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Original Article

Use of serological markers for evaluation patients with rheumatoid arthritis

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ABSTRACT

Objective: The aim of this study was to determine the frequency of antinuclear antibody, rheumatoid factor, and cyclic citrullinated peptide antibody in patients with rheumatoid arthritis and to compare cyclic citrullinated peptide antibody with rheumatoid factor. Methods: Our study was conducted in princess Iman Center for research and laboratory sciences at King Hussein Medical Center in a period from August 2011 to November 2011. In this study 115 patients from arthritis clinic were examined. For all we measured the antinuclear antibody (indirect immunofluorescence), cyclic-citrullinated peptide (enzyme linked immunosorbent assay), rheumatoid factor (agglutination assay).Results: Out of 115 patients with arthritis, 97 were females and 18 were males. Median age was 57.5 years for males and 48.5 years for females. 60% (69) of patients were positive for antinuclear antibody. 55% (64) of patients were positive for three serological markers (cyclic-citrullinated peptide antibody, antinuclear antibody and rheumatoid factor). For these patients further investigations were done such as dsDNA and extractable nuclear antibody (ENA), and were negative for both. Only 5 patients of 115 were positive for antinuclear antibody alone with speckled pattern, of them 4 had high titer(> 1/160) and positive for ENA and 1 had low titer (1/80) and negative for ENA. The incidence of cyclic-citrullinated peptide antibody and rheumatoid factor was 79.1 %(91) and 81.7 %(94) respectively. 23.4% (27) of patients had positive for both serological markers (anti-ccp and RF).Conclusion: For evaluation patients with suspected rheumatoid arthritis recommended perform cyclic-citrullinated peptide antibody and IgM- rheumatoid factor. The results of both tests are informative, since a positive result for either test increase diagnostic sensitivity, while the specificity is increased when both tests are positive.

1. Introduction

Rheumatoid arthritis is a chronic, severe, progressive inflammatory autoimmune disease of uncertain etiology involving multiple peripheral joints [1]. Rheumatoid arthritis can also produce diffuse inflammation in the lungs, pericardium, pleura, and sclera, and also nodular lesions, most common in subcutaneous tissue. About 1% of the world's population is afflicted by rheumatoid arthritis, and is much more common in women than in men and generally occurs between the ages of 40 and 60years. The disease onset is usually gradually, with the predominant symptoms being pain, morning stiffness, and swelling of many joints [2]. Early tends to affect smaller joints of hand and feet and later on as the disease progresses, symptoms often spread to the knees, ankles, elbows, hips and shoulders [3,4]. Rheumatoid arthritis is diagnosed according to clinical findings and serologic testing. The main useful serological markers are rheumatoid factors and antibodies to citrullinated peptides. Rheumatoid factor (RF) is IgM autoantibody directed against the Fc portion of IgG. It is found in 75 to 80% of rheumatoid arthritis patients, but has a low specificity because it may be found in healthy elderly individuals and patients with other autoimmune diseases or infections [5,6]. Anti cyclic-citrullinated peptide antibody (Anti-ccp) is autoantibody that bind antigenic determinant of unusual amino acid citrulline formed by posttranslational modification of arginine residues. The sensitivity of Anti-ccp for RA varies from about 50% to 75%, while specificity is relatively high, usually over 90 % [7,8].

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2. Materials and Methods

Our study was carried out in princess Iman Center for research and laboratory sciences at King Hussein Medical Center, Jordan.115 patients from arthritis clinic were examined.110 patients were diagnosed clinically as rheumatoid arthritis according to clinical findings(morning stiffness, arthritis of 3 or more joint areas, arthritis of hand joint, symmetric arthritis, rheumatoid nodules and radiological changes). Six milliliters of venous blood were collected from each patient and sent to the clinical immunology laboratory for serology testing. Anti-nuclear antibody was determined quantitatively by indirect immunofluorescence assay using BI0-RAD, KALLESTADTM HEp-2 cell line substrate reagent kits (USA). Anti-cyclic citrullinated peptide antibodies were determined quantitatively by Enzyme-Linked Immunosorbent assay (ELISA) using EUROIMMUN reagent kits(Germany) and Elisa washer (PW40 BIO-RAD) and Elisa reader (Model 680 BIO-RAD). Rheumatoid factor -IgM was determined qualitatively and semi-quantitatively by latex agglutination assay using Ccromatest.LiNEAR Chemicals.S.L (Spain). To evaluate assay reproducibility, 3 positive and 3 negative controls were assayed in each analytical run.

3.Results

Out of 115 patients with arthritis, 97 were females and 18 were males. Median age was 57.5 years for males and 48.5 years for females.110 patients were diagnosed clinically as rheumatoid arthritis. The prevalence of antinuclear antibody, anti-cyclic citrullinated peptide antibody, and rheumatoid factor were 60% (69), 79.1% (91) and 81.7% (94) respectively table (1).

Table- 1: prevalence of ANA, Anti-CCP, RF.

Serological marker	Number of patients	Percentage
ANA	69	60%
Anti-CCP	91	79.1%
RF	94	81.7%

23.4% (27) of patients had positive results for both serological markers (Anti-CCP and RF). 55% (64) of patients were positive for three markers (ANA, Anti-CCP, and RF) table (2).For these patients further investigations were done such as dsDNA and ENA (extractable nuclear antigens), and were negative for both. Only 5 patients of 115 were positive for antinuclear antibody alone with speckled pattern, of them 4 had high titer (> 1/160) and positive for ENA and 1 had low titer (1/80) and negative for ENA.

Table-2: percentage of patients with positive results for more than one marker

Serological markers	Number of patients	Percentage
Anti-CCP + RF	27	23.4%
Anti-CCP + RF + ANA	64	55%

Sixty four of patients (70.3%) with positive results for Anti-CCP had high concentration, whereas 27 (29.7%) showed a positive reaction low at low concentration.89.4% (84) of IgM-RF positive patients had high titer (≥ 1/64), and 10.6% (10) had low titer (1/8- 1/32).

4.Discussion

When RA is clinically suspected, immunological studies are required, such as testing for the presence of rheumatoid factor and anti-cyclic citrullinated peptide.RF was the first autoantibody detected in patients with RA. It was discovered in the early twentieth century and became the primary serological test used in the diagnosis of RA [9]. Rheumatoid factor also found in many other diseases, including Sjogren's syndrome, systemic lupus erythematosus, mixed connective tissue disease, chronic infection and in healthy elderly population. Because of this low specificity, new serological test such as anti- cyclic citrullinated protein antibodies is used for diagnosing rheumatoid arthritis. The detection of anti-CCP is useful for the diagnosis of RA because of its similar sensitivity but higher specificity compared with RF. In our study we found high prevalence of RF and anti-CCP antibodies in patients with rheumatoid arthritis. Also we found moderate prevalence of antinuclear antibodies with low titer and negative for dsDNA and ENA. This is important to role out systemic lupus erythematosus. The combination of two biomarkers (RF and CCP) together provide important diagnostic tool about rheumatoid arthritis.

5. Conclusion

For evaluation patients with suspected rheumatoid arthritis recommended perform cyclic-citrullinated peptide antibody and IgM- rheumatoid factor. The results of both tests are informative, since a positive result for either test increase diagnostic sensitivity, while the specificity is increased when both tests are positive.

6.Reference

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