ENDOCRINOLOGY RESEARCH AND PRACTICE

SOCIETY OF ENDOCRINOLOGY AND METABOLISM OF TURKEY

ORIGINAL ARTICLE
Endocrinol Res Pract. 2025;29(3):223-228

Frequency and Characteristics of Antibody Negative Chronic Thyroiditis: An Experience from a Tertiary Center

ABSTRACT

Objective: Limited literature is relevant to antibody-negative chronic thyroiditis (AN-CT). The aim was to investigate the frequency and characteristics of AN-CT and explore the presence of other autoimmune and autoinflammatory diseases in patients with AN-CT.

Methods: Consecutive participants in the follow-up above 18 years old diagnosed with hypothyroidism caused by chronic thyroiditis (CT) between December 2016 and March 2024 were included in the study. A total of 767 euthyroid patients with CT under levothyroxine (LT4) treatment were analyzed retrospectively. The patient group was divided into 2 subgroups: antibody-negative and antibody-positive. Characteristics and comorbid conditions were compared between the 2 groups.

Results: There were 582 patients (75.9%) with classic Hashimoto's thyroiditis (antibody-positive) and 185 patients (24.1%) with AN-CT in the study group. The female/male ratio was similar in the 2 groups ($P = .730$). The median body mass index was comparable between the 2 groups ($P = .486$). Median age ($P = .003$) and thyroid nodule frequency ($P = .011$) were significantly higher in the AN-CT group. The duration of hypothyroidism was shorter ($P = .022$), and the daily LT4 dose to achieve euthyroidism was lower ($P < .001$) in patients with AN-CT. The presence of other autoimmune and autoinflammatory diseases did not differ between the 2 groups.

Conclusion: In this study group, AN-CT frequency was 24.1%. Older age, shorter duration of hypothyroidism, higher thyroid nodule frequency, and lower daily LT4 dose to achieve euthyroidism were associated with AN-CT. However, patients with AN-CT had similar behavior relevant to other autoimmune and autoinflammatory disorders when compared with Hashimoto's patients.

Keywords: Chronic thyroiditis, antibody-negative chronic thyroiditis, frequency, comorbidities

Introduction

Various antibody-negative autoimmune diseases, including autoimmune thyroid diseases,[1] have been described. There are several factors underlying seronegative autoimmune diseases. Laboratory limitations related to detection methods, rapid autoantibody clearance, immunodeficiencies, immunosuppression, antigen depletion, and immunosenescence with progressive aging may lead to seronegative autoimmune disorders.[1] The presence of undefined autoantibodies is another possibility.[1] Although high sensitivity of modern assay methods for detecting autoantibodies against thyroid peroxidase (TPOAb) and thyroglobulin (TgAb), a significant percentage of patients with chronic thyroiditis have negative thyroid autoantibodies tests.[2,3] Morbid obesity is the most common cause of incorrect diagnosis for antibody-negative chronic thyroiditis (AN-CT). Obesity can lead to elevated thyroid-stimulating hormone (TSH) and hypoechogenic appearance of the thyroid gland on ultrasonography in the absence of autoimmunity.[4] This appearance may be related to increased fat tissue in the neck.[4] The relevant studies available for AN-CT are limited in the literature. The presence of primary hypothyroidism, typical ultrasonographic appearance due to lymphocytic infiltration of the thyroid gland, and absence of measurable antibodies to TPOAb and/or TgAb are the main diagnostic criteria for AN-CT.[2,5] It was first described in 1988 by Baker et al[6] They reported a case without serologic evidence of an autoimmune thyroid disorder.[6] A 20-year-old woman had a thyroidectomy for neck compression caused by a goiter.[6] Histological examination of the thyroid gland revealed pathological changes compatible with classic Hashimoto's thyroiditis (CHT).[6] This result was explained by the possibility of intrathyroidal autoantibody production in autoimmune thyroid disease.[6,7] The first case series of AN-CT was

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Received: February 5, 2025
Revision Requested: March 7, 2025
Last Revision Received: March 16, 2025
Accepted: April 7, 2025
Publication Date: June 11, 2025

Cite this article as: Sezer H, Canbaz HB. Frequency and characteristics of antibody negative chronic thyroiditis: an experience from a tertiary center. *Endocrinol Res Pract.* 2025;29(3):223-228.

