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ORIGINAL ARTICLE - FOOD FOR THOUGHT

Association of antithyroid peroxidase antibody with fibromyalgia in rheumatoid arthritis

Jowairiyya Ahmad[1] · Helena Blumen[2] · Clement E. Tagoe[3,4]

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Abstract To investigate how autoimmune thyroiditis (ATD) affects the clinical presentation of established rheumatoid arthritis (RA) with particular reference to fibromyalgia and chronic widespread pain (CWP). A cohort of 204 patients with RA for whom the presence or absence of autoimmune thyroid antibodies was documented was examined for the relationships between thyroid autoantibodies and fibromyalgia or CWP. We identified 29 % who tested positive for antithyroid peroxidase antibodies (TPOAb). The anti-thyroglobulin antibody (TgAb) was found in 24 %. Among the thyroid autoantibody-positive patients, 40 % had a diagnosis of fibromyalgia or CWP versus 17 % for antibody negative patients. Logistic regression analyses (adjusted by age, sex, diabetes and BMI) indicated that TPOAb-positive patients were more likely to have fibromyalgia or CWP, with an odds ratio (OR) of 4.641, 95 % confidence interval (CI) (2.110–10.207) $P < .001$. Adjusting for spinal degenerative disc disease did not change the association with fibromyalgia, OR 4.458, 95 % CI (1.950–10.191), $P < .001$. The OR between TgAb and fibromyalgia was not significant ($P > .05$). Additional logistic regression analyses (adjusted by age, sex and BMI) indicated a significant relationship between TPOAb and fibromyalgia or CWP in patients without diabetes and those without hypothyroidism (OR of 4.873, 95 % CI (1.877–12.653), $P = .001$ and OR of 4.615 95 % CI (1.810–11.770), $P = .001$, respectively). There may be a positive association between the ATD antibody TPOAb, and fibromyalgia syndrome and CWP in patients with established RA.

Keywords Autoimmune thyroid disease · Chronic lymphocytic thyroiditis · Hashimoto thyroiditis · Fibromyalgia · Chronic widespread pain · Rheumatoid arthritis

Introduction

Autoimmune thyroid disease (ATD) is the commonest autoimmune disease with a prevalence of over 10 % worldwide [1]. Data from the National Health and Nutrition Examination Survey (NHANES III) suggest the prevalence goes up to about 20 % in older post-menopausal women in the disease-free population [2]. Similar to many autoimmune diseases, thyroid autoimmunity is characterized by a female to male preponderance of about 9:1 [3]. Clinically, patients may have Graves' disease, chronic lymphocytic thyroiditis (CLT) or the goitrous form of CLT, Hashimoto thyroiditis (HT). Graves' disease is characterized by autoantibodies to the thyrotropin [thyroid-stimulating hormone (TSH)] receptor, while perhaps 95 % of CLT and HT patients are positive for the antithyroid peroxidase antibody (TPOAb) and/or the anti-thyroglobulin antibody (TgAb) [4, 5]. CLT has been associated with a high prevalence of hypothyroidism in about 10–20 % of affected individuals particularly in the presence of TPOAb [2]. Histologically, ATD is characterized by the infiltration of the thyroid gland by inflammatory cells, chiefly lymphocytes. In the specific

✉ Clement E. Tagoe
ctagoe@aol.com; ctagoe@montefiore.org

1 Division of Rheumatology, Department of Medicine, Thomas Jefferson University, Philadelphia, PA, USA

2 Division of Geriatrics, Department of Medicine, Albert Einstein College of Medicine, Bronx, NY, USA

3 Division of Rheumatology, Department of Medicine, Albert Einstein College of Medicine, Bronx, NY, USA

4 Division of Rheumatology, Montefiore Medical Center, 111 East 210th Street, Bronx, NY 10467-2490, USA

case of CLT, the thyrocyte cytoplasm may undergo oxyphilic change, appearing granular and pink, known as Hürthle or Askanazy cells [6]. Eventually as a terminal outcome of the inflammatory process, there is organ destruction and fibrosis [7]. Despite the nosological distinctions made between Graves' disease and CLT, considerable overlap is seen in the clinical presentation of ATD.

