Original Article

Serum Anti-Mcv Antibodyand Its Correlation With Disease Activity In Local Pakistani Rheumatoid Arthritis Patients

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Objective: To investigate the correlation of anti-mutated citrullinated vimentin (anti-MCV) titers with clinical manifestations and disease activity in a cohort of patients with established diagnosis of rheumatoid arthritis.

Material and Methods: A total of 58 patients attending the Rheumatology outpatient department of Fatima Memorial Hospital, Lahore were recruited in the study. Data of disease related parameters such as disease duration, medications, degree of pain (visual analog scale, VAS), disease activity score 28 (DAS 28), and health assessment questionnaire (HAQ) were recorded. Laboratory workup included erythrocyte sedimentation rate (ESR>20mm/hr considered positive), rheumatoid factor (determined by ELISA technique), anti-CCP antibody (ELISA Immco Diagnostics, USA) and anti-MCV antibody (Cusabio Biotech Co., Ltd, China).

Results: The anti-MCV antibody levels did correlate with the number of tender joints (p=0.001), swollen joints (p=0.001), VAS (p=0.330), ESR (p=0.001), DAS28 scores (p=0.001). However, no significant correlation of aMCV titers with HAQ scores (p=0.090) and anti-CCP titers (p=0.685) and serum RF titers (p=0.621) was observed.

Conclusion: In Significant correlation was noticed between the serum anti-MCV antibody titers and DAS-28 and other disease activity parameters besides HAQ-DI and anti-CCP and RF titers.

Key words: Rheumatoid Arthritis, Anti-Mutated Citrullinated Vimentin Antibody (anti-MCV),disease activity.

Introduction

Rheumatoid arthritis (RA) is an autoimmune disorder characterized by symmetric and erosive synovitis. It causes progressive joint destruction and disability. It is the most common type of inflammatory arthritis, affecting 0.5 to 1% of the general population worldwide, with a female to male ratio of 2.5:1. The disease may start at any age, but it is most common among those aged from 40-70 years.[1] The disease progresses rapidly within first two years of onset and can lead to irreversible erosive joint destruction. Early diagnosis is important as these patients can be treated early and deformities can be prevented.[2]

Early diagnosis of rheumatoid arthritis depends mainly on clinical symptoms which are usually mild and nonspecific, and patients usually do not fulfill the American College of Rheumatology (ACR) criteria for the diagnosis.[3] When clinical diagnosis of RA is made, irreversible joint erosions usually have occurred. Early therapeutic intervention results in earlier disease control and consequently less joint damage.[4] There is no single specific test or finding that can diagnose rheumatoid arthritis. Rheumatoid factor is the only serological test included in the ACR criteria. RF is an antibody against Fc region of IgG. It has been used as a diagnostic marker of RA for decades. However, this auto-antibody lacks specificity. It may be detected in patients of autoimmune diseases and infectious disorders. It may even be present in sera of apparently healthy elderly individuals. Up to 25% of patients having rheumatoid arthritis show negative rheumatoid factor test (seronegative).[5] Therefore, detection of specific auto antibodies are needed for early diagnosis. The RF assay in its current form lacks sensitivity (54-88%) and specificity (40-92%). However, it has been established that high titers of RF depicts aggressive disease.[6]

Other RA associated antibodies such as anti-perinuclearfactor (APF), anti-keratin antibody (AKA), anti-fill grin antibody and anti-cyclic citrullinated peptide antibody have been discovered. These all belong to the family of anti-citrullinated protein /peptide antibody (ACPA).[7] All these antibodies recognize the antigenic epitome containing citrulline[8] that is generated byylargininedeiminase (PAD).[9] Many citrullinated proteins called as antigens include fibrin, Ebstein-Barr virus nuclear antigen, alpha-enolase and vimentin.[10] Process of citrullination is increased in inflammatory conditions. Citrullinated peptides are synthesized as antigens for diagnostic immunoassays. Many assays for detecting anti-

citrullinated peptide antibodies (ACPA´s) are available employing filaggrin derived peptides (CCP-assay), viral citrullinated peptides (VCP-assay), mutated citrullinated vimentin (MCV-assay). It has been shown that ACPA have a higher specificity than rheumatoid factor in diagnosing rheumatoid arthritis.[11] ACPA´s can be detected years before the appearance of first symptoms of RA.[12] Although the presence of ACPA has been accepted to be a reliable diagnostic and prognostic tool in RA, it association with disease activity and severity remains unclear. Anti-MCV antibody concentrations have been shown to have correlation with disease activity score (DAS28), prognostic for disease severity, and being treatment sensitive, enabling their use in monitoring response to therapy. In the present study, we have investigated the correlation of serum anti-MCV antibody with clinical manifestations and disease activity in established cases of rheumatoid arthritis.

Materials and Methods

A total of consecutive 58 patients attending the Rheumatology outpatient department of Fatima Memorial Hospital, Lahore were recruited in the study. All the patients fulfilled the American College of Rheumatology criteria for RA and were diagnosed by the rheumatologist. The study was approved by the Ethical and Review Committee of University of Health Sciences, Lahore. Informed written consent was taken from each study participant. Demographic data was collect during clinical evaluation of the patients. Patients with other connective disease, acute or chronic infectious diseases or malignancy were excluded from the study to avoid false positive results associated with other conditions.[12]

Purposefully designed proforma was used to record the data of the subjects including age, gender, duration of disease, medications, degree of pain (visual analog scale, VAS) and clinical characteristics. Stanford Health Assessment repeated Questionnaire-Disability Index (HAQ-DI) was used to get a score so as to access the functional disability of RA.[13] Disease activity was estimated in all patients using the disease activity score of 28 joints and for four variables, with the help of a preprogrammed calculator (DAS-28).[14]

Laboratory workup included erythrocyte sedimentation rate (ESR>20mm/hr considered positive), rheumatoid factor (determined by ELISA technique), anti-CCP antibody (ELISA Immco Diagnostics, USA) and anti-MCV antibody (ELISA Cusabio Biotech Co., Ltd, China).