DOI: 10.5152/erp.2025.25643

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reported in 2014.[8] The prevalence of AN-CT was reported to be lower than 10% in previous studies.[9,10] In the following years, the number of patients diagnosed with AN-CT increased.[2,3] Antibody-negative chronic thyroiditis is considered a less severe phenotype of CHT.

It is well known that there is a significant correlation between CHT and various autoimmune disorders such as Type 1 diabetes mellitus (T1DM), celiac disease (CD), pernicious anemia, vitiligo, Sjögren's syndrome (SS), systemic lupus erythematosus (SLE), myasthenia gravis (MG), rheumatoid arthritis (RA), Addison's disease (AD), premature ovarian insufficiency (POI), and autoimmune liver diseases.[11-16] In addition, CHT may be a part of autoimmune poly glandular syndromes 2 or 3.[17] There are also case studies of the combination of CHT and several chronic autoinflammatory diseases in the literature. The association of CHT with multiple sclerosis (MS), inflammatory bowel disease (IBD), especially ulcerative colitis (UC), sarcoidosis, familial Mediterranean fever (FMF), psoriasis, and ankylosing spondylitis (AS) were reported.[18-26] Genetic susceptibility, HLA status, some common immunopathogenic mechanisms, and triggering environmental factors are underlying mechanisms of CHT-associated diseases.[13] Most studies investigated the coexistence of CHT and other autoimmune and autoinflammatory disorders. However, in English literature, studies evaluating the association of other autoimmune and autoinflammatory conditions with AN-CT are scarce.

In this study, the frequency and characteristics of AN-CT were investigated, and the presence of other autoimmune and autoinflammatory diseases was explored in patients with AN-CT.

Material and Methods

Ethical committee approval for this present retrospective study was obtained on March 25, 2024, with decision number 2024.136. IRB2.061 from the Koç University School of Medicine. This was a retrospective archive screening study, and data sources were analyzed anonymously since the consent form was not obtained from the patients. Consecutive patients in the follow-up above 18 years old diagnosed with primary hypothyroidism caused by chronic thyroiditis (CT) in a single tertiary center between December 2016 and March 2024 were included in the study. All patients were in euthyroid status under levothyroxine (LT4) treatment.

Patients with CT were divided into 2 subgroups according to TPOAb and TgAb titers: group 1 CHT (antibody positive) and group 2 AN-CT. Positive TPOAb was defined as >35 IU/mL, and positive TgAb was defined as >115 IU/mL. CHT was defined in the presence of autoantibodies for either TPOAb, TgAb, or both. Furthermore, a thyroid ultrasonography (USG) examination confirmed CT. The diagnosis of CHT was made by the roughness of the thyroid parenchyma, hypoechoic, and heterogeneous thyroid structure at USG examination. The USG examinations were performed using an 8-18 MHz linear array transducer. At least one of the patients' USG scans was performed by 1 of 4 well-experienced radiologists. Their specific area was ultrasound imaging. The diagnosis of AN-CT was confirmed in patients who had signs of CT on USG examination and negative thyroid antibody tests for both TPOAb and TgAb. Positivity and negativity of antibodies were verified on at least 2 separate measurements for each patient in the study.

MAIN POINTS

- Approximately 25% of adult primary hypothyroidism attributed to chronic thyroiditis tested negative for antibodies.
- Older age and a shorter duration of hypothyroidism were associated with antibody-negative chronic thyroiditis (AN-CT).
- The frequency of thyroid nodules was higher in individuals with AN-CT.
- The daily levothyroxine dosage required to attain euthyroidism was reduced in AN-CT patients.
- The frequency of various autoimmune and autoinflammatory illnesses was comparable between antibody-negative and antibody-positive chronic thyroiditis.

