ORIGINAL ARTICLE

DOI: 10.4274/hamidiyemedj.galenos.2023.05706

Hamidiye Med J 2023;4(1):70-76

Association of Chronic Lymphocytic Thyroiditis with the Surgical Diseases of the Thyroid Gland

Tiroid Bezinin Cerrahi Hastalıklarında Kronik Lenfositik Tiroidit Birlikteliği

Salih Celepli[1], Baki Türkoğlu[1], İrem Bigat[2], Muharrem Öztaş[1], Pınar Celepli[3], Levent Dönmez[4]

[1]*University of Health Sciences Türkiye, Gülhane Training and Research Hospital, Clinic of General Surgery, Ankara, Türkiye*

[2]*TOBB University of Economics and Technology, Department of Biomedical Engineering, Ankara, Türkiye*

[3]*Ankara Training and Research Hospital, Clinic of General Surgery, Ankara, Türkiye*

[4]*Akdeniz University Faculty of Medicine, Department of Public Health, Antalya, Türkiye*

ABSTRACT

Background: The incidence of chronic lymphocytic thyroiditis (CLT), the most common cause of hypothyroidism, has increased rapidly in the last three decades, and it is argued that these cases have a higher risk of being affected by malignant neoplasia. In this study, we aimed to investigate the relationship between CLT and papillary thyroid carcinoma (PTC).

Materials and Methods: The data sets created by retrospectively screening the data of 780 patients who underwent surgical treatment for thyroid gland diseases in our clinic between 2010 and 2020 were analyzed with the logistic regression analysis, chi-square test or Fisher's Exact chi-square test using IBM SPSS Statistics 22. A p-value less than 0.05 was considered statistically significant.

Results: The patients 75.9% of the cases were female and 24.1% were male and it was observed that the risk of CLT in female patients was 2.5 times higher than in male patients, and CLT positivity decreased as patient age increased. The malignant group has a higher rate CLT coexistence and greater thyroid-stimulating hormone (TSH) values compared to the benign group (4.20±13.03 vs. 2.81±11.75). A lower cytological diagnosis success was observed in association with CLT (35.51% vs. 47.22%).

Conclusion: It was observed that the association of CLT and PTC was higher in the presence of high TSH and autoantibodies in young women. The success of aspiration biopsies performed for diagnostic purposes was found to be lower. We consider that patients with CLT should be closely evaluated in terms of malignancy and especially the development of PTC due to the difficulties in the diagnosis and follow-up of these cases, and there is a need to develop new imaging and cytopathological diagnosis methods for these patients.

Keywords: Chronic lymphocytic thyroiditis, thyroid gland, surgical diseases

ÖZ

Amaç: Hipotiroidinin en yaygın nedeni olan kronik lenfositik tiroiditin (KLT), insidansı son 3 dekatta hızla artmıştır, ve bu olguların malign neoplazilerden etkilenme riskinin daha yüksek olduğu tartışılmaktadır. Bu çalışmada KLT ile papiller tiroid karsinomu (PTK) arasındaki ilişkiyi araştırmayı amaçladık.

Gereç ve Yöntemler: Kliniğimizde 2010-2020 yılları arasında tiroid cerrahisi uygulanan 780 hastanın verileri retrospektif olarak incelendi ve oluşturulan data setler, IBM SPSS Statistics 22 kullanılarak lojistik regresyon analizi, ki-kare testi veya Fisher's Exact test ile analiz edildi. P-değeri <0,05 istatistiksel olarak anlamlı kabul edildi.

Bulgular: Hastaların %75,9'u kadın, %24,1'i erkek olup, kadın cinsiyette KLT riskinin erkeklere göre 2,5 kat daha yüksek olduğu, ve yaş arttıkça KLT pozitifliğinin azaldığı görüldü. Malign grupta benign gruba göre daha yüksek oranda KLT birlikteliği ve daha yüksek tiroid stimüle edici hormon (TSH) değerleri olduğu görülmektedir (4,20±13,03'e karşı 2,81±11,75). KLT birlikteliğinde sitolojik tanı başarısının düşük olduğu görülmektedir (%35,51'e karşı %47,22).

