Association of Anti-cyclic Citrullinated Peptide (CCP) Antibodies and Functional Status in Rheumatoid Arthritis

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Key Words: Rheumatoid arthritis, Anti-cyclic citrullinated peptide antibodies, Rheumatoid factor, Anti-perinuclear factor, Autoantibody

 목적: 류마티스 관절염에서 항-CCP 항체와 임상 소견 및 검사실 소견 사이의 상관성을 확실히

방법: 미국 류마티스학회의 기준에 의해 진단된 114명의 류마티스 관절염 환자를 대상으로 하였다. 임상 소견으로 나이, 성별, 혈종의 기간, 기능적 상태를 조사하였고, 검사실 소견으로는 종 백혈구 수, 혈색소, 혈소판 수, 적혈구 완성속도, C-반응단백을 검사하였다. 항-CCP 항체와 함께 분석한 자가항체는 류마티스 인자, 항핵항체, 항핵주위인자였다.

결과: 항-CCP 항체는 대상 환자의 67.5% (77/114)에서 양성이었고, 류마티스 관절염의 기능적 상태가 나빠수록 항-CCP 항체의 양성률이 의미 있게 높아졌다 (functional class I/II vs III/IV, p<0.0001, OR=1.67). 항-CCP 항체 양성율은 류마티스 인자(p<0.0001), 항핵주위인자(p=0.018)의 양성과는 상관성이 있었으나 다른 임상적 검사실적 소견과는 연관성이 없었다.

결론: 항-CCP 항체가 류마티스 관절염의 나쁜 기능적 상태와 연관성이 있었기 때문에 항-CCP 항체의 류마티스 관절염의 예후에 미치는 영향에 대한 추가적인 연구가 필요할 것으로 생각된다.
INTRODUCTION

Rheumatoid arthritis (RA) is one of the most prevalent systemic rheumatic diseases, affecting 1~2% of the population worldwide (1). RA has been diagnosed according to clinical presentations and rheumatoid factor (RF) is one of the classification criteria proposed by the American College of Rheumatology (ACR) (2). However, RF has a low specificity because it may be found in healthy elderly individuals and in patients with other autoimmune diseases or chronic infections (3-5). Early intervention with highly effective disease modifying antirheumatic drugs (DMARDs) results in a better control of the disease. Therefore, it is important to differentiate between RA and self-limiting arthritis (6-9).

 Recently, a new serological test, the anti-cyclic citrullinated peptide (CCP) antibodies enzyme linked immunosorbent assay (ELISA) was developed and it has an excellent specificity for the diagnosis of RA, especially in patients with early disease (10-12). In this study we evaluated the relationship between anti-CCP antibodies and various clinical and laboratory parameters in RA patients.

MATERIALS AND METHODS

One hundred and fourteen patients (95 women and 19 men; mean age, 51.1 years; range, 23~80 years) attending the rheumatology unit of the Dong-A University Hospital were included. All patients were diagnosed RA according to the revised criteria of ACR (2).

For analysis of specificity, 202 non-RA controls were selected: systemic lupus erythematosus (SLE) (n=31), Sjogren’s syndrome (n=3), mixed connective tissue disease (MCTD) (n=4), systemic sclerosis (n=1), polymyositis (n=3), osteoarthritis (n=40), Raynaud syndrome (n=1), palindromic rheumatism (n=4), fibromyalgia syndrome (n=9), ankylosing spondylitis (n=4), adult-onset Still’s disease (n=4), juvenile RA (n=4), gout (n=9),

Bechter’s disease (n=8), unclassified arthritis (n=11), other diseases (n=10), and healthy subjects (n=56). The serum samples were aliquoted and stored at -20℃ until use.

Among the RA patients, the variables recorded were age, gender, time from diagnosis, and functional status (13). Laboratory parameters tested were WBC, hemoglobin, platelet count, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP). Analyzed autoantibodies were RF, anti-CCP, antinuclear antibodies (ANA), and anti-permucular factors (APF).

Anti-CCP antibodies were determined by an ELISA using a commercial anti-CCP assay (Euro-Diagnostica, Malmö, Sweden). The assay was performed according to the manufacturer’s protocol. RF was measured by immunoturbidimetry (LX-2200, Eiken Chemical Co., Tokyo, Japan). ANA was assayed by indirect immunofluorescence on HEp-2 cells (fluoroHEPANA, MBL, Japan), and APF by indirect immunofluorescence (IT-APF, ImmunoThink, Seoul, Korea).

Statistical analysis was performed using the SPSS 10.1 (SPSS, Chicago, USA). Subgroups of RA patients who were positive and negative for anti-CCP were compared by means of Student’s t-test (for continuous variables) and the chi-square test (for discrete variables). Odds ratio and 95% confidence interval between anti-CCP positivity and functional class were calculated using chi-square statistics. Correlations between anti-CCP and autoantibodies were analyzed by using Pearson correlation coefficient. The level of statistical significance was established at p < 0.05.

RESULTS

1. Association of anti-CCP with RA

The demographic and clinical characteristics of RA patients according to anti-CCP are shown in Table 1. Anti-CCP were found in 77 (67.5%) of 114 RA patients and anti-CCP positive RA patients had a mean antibody concentration of 564.5 (range, 27~4,717) unit. Only 8 of 202 control sera (4.0%) showed a positive