Exclusion criteria were as follows: being under 18 years old, pregnancy, breastfeeding, central hypothyroidism, euthyroid CT without LT4 treatment, history of Graves' disease, postpartum or subacute thyroiditis, history of radiotherapy to the neck or thyroid operation, having antibodies measured once, having USG performed in another center, obesity [body mass index (BMI) >30 kg/m^2], organ transplantation, being under immunosuppressive treatment or having immunodeficiencies, being under immune checkpoint inhibitor, corticosteroid, immunomodulator medications, amiodarone, or lithium treatment. A total of 11 232 patients' electronic medical files with a diagnosis of hypothyroidism or autoimmune thyroiditis were screened. Seven hundred sixty-seven patients were eligible for the study.

Characteristics of the participants, including age, gender, BMI, family history of primary hypothyroidism in first-degree relatives, duration of hypothyroidism (years), daily LT4 dose to achieve euthyroid status (μg), presence of thyroid nodule, other autoimmune and autoinflammatory disorders (vitamin B12 deficiency, T1DM, CD, MG, POI, AD, RA, IBD, SLE, SS, psoriasis, MS, sarcoidosis, FMF, AS, vitiligo, and autoimmune liver diseases), and laboratory findings (blood samples for TPOAb, TgAb, TSH value in euthyroid status under LT4 treatment, and vitamin B12) were reviewed. Data regarding the diagnosis and treatment of other autoimmune and autoinflammatory diseases were obtained from the patient's electronic medical files at the tertiary center. A specialist in internal medicine, endocrinology, dermatology, rheumatology, neurology, chest diseases, and gastroenterology at the tertiary center performed the ongoing follow-up of the patients for these comorbid disorders. Demographic, clinical, and biochemical findings were obtained from the medical records.

Demographic, clinical, and biochemical parameters, as well as comorbid diseases, were compared between autoantibody-negative and autoantibody-positive groups.

Assays

Serum TPOAb, TgAb, TSH, and vitamin B12 measurements were performed using the electrochemiluminescence immunoassay method. The minimum and maximum detectable TgAb concentrations were 10 IU/mL and 4000 IU/mL, respectively. The minimum and maximum detectable TPOAb concentrations were 9 IU/mL and 600 IU/mL, respectively. The normal range of TSH was defined as 0.4-4.2 mIU/L. Vitamin B12 deficiency was defined as a serum concentration of B12 lower than 180 pg/mL. The unit of vitamin B12 is pg/mL. Roche Cobas 503 PRO analyzer device was used to analyze biochemical parameters. Immunochemistry tests were performed using the Roche Cobas 801 PRO module.

Statistical Analysis

Statistical analysis was performed using IBM SPSS version 27 (IBM SPSS Corp.; Armonk, NY, USA). Basal study parameter distribution was defined as percentage, frequency, mean, SD, and median. Non-parametric tests were used for data that did not fit the normal distribution. Differences in values between the groups were analyzed using the Mann–Whitney *U*, Chi-Square, and Fisher's Exact tests. The Chi-Square test was used to compare categorical data. A *P* value <.05 was identified as the statistically significant value of the variables.

Results

The study population included 767 consecutive participants in the follow-up with primary hypothyroidism caused by CT (CHT = 582 patients, AN-CT = 185 patients) from 2016 to 2024. The mean patient age was 53.4 ± 14.0 years. Among 767 patients, 669 (87.2%) were women and 98 (12.8%) were men. The mean BMI was 25.3 ± 3.0 kg/m^2. The frequency of AN-CT was 24.1%. There was a positive family history of hypothyroidism in 27.5% of the patients. The mean duration of hypothyroidism was 11.1 ± 7.5 years, of which 32.9% of patients had thyroid nodules. Median TPOAb and TgAb values were 124 IU/mL and 100 IU/mL, respectively. The mean daily LT4 dose to achieve euthyroidism was 73.7 ± 34.4 µg. Of the patients, 27.8% had other autoimmune and autoinflammatory diseases. Table 1 shows the study population's demographic, clinical, and biochemical features. The frequency of vitamin B12 deficiency was 17.7%, T1DM 2.3%, and RA 1.4% (Table 2).

