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THE ROLE OF ANTI-CYCLIC CITRULLINATED PEPTIDE ANTIBODIES IN PREDICTING RHEUMATOID ARTHRITIS

ULOGA PROTU-CIKLIČKIH CITRULINSKIH PEPTIDNIH ANTITIJELA U PREDVIĐANJU REUMATOIDNOG ARTRITISA

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Summary

The study presents the results of predicting role of anti-cyclic citrullinated peptide antibodies in rheumatoid arthritis, compared to rheumatoid factor. 32 patients with rheumatoid arthritis were identified from a retrospective chart review.

The results of our study show that presence of the rheumatoid factor has less diagnostic and prognostic significance than the anti-cyclic citrullinated peptide, and suggests its superiority in predicting an erosive disease course.

Keywords

rheumatoid arthritis, anti-cyclic citrullinated peptide antibody, rheumatoid factor

Sažetak

Rad prikazuje rezultate o ulozi protu-cikličkih citrulinskih peptidnih antitijela u predviđanju reumatoidnog artritisa, u poređivanju s reumatoidnim faktorom. 32 bolesnika s reumatoidnim artritisom su ispitivani u retrospektivnom radu.

Rezultati našeg istraživanja pokazuju da je prisutnost reumatoidnog faktora s manjim dijagnostičkim i prognostičkim značajem uporedivši sa protu-cikličkim citrulinskim peptidnim antitijelima i sugerira njihovu superiornost u predviđanju erozivnog tijeka bolesti.

Ključne riječi

reumatoidni artritis, protu-ciklička citrulinska peptidna antitijela, reumatoidni faktor

Intoduction

Rheumatoid arthritis (RA) is an autoimmune disease of unknown etiology that is characterized by symmetric, erosive synovitis and multi-system involvement. The diagnosis of RA was concluded on diagnostic criteria of American College of Rheumatology (ACR). Rheumatoid Factor (RF) is very useful laboratory test for diagnostic evaluation of RA. Anti-CCP, which stands for anti-cyclic citrullinated peptide antibody, is a new and exciting blood test to help rheumatologists confirm a diagnosis of RA (1). Citrullinated peptides are considered to be potential autoantigens driving the immune response in RA. Autoantibodies against citrullinated antigens have been shown

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to be highly specific for RA (2). Anti-cyclic citrullinated peptide (anti CCP) antibodies, first described in 1998, were shown to be highly specific (95%) in the diagnosis of RA and slightly less sensitive than IgM RF (60-70%) (3). The second generation of anti CCP antibodies (anti CCP-2) increased the sensitivity to 80 percent, while retaining the specificity (98%) (4). While the rheumatoid factor is more common in rheumatoid arthritis patients, many patients with a positive test do not have rheumatoid arthritis. Furthermore, the presence of the rheumatoid factor has less prognostic significance than the CCP. Both blood tests are recommended in the initial evaluation of a patient with suspected rheumatoid arthritis. Measurement of anti-CCP helps to differentiate RA from other arthropathies; furthermore, as a prognostic marker it may predict persistent, erosive and more aggressive synovitis (5).

Objective of study

The aim of this study was to compare the diagnostic and prognostic role of rheumatoid factor versus anti-cyclic citrullinated peptide, as predictor factor in early diagnosis RA.

Material and methods

In this study, in Internal Clinic - Rheumatology Department, 32 patients with RA from a retrospective chart review of inpatients and outpatients were investigated. All patients were diagnosed according to 1987 revised classification criteria of the American College of Rheumatology. The mean age of the patients was 59.2±11.02 years with average illness duration of 3.53 years. Parameters of illness activity (DAS28 score) are presented. Value of anti-CCP antibody was measured in all patients using Elescys and Cobas immunoassay analyzers and value of rheumatoid factor with (RF). Patients with rheumatoid arthritis involved in the study were part of the third and fourth anatomic phase of radiological changes according to Steinbrocker, revised by ACR 1991. We have done statistical analysis of the results we obtained through the structure indicators and estimates of arithmetic averages. We have identified homogeneity set of statistics on the basis of the variation interval, standard deviation and coefficient variation. We tested with the T-test of arithmetic averages for small samples to find the difference between arithmetic average, and we tested with the χ^2 test. The obtained results are presented in form of tables.

