

The prevalence of anti-cyclic citrullinated peptide (anti-CCP) antibodies in patients with thyroid autoimmunity

Tiroid otoimmünitesi olan hastalarda anti-siklik sitrülünlenmiş peptit (anti-CCP) antikor yaygınlığı

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Abstract

Aim: Anti-cyclic citrullinated peptide (anti-CCP) antibodies are one of the diagnostic markers of rheumatoid arthritis (RA), but can also be found in other diseases such as systemic lupus erythematosus, primary Sjogren's syndrome. So far, there has been no data available which identified prevalence of anti-CCP in patients with thyroid autoimmunity (TA). We aimed to identify anti-CCP prevalence in adult patients with TA.

Material and Methods: We reviewed retrospectively medical records of 1282 patients including TPO-Ab, TRAb, rheumatoid factor (RF), anti-CCP antibodies in the computer database between the dates of January 2010 and October 2014. TA diagnosis was made if thyroid autoantibodies were higher than the upper limit of normal. Anti-CCP and RF positivity were considered if the values exceeded the upper limit of normal. Patients with or without TA were compared in terms of the prevalence of anti-CCP antibodies.

Results: In group with TA, TPO-Ab, TRAb, CCP, and RF were detected in 332 (99%), 7 (2%), 44 (13%), and 78 (23%) patients respectively. In group without TA, CCP was detected in 70 patients (7.4%), and RF was detected in 378 (20%) patients. The positive rates of anti-CCP were significantly higher in patients with TA than the patients without TA (13% vs. 7.4%, $p < 0.001$). However, there was no difference in RF positivity between the groups.

Conclusion: Our study indicates an increased prevalence of anti-CCP antibodies in patients with TA. It is suggested that anti-CCP antibodies can also be shown in patients with TA in addition to RA.

Key words: Thyroid autoimmunity, anti-cyclic citrullinated peptide antibodies, rheumatoid factor

Öz

Amaç: Anti-CCP antikorları romatoid artrit (RA) tanı koydurucu belirteçlerinden bir tanesi olmakla birlikte sistemik lupus eritematosus (SLE), primer Sjögren sendromu (pSS) gibi diğer hastalıklarda da saptanabilmektedir. Yetişkinlerde tiroid otoimmünitesi (TO) ve anti-CCP pozitifliğiyle ilgili günümüze kadar herhangi bir veri yayınlanmamıştır. Biz bu çalışmada yetişkin TO olan hastalarda anti-CCP pozitifliği yaygınlığını saptamayı amaçladık.

Yöntem ve Gereçler: Ocak 2010-Ekim 2014 tarihleri arasında anti-CCP, RF ve anti-tiroid peroksidoz (anti-TPO) ve/veya TSH reseptör antikor (TRAb) istenen 1282 hastanın kayıtları tıbbi kayıt sisteminden retrospektif olarak incelendi. TO, tanısı tiroid otoantikorlarının normal değerlerinin üst sınırının üzerinde saptanması ile kondu. RF ve anti-CCP pozitifliği değerler normal aralığın üzerinde olduğu zaman düşünüldü.

Bulgular: TO olan grupta, TPO-Ab, TRAb, CCP ve RF pozitifliği sırasıyla 332 (%99), 7 (%2), 44 (%13), ve 78 (%23) olarak saptandı. TO olmayan grupta 70 kişide Anti-CCP pozitifliği (%7.4) ve 378 kişide RF pozitifliği (%20) saptandı. Anti-CCP pozitiflik oranı TO olan grupta TO olmayan gruba göre anlamlı olarak daha yüksek saptandı (%13 vs. %7.4, $p < 0.001$). Ancak RF pozitifliği yönünden gruplar arasında anlamlı olarak fark yoktu.

Sonuç: Bizim çalışmamız TO olan hastalarda anti-CCP prevalansının arttığını göstermiştir. Bu da bize Anti-CCP antikorlarının RA'ya ek olarak TO olanlarda da görülebileceğini düşündürür.