Sonuç: Genç kadınlarda yüksek TSH ve otoantikor varlığında, KLT ve PTK birlikteliğinin yüksek olduğu gözlendi. Tanısal amaçlı yapılan aspirasyon biyopsilerinin başarısının ise daha düşük olduğu saptandı. KLT'li olguların malignite ve özellikle de PTK gelişimi açısından yakından izlenmesi gerektiği, bu olgularda tanı ve takipte zorluklar olduğu, görüntüleme yöntemleri ve sitopatolojik tanı yöntemlerinde yeni metodların geliştirilmesine ihtiyaç duyulduğunu düşünmekteyiz.

Anahtar Kelimeler: Kronik lenfositik tiroidit, tiroid bezi, cerrahi hastalıklar

Address for Correspondence: Salih Celepli, University of Health Sciences Türkiye, Gülhane Training and Research Hospital, Clinic of General Surgery, Ankara, Türkiye
Phone: +90 505 279 55 90 E-mail: salih_celepli@hotmail.com **ORCID ID:** orcid.org/0000-0002-3596-7938

Received: 12.04.2022 **Accepted:** 27.01.2023

Introduction

Chronic lymphocytic thyroiditis (CLT) is the most common cause of hypothyroidism in regions where individuals have an adequate dietary iodine intake, and it is thought that environmental factors and genetic disposition are effective in its occurrence (1,2). The incidence of CLT has increased rapidly in the last three decades, and today, it has become one of the most common thyroid diseases with an incidence of 0.3-1.5 per 1,000 people (3). Hashimoto's thyroiditis (HT), one of the most common autoimmune diseases, is a subtype of CLT characterized by thyroid gland-specific autoantibodies (4). Antibody positivity is present in more than 10% of women with CLT, with approximately 2% showing clinical symptoms, while its prevalence among men is one-tenth of that in women (5).

It has been reported that patients with CLT are more likely to be affected by malignant neoplasms than those without CLT (6). In these patients, long-term high thyroid stimulating hormone (TSH) levels may result in a predisposition to the development of papillary thyroid carcinoma (PTC) by stimulating follicular epithelial proliferation (7,8). In the literature, this hormone level being close to the upper limit for a long time has been associated with a higher incidence and more advanced stages of thyroid cancer (9).

Although studies in the literature suggest that the risk of PTC is increased in patients with CLT, the effects of this association are still discussed due to conflicting results. It has been reported that the presence of CLT induces the production of pro-inflammatory cytokines and the emergence of thyroid cancer through oxidative stress (10). In addition, it has been shown that clonal RET-PTC expression, which is specific for PTC, is also detected in hyperplastic thyroid nodules and CLT, albeit at low levels (11). Ahn et al. (12) reported that patients with PTC were four times more likely to have CLT compared to those with other thyroid diseases, and there was a relationship between chronic inflammation in the thyroid gland and cancer development. In another study, the mean prevalence of PTC was determined to be 1.2%, and the mean risk ratio was 0.69 in patients with CLT (13). In another study, it was reported that PTC cases with CLT tended to have a better prognosis, including a smaller tumor size, less lymph node metastasis frequency, and higher disease-free and overall survival rates, compared to patients without this coexistence (14).

In this study, we aimed to identify patients with benign and malignant thyroid diseases that underwent surgical treatment in our clinic and to evaluate the association of CLT with these diseases as a factor that could be important in the clinical presentation and diagnosis of especially PTC cases.

Material and Methods

Our study was carried out after obtaining approval from the Ethics Committee of University of Health Sciences Türkiye, Gülhane Training and Research Hospital, dated 10.11.2021 and numbered 2021/86. The data of patients who underwent surgery due to thyroid gland diseases in our clinic between 2010 and 2020 were retrospectively screened and recorded in a database. The study included 780 patients with complete data, including surgical and pathological reports available in the hospital information system and archive files. Cases with missing data were excluded from the study. Cytological diagnoses were classified in six categories using the Bethesda System (2017) as follows: Bethesda 1, non-diagnostic/unsatisfactory; 2, benign; 3, atypia of uncertain significance or follicular lesion of uncertain significance (AUS/FLUS); 4, follicular neoplasm (FN) or suspected FN; 5, suspicion of malignancy; and 6, malignant (15).