Classically, ATD is viewed as a single-organ autoimmune disease. However, it is frequently found in association with other autoimmune conditions and well-differentiated connective tissue diseases (CTD). Most musculoskeletal associations of ATD have been described with reference to CLT/HT in part because the rheumatic manifestations of Graves' disease occur much less frequently [8]. ATD has been described in up to 25 % of rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) patients, respectively [9]. The association remains equally high with seropositive Sjögren's syndrome (SS) [10]. Biro et al. [11] showed that 51 % of HT patients had associated well-defined systemic autoimmune diseases including mixed connective tissue disease (MCTD), SS, SLE, RA, systemic sclerosis (SSc) and polymyositis/dermatomyositis. The inverse relationship is equally true, and the prevalence of ATD has been shown to be increased when patients with differentiated autoimmune and CTD are studied [12].

Non-endocrine associations of hypothyroidism and autoimmune thyroiditis have been described including rheumatic manifestations such as osteoarthritis and erosive osteoarthritis, inflammatory arthritis resembling RA, calcium pyrophosphate dihydrate deposition disease (CPPD), myositis, spinal degenerative disc disease (DDD), carpal tunnel syndrome and Raynaud's phenomenon [13, 14]. Non-rheumatic associations include chronic fatigue syndrome, encephalitis, psychological symptoms, endocrine and dermatologic findings [15]. Ott et al. [15] have suggested that the symptom load and quality of life issues associated with HT may be related to the autoimmune disease as well as its endocrine consequences.

Recent reports clearly suggest rheumatic complications in euthyroid persons with ATD but without well-differentiated CTD. Similarly, ATD has been linked independently with fibromyalgia and chronic widespread pain (CWP) [16, 17]. This expands the argument that autoimmune thyroiditis itself may exert immunological sequelae beyond the confines of the thyroid gland [15]. We therefore hypothesized that ATD might express a symptom burden distinct from any associated CTD. The aim of this study was thus to examine whether the rheumatic manifestations of ATD presenting as CLT, which have been well-described in the absence of well-defined CTDs are present in association with RA, with specific reference to fibromyalgia and CWP.

Methods

We performed a retrospective cohort analysis of 204 patients with a diagnosis of established RA for whom the presence or absence of the autoimmune thyroid autoantibodies TPOAb and/or TgAb was documented. Paired thyroid antibody data were available for 92 % of the study patients. Patients were included from those attending adult rheumatology outpatient follow-up in a tertiary care center. Common indications for assessment of thyroid function and thyroid autoantibodies included suspicion of hypothyroidism, weight change, fatigue, palpitations, presence of goiter and previously abnormal thyroid studies. The associations between thyroid autoantibodies and fibromyalgia or CWP were examined. The presence of osteoarthritis was ascertained using American College of Rheumatology (ACR) classification criteria [18–20]. The 1987 revised classification criteria for RA were employed [21]. The post hoc application of the 2010 ACR/European League Against Rheumatism (EULAR) RA classification criteria did not change the diagnoses for the study cohort [22]. Fibromyalgia and CWP were diagnosed based on the 1990 ACR criteria [23]. Patients were excluded if antibody testing had preceded the diagnosis of fibromyalgia of CWP. Positive values for TPOAb and TgAb were >5 and >10 IU/mL, respectively, and seropositivity for one or both of the antibodies indicated the presence of CLT [6]. The normal range for the TSH was 0.4–4.6 μIU/mL. Normal values for the acute phase reactants erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were 0–20 mm/Hr and 0.0–0.8 mg/dL, respectively. Serum IgM rheumatoid factor was determined by rate nephelometry. The presence of anti-citrullinated protein antibodies (ACPA) was documented by a second generation anti-cyclic citrullinated peptide assay using a normal cut-off value of <20.0 AU.

Covariates

Because of the possibility of a number of covariates acting as confounders due to their known associations with pain syndromes, we did further regression analyses adjusting for those covariates, namely diabetes, spinal DDD and hypothyroidism. Diabetes is well known to be associated with generalized somatic pain because of its association with small fiber neuropathy, a potential confounder of fibromyalgia and CWP [24]. We also analyzed spinal DDD because it is a potential cause of spinal radiculopathy, spinal stenosis and secondarily generalized pain. Hypothyroidism is highly associated with ATD, but has also been described in the literature as being associated with generalized pain as well as with osteoarthritis [25].

