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ORIGINAL ARTICLE

Anti-mutated citrullinated vimentin antibodies in rheumatoid arthritis patients: Relation to disease activity and manifestations

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Abstract *Aim of the work:* To evaluate the frequency of anti-mutated citrullinated vimentin antibodies (MCV) in rheumatoid arthritis (RA) patients and to correlate it with disease activity and various disease manifestations.

Patients and methods: Fifty RA patients were recruited from the rheumatology and rehabilitation outpatient clinic, Kasr Al-Aini. Thirty healthy subjects served as controls. All patients were subjected to full history taking and clinical examination including general and joint assessment. Disease activity was assessed by the disease activity score (DAS-28) and functional ability was evaluated by the Modified Health Assessment Questionnaire (MHAQ). Anti-MCV and anti-cyclic citrullinated peptide (anti-CCP) were assayed by ELISA in patients and controls. Plain X-ray was performed on the hands and wrists and Sharp score was used to assess the erosions and joint space narrowing.

Results: A highly significant elevation of serum anti-MCV in RA patients (135.82 ± 126.81 U/ml) compared to controls (13.63 ± 8.48 U/ml) ($p < 0.0001$) was found. Anti-MCV showed a sensitivity of 84% and specificity of 80%. There was a significant difference between anti-MCV positive and anti-MCV negative patients as regards MHAQ (1.07 ± 0.74 vs. 0.52 ± 0.37, $p = 0.005$) and Sharp erosion score (12.93 ± 23.55 vs. 4 ± 2.2, $p = 0.02$). Anti-CCP showed a

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sensitivity of 70% and specificity of 100%. There was a significant difference between the specificities of both markers ($p = 0.03$). There was no significant correlation of the anti-MCV with the clinical manifestations, MHAQ, DAS28 or Sharp score. Anti-MCV significantly correlated with anti-CCP ($p < 0.0001$).

Conclusion: Anti-MCV test has a significant association with the functional disability and *radiologic* progression in RA and could be considered as a promising biomarker.

1. Introduction

Rheumatoid arthritis (RA) is a common systemic autoimmune disease. Its prevalence is between 0.5% and 1% worldwide. It is mainly characterised by persistent joint inflammation that results in loss of joint function and morbidity [1]. The American College of Rheumatology (ACR) 1987 revised criteria could still be used in the classification of RA and is primarily based on clinical parameters. The only serological criteria being IgM rheumatoid factor (IgM RF). However, the criteria may be insufficient for the diagnosis of early RA, as they are based upon measurements of disease classification predominately featuring manifestations typical of later-stage disease [2].

Numerous serological markers of RA have been described over the past 50 years. Among all these, Anti-Cyclic Citrullinated Peptide (CCP) antibodies have been proven to be highly specific, diagnostic and prognostic markers in RA [3]. In July 2010, the 2010 ACR/European League against Rheumatism (EULAR) rheumatoid arthritis classification criteria was introduced. These new classification criteria included anti-CCP testing [4], overruled the "old" ACR criteria 1987 [5] and are adapted for early RA diagnosis. The newest member of this autoantibody family is anti-mutated citrullinated vimentin (MCV) [3].

Vimentin is a protein found in mesenchymal and endothelial cells, monocytes and activated macrophages, citrullinated by peptidyl arginine deaminase enzyme [6]. In RA this ccitrullinated peptide activates T-lymphocytes by binding on HLA-DR4 on the surface of antigen presenting cells and may contribute to certain pathways in the pathogenesis of RA [7]. Studies on the diagnostic accuracy of anti-CCP antibodies report a higher sensitivity (up to 78%) and specificity (up to 95%) of anti-MCV. Besides the higher sensitivity it has been shown that anti-MCV is an even better prognostic marker for the outcome of RA, it correlates well with the disease activity score [7].

The aim of this work is to evaluate the frequency of anti-MCV antibodies in RA patients and to correlate its relation to disease activity and manifestations.

2. Patients and methods

Fifty RA patients attending the Kasr Al Aini Rheumatology and Rehabilitation Outpatient Clinic, and 30 healthy controls were involved in this study. All patients were previously diagnosed according to the 2010 ACR/EULAR RA classification criteria [4].

All patients gave informed consent to participate in the study, which was approved by the Kasr Al Aini medical ethics committee. Patients were subjected to detailed history, general and musculoskeletal examination and measurement of the 28-joint count of tender and swollen joint with calculation of the disease activity score (DAS-28) for each RA patient by DAS-28 score calculator [8].

Modified Health Assessment Questionnaire (MHAQ) was used for assessing the functional ability of the patients [9,10].

2.1. Laboratory tests

All patients were subjected to routine laboratory investigations.

Rheumatoid factor was assayed with a quantitative immuno-nephelometry test (Behring, Marburg, Germany).

Anti-CCP was measured using the Immunoscan CCPlus® test kit using enzyme-linked immunosorbent assay (ELISA) for qualitative and semiquantitative detection of IgG antibodies to Cyclic Citrullinated Peptides (CCP) in human sera. Normal reference level is up to 25 U/ml.

Anti-MCV was measured using an indirect solid phase ELISA for the quantitative measurement of IgG class autoantibodies against Mutated Citrullinated Vimentin (MCV) in human serum (using kit from ORGENTEC Diagnostika GmbH). Normal reference level is up to 20 U/ml.

2.2. Conventional radiography

Sharp score was calculated to evaluate radiographic changes in RA patients and included the Sharp erosion score and the joint space narrowing (JSN) score [11].

Statistical methods: Comparison was done using Student's *t* test for independent samples comparing 2 groups and the Mann Whitney *U* test. Comparison of numerical variables between more than two groups was done using the Kruskal Wallis test. For comparing categorical data, Chi square (χ^2) test was performed. Correlation between various variables was done using Spearman rank correlation equation for non-normal variables. A linear multiple regression analysis for anti-MCV levels (dependent variable) was performed to assess the effect of possible independent variables. *p*-values less than 0.05 were considered statistically significant. All statistical calculations were done using computer programs SPSS version 15 for Microsoft Windows.

3. Results

The study included fifty RA patients, 47 females (94%) and 3 males (6%). The demographic, clinical and laboratory characteristics of the RA patients are demonstrated in Tables 1 and 2.

Serum Anti-MCV levels in the patients were detected with a mean of 135.82 ± 126.81 U/ml. These values were significantly