Results

In table 1, we have presented gender structure of patients. There were more females than males (87.5% vs. 12.5%), which is statistically significant ($p<0.00012$). The average age of all patients was 59.2± 11.02 years old. Range of age was 27-85 year.

Table 1. **Gender structure of patients**
Tablica 1. **Spolna struktura bolesnika**

Parameters	Gender		Total	χ^2-test	
	Female	Male			
N	28	4	32		
%	87.5	12.5	100.0	χ^2 =18	p=0.00002
Average age ± SD	59.4 ± 11.76	57.5 ± 2.38	59.2 ± 11.02	Shl=1	p<0.00012
Age range			27-85		

Table 2. **Relationship between positive anti-CCP and rheumatoid factor in patients with rheumatoid arthritis**
Tablica 2. **Odnos između pozitivnog anti-CCP i reumatoidnog faktora u bolesnika s reumatoidnim artritisom**

Test	Positive		Negative		Total	
Anti CCP	28	87.5%	4	12.5%	32	100.0%
RF	21	65.6%	11	34.4%	32	100.0%

Table 3. **Presence of anti-CCP according to the X-ray stage**
Tablica 3. **Prisutnost anti-CCP u odnosu na rentgenološki stupanj**

X-ray stage	Positive		Negative		Total	
I	0	0.0%	2	50.0%	2	6.3%
II	0	0.0%	2	50.0%	2	6.3%
III	23	82.1%	0	0.0%	23	71.9%
IV	5	17.9%	0	0.0%	5	15.6%
Grand total	28	100.0%	4	100.0%	32	100.0%

In table 2 we show that anti-CCP antibodies were positive in 28 patients (87.5%), while rheumatoid factor was positive in 21 patients (65.63%) of RA. In 8 patients with negative IgM-FR, positive anti-CCP were found (28.57%).

In all patients with positive anti-CCP advanced X-ray changes were shown (III and IV Steinbrocker stage): 23 (82.14%) with stage III and 5 (17.86 %) with stage IV (table 3).

Discussion

Of the total number of 32 patients, 28 were female and 4 were male. This gender structure is consistent with other authors, who also found similar data, as it is known that rheumatoid arthritis attacks more women than men (6). In many cases of RA, clinical symptoms are milder and patients who do not fulfill all ACR classification criteria for RA. Therefore, the detection of a disease-specific autoantibody like anti-CCP is of great diagnostic and therapeutic importance. Nell et al. concluded that anti-CCP antibodies were detected in roughly 50-60 % of patients with RA (7,8). Compared to RF-IgM and RF-Latex that have moderate sensitivities and good specificities, the anti-CCP antibody test has priority of having moderate sensitivity and excellent specificity. The combination of anti-CCP antibody and IgM-RF positivity improved specificity over RF positivity alone (Bas et al.) (9,10) as shown also in our study. In our study the specificity of the anti-CCP antibody test (87.5 %) was significantly higher ($p<0.001$) than that for RF-IgM (65.63 %). This study also demonstrated the additional prognostic value of anti-CCP antibodies in patients with severe joint destruction and active disease compared with the RF. In all patients with positive anti-CCP advanced X-ray changes were shown (in III and IV Steinbrocker stage), in 23 (82.14 %) with stage III and 5 (17.86 %) with stage IV. This set of diagnostic and prognostic markers would allow the clinician to choose a more powerful disease modifying anti-rheumatic drugs early in the course of disease, even when clinical judgment might not yet indicate the need for such drugs.

Conclusion

This study shows that the presence of the rheumatoid factor has less diagnostic and prognostic significance than the anti-CCP and suggests the superiority of anti-CCP over IgM-RF in predicting an erosive disease course. We can conclude that anti-CCP is proven to be important diagnostic test, especially for early detection to rheumatoid arthritis patients with negative RF.

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