Statistical Analysis

The statistical analyses of the study were performed using IBM SPSS Statistics version 22. Comparisons between groups were undertaken with either the chi-square test or the Fisher's Exact chi-square test. The relationship of independent variables (age, gender, and presence of malignant and benign lesions) with CLT positivity was evaluated with the multivariate logistic regression analysis. $P<0.05$ was accepted as the statistical significance limit.

Results

Of the 780 cases included in the study, 75.9% of the cases were female and 24.1% were male. The association of patients with CLT is summarized in Table 1. When the patients were evaluated according to age groups, it was determined that the association of CLT was higher in the 41-60 years range than in the remaining age groups in both genders (Table 1). The multivariate analysis was performed using the binary logistic regression model for the analysis of CLT association. Histopathological diagnosis (malignant/benign), gender, age and TSH were included in the model. As a result of the multivariate analysis, it was observed that the risk of CLT was 2.461 times higher in women than in men, and therefore, gender was associated with the diagnosis of CLT ($p<0.01$). In addition, as patient age increased, CLT positivity decreased (odds ratio =0.978; $p<0.05$) (Table 2).

Among the 780 thyroidectomy cases, 378 (48.46%) were malignant and 402 (51.54%) were benign. The rate of patients with CLT was found to be higher in the malignant group than in the benign group (39.2% vs. 35.3%). The most common (64.2%) benign diagnosis was Nodular Goiter (NG).

The association of CLT with NG and Graves' disease was statistically significant (p<0.05 and p<0.01, respectively).

Among the cases included in our study, there was one medullary thyroid carcinoma and two Hurthle cell carcinomas. Since the number of these cases was insufficient for a statistical evaluation, they were grouped under the category of "other thyroid cancers" together with follicular thyroid carcinomas. In addition, for the same reason, six cases with a diagnosis of Hurthle cell adenoma were evaluated under the category of "Benign Thyroid Nodules (BTN)" including follicular adenomas (Table 3).

When the TSH levels of the patients were divided into levels as in the study of Lun et al. (16), it was observed that the malignant cases had higher mean TSH values than the

Table 1. CLT association according to the age and gender of the patients

		Female			Male		
		CLT (+)	**CLT (-)**	**Total**	**CLT (+)**	**CLT (-)**	**Total**
Mean age		41.50±11.96	45.20±13.16	**43.64±12.77**	44.71±13.57	49.29±15.38	**48.30±15.05**
Age	⩽20	5 (62.5%)	3 (37.5%)	**8 (100.0%)**	0 (0.0%)	2 (100.0%)	**2 (100.0%)**
	21-40	107 (48.2%)	115 (51.8%)	**222 (100.0%)**	16 (30.77%)	36 (69.23%)	**52 (100.0%)**
	41-60	115 (40.49%)	169 (59.51%)	**284 (100.0%)**	20 (20.2%)	79 (79.8%)	**99 (100.0%)**
	>60	22 (28.21%)	56 (71.79%)	**78 (100.0%)**	4 (11.43%)	31 (88.57%)	**35 (100.0%)**
Total		**249 (42.06%)**	**343 (57.94%)**	**592 (100.0%)**	**40 (21.28%)**	**148 (78.72%)**	**188 (100.0%)**
		592 (75.90%)			**188 (24.10%)**		
		p=0.081			**p=0.503**		

CLT: Chronic lymphocytic thyroiditis

Table 2. Factors affecting CLT positivity (results of the logistic regression analysis)

Independent variables	B ± SE	OR (95% CI)	p
†Female gender[a]	0.900±0.308	2.461 (1.345-4.501)	0.003
†Malignant diagnosis[b]	-0.030±0.329	0.971 (0.510-1.850)	0.928
†Benign diagnosis[c]	-0.229±0.323	0.795 (0.422-1.498)	0.478
†Age	-0.022±0.009	0.978 (0.960-0.996)	0.015
†TSH value	-0.008±0.016	0.992 (0.962-1.023)	0.604
Constant	-0.078±0.593	0.925	0.896

