



Review

Rheumatic and autoimmune thyroid disorders: A causal or casual relationship?



Khalil Bourji, Mariele Gatto, Franco Cozzi, Andrea Doria*, Leonardo Punzi

Rheumatology Unit, Department of Medicine-DIMED, University of Padova, Italy

ARTICLE INFO

Article history:

Received 7 September 2014

Accepted 23 September 2014

Available online 12 October 2014

ABSTRACT

A number of dysfunctions may affect the thyroid gland leading either to hyper- or hypothyroidism which are mediated by autoimmune mechanisms. Thyroid abnormalities may represent an isolated alteration or they may be the harbinger of forthcoming disorders as is the case of well-characterized polyendocrine syndromes. Also, they may precede or follow the appearance of rheumatic manifestations in patients affected with connective tissue diseases or rheumatoid arthritis. The mechanisms by which autoimmune thyroid disorders may be linked to systemic autoimmune diseases have not been fully unraveled yet, however alterations of common pathways are suggested by shared genetic variants affecting autoantigen presentation and regulation of the immune response. On the other hand, the higher prevalence of autoimmune thyroid disorders over rheumatic diseases compels the chance of a mere causal concomitancy in the same patient.

The aim of our paper is to provide an overview of available data on thyroid involvement in different rheumatic diseases and to go over the main rheumatic manifestations in the context of autoimmune thyroid diseases.

© 2014 Elsevier B.V. All rights reserved.

Contents

1. Introduction	57
2. Thyroid involvement in rheumatic diseases	58
2.1. Sjögren syndrome (SS)	58
2.2. Systemic Lupus Erythematosus (SLE)	58
2.3. Rheumatoid arthritis (RA)	58
2.4. Systemic sclerosis (SSc)	58
2.5. Polymyalgia rheumatica (PMR) and vasculitis	59
3. Rheumatic manifestations in thyroid diseases	59
3.1. Joint and bone manifestations	59
3.2. Muscular manifestations	60
3.3. Neurologic manifestations	60
4. Anti-thyroid drug (ATD) induced RM	60
5. Conclusions	61
Take-home messages	61
Conflicts of interest	61
References	61

1. Introduction

Thyroid gland involvement in autoimmune diseases (AIDs) is well described and a pathogenic link may exist between immune-mediated thyroid disorders and rheumatic diseases with autoimmunity being a common feature [1,2]. However, thyroid affections are more common in the general population than AIDs; therefore, casual occurrence should be carefully considered.

* Corresponding author at: Rheumatology Unit, Department of Medicine, University of Padova, Via Giustiniani, 2, 35128 Padova, Italy. Tel.: +39 049 8212190; fax: +39 049 8212191.

E-mail address: adoria@unipd.it (A. Doria).

In this paper we report an overview on previous and recent papers analyzing thyroid involvement in different rheumatic diseases, and go over the main rheumatic manifestations (RM) in the context of thyroid diseases and anti-thyroid drug uses.

2. Thyroid involvement in rheumatic diseases

Autoimmune thyroid diseases are the most frequent autoimmune endocrine disorders. Chronic autoimmune thyroiditis (CAT), also called chronic lymphocytic thyroiditis or Hashimoto's thyroiditis, represents the cornerstone of this category. It is the most common and extensively studied organ-specific autoimmune disorder in humans [3].

2.1. Sjögren syndrome (SS)

SS is a chronic autoimmune disorder that affects exocrine glands mainly salivary and lachrymal glands with lymphocytic infiltration and clinical mouth and eye dryness. SS is commonly associated with autoimmune thyroid manifestations. Retrospective studies carried out in cohorts of patients either with primary autoimmune thyroid affections or with primary SS, reported a high prevalence of both entities [4,5]. A highly significant association between the presence of thyroid auto-antibodies and sicca syndrome has been reported [6]. A study by Kelly et al. [7] showed a prevalence of thyroid alterations of 14% among 100 SS patients, with hypothyroidism being found in 11% and hyperthyroidism in 3%. Later on, Perez et al. [8] studied the thyroid function of 33 patients with SS and found thyroid disease and thyroid dysfunction in 45% of these patients, being autoimmune thyroiditis in 24%, hypothyroidism in 33% and hyperthyroidism in 6%. Anti-thyroperoxidase (TPO) antibodies, anti-thyroglobulin (TG) antibodies, anti-thyroxine antibodies and antitriiodothyronine antibodies were positive in 45%, 18%, 42% and 36% of patients, respectively. This study suggests that SS and thyroid disease are more frequently associated than previously thought.

In 1996, we evaluated the prevalence of thyroid disorders in 121 consecutive patients with primary SS classified according to Vitali's criteria [9], in 74 patients with rheumatoid arthritis (RA) and in 404 controls. As compared with controls, patients with SS were more likely to have anti-microsomal (Mi) antibodies (9% vs. 17.6%; $p < 0.05$), and both SS and RA patients displayed significantly higher levels of anti-TG antibodies compared with controls (13.4% and 10.9% vs. 1%, respectively, $p < 0.0001$). The prevalence of CAT was 7.4% in SS and 6.7% in RA. Our results supported the concept that thyroid disease is more common in primary SS than in RA and controls [10]. Another large cohort study showed a prevalence of 36% of thyroid disease in patients with a diagnosis of SS; however, this prevalence was not significantly higher than in controls [11].