Table 1 Baseline characteristics of patients with and without autoimmune thyroid disease (ATD)

	ALL ($N = 204$)	ATD ($N = 74$)	No ATD ($N = 130$)	P value (ATD vs. no ATD)
Age, mean ± SD (years)	58.23 ± 13.06	61.08 ± 13.11	56.69 ± 13.29	$P = .03$*
Female sex (%)	92	92	91	$P = .73$
BMI, mean ± SD (kg/m^2)	31.13 ± 6.89	31.10 ± 5.86	30.94 ± 7.23	$P = .87$
Diabetes II (%)	26	27	23	$P = .53$
Osteoarthritis (%)	63	75	56	$P = .01$*
Fibromyalgia or chronic widespread pain (%)	25	40	17	$P < .01$**
Hypothyroidism (%)	19	38	8	$P < .001$***
ACPA positive (%)	65	68	60	$P = .30$
TSH, mean ± SD (μIU/mL)	4.05 ± 22.08	3.98 ± 5.41	1.75 ± 2.41	$P < .001$***
ESR, mean ± SD (mm/Hr)	33.62 ± 24.05	33.70 ± 22.24	32.24 ± 24.93	$P = .70$
CRP, mean ± SD (mg/dL)	0.85 ± 1.74	0.65 ± 2.45	0.74 ± 0.98	$P = .49$

* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$

Statistics

Student's t test was used to study the associations of patient characteristics for continuous variables. The Chi-square test was used for categorical variables. Multivariable binary logistic regression analysis was used to test the association of fibromyalgia and chronic pain between patients with positive antithyroid autoantibodies and negative antibodies adjusted by independent variables screened as significant in our bivariate analysis or considered potentially significant covariates, namely; age, sex, BMI, hypothyroidism, diabetes and spinal DDD. Spearman's rank correlation test was used for correlations of TPOAb and TgAb, with BMI, ESR, CRP and TSH. A two-sided P value of <.05 was considered significant. Statistical analyses were performed using IBM® SPSS® Statistics version 20.0 (IBM, Armonk, New York, USA).

Ethics

The study was approved by the institutional review board of the Albert Einstein College of Medicine, New York.

Results

Sample characteristics of patients with and without ATD are summarized in Table 1. Among 204 patients, we identified 29 % who tested positive for TPOAb. Twenty-four percent of patients tested positive for TgAb, and 36 % were positive for either antibody. Nineteen percent of study patients were clinically hypothyroid. The seropositivity rate for RA was represented by 63 % for ACPA and 60 % for rheumatoid factor, respectively. Seventy-five percent of the cohort were either RF or ACPA positive. The mean age was significantly different between the thyroid antibody-positive group and the negative group at 61.08 versus 56.69 years, respectively, but there was no significant difference in sex, BMI or the prevalence of type II diabetes between patients with ATD and those without. The presence of ACPA positivity was not significantly different between ATD and non-ATD patients. There was also no significant difference between ATD and non-ATD patients in terms of the acute phase reactants ESR and CRP. Statistically significant differences between those with TPOAb and/or TgAb, and those without were seen with respect to fibromyalgia and CWP, osteoarthritis, hypothyroidism and the level of TSH. Among the thyroid autoantibody-positive patients, 40 % had a diagnosis of fibromyalgia or CWP, while 17 % of antibody negative patients had fibromyalgia or widespread pain. Degenerative intervertebral disc disease of the spine was documented in 55 % and orthopedic procedures including spinal surgery were performed in 17 % of the cohort.

The clinical characteristics of patients with TPOAb, TGAb, and both TPOAb and TGAb are summarized in Table 2. Further analysis of the ATD group showed no statistically significant differences between TPOAb-positive and TgAb-positive patients with regard to age, sex, BMI, prevalence of type II diabetes, presence of osteoarthritis, hypothyroidism, seropositivity for ACPA, level of TSH or the level of the serum acute phase reactants ESR and CRP. However, there was a significant difference in terms of the presence of fibromyalgia or CWP when having both antibodies, seen in 17.6 % of patients, was compared to having TPOAb alone, and when the presence of TPOAb was compared with TgAb, with P values of .03 and .02, respectively.