CLT: Chronic lymphocytic thyroiditis, TSH: Thyroid-stimulating hormone, B ± SE: Cox regression coefficient and its standard error, OR: Odds ratio, CI: Confidence interval
Dependent variable: CLT positivity, †reference categories, [a]male, [b]non-malignant diagnosis, [c]non-benign diagnosis

Table 3. CLT positivity according to the histopathological diagnosis groups

		CLT (+)	CLT (-)	Total	p	Total
Benign	NG/NH	80 (31.0%)	178 (68.9%)	258 (64.2%)	**0.046***	**402 (51.54%)**
	MNG	2 (11.1%)	16 (88.9%)	18 (4.5%)	0.102	
	GD	26 (65.0%)	14 (35.0%)	40 (9.9%)	**0.008***	
	BTN	34 (39.5%)	52 (60.5%)	86 (21.4%)	0.952	
	Total benign	**142 (35.3%)**	**260 (64.7%)**	**402 (100.0%)**	0.258	
Malignant	PTC	138 (39.0%)	216 (61.0%)	354 (93.7%)	0.432	**378 (48.46%)**
	OTC	10 (41.67%)	14 (58.3%)	24 (6.3%)	0.737	
	Total malignant	**148 (39.2%)**	**230 (60.8%)**	**378 (100.0%)**	0.438	
Total		**290 (37.18%)**	**490 (62.82%)**	**780 (100.0%)**		

CLT: Chronic lymphocytic thyroiditis, PTC: Papillary thyroid carcinoma, OTC: Other thyroid carcinomas, NG/NH: Nodular goiter/hyperplasia, MNG: Multinodular goiter, GD: Graves' disease, BTN: Benign thyroid nodules, percentages are taken as column percentages in totals. Percentage of rows in total and grand total are taken.
*Significant p-values are shown in bold (p<0.05)

benign cases (3.70±9.76 vs. 2.53±8.50) (Table 4). The highest mean TSH value was 4.20±13.03 in the CLT (+) malignant group, and the lowest value was 2.03±2.57 in the CLT (-) benign case group. It was found that there was a higher rate of patients with a TSH value of ⩽0.35 in the benign group compared to the malignant group (24.38% vs. 15.34%). The TSH range with the highest rate (30.76%) of patients was 1.91-4.94, which was seen at a higher rate among the malignant cases compared to the benign cases (37.57% vs. 24.38%). The TSH level with the highest rate of malignant cases (37.57%) was 1.91-4.94, and the TSH range with the highest number of benign (28.86%) was observed to be 0.36-1.35. In addition, when 1.35 was determined as a threshold value for TSH, although 64.55% of the malignant cases were above this limit, 53.24% of the benign cases were below this limit.

Antithyroglobulin antibody (ATG) was positive in 32.01% of the malignant cases and 15.42% of the benign cases. It was observed that this antibody was positive at a higher rate in the malignant cases with concomitant CLT than in those without CLT (41.22% vs. 26.09%).

When evaluated in terms of anti-tyrosine peroxidase antibody (ATPO), positivity was observed in 17.72% of the malignant cases and 10.20% of the benign cases. The rate of ATPO-positive cases was higher in the malignant cases with concomitant CLT than in those without CLT (26.35% vs. 13.48%). Similarly, in the benign group, ATPO positivity was seen at a higher rate (15.49% vs. 7.31%) in those with CLT coexistence compared to those without CLT.

Table 5 shows the distribution of cytological and histopathological diagnoses according to the coexistence of CLT. It was observed that cytological diagnoses were made at a lower rate in PTC cases with CLT coexistence than in those without CLT (35.51% vs. 47.22%). The percentage of accuracy in cases with a cytological malignant diagnosis (DC-6; PTC) was higher than in those without CLT (85.71% vs. 73.13%). Suspicion of malignancy (DC-5) was higher in those with CLT than in those without CLT (9.31% vs. 3.47%).