The median age was significantly higher in patients with AN-CT compared to those with CHT (*P* = .003), as shown in Table 3. The female/male ratio was similar in the 2 groups (509/73 for CHT, 160/25 for AN-CT, *P* = .730). Median BMI was comparable between the 2 groups (*P* = .486). The 2 groups had a similar positive family history of hypothyroidism (*P* = .335). A higher thyroid nodule frequency was found in patients with AN-CT (*P* = .011). The duration of hypothyroidism was shorter in the AN-CT group (*P* = .022). Daily LT4 dose to achieve euthyroidism was lower in patients with AN-CT when compared with CHT patients (*P* < .001). The presence of other autoimmune and autoinflammatory diseases did not differ between the 2 groups (Table 4).

Table 1. Demographic, Clinical, and Biochemical Parameters of the Whole Study Group

Parameters	Total (n = 767)
Age (years), mean ± SD	53.4 ± 14.0
Gender, n (%) Female Male	 669 (87.2) 98 (12.8)
BMI (kg/m^2), mean ± SD	25.3 ± 3.0
CHT, n (%) AN-CT, n (%)	582 (75.9) 185 (24.1)
Positive family history for hypothyroidism, n (%)	221 (27.5)
Duration of hypothyroidism, years, mean ± SD	11.1 ± 7.5
Presence of thyroid nodule, n (%)	252 (32.9)
Positive TPOAb, n (%)	515 (88.5)
Positive TgAb, n (%)	371 (63.8)
TPOAb, IU/mL, median	124
TgAb, IU/mL, median	100
Daily levothyroxine dose to achieve euthyroidism (µg) mean ± SD	73.7 ± 34.4
TSH in euthyroid status, µIU/mL, mean ± SD	2.2 ± 1.1
Other autoimmune/autoinflammatory disorders, n (%)	213 (27.8)

AN-CT, antibody negative chronic thyroiditis; BMI, body mass index; CHT, classic Hashimoto's thyroiditis; TgAb, thyroglobulin antibody; TPOAb, thyroid peroxidase antibody; TSH, thyroid stimulating hormone.

Discussion

The results of this study, which included 767 consecutive euthyroid CT individuals under LT4 treatment, revealed that the frequency of AN-CT was 24.1%. Older age, shorter duration of hypothyroidism, higher thyroid nodule frequency, and lower daily LT4 dose to achieve euthyroidism were associated with AN-CT. The presence of other autoimmune and autoinflammatory diseases was similar in the CHT and AN-CT groups.

Antibody-negative chronic thyroiditis prevalence was reported to be between 2% and 8% in previous studies.[9,10,27] Rago et al[9] followed up 482 healthy subjects over 3 years. A hypoechogenic pattern on thyroid USG was found in 41 out of 482 subjects.[9] In 29 out of 41 individuals, thyroid autoantibodies were negative.[9] In addition, thyroid dysfunction was found in 4 out of 29 subjects with negative TPOAb and/or TgAb.[9] Few data are available for AN-CT in the country. Bağcı Akmeşe et al[27] showed that patients with antibody-negative Hashimoto's thyroiditis constituted nearly 2% of cases. These study results may be explained by different methodologies and inclusion criteria. In the following years, AN-CT accounted for a significant proportion of patients with autoimmune hypothyroidism.[2,3,8] A recent study reported that both TPOAb and TgAb were negative in 34.6% of the patients with CT.[3] Their study group was similar to the present study population. They included patients with primary hypothyroidism caused by CT, like us. The frequency of AN-CT was 24.1% among CT patients in this study. The elevated frequency may be due to increased measurement of thyroid autoantibodies, TSH, and