At the end of study, patients were divided into anti-MCV positive and anti-MCV negative and comparisons between the two groups were performed in all the above mentioned characteristics. Spearman's rho correlation was used to observe correlation between non-normally distributed quantitative variables. The level of two-sided statistical significance was set at 0.05. All data was analyzed using Statistical Package for social sciences, version 17.

Results

The socio-demographic and disease related characteristics of the patient with rheumatoid arthritis are summarized in table-1. Among the58 rheumatoid arthritis patients (47 were females and 11 were males), 20 were found to be anti-MCV positive (34.5%) and 38(65.5%) were anti-MCV negative. Mean age± SEM of the RA group was 44±1.2 years. All the patients (n=58) were using methotrexate, while 35 were using steroids.Correlation of serum aMCV titers with various disease variables like TJC, SJC, VAS, DAS-28 was determined. There was a significant correlation of serum aMCV titers with TJC (=0.515, n=58, p=0.000), SJC (=0.598, n=58, p=0.00), VAS (=0.330, n=58, p=0.012) and ESR (=0.560, n=58, p=0.00). There was also a significant (=0.626, n=58, p=0.000) correlation of serum aMCV titers with DAS-28 scores. But no significant correlation of serum aMCV titers with serum RF titers (= -0.066, n=58, p=0.621), serum aCCP titers (rho= -0.054, n=58, p=0.685), HAQ-DI (=0.225, n=58, p=0.090), was observed. (**Table-2**)

Table-1: Disease related characteristics of RA patients.

Characteristics	P-value
Drug treatment Methotreaxte	58
Steroid	35
Disease duration years	5(4-8)
TJC	10(5.25-16)
SJC	4(0.0-7.0)
VAS	50(31-73.75)
ESR(mm/1sthr)	44(25-63.8)
DAS-28 Score	5.37(4.35-6.49)
HAQ-D1Score	1.9(1.0-2.38)
Serum RF titer(IU/ml)	27.76(2.51-32.9)
Serum aCCP titer(IU/ml)	1.8(0.00-340.5)

Table-2: Correlation of serum amcv antibody titers and other disease variables.

Characteristics	N	Spearman rho corilation cofficient (rho)	P-value
ESR	58	0.560	0.001*
TJC	58	0.515	0.001*
SJC	58	0.598	0.001*
VAS	58	0.330	0.012*
DAS-28	58	0.626	0.001*
HAQ-DI	58	0.225	0.090
RF titiers	58	-0.066	0.621
ACCP titers	58	-0.054	0.685

**p-value of <0.05 is considered as statistically significant*

Discussion

The modern trend of RA treatment is to start it as early as possible. Early control of inflammation in RA results in reduced joint damage. It is therefore important to differentiate between RA and other forms of arthritis at early stage, so that the rheumatologists are able to use potentially toxic and expensive drugs to those patients, where the benefits clearly outweigh the risk. Joint erosions and deformities are the major adverse outcomes. The association of anti-MCV positivity and joint destruction in patients with established rheumatoid arthritis has been documented.[15] Follow-up parameters of disease activity in RA patients are duration of morning stiffness, degree of joint pain, HAQ, DAS-28, ESR and serum RF positivity. Although the presence of anti-MCV has recently been accepted to be a reliable diagnostic and prognostic tool in RA, its association with disease activity and severity remains unclear. In the present study, we have investigated the correlation of levels of serum anti-MCV with clinical manifestations and disease activity. There was a significant correlation of serum aMCV titers with TJC (rho=0.515, n=58, p=0.000), SJC (rho=0.598, n=58, p=0.00), VAS (rho=0.330, n=58, p=0.012) and ESR (rho=0.560, n=58, p=0.00). There was also a significant (rho=0.626, n=58, p=0.000) correlation of serum aMCV titers with DAS-28 scores. But no significant correlation of serum aMCV titers with serum RF titers (rho= -0.066, n=58, p=0.621), serum aCCP titers (rho= -0.054, n=58, p=0.685), HAQ-DI (rho=0.225, n=58, p=0.090), was observed.These results are in concordance with findings of other researchers. Bang, et al. (2007), reported a significant correlation of anti-MCV antibodies with DAS28 in 42 German RA patients.[16] Mathsson, et al. (2008), also reported that anti-MCV positive patients had higher disease activity according to physician assessment and DAS28 and had more swollen and tender joints than anti-MCV negative patients.[17] Similarly, Wagner, et al. (2008) also reported a significant correlation between anti-MCV and disease activity in a sub-group of 86 Austrian RA patients.[18] Innala, et al. (2008) concluded that anti-MCV titer was significantly correlated with DAS-28, SJC and ESR.[19] Mansour, et al. (2010) also found that anti-MCV positive RA patients had a significantly higher DAS28 scores and SEN-scores than anti-MCV negative patients, who were found to have more benign disease with lower incidence of erosions.[20]

Conclusion

Significant direct correlation exists between serum anti-aMCV antibody with DAS-28 and other disease activity parameters like ESR, TJC and SJC besides HAQ-DI, anti-CCP and RF titers.

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