Discussion

CLT is an autoimmune thyroid disease characterized by damage to thyroid follicle epithelial cells and progressive loss of function (17). In the literature, the association of CLT with TC, and especially PTC is commonly reported (8-36.4%) (18). In a study by Pagni et al. (19), CLT was frequently seen at the first presentation in both multinodular (23.8%) and solitary nodule (27.7%) cases. In our study, the rate

Table 4. Evaluation of histopathological features in relation to TSH and autoantibody levels

		Malignant			Benign			Total n (%)
		CLT (+) n (%)	CLT (-) n (%)	Total n (%)	CLT (+) n (%)	CLT (-) n (%)	Total n (%)	
Mean TSH (mIU/L)		4.20±13.03	2.93±4.68	3.70±9.76	2.81±11.75	2.03±2.57	2.53±8.50	3.09±9.11
TSH (mIU/L)	⩽0.35	28 (18.92%)	30 (13.04%)	58 (15.34%)	38 (26.76%)	60 (23.08%)	98 (24.38%)	156 (20.0%)
	0.36-1.35	20 (13.51%)	56 (24.35%)	76 (20.11%)	24 (16.90%)	92 (35.38%)	116 (28.86%)	192 (24.62%)
	1.36-1.90	22 (14.86%)	46 (20.0%)	68 (17.99%)	26 (18.31%)	44 (16.92%)	70 (17.41%)	138 (17.69%)
	1.91-4.94	68 (45.95%)	74 (32.17%)	142 (37.57%)	44 (30.99%)	54 (20.77%)	98 (24.38%)	240 (30.76%)
	4.95⩽	10 (6.76%)	24 (10.43%)	34 (8.99%)	10 (7.04%)	10 (3.85%)	20 (4.98%)	54 (6.92%)
	Total	**148 (18.97%)**	**230 (29.49%)**	**378 (48.46%)**	**142 (18.21%)**	**260 (33.33%)**	**402 (51.54%)**	**780 (100.0%)**
		378 (48.46%)			**402 (51.54%)**			
Thyroid antibodies (IU/mL)	ATG (+)	61 (41.22%)	60 (26.09%)	121 (32.01%)	27 (19.01%)	35 (13.46%)	62 (15.42%)	183 (23.46%)
	ATPO (+)	39 (26.35%)	31 (13.48%)	67 (17.72%)	22 (15.49%)	19 (7.31%)	41 (10.20%)	108 (13.85%)
	Total	**148 (18.97%)**	**230 (29.49%)**	**378 (48.46%)**	**142 (18.21%)**	**260 (33,33%)**	**402 (51.54%)**	**780 (100.0%)**
		378 (48.46%)			**402 (51.54%)**			

CLT: Chronic lymphocytic thyroiditis, TSH: Thyroid-stimulating hormone, ATG: Anti-thyroglobulin antibody, ATPO: Anti-tyrosine peroxidase antibody. Grand totals are given along the row, others are given in % along the column

of association with CLT was found to be similar in the benign and malignant diagnosis groups. Although the most common benign diagnosis was NG, the most common benign diagnosis with CLT was Graves' disease. The coexistence of CLT with PTC, which is the most common malignant lesion, was similar to the literature. In addition, the rate of CLT was higher in the DTC group than in the PTC group, which we attributed to the low rate of DTC cases (6.3%).

In a study by Uhliarova and Hajtman (14) investigating the relationship between TC and HT, 82% of the cases were female and 18% were male. In our study, the rate of female patients was lower (75.9%). We observed that the risk of CLT was 2.5 times higher in women than in men, and therefore gender was associated with the diagnosis of CLT. While the mean age was 46 years in the study of Uhliarova and Hajtman (14), it was 44 years in our study. Although the mean age was similar in our benign and malignant groups, we observed that it was lower in the groups with CLT coexistence. The age range with the highest incidence of all cases was 41-60 years. The rate of CLT coexistence was higher in both genders at the ages of 41-60 years compared to the remaining age groups. It was also observed that CLT positivity decreased as patient age increased (odds ratio =0.978; p<0.05).