Anahtar Kelimeler: Tiroid otoimmünitesi, anti-siklik sitrülünlenmiş peptid antikorları, romatoid faktör

Introduction

Anti-cyclic citrullinated peptide (anti-CCP) antibodies are a marker for the diagnosis of rheumatoid arthritis (RA) [1]. The specificity of the anti-CCP antibody in the diagnosis of RA has been reported to be about 95 %. Anti-CCP positivity can also be found in several autoimmune diseases including systemic lupus erythematosus (SLE), systemic sclerosis (SSc), primary Sjögren's syndrome (pSS) [2-4], and they can be detected many years before RA onset [5]. Autoimmune thyroid diseases (AITD) result from a dysregulation of the immune system leading to an immune attack on the thyroid. AITD are T cell-mediated organ-specific autoimmune disorders. Graves' disease (GD) and Hashimoto thyroiditis (HT) are the major forms of AITD. The predominant autoantibody produced in GD is directed against the thyrotropin (TSH) receptor [6], while the main autoantibodies produced in up to 90% of HT patients are the antithyroid peroxidase antibody (TPOAb) and the antithyroglobulin antibody (TgAb). Although specific antibodies for AITD [TPOAb, TgAb, TRAb (thyrotropin receptor antibody)], they have been reported in many patients with other organ specific, or systemic autoimmune disorders (Sjögren's syndrome, rheumatoid arthritis, systemic lupus erythematosus, systemic sclerosis, cryoglobulinemia, sarcoidosis, psoriatic arthritis) [7].

To the best of our knowledge, no study has investigated the prevalence of anti-CCP antibodies in adults with TA to date. The present study aimed to determine the prevalence of anti-CCP antibodies in patients with TA.

Patients and Methods

In this retrospective study, results of investigations were carried out between January 2010 and October 2014 including thyroid peroxidase antibody (TPOAb), TSH-receptor antibody (TRAb), rheumatoid factor (RF), anti-CCP antibodies were obtained from computer database of Ankara Numune Training and Research Hospital (Ankara, Turkey). 1282 patients were included in the study. TPOAb, TRAb, RF and anti-CCP antibodies were determined by immunoenzymatic method, radioimmunoassay, immunoturbidimetric method and enzyme immunoassay, respectively. TA diagnosis was made if thyroid autoantibodies were higher than the upper limit of normal (ULN) ([TPOAb $nr < 34$ IU/mL] and/or [TRAb $nr < 8$ U/L]). Anti-CCP and RF positivity were considered if the values exceeded the upper limit of normal (ULN < 5 RU /mL) and (ULN < 14 IU/mL), respectively.

Patients with or without TA were compared in terms of the prevalence of anti-CCP antibodies by chi-square test, and the gender distribution in both groups, RF and anti-CCP positivity in between sexes were analyzed by chi-square test. The average of age was compared by student t test. Student's t test was used to study the associations of patient characteristics for continuous variables. Statistical analysis was performed on SPSS (PAWS Statistics) version 18 was used for analysis. A value of $p < 0.05$ was considered statistically significant.

Results

Demographic and laboratory characteristics of with TA and without TA patients are given in Table 1. No difference was determined in age between the groups [50±19 (15-93) vs. 50±15 (17-96) years with TA and without TA, respectively]. In TA group, TPOAb, TRAb, anti-CCP, and RF were detected in 332 (98.8%), 7 (2%), 44 (13%) and 78 (23%) patients in the same order. In group without TA, anti-CCP was detected in 70 patients (7.4%), and RF was detected in 378 patients (20%). The positive rates of anti-CCP were significantly higher in patients with TA than the patients without TA (13% vs. 7.4%, $p<0.001$). However, there was no difference in RF positivity between the groups. Among the correlations, TPOAb, RF and anti-CCP are demonstrated in Table 2. In the overall patient evaluation, the significant correlation was determined between anti-CCP with RF and TPOAb ($r=0.35$, $p<0.001$ vs. $r=0.27$, $p=0.01$, respectively). No correlation was determined between TRAb with anti-CCP and RF. There was no difference in gender in terms of anti-CCP and TRAb positivity. While anti-TPO positivity was significantly higher in women compared to men (27% vs. 19.2%, $p=0.02$), RF positivity was detected higher in men (28.9% vs. 20.4%, $p=0.04$).