Table 2. Other Autoimmune and Autoinflammatory Disorders of the Whole Study Group

Comorbid Conditions, n (%)	Total (n = 767)
Vitamin B12 deficiency	136 (17.7)
Type 1 diabetes mellitus	18 (2.3)
Rheumatoid arthritis	11 (1.4)
Premature ovarian insufficiency	9 (1.2)
Psoriasis	8 (1.0)
Myasthenia gravis	7 (0.9)
Coeliac disease	7 (0.9)
Vitiligo	7 (0.9)
Autoimmune liver diseases	6 (0.8)
Systemic lupus erythematosus	4 (0.5)
Sjögren's disease	4 (0.5)
Familial Mediterranean fever	4 (0.5)
Multiple sclerosis	3 (0.4)
Sarcoidosis	3 (0.4)
Ankylosing spondylitis	3 (0.4)
Addison's disease	3 (0.4)
Inflammatory bowel disease	1 (0.1)
Total	234 disorders in 213 patients

increased examination of thyroid USG. Further studies with larger sample sizes are needed to support this opinion.

A study by Iwamoto et al[3] showed that patients with thyroid antibody negative were older than those with thyroid antibody positive. There was also a male predominance in the AN-CT group.[3] This study suggested that older age and male gender were independent factors for AN-CT.[3] It is well known that females are 2-10 fold more prone to a series of autoimmune diseases such as MS, RA, SLE, MG, CHT, and SS.[28] The immune system exhibits remarkable changes during aging, known as immunosenescence. Several factors, such as genetics, nutrition, lifestyle, exposure to microorganisms, and gender, can influence immunosenescence.[29] Age-related changes in the immune system are different between women and men.[29] Some authors show that immunosenescence develops earlier in men than women.[30] Older age and male predominance in patients with AN-CT may explain dynamic changes in the immune system during aging. However, trials are not available whether autoantibodies are unchanged or reduced during aging in Hashimoto's patients. Future studies must elucidate these interactions in patients with chronic autoimmune thyroiditis. In other studies, the female/male ratio and mean age were similar between the CHT and AN-CT groups.[2,7] No gender differences between the 2 groups were found. However, the patients with AN-CT were older, and supporting this study result, the duration of hypothyroidism was shorter. This may be because AN-CT is a less severe phenotype of CHT. In this context, hypothyroidism may occur at older ages in AN-CT patients.

A study investigated the positive family history of thyroid disorders among antibody-negative and antibody-positive patients.[8] They found no significant differences between the 2 groups.[8] The history of hypothyroidism was evaluated in family members. A similar family history of hypothyroidism ratio was shown in comparison to the 2 groups. In a study, the presence of thyroid nodules was more common in the AN-CT group (51.2%) when compared to the CHT group (38.2%).[3] However, it did not reach statistical significance ($P = .074$).[3] Two other studies reported that thyroid nodules were comparable between the 2 groups.[8,27] It was found that thyroid nodules were significantly higher in patients with AN-CT. This study result may be associated with the older age of individuals with AN-CT. It is known that there are structural differences between AN-CT and CHT on ultrasonographic examination.[3] However, insufficient studies are available on the frequency of thyroid nodules in patients with AN-CT. To explain this issue, further studies involving different geographical areas with a larger sample size are needed. The required daily LT4 dose to correct hypothyroidism was lower in patients with AN-CT when compared with CHT patients.[2] It is considered that AN-CT was a milder phenotype of CT.[2,8] Based on the lower daily LT4 requirement, this data was confirmed with a larger study population than in previous studies.