It has been reported that TSH levels close to the upper normal limit support the development of PTC by stimulating follicular proliferation in patients with autoimmune thyroid disease (16). In the literature, it is suggested that the risk of more advanced stages of thyroid cancer increases in patients with high serum TSH levels (9). Lun et al. (16) compared the mean serum TSH concentrations and ATG and ATPO positivity rates in patients with benign thyroid nodules and PTC cases in order to evaluate the effect of HT on the development of malignancy. According to the results of that study, there were significantly higher mean TSH concentrations and ATG and ATPO positivity rates in the PTC cases compared to the patients with benign thyroid nodules. In addition, it was noted that the serum TSH levels were higher in patients with PTC associated with CLT than in those without CLT. Similarly, in our study, the mean serum TSH values were found to be higher in the malignant cases compared to the benign group. In addition, it was determined that the mean TSH value was higher in malignant cases with CLT coexistence than in those without CLT. When the TSH values were divided into levels as in the study by Lun et al. (16), it was seen that there was a higher rate of benign cases with a TSH value of ⩽0.35 compared to the malignant group (24.38% vs. 15.34%). The TSH range in which all the cases had the highest rate (30.76%) was 1.91-4.94, and there were more malignant than benign cases with a TSH value in this range (37.57% vs. 24.38%). The TSH

Table 5. Comparison of histopathological/cytological diagnoses (Bethesda system) in cases with and without CLT

		Malignant		Benign	Total	
		PTC	OTC			
CLT (+)	DC-1	62 (44.93%)	10 (100.0%)	64 (45.08%)	136 (46.89%)	780 (100.0%)
	DC-2	2 (1.45%)	0	26 (18.32%)	28 (9.67%)	
	DC-3	4 (2.90%)	0	13 (9.15%)	17 (5.86%)	
	DC-4	2 (1.45%)	0	13 (9.15%)	15 (5.17%)	
	DC-5	19 (13.76%)	0	8 (5.63%)	27 (9.31%)	
	DC-6	49 (35.51%)	0	18 (12.67%)	67 (23.10%)	
	Total	**138 (100.0%)**	**10 (100.0%)**	**142 (48.97%)**	**290 (100.0%)**	
		148 (51.03%)				
CLT (-)	DC-1	85 (39.35%)	8 (57.14%)	148 (56.92%)	241 (49.18%)	
	DC-2	4 (1.86%)	1 (7.15%)	50 (19.23%)	55 (11.22%)	
	DC-3	11 (5.09%)	5 (35.71%)	27 (10.39%)	43 (8.78%)	
	DC-4	2 (0.92%)	0	13 (5.0%)	15 (3.06%)	
	DC-5	12 (5.56%)	0	5 (1.92%)	17 (3.47%)	
	DC-6	102 (47.22%)	0	17 (6.54%)	119 (24.29%)	
	Total	**216 (100.0%)**	**14 (100.0%)**	**260 (53.06%)**	**490 (100.0%)**	
		230 (46.94%)				

CLT: Chronic lymphocytic thyroiditis, PTC: Papillary thyroid carcinoma, OTC: Other thyroid carcinomas, DC: Diagnostic category, %s are given along the line. Totals are given along the columns

level with the highest number of malignant cases was 1.91-4.94, and the benign cases were mostly seen to have a TSH value in the range of 0.36-1.35, which is in agreement with the literature. Most of the cases with malignant diagnoses (64.55%) had a TSH value of ⩾1.35, and most of the benign cases (53.24%) had a TSH value of ⩽1.35, which is consistent with the results reported in the literature. When evaluated in terms of autoantibody positivity, ATG positivity was proportionally higher in the malignant cases compared to the benign group (15.42% vs. 32.01%). There was higher ATG positivity in both the malignant and benign groups with CLT compared to those without CLT. In terms of ATPO, which is more specific for HT, it was seen that this autoantibody was positive in 17.72% of the malignant cases and 10.20% of the benign cases. We consider that the reason for our different ATPO values compared to the literature is that we included all the patients with CLT in our study, while Lun et al. (16) evaluated only patients with the tissue diagnosis of HT.