Table 1: Demographic and laboratory characteristics of TA and non-TA patients

	With TA (n=336)	Without TA (n=946)	p value
Age at entry, years, Mean ± SD, range	50±19 (15-93)	50±15 (17-96)	0.63
Sex			
Females, n (%)	301 (90)	804 (85)	0.03
Males, n (%)	35 (10)	142 (15)	
TPOAb positivity, n (%)	332 (98.8)	-	
TRAb positivity, n (%)	7 (2)	-	
Anti-CCP positivity, n (%)	44 (13)	70 (7.4)	0.001
RF positivity, n (%)	78 (23)	190 (20)	0.56

TA, thyroid autoimmunity; TPOAb, thyroid peroxidase autoantibody; TRAb, TSH receptor antibody; Anti-CCP, anti-cyclic citrullinated peptide antibodies; RF, rheumatoid factor

Table 2: The correlations between TPOAb and anti-CCP antibodies

	TPOAb	Anti-CCP	RF
TPOAb	-	$r=0.27$, $p=0.01$	NS
Anti-CCP	$r=0.27$, $p=0.01$	-	$r=0.35$, $p<0.001$

TPOAb, thyroid peroxidase autoantibody; Anti-CCP, anti-cyclic citrullinated peptide antibodies; RF, rheumatoid factor; NS, nonsignificant

Discussion

Anti-CCP antibodies is a widely used serological markers in the diagnosis of RA [1]. It can be detected positive in up to 90% in the RA patients. It gives information about the prognosis of the diseases like the diagnosis. Anti-CCP positive RA patients are more erosive than negative ones. These antibodies can be detected positive in serum before 10-15 years of development RA [5]. Clinically manifested by polyarthritis, anti-CCP positivity and longer than 6 weeks can be classified as RA according to 2010 ACR/EULAR classification criteria for RA [8]. Anti-CCP positivity can also be found several autoimmune diseases including systemic lupus erythematosus (SLE), systemic sclerosis (SSc), primary Sjögren's syndrome (pSS) (2-4). TA is characterized by the formation of thyroid autoantibodies. Thyroid autoantibodies, indicators for the diagnosis of autoimmune thyroid disease, were found in 3-9% of the general population, with the prevalence increasing markedly in women above the age of 45 years [9]. While in the studies, RF and ANA were detected higher in autoimmune thyroid disease group than the healthy population, several studies have been published reporting high prevalence of thyroid autoantibodies in patients with RA [10]. The prevalence of antinuclear antibodies in children with thyroid autoimmunity was investigated by Segni et al. and the correlation wasn't detected between thyroid autoimmunity and anti CCP positivity [11].

However, until now there has been no data available which identified prevalence of anti-CCP in patients with thyroid autoimmunity. In our study, anti CCP positivity was significantly higher in TA group than the others. there was no significantly difference for RF. At the same time there was a significant correlation between anti CCP and RF, but there was no correlation between TPOAb with anti-CCP in all patients. Autoimmunity plays a crucial role in the etiology of RA, an association between this disorder and thyroid autoimmunity may exist. Some autoantibodies against specific non- thyroid antigens has been described in patients with AITD, such as ANA. ANA positivity varies from 9%-35%. thyroid autoantibodies have been described in patients with rheumatologic diseases. AITD is associated with RA due to similar immunological mechanisms and genetic susceptibility [12]. The association presence of the HLA DR3 and DR4 antigens with RA and Hashimoto have been evidenced by some authors [13,14].

A study that was designed ANA in children with thyroid autoimmunity. ANA positivity was found 71%, anti-ENA was found 4.3%, anti-dsDNA antibodies were found in 1.1%, RF was detectable in 3.2%, and anti-CCP were found in none in adults [15].

In conclusion, our study indicates an increased prevalence of anti-CCP antibodies in patients with TA and it suggests that anti-CCP antibodies can also be shown in TA in addition to RA. This study completely was obtained from patient medical records, therefore it does not reflect real population. Prospective larger studies for evaluating anti-CCP prevalence in patients with TA are still warranted.

Conflict of interest

The authors report no conflict of interest.

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