and immunoglobin

There was a significant positive correlation between serum anti-CCP and complement C3, C4, IgG, IgA and IgM (r=0.462, 0.554, 0.558, 0.772, 0.741, P < 0.05).

### 4. Discussions

RA is a chronic, progressive, and inflammatory synovitis-based systemic autoimmune disease, disease development can eventually lead to joint deformity and loss of function, with high morbidity and high morbidity characteristics. Studies have shown that, RA in the first year of the disease there is a short period of treatment, during which the patient's synovitis is reversible, the effective time to alleviate and control the disease[8]. Therefore, the early diagnosis of RA is of great significance, while the sensitivity and specificity of high serum specificity is the main basis for improving the accuracy of early diagnosis.

RF is the most commonly used and necessary laboratory tests, with high sensitivity, but its specificity is not high, and also positively expressed in many chronic infectious diseases and connective tissue disease, clinical diagnosis has a certain missed diagnosis and misdiagnosis[9]. Citrulline is the main antigenic determinant of anti-filaggrin-related antibodies in serum of RA patients. The synthetic anti-citrullinated protein antibody (ACPA) was included in the American College of Rheumatology (ACR)/European Anti-rheumatism Union (EULAR) RA diagnostic criteria, and ACPA often exists before the clinical incidence of RA, and related with its disease progression and prognosis[10,11]. There are many types of ACPA antibodies, among which anti-CCP antibody is the most widely used antibody with high sensitivity and specificity, and its specificity is higher than that of RF[12]. The results showed that serum anti-CCP levels in patients with RA were significantly higher than those with low activity and remission, especially in the high-activity group, it is suggested that anti-CCP antibody is involved in the pathogenesis of RA and is closely related to the disease activity of RA.

Recent studies have shown that cellular immunity and humoral immunity involved in the physiological and pathological process of RA, the immune parameters detection in humoral immunity has important reference value in the diagnosis of RA[13]. Complement is the main component of non-specific immunity, has important role of specific immune guidance and maintenance of immune self-stabilizing, complement deficiency often lead to autoimmune diseases[14]. C3 is an important complement protein in the complement system, exists in the intersection of two activation pathways, and plays a pivotal role in the complement system activation process, with the important function of immune regulation. C4 is the second activated molecule in the classical activation pathway. It has functions of regulating complement activation, preventing immune complex deposition and neutralizing virus, and is related to immune recognition and maintenance of immune self-stabilizing function. There is controversy on the study of serum complement levels in patients with RA. It is generally believed that RA patients showed increased C3 and C4, but there were also reports show that their levels were reduced[15,16]. The results show that RA patients with C3, C4 were significantly higher than the healthy population, and the higher the degree of RA activity, the more obvious the level of increase, suggesting that serum complement is also associated with RA disease activity.

Immunoglobin IgG, IgA and IgM are important components of humoral immunity, IgG, IgA and IgM increased levels can cause a series of immune response, leading to tissue damage, and can be directly involved in the pathogenesis of RA[17]. IgG is the main component of immunoglobulin, with anti infection effect; IgA is the main component of defense system of organism mucosal immune; IgM is first appeared in humoral immune response, plays an important role in the body defense in early[18]. The results of this study show that serum IgG, IgA and IgM levels of RA patients were higher than those of healthy people, and the activity period was higher than that of remission stage, the higher the activity level, the higher the immunoglobulin level, indicating that serum
The results of this study are consistent with the results of Liu Yan-qing et al. [19] on immuno competent level changes in patients with RA.

Correlation analysis showed that anti-CCP antibody complement and immunoglobulin levels were increased, and related to RA disease activity, which can be used as an important index for early diagnosis and monitoring of RA.

In conclusion, the results of this study show that serum anti-CCP antibody, as well as the difference in the disease activity of RA patients, are related to the inclusion criteria and exclusion criteria of the study, as well as the difference in the disease activity of RA patients.

In conclusion, the results of this study show that serum anti-CCP antibody, complement and immunoglobulin levels in patients with RA increased, and related to RA disease activity, which can be used as an important index for early diagnosis and monitoring of RA.

References