In a study performed by Uhliarova and Hajtman (14), it was reported that the accuracy of Fine Needle Aspiration Biopsy (FNAB) in the diagnosis of malignancy was significantly higher in patients without CLT. In other words, the coexistence of CLT negatively affected the accuracy of FNAB in terms of malignancy diagnosis. In our study, it was seen that the diagnostic accuracy rate in patients with the cytological diagnosis of PTC (DC-6) was higher than those without CLT. Suspicion of malignancy (DC-5) as a cytological diagnosis was observed at a higher rate in those with CLT coexistence. One of the limitations of this study is the high rate (48.3%) of patients that could not be diagnosed cytologically (DC-1). Although the results of our study are similar to the literature in terms of cytological diagnoses, a lower accuracy rate was observed. Despite this, the presence of CLT had a negative effect on the accuracy rate of cytological diagnoses and increased the suspicious diagnosis rate. In the literature, gene expression classifiers and next-generation sequencing have been used with an attempt to improve the poor accuracy of FNAB in the presence of CLT, but convincing results have not yet been reported (20,21). We consider that studies in the field of molecular and genetics can make important contributions to the development of new methods for the accurate diagnosis of malignancies, especially in cases with CLT coexistence.

Conclusion

In our study, as reported in the literature, a relationship was found between CLT and PTC, which is the most common thyroid cancer. It is noteworthy that female gender and patient age were the most significant factors in this association. The TSH and autoantibody levels in cases with the coexistence of PTC and CLT had higher serum values compared with the other diagnostic groups. In the literature, it has been reported that suppressing TSH levels may prevent the development of malignancies, and we consider that CLT cases with high TSH and autoantibody levels should be evaluated more carefully in terms of malignancy development. Although the success rate in cytological diagnoses is lower in cases with CLT, further studies should be conducted to improve the success of diagnostic methods to ensure that malignancies are not overlooked during the follow-up of these patients.

Ethics

Ethics Committee Approval: Our study was carried out after obtaining approval from the Ethics Committee of University of Health Sciences Türkiye, Gülhane Training and Research Hospital, dated 10.11.2021 and numbered 2021/86.

Informed Consent: Retrospective study.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Concept: S.C., P.C., Design: S.C., B.T., M.Ö., Data Collection or Processing: B.T., İ.B., M.Ö., Analysis or Interpretation: İ.B., L.D., Literature Search: S.C., B.T., M.Ö., P.C., Writing: S.C., B.T., İ.B., M.Ö., L.D.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Campos LA, Picado SM, Guimarães AV, Ribeiro DA, Dedivitis RA. Thyroid papillary carcinoma associated to Hashimoto's thyroiditis. Braz J Otorhinolaryngol. 2012;78:77-80. [Crossref]
2. Tomer Y, Huber A. The etiology of autoimmune thyroid disease: a story of genes and environment. J Autoimmun. 2009;32:231-239. [Crossref]
3. Ralli M, Angeletti D, Fiore M, D'Aguanno V, Lambiase A, Artico M, et al. Hashimoto's thyroiditis: An update on pathogenic mechanisms, diagnostic protocols, therapeutic strategies, and potential malignant transformation. Autoimmun Rev. 2020;19:102649. [Crossref]
4. Caturegli P, De Remigis A, Chuang K, Dembele M, Iwama A, Iwama S. Hashimoto's thyroiditis: celebrating the centennial through the lens of the Johns Hopkins hospital surgical pathology records. Thyroid. 2013;23:142-150. [Crossref]
5. Hiromatsu Y, Satoh H, Amino N. Hashimoto's thyroiditis: history and future outlook. Hormones (Athens). 2013;12:12-18. [Crossref]
6. Chen YK, Lin CL, Cheng FT, Sung FC, Kao CH. Cancer risk in patients with Hashimoto's thyroiditis: a nationwide cohort study. Br J Cancer. 2013;109:2496-2501. [Crossref]
7. Boelaert K, Horacek J, Holder RL, Watkinson JC, Sheppard MC, Franklyn JA. Serum thyrotropin concentration as a novel predictor of malignancy in thyroid nodules investigated by fine-needle aspiration. J Clin Endocrinol Metab. 2006;91:4295-301. [Crossref]
8. Jankovic B, Le KT, Hershman JM. Clinical Review: Hashimoto's thyroiditis and papillary thyroid carcinoma: is there a correlation? J Clin Endocrinol Metab. 2013;98:474-482. [Crossref]