Numerous studies have investigated the association between CHT and other autoimmune/autoinflammatory disorders in the literature. However, there is no available data for AN-CT. The frequency of other autoimmune diseases was 14.3% in CHT.[12] Two studies reported that the most common other autoimmune disorders were chronic autoimmune gastritis,[11,12] vitiligo,[11,12] RA,[11,12] SLE,[12] AD,[12] and CD[12] in patients with CHT. A study found that vitiligo was significantly associated with autoimmune thyroid disorders.[31] Ionescu et al[32] reported a case series of concomitant MG and CHT. They claimed that the thymus could play a major role in the pathogenesis of the coexistence of these 2 diseases.[32] Two studies found a significant association between psoriasis and CHT.[24,25] A high prevalence of the association between CHT and UC has been known.[19] However, CHT coexisting with Crohn's disease has been rarely reported.[33] Familial Mediterranean fever's frequency is very high in some ethnic populations.[34] Familial Mediterranean fever coexisting with other autoimmune diseases is rare. Several case reports exist in children and adults.[21,22] Ergul et al[21] reported a child case who had both FMF and CHT. A 21-year-old female patient coexisted with these 2 diseases in the literature.[22] Premature ovarian insufficiency is described as a loss of ovarian reserve before the age of 40 years. Thyroid autoimmunity is significantly associated with early decreased ovarian reserve. The first most common disease related to POI is autoimmune thyroid disorders.[35] Hsieh et al[16] showed that Hashimoto's patients had a

Table 3. Comparison of Demographic, Clinical, and Biochemical Parameters in Patients with Classic Hashimoto's Thyroiditis and Antibody-Negative Chronic Thyroiditis

Parameters	CHT (n = 582)	AN-CT (n = 185)	*P*
Age (years), median	52	57	**.003**[a]
Gender, n (%)			
Female	509 (87.5)	160 (86.5)	.730[b]
Male	73 (12.5)	25 (13.5)	
BMI (kg/m^2), median	25	25	.486[a]
Positive family history of hypothyroidism, n (%)	165 (28.4)	46 (24.9)	.335[b]
Duration of hypothyroidism, years, median	10	9	**.022**[a]
Presence of thyroid nodule, n (%)	177 (30.4)	75 (40.5)	**.011**[b]
TPOAb, IU/mL, median	207	11	**<.001**[a]
TgAb, IU/mL , median	195	15	**<.001**[a]
Daily levothyroxine dose to achieve euthyroidism (μg), median	75	60	**<.001**[a]
TSH in euthyroid status, μIU/mL, median	2.1	2.2	.595[a]
Other autoimmune/autoinflammatory disorders, n (%)	160 (27.5)	53 (28.6)	.759[b]

Bold characters indicate significant differences.
AN-CT, antibody negative chronic thyroiditis; BMI, body mass index; CHT, classic Hashimoto's thyroiditis; TgAb, thyroglobulin antibody; TPOAb, thyroid peroxidase antibody; TSH, thyroid stimulating hormone.
[a]Mann–Whitney *U* test.
[b]Chi-square test.

Table 4. Comparison of Other Autoimmune and Autoinflammatory Disorders in Patients with Classic Hashimoto's Thyroiditis and Antibody-Negative Chronic Thyroiditis

Comorbid Conditions, n (%)	CHT (n = 582)	AN-CT (n = 185)	*P*
Vitamin B12 deficiency	100 (17.2)	36 (19.5)	0.408[b]
Type 1 diabetes mellitus	16 (2.7)	2 (1.1)	0.268c
Rheumatoid arthritis	9 (1.5)	2 (1.1)	1.000[c]
Premature ovarian insufficiency	7 (1.2)	2 (1.1)	1.000[c]
Psoriasis	5 (0.9)	3 (1.6)	0.408[c]
Myasthenia gravis	6 (1.0)	1 (0.5)	1.000[c]
Coeliac disease	6 (1.0)	1 (0.5)	1.000[c]
Vitiligo	4 (0.7)	3 (1.6)	0.368[c]
Autoimmune liver diseases	5 (0.9)	1 (0.5)	1.000[c]
Systemic lupus erythematosus	2 (0.3)	2 (1.1)	0.247[c]
Sjögren's disease	3 (0.5)	1 (0.5)	1.000[c]
Familial Mediterranean fever	3 (0.5)	1 (0.5)	1.000[c]
Multiple sclerosis	3 (0.5)	0 (0)	1.000[c]
Sarcoidosis	1 (0.2)	2 (1.1)	0.146[c]
Ankylosing spondylitis	3 (0.5)	0 (0)	1.000[c]
Addison's disease	2 (0.3)	1 (0.5)	0.564[c]
Inflammatory bowel disease	1 (0.2)	0 (0)	1.000[c]
Total	176 disorders in 160 patients	58 disorders in 53 patients	

