

## Frequency of rheumatic diseases in patients with autoimmune thyroid disease

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**Abstract** We aimed to investigate the frequency of rheumatic diseases in patients suffering from autoimmune thyroid diseases (ATD). Sixty-five patients (56 F, 9 M), who were followed by diagnosis of ATD, were questioned and examined for the presence of rheumatic disease. Basic laboratory tests and antithyroid antibodies, antinuclear antibody and rheumatoid factor (RF) levels were also measured by appropriate methods. Various rheumatic diseases were detected in 40 (62%) of patients with ATD. The most frequent rheumatic conditions were fibromyalgia, recurrent aphthous stomatitis, osteoarthritis, keratoconjunctivitis sicca and xerostomia and carpal tunnel syndrome which were detected in 20 (31%), 13 (20%), 10 (15%), 9 (14%) and 8 (12%) of patients, respectively. Autoimmune diseases, except Sjogren's syndrome, which were detected in ten patients with ATD, are as follows—vitiligo: two; autoimmune hepatitis: two; oral lichen planus: one, ulcerative colitis: one, inflammatory arthritis in four patients (two of them had rheumatoid arthritis, one had psoriasis and psoriatic arthritis and one had mixed collagen tissue disease). RF was positive in two patients, one of them had rheumatoid arthritis and FANA was positive in six (9%) patients; all of them

had hypothyroidism. The frequency of rheumatic diseases seems to be higher in patients suffering from ATD. Initial evaluation and a regular checking for rheumatic diseases in patients suffering from ATD were recommended.

### Background

Autoimmune thyroid diseases (ATD) are organ-specific autoimmune disorders characterized by the presence of antibodies against the thyroglobulin, thyroid peroxidase, or thyrotropin receptor autoantigens [1]. The association between rheumatologic and thyroid disorders has long been known, the most common being the association of rheumatoid arthritis, Sjogren's syndrome (SS) and ATD [2–5]. However, the occurrence of rheumatic diseases among patients with ATD remains unclear. In this trial, we examined the patients who were followed by the diagnosis of ATD for the presence of rheumatic disease.

### Patients and methods

The study consisted of 65 consecutive patients, who had followed the diagnosis of ATD at our Endocrinology Outpatient Clinic between 2001 and 2005. Patients were questioned and examined by a rheumatologist for joint pain and swelling, Raynaud's phenomenon (RP), aphthous stomatitis, photosensitivity, rashes, sicca symptoms, constitutional symptoms, carpal tunnel syndrome (CTS) and were tested for erythrocyte sedimentation rate (ESR), CBC, antinuclear antibody testing by immune fluorescence (FANA), rheumatoid factor

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(RF, by nephelometry) levels, serum antithyroglobulin (ATG, by radioimmunoassay) and antithyroidperoxidase antibody (ATPO, by radioimmunoassay) levels. Dilutions of 1/80 or higher FANA were accepted as positive. Patients were tested by electroneuromyography (EMNG) when symptoms or physical findings of CTS (Tinel's and Phallen's tests) were positive. Diagnosis of osteoarthritis was done by the clinical and radiological features. Schirmer's test was performed in the presence of sicca symptoms. Thyroid status was determined by serum TSH (third generation; immunometric assay, normal range 0.4–4  $\mu$ IU/ml), free T3 (chemiluminescent immunoassay method; 0.8–1.9 ng/l) and free T4 levels (competitive immunoassay method; 1.8–4.2 pg/ml) (DPC, Immulite 2000, CA).

In statistical analysis, results were given as mean  $\pm$  standard deviation or proportion as appropriate. Differences between the groups were evaluated by Chi-square for discrete variables,  $P < 0.05$  was considered as significant.

## Results

Fifty-six (87.5%) of the ATD patients were woman. Mean age of the patients was  $43 \pm 10$  (range 18–62) years; mean duration of thyroid disease was  $1, 65 \pm 1, 22$  (range 1–6) years. Thyroid function results were as follows: 50 (77%) patients had hypothyroidism, 12 (18%) had hyperthyroidism and 3(5%) were euthyroid. Levels of serum ATG:  $901 \pm 1137$  (range 20–3000) IU/l; Levels of serum ATPO:  $878 \pm 406$  (range 10–3000) IU/l.

Various rheumatic symptoms or findings that lead us to diagnose rheumatic diseases were detected in 40 (62%) of the patients with ATD. Twenty (31%) patients, all woman, met the ACR criteria for the diagnosis of fibromyalgia (FM) [6]. Recurrent aphthous stomatitis was detected in 13 (20%) of the patients. None of them fulfilled ISG criterias for diagnosis of Behçet's

disease [7]. Keratoconjunctivitis sicca and xerostomia (KCS-X) was found in 9 (14%) of the patients. This diagnosis was done by clinical features and Schirmer's test; we did not perform the biopsy of minor salivary gland. Inflammatory arthritis was found in four patients; two of them had rheumatoid arthritis, one had psoriatic arthritis, one had mixed connective tissue disease. Other autoimmune diseases detected in patients with ATD were as follows (total six patients)—vitiligo: two patients; autoimmune hepatitis: two patients; oral lichen planus: one patient and ulcerative colitis: one patient. CTS was found in eight patients by EMNG examination, lateral epicondylitis was found in two patients. Results are outlined in Table 1.