9. Zafon C, Obiols G, Baena JA, Castellví J, Dalama B, Mesa J. Preoperative thyrotropin serum concentrations gradually increase from benign thyroid nodules to papillary thyroid microcarcinomas then to papillary thyroid cancers of larger size. J Thyroid Res. 2012;2012:530721. [Crossref]
10. Ma H, Yan J, Zhang C, Qin S, Qin L, Liu L, et al. Expression of papillary thyroid carcinoma-associated molecular markers and their significance in follicular epithelial dysplasia with papillary thyroid carcinoma-like nuclear alterations in Hashimoto's thyroiditis. Int J Clin Exp Pathol. 2014;7:7999-8007. [Crossref]
11. Cancer Genome Atlas Research Network. Integrated genomic characterization of papillary thyroid carcinoma. Cell. 2014;159:676-690. [Crossref]
12. Ahn D, Heo SJ, Park JH, Kim JH, Sohn JH, Park JY, et al. Clinical relationship between Hashimoto's thyroiditis and papillary thyroid cancer. Acta Oncol. 2011;50:1228-1234. [Crossref]
13. Sulaieva O, Selezniov O, Shapochka D, Belemets N, Nechay O, Chereshneva Y, et al. Hashimoto's thyroiditis attenuates progression of papillary thyroid carcinoma: deciphering immunological links. Heliyon. 2020;6:e03077. [Crossref]
14. Uhliarova B, Hajtman A. Hashimoto's thyroiditis - an independent risk factor for papillary carcinoma. Braz J Otorhinolaryngol. 2018;84:729-735. [Crossref]
15. Cibas ES, Ali SZ. The 2017 Bethesda System for Reporting Thyroid Cytopathology. J Am Soc Cytopathol. 2017;6:217-222. [Crossref]
16. Lun Y, Wu X, Xia Q, Han Y, Zhang X, Liu Z, et al. Hashimoto's thyroiditis as a risk factor of papillary thyroid cancer may improve cancer prognosis. Otolaryngol Head Neck Surg. 2013;148:396-402. [Crossref]
17. Bliddal S, Nielsen CH, Feldt-Rasmussen U. Recent advances in understanding autoimmune thyroid disease: the tallest tree in the forest of polyautoimmunity. F1000 Res. 2017;6:1776. [Crossref]
18. Schatz-Siemers N, Brandler TC, Oweity T, Sun W, Hernandez A, Levine P. Hürthle cell lesions on thyroid fine needle aspiration cytology: Molecular and histologic correlation. Diagn Cytopathol. 2019;47:977-985. [Crossref]
19. Pagni F, Jaconi M, Delitala A, Garancini M, Maternini M, Bono F, et al. Incidental papillary thyroid carcinoma: diagnostic findings in a series of 287 carcinomas. Endocr Pathol. 2014;25:288-296. [Crossref]
20. Papoian V, Rosen JE, Lee W, Wartofsky L, Felger EA. Differentiated thyroid cancer and Hashimoto thyroiditis: Utility of the Afirma gene expression classifier. J Surg Oncol. 2020;121:1053-1057. [Crossref]
21. Molnár C, Bádon ES, Mokánszki A, Mónus A, Beke L, Győry F, et al. High Genetic Diversity and No Evidence of Clonal Relation in Synchronous Thyroid Carcinomas Associated with Hashimoto's Thyroiditis: A Next-Generation Sequencing Analysis. Diagnostics (Basel). 2020;10:48. [Crossref]