AN-CT, antibody negative chronic thyroiditis; CHT, classic Hashimoto's thyroiditis.
[b]Chi-square test.
[c]Fisher-exact test.

higher risk of ovarian failure. Autoimmune thyroid diseases are more common in patients with AS. A study reported that the frequency of CHT was more frequent in AS patients when compared to sex- and age-matched healthy control groups.[26] Classic Hashimoto's thyroiditis was the most common comorbid disease in patients with MS.[18] In the present study, the 3 most frequent comorbid diseases were vitamin B12 deficiency, T1DM, and RA. Other autoimmune and autoinflammatory disorders were found in 28.6% of the antibody-negative group and 27.5% of the CHT group. No significant differences existed in other autoimmune and autoinflammatory disorders between the CHT and AN-CT groups. Antibody-negative chronic thyroiditis is a milder form of CHT in terms of daily LT4 dose to achieve euthyroidism and duration of hypothyroidism. However, these patients have similar behaviors relevant to other autoimmune and autoinflammatory disorders in comparison with Hashimoto's patients.

This present study has a few limitations. It is a single-center retrospective study with a small sample size. However, the findings are important for understanding the characteristics and behavior of AN-CT. Patients with AN-CT had similar behavior relevant to other autoimmune and autoinflammatory disorders when compared with Hashimoto's patients. This study demonstrated that overlap syndromes could occur in patients with AN-CT. The findings were shared to increase awareness of the coexistence of AN-CT and other autoimmune and autoinflammatory disorders. A shorter duration of hypothyroidism and a lower daily LT4 dose to achieve euthyroidism were associated with AN-CT. It was not possible to assess the patients' serum TSH levels during the initial presentation. It would be better to know whether patients with AN-CT initially presented with subclinical or overt hypothyroidism. Studies mainly found that lower serum TSH and higher serum FT4 levels were associated with AN-CT compared to CHT. The initial clinical severity and course of other autoimmune and autoinflammatory diseases can be compared between antibody-negative and antibody-positive groups. Just like hypothyroidism, other autoimmune and autoinflammatory diseases may be less severe in patients with AN-CT. Future studies will be needed to compare the differences in the severity of comorbid diseases.

In conclusion, the current study is the first to demonstrate the presence of other autoimmune and autoinflammatory disorders in patients with AN-CT. Although AN-CT patients have similar behavior relevant to other autoimmune and autoinflammatory disorders, they seem to have less severe thyroid disease in terms of daily LT4 dose to achieve euthyroidism and duration of hypothyroidism when compared with Hashimoto's patients.

Data Availability Statement: The data that support the findings of this study are available upon request from the corresponding author.

Ethics Committee Approval: This study was approved by the Ethics Committee of Koç University School of Medicine (Approval No: 2024.136.IRB2.061; Date: March 25, 2024).

Informed Consent: Written informed consent was obtained from all participants who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – H.S.; Design – H.S.; Supervision – H.S.; Resources – H.S.; Materials – H.S.; Data Collection and/or Processing – H.S., H.B.C.; Analysis and/or Interpretation – H.S., H.B.C.; Literature Search – H.S., H.B.C.; Writing Manuscript – H.S.; Critical Review – H.S., H.B.C.

Declaration of Interests: The authors have no conflicts of interest to declare.

Funding: This study received no funding.

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