Fibromyalgia associates with antithyroid peroxidase antibody positivity

The results of our logistic regression analyses adjusted by age, sex, diabetes and BMI are summarized in Table 3. We

Table 2 Baseline characteristics of patients with TPOAb and TgAb (both) compared to TPOAb- or TgAb-positive ATD, respectively

	TPOAb and TgAb (both) ($N = 34$)	TPOAb ($N = 59$)	TgAb ($N = 49$)	P value (both vs. TPOAb)	P value (both vs. TgAb)	P value (TPOAb vs. TgAb)
Age, mean ± SD (years)	62.85 ± 11.71	62.24 ± 13.66	55.73 ± 14.89	$P = 0.98$	$P = .08$	$P = .20$
Female sex (%)	91	94	93	$P = .94$	$P = .45$	$P = .59$
BMI, mean ± SD (kg/m^2)	32.24 ± 6.35	30.70 ± 5.14	29.05 ± 5.11	$P = .57$	$P = .15$	$P = .43$
Diabetes II (%)	35	24	13	$P = .27$	$P = .09$	$P = .59$
Osteoarthritis (%)	76	82	67	$P = .71$	$P = .65$	$P = .49$
Fibromyalgia or chronic widespread pain (%)	31	69	27	$P = .03$*	$P = .62$	$P = .02$*
Hypothyroidism (%)	44	44	20	$P = .77$	$P = .26$	$P = .22$
ACPA positive (%)	65	80	65	$P = .81$	$P = .22$	$P = .21$
TSH, mean ± SD (μIU/mL)	4.28 ± 5.19	4.73 ± 39.09	2.45 ± 3.15	$P = .61$	$P = .34$	$P = .27$
ESR, mean ± SD (mm/Hr)	33.38 ± 20.54	33.25 ± 21.46	34.87 ± 27.57	$P = .70$	$P = 71$	$P = .55$
CRP, mean ± SD (mg/dL)	0.65 ± 0.67	0.69 ± 0.76	0.59 ± 0.60	$P = .69$	$P = .72$	$P = .96$

* $P < 0.05$

Table 3 Binary logistic regression analyses adjusted for age, sex, diabetes and BMI

	TPOAb-adjusted OR (95 % CI)	TgAb-adjusted OR (95 % CI)	Both-adjusted OR (95 % CI)
Fibromyalgia	4.641 (2.110–10.207)	1.664 (.762–3.631)	1.97 (.806–4.823)
	$P < .001$	$P = 0.201$	$P = 0.137$
Spinal degenerative disc disease (DDD)	1.469 (0.700–3.082)	1.437 (0.661–3.124)	1.098 (0.452–2.666)
	$P = 0.309$	$P = 0.360$	$P = 0.837$
Hypothyroidism	6.728 (2.930–15.45)	3.759 (1.617–8.736)	4.110 (1.667–10.135)
	$P < .001$	$P < .01$	$P < .01$
Fibromyalgia (adjusted for age, sex, diabetes, BMI and spinal DDD	4.458 (1.950–10.191)	1.330 (0.572–3.092)	1.978 (0.776–5.042)
	$P < .001$	$P = .508$	$P = .153$

found that TPOAb-positive patients were more likely to be diagnosed with fibromyalgia and report the presence of CWP, with an odds ratio (OR) of 4.641, 95 % confidence interval (CI) (2.110–10.207), $P < .001$. The OR between TgAb and fibromyalgia was not significant, with a P value >.05. Patients who were both TPOAb- and TgAb-positive were numerically more likely to be diagnosed with fibromyalgia with an OR of 1.97, 95 % CI (0.806–4.823), but this relationship was not statistically significant with a P value of .137. The TPOAb was also strongly associated with hypothyroidism with an OR of 6.728, 95 % CI (2.930–15.45), $P < .001$, and TgAb antibody had a less robust, yet significant association with hypothyroidism with an OR of 3.759, 95 % CI (1.617–8.736), $P < .01$. The presence of both antibodies was associated with hypothyroidism with an OR of 4.110, 95 % CI (1.667–10.135), $P < .01$. The association between fibromyalgia and TPOAb remained strong when the analysis was adjusted for the presence of spinal DDD as an additional covariate, with an OR of 4.458, 95 % CI (1.950–10.191), $P < .001$. No association with TgAb could be seen with a similar evaluation. Our analysis showed no significant associations between the presence of antithyroid autoantibodies and the presence of spinal DDD.