Differences of all parameters were analyzed by Chi-square test and there was no significant difference between the hypothyroid and hyperthyroid groups ( $P > 0.05$  for all of them). RF was positive in two patients, one of them had rheumatoid arthritis and FANA was positive in 6 (9%) patients; all of them had hypothyroidism.

## Discussion

The existence of ATD among patients with systemic autoimmune diseases such as systemic lupus erythematosus, SS, or rheumatoid arthritis has been well recognized [2–5]. In addition, the frequencies of autoimmune diseases and positivity of certain autoantibodies in patients with ATD was also studied previously [8, 9]. In this trial, in addition to systemic rheumatic diseases and certain autoantibodies, we explore the frequency of other rheumatic conditions including FM, RP, aphthous stomatitis and local rheumatic diseases in patients with ATD.

We found high frequency of rheumatic diseases in patients with ATD. The most frequently associated disease was FM, which is detected in 31% of patients; it was reported as 3.6% in healthy Turkish female population

**Table 1** Distribution of rheumatic disease in thyroid patients

Thyroid status/rheumatic disease	Euthyroid (n = 3)	Hypothyroid (n = 50) (%)	Hyperthyroid (n = 12)	Total (n = 65) (%)	$P^*$
Fibromyalgia	–	17 (34)	3 (25)	20 (31)	>0.05
Recurrent aphthous stomatitis	–	9 (18)	4 (33)	13 (20)	>0.05
Osteoarthritis	1	6 (12)	3 (25)	10 (15)	>0.05
KCS-X	1	5 (10)	3 (25)	9 (14)	>0.05
CTS	–	5 (10)	3 (25)	8 (12)	>0.05
Raynoud's phenomenon	1	3 (6)	1	5 (8)	>0.05
Inflammatory arthritis	–	3 (6)	1	4 (6)	>0.05
Autoimmune disease <sup>a</sup>	–	9	1	10 (15)	>0.05

\*Statics were performed between the patients with hyperthyroidism and hypothyroidism

<sup>a</sup> Including inflammatory arthritis group

[10]. The common association of FM with other rheumatic disorders has been well documented in several studies [11]. For example, Middleton et al. [12] reported that at least 22% of SLE patients also have FM; Yavuz et al. [13] reported that the frequency of FM was 9.2% in patients with Behçet's disease. Frequency of FM was reported as 8.8% by Cakır et al. [14] in patients with thyroid disease including autoimmune and nonautoimmune etiologies. It is nearly 9 times more common than healthy controls in the present study. Thus, FM should be considered for ATD patients with widespread pain and other nonspecific multiple complains.

We found that 10 (15%) of patients with ATD have had autoimmune disease, other than Sjögren's syndrome. Gaches et al. [7] reported that 13.7% of the ATD patients have had at least one autoimmune disease, most frequently lupus and Sjögren's syndrome. Although we did not perform the minor gland biopsy, objective findings of dry eye and xerostomia were found in 9 (14%) patients. Five of them also had another autoimmune disease. Tektonidou et al. [9] reported that prevalence of Sjögren's syndrome among ATD patients is 9%, which is significantly higher than in Grece population. They also reported that 35% of the ATD patients have had ANA positivity. But there was no knowledge about titer of ANA, which they accept as positive. We found 9% of ATD patients have positive FANA at least 1/80 titers.

Raynaud's phenomenon is a frequent condition, which is accompanied with autoimmune connective diseases. Frequency of RP was found to be 8%, which is comparable to the 5.6% reported in healthy Turkish population [15]. There was no knowledge about ATD and RP in the literature; this is the first report about RP and ATD.

Recurrent aphthous stomatitis was detected in 20% of the patients. This is similar to the frequency of recurrent aphthous stomatitis in the healthy Turkish population [16]. We could not find knowledge about recurrent aphthous stomatitis and ATD in the literature.

Carpal tunnel syndrome is another frequent condition reported in thyroid patients. Cakır et al. [15] reported that 9.5% of patients with thyroid disease have had CTS, but this had been more frequent among hypothyroid patients (30.4%). Similarly, we found the CTS prevalence of 12% in ATD and 25% in hypothyroid group.

Osteoarthritis was found in 15% of the patients. Five of them had Heberden's nodules; others had knee osteoarthritis. Unfortunately, we had taken radiography if patients have complained. Therefore, asymptomatic osteoarthritis may be more common than 15%.

There were many limitations in our study. For example, we did not perform the minor salivary gland biopsy for the diagnosis of Sjögren's syndrome. The number

of patients was also low. Diagnosis of FM may be done by a blind method as performed by Yavuz et al. [13]

In conclusion, not only autoimmune connective tissue diseases, but also the frequency of other musculoskeletal diseases was found in high prevalence among patients with ATD. High frequency of these associations suggests the need for a long-lasting survey of those patients having ATD. Initial evaluation and a regular checking for rheumatic diseases in the patients who have ATD are recommended.

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