In a study on 1138 patients with Systemic Lupus Erythematosus (SLE), 169 had a diagnosis of SS. Thyroid diseases were more frequently observed in patients with SLE-SS than in SLE alone (29.6% vs. 12.7%; $p < 0.05$) [12]. More recently, Caramaschi et al. reported a prevalence of 27% of Hashimoto thyroiditis among patients with SS diagnosis [13].

2.2. Systemic Lupus Erythematosus (SLE)

A correlation between SLE and thyroid-AIDs has been suggested since a long time by White et al. [14] and Hijmans et al. [15]. However, these results were challenged by Scofield in 1996, who found SLE patients to have just slight or no risk of autoimmune thyroid disease compared with age- and sex-matched population [16]. Later on, the same author observed more thyroid diseases in patients with SLE-SS than in SLE alone [12]. In a cross sectional study on 133 patients (69 affected with SLE and 64 affected with RA), Chan et al. [17] observed that 13 % of SLE patients and 6.3% of RA patients had subclinical hypothyroidism. Furthermore, anti-TPO antibodies were detected in

23.2% of SLE and 10.9% of RA patients. In another large cohort study, involving 300 patients with SLE, the prevalence of hypothyroidism in SLE was higher than in the normal population (5.7% vs. 1%), while that of hyperthyroidism (1.7%) was not significantly different. In addition, 14% of SLE patients had anti-thyroid antibodies, rising up to 68% in the subgroup with thyroid disease ($p < 0.001$) [18].

On the other hand, antinuclear antibody (ANA) positivity can often be found in patients affected with Hashimoto's thyroiditis bearing no pathogenic effect.

2.3. Rheumatoid arthritis (RA)

The presence of a correlation between RA and thyroid dysfunction is still debated. Since the first studies published about this topic, conflicting evidences were reported [19,20]. In a prospective controlled study by Shiroky et al., evidence of thyroid diseases was observed in 30% of women with RA (mostly hypothyroidism) compared with 11% in a matched control group [21]. However, another study showed similar percentages but with no significant difference between cases and controls [22].

More recent studies suggest that there is no difference in the prevalence of thyroid disease in patients with RA compared with the general population or with patients affected with other rheumatic diseases. Accordingly, McCoy et al. did not demonstrate a significant difference in the presence or development of thyroid disease in RA patients when compared to non-RA patients [23]. Furthermore, a Colombian study carried out in a cohort of 800 patients with RA found that the prevalence of autoimmune thyroid disease was 9.8% and the anti-TPO antibodies were positive in 37.8% while the anti-TG antibodies were positive in 20.8% of patients [24].

2.4. Systemic sclerosis (SSc)

Since the pioneering study by Becker et al. [25] reporting just one case of scleroderma out of 506 patients followed at the *Mayo Clinic* for Hashimoto's thyroiditis, several studies investigated a possible relationship between SSc and autoimmune thyroid disorders [26,27]. Some years later, Molteni et al. [28] evaluated the frequency of anti-thyroid antibodies and analyzed genetic association with the HLA class II antigens in 85 patients with SSc. The proportions of patients with anti-TG and anti-TPO antibodies were 12% and 19%, respectively. Subjects with positive anti-TPO antibodies showed a higher frequency of the HLA-DR15 allele compared with anti-TPO negative patients, suggesting that HLA-DR15 may be an immunogenic marker associated with antibodies against TPO. Later on, another Italian research group showed that TSH (thyroid stimulating hormone) levels and anti-TPO antibodies were significantly higher in female patients with SSc than in the sex-matched control group (mean TSH levels 3.6 vs. 1.6 $\mu\text{U}/\text{ml}$, TPO 115 vs. 24 IU/ml, $p < 0.05$) yet no statistically significant difference was noticed in the prevalence of subclinical hyperthyroidism among these groups [29]. Higher prevalence of hypothyroidism in 110 SSc patients compared with 80 healthy controls was reported in a Mexican cross-sectional study (19% vs. 1.3%, $p < 0.01$) [30].

Assessing the thyroid function of 160 female patients 79 with SSc and 81 with osteoarthritis (OA), Marasini et al. found 31 out of 160 women (19%) displaying thyroid dysfunction, being either hyperthyroidism in 6 (4%) or hypothyroidism in 25 (16%). Hyperthyroidism was observed more frequently in women with OA compared with SSc while prevalence of hypothyroidism was higher in SSc patients, yet not statistically significant [31]. Recently, Danielidis et al. [32] reported an increase in prevalence of anti-TPO antibodies but not of anti-TG antibodies in SSc patients compared to healthy controls (27.5% vs. 14%, $p = 0.016$) with a statistical significance only in limited cutaneous SSc.

Download English Version:

<https://daneshyari.com/en/article/3341451>

Download Persian Version:

<https://daneshyari.com/article/3341451>

[Daneshyari.com](https://daneshyari.com)