Acute phase reactants do not correlate with antithyroid autoantibodies

Spearman's rank correlation testing comparing TPOAb and TgAb with BMI, ESR, CRP, and TSH showed significant associations between antibodies and TSH. There was no significant association between the antibodies and hence ATD and the serum acute phase reactants ESR or CRP (Table 4). Not surprisingly, the presence of TPOAb correlated with the presence of TgAb very significantly ($P < .001$). Also expected was the significant correlation between TPOAb and the level of TSH. The association of TgAb and TSH, as well as that between ESR and CRP, was also significant (Table 4). The relationship between BMI and CRP was very significant ($P < .01$), while BMI was

Table 4 Correlations by linear regression

	TPOAb	TgAb	BMI	ESR	CRP	TSH
TPOAb	–	0.563***	0.105	0.086	0.085	0.350***
TgAb	–		0.060	0.043	0.023	0.295***
BMI	–			0.156*	0.209**	0.135
ESR	–				0.522***	0.122
CRP	–					0.156*
TSH	–					–

* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$

Table 5 Logistic regression analysis adjusted for covariates diabetes, spinal degenerative disc disease and hypothyroidism

Covariates (age, sex and BMI)	TPOAb	TgAb	Both
Fibromyalgia or chronic widespread pain			
Without diabetes	4.873 (1.877–12.653), $P = .001$**	1.458 (0.587–3.625), $P = .417$	1.619 (0.535–4.893), $P = .393$
With diabetes	3.085 (0.705–13.499), $P = .135$	2.295 (0.457–11.527), $P = .313$	2.625 (0.512–13.462), $P = .247$
Degenerative disc disease			
Without diabetes	1.335 (0.564–3.160), $P = .510$	1.414 (0.597–3.352), $P = .431$	1.044 (0.373–2.922), $P = .934$
With diabetes	1.746 (0.363–8.386), $P = .486$	1.417 (0.228–8.788), $P = .708$	1.213 (0.192–7.685), $P = .837$
Hypothyroidism			
Without diabetes	8.834 (2.735–28.529), $P < .0001$***	4.143 (1.410–12.176), $P = .010$*	3.558 (1.079–11.730), $P = .037$*
With diabetes	5.859 (1.538–22.316), $P = .010$*	3.291 (0.828–13.079), $P = .091$	5.077 (1.170–22.033), $P = .030$*
Fibromyalgia or chronic widespread pain			
Without hypothyroidism	4.615 (1.810–11.770), $P = .001$**	1.217 (0.473–3.129), $P = .684$	1.505 (0.473–4.791), $P = .489$
With hypothyroidism	4.511 (0.749–27.181), $P = .100$	3.532 (0.614–20.320), $P = 158$	2.649 (0.502–13.971), $P = .251$
Degenerative disc disease			
Without hypothyroidism	1.359 (0.534–3.456), $P = .520$	0.964 (0.380–2.444), $P = .939$	0.708 (0.223–2.246), $P = .558$
With hypothyroidism	1.337 (0.201–8.914), $P = .764$	2.823 (0.373–21.333), $P = .315$	1.557 (0.202–12.009), $P = .671$

* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$

found to be significantly associated with ESR. Lastly, CRP and TSH were also found to be significantly correlated ($P < .05$) (Table 4).

Antithyroid peroxidase antibodies retain their association with fibromyalgia after adjustment for covariates

When we examined the association between TPOAb and fibromyalgia or CWP in patients with and without diabetes separately, we found a significant relationship between TPOAb and fibromyalgia in patients without diabetes with an OR of 4.873, 95 % CI (1.877–12.653), $P = .001$, but not in patients with diabetes (Table 5). In addition, there was no statistically significant association with TgAb or the presence of both autoantibodies. There was no significant association between ATD and spinal DDD in the absence or in the presence of diabetes. The association of TPOAb with hypothyroidism was maintained in the absence of diabetes with an OR of 8.834, 95 % CI (2.735–28.529), $P < .0001$, while the association of TgAb with hypothyroidism also remained significant with an OR of 4.143, 95 % CI (1.410–12.176), $P = .010$. Finally, in the presence of diabetes, TPOAb remained associated with hypothyroidism with an OR of 5.859, 95 % CI (1.538–22.316), $P = .010$.

Importantly, the association of the TPOAb with fibromyalgia was maintained in the absence of hypothyroidism with an OR of 4.615, 95 % CI (1.810–11.770), $P = .001$, suggesting that the known association of widespread pain with hypothyroidism was not the cause of the association described in the study. The presence of spinal DDD did not have any associations with thyroid autoantibody positivity and hence ATD, either in the absence or in the presence of hypothyroidism (Table 5).

Discussion

This study shows a positive association between ATD and the presence of TPOAb, and fibromyalgia or CWP in patients with established RA. There was a significant difference in age between ATD and non-ATD patients that

might reflect the age dependence of antithyroid autoantibody accrual noted in population studies [2]. However, the association holds after controlling for age, sex, diabetes and BMI. Further adjustment for diabetes, spinal DDD and hypothyroidism also showed an association between TPOAb and fibromyalgia or widespread pain. There was no demonstrable effect of the presence of ACPA antibodies or the level of serum acute phase reactants ESR and CRP on the association. This finding is relevant to the current practice of rheumatology where measures of disease activity often involve patient assessments of global health (PGA). The disease activity score in 28 joints (DAS28) and Clinical Disease Activity Index (CDAI) both rely on joint counts and the PGA. Tender joint counts can be falsely exaggerated by the generalized tenderness associated with fibromyalgia syndrome. Various health assessment questionnaires similarly rely heavily on patient reports of global health or pain [26]. The possibility of contamination of RA clinical studies with chronic pain or fibromyalgia patients is low because such patients ultimately fulfill exclusion criteria. However, in real-world rheumatology practice, fibromyalgia and chronic pain are an ever present condition impacting management decisions [27].

The strength of the association mimicked the pattern seen for the association between antithyroid autoantibodies and TPOAb, and hypothyroidism [28]. It is generally accepted that the initial immunological reaction in ATD is a T-cell response to antigen presentation by HLA class II expressing thyrocytes and that the humoral response likely comes later [6, 28]. It has also been described that the TgAb response appears to precede the appearance of TPOAb. This transition seems to presage the development of end-organ damage and eventual hypothyroidism and suggests an escalation of the immunological process [29]. Similar to the intermediate OR seen for both antibodies for hypothyroidism, we found the presence of both TPOAb and TgAb correlated less well with the presence of fibromyalgia or chronic pain but more so than TgAb alone. The lack of association with the serum acute phase reactants suggests that the presence of fibromyalgia was dissociated from an active inflammatory response. The relationship between TPOAb and fibromyalgia may not be causal and may reflect the complexity or intensity of immunological dysfunction rather than a direct causal association of the antibody with pain generation [24].

Chronic generalized pain has been shown to be closely influenced by a number of factors including diabetes, spinal DDD, depression and hypothyroidism. We therefore did further analyses correcting for those variables. We omitted depression because it was insignificantly represented in our study population and would have been impossible to analyze statistically. Spinal DDD can be a source of secondarily generalized pain independent of the presence of fibromyalgia syndrome but did not appear to be a significant cause in our sample perhaps because of sample size or more likely because the condition was not further sub-classified into the progressive diseases like spinal stenosis and spinal radiculopathy which are the more proximate causes of secondarily generalized pain. Importantly, the association of TPOAb with fibromyalgia and CWP remained after controlling for diabetes, spinal DDD and hypothyroidism.

The close relationship of ATD with rheumatologic disease has led to speculation on possible reasons for the association [30, 31]. There are considerable similarities in genetics and a significant overlap in clinical presentation between several CTD and ATD even in the absence of well-defined CTD [16, 31]. There may therefore at least in some ATD patients be a generalized autoimmune process with systemic clinical manifestations.

Our study has a number of limitations including the sample size and retrospective design. However, we think that selection bias was mitigated by the fact that the sample was drawn from several providers and that thyroid antibody testing was not dependent on the diagnosis of RA or generalized pain. Secondly, because the reporting of TPOAb and TgAb values changed over time at our institution, the upper limits for several patients could not be determined and were simply documented as being above an arbitrary value. Quantitative evaluation of the clinical correlation of the presence of generalized pain with the levels of the antibodies was therefore not possible. We also omitted the traditional measures of disease activity in favor of serum acute phase reactants for the reasons elaborated above. Despite these limitations, we think our sample is representative of the general RA population given similar rates of ACPA positivity, ATD, diabetes and hypothyroidism as described elsewhere [9, 32].

We have described an association between the TPOAb of ATD, the commonest autoimmune disease, and fibromyalgia or CWP in established RA. We suggest that the determination of antithyroid antibodies in RA patients could be of prognostic significance since as shown here it is associated with chronic pain syndromes independent of the RA itself. It could perhaps prevent the unnecessary escalation of potentially toxic RA pharmacologic treatments in ATD patients with chronic pain and encourage a shift of emphasis to pain management modalities.

Conclusion

There may be an association of TPOAb with fibromyalgia and CWP. The assessment of antithyroid autoantibodies in the early workup of RA patients might provide important prognostic and clinical information regarding their risk for chronic pain syndromes.

Conflict of interest The authors have no conflicts of interest to declare.

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