Endokrynologia Polska/Polish Journal of Endocrinology
Tom/Volume 61; Numer/Number 6/2010
ISSN 0423–104X

Comparison of the prevalence and sonographic features of thyroid nodules accompanying autoimmune thyroid diseases

Porównanie częstości występowania i cech sonograficznych guzków tarczycy towarzyszących autoimmunologicznym chorobom tarczycy

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Abstract

Introduction: The coexistence of thyroid nodules and autoimmune thyroid disease (ATD) has been widely reported. The aim of our study was to retrospectively evaluate the prevalence and sonographic features of malignancy of thyroid nodules in ATD patients.
Material and methods: We retrospectively analysed data from 500 patients with ATD in our hospital. We recorded ultrasonographic, histopathological and laboratory features of these patients. Thyroid ultrasonography was performed on all the patients, as well as fine needle aspiration biopsy (FNAB) of the thyroid nodule, when required. Patients underwent operations depending on the result of the FNAB.
Results: Of the 500 with ATD (400 female and 100 male; mean age = 42.4 years), 300 (60%) had Hashimoto's thyroiditis (HT) and 200 (40%) presented with Graves' disease (GD). The frequency of thyroid nodules was statistically significantly higher in those with GD (37.8%) than in those with HT (24.3%) ($p < 0.001$). One hundred and forty-nine nodules underwent FNAB (37.8%, 76 out of 200 had GD and 24.3%; 73 out of 300 had HT). The results of the cytological examination were: non-diagnostic cytology, benign, malignant and indeterminate in 19.4%, 73.8%, 2% and 4.5% of the nodules, respectively. When 55 GD and 32 HT patients, on whom total thyroidectomy had been carried out, were evaluated, the incidence of thyroid carcinoma was similar between patients with GD (n = 3, 5.5%) and HT (n = 2, 6.3%) ($p > 0.05$).
Conclusions: We observed that the prevalence of thyroid nodules in patients with GD was higher than patients with HT. However, in general, the characteristics of the nodules and FNAB results were similar in both ATDs.
(Pol J Endocrinol 2010; 61 (6): 658–664)

Key words: *thyroid nodule, Hashimoto's thyroiditis, Graves' disease*

Streszczenie

Wstęp: W licznych doniesieniach stwierdza się współwystępowanie guzków tarczycy i autoimmunologicznych chorób tarczycy. Celem pracy była retrospektywna ocena występowania i sonograficznych cech złośliwości guzków tarczycy u pajcentów z autoimmunologicznymi chorobami tarczycy (ATD, *autoimmune thyroid disease*).
Materiał i metody: Analizie retrospektywnej poddano dane 500 pacjentów z ATD, u których przeprowadzono badania ultrasonograficzne, histopatologiczne i laboratoryjne. U wszystkich pacjentów wykonano badanie ultrasonograficzne oraz, w zależności od wymagań, biopsję aspiracyjną cienkoigłową (BAC). Pacjentów poddano operacji w zależności od wyniku BAC.
Wyniki: Spośród 500 pacjentów z ATD (400 kobiet i 100 mężczyzn, średnia wieku: 42,4 lat), u 300 (60%) stwierdzono zapalenie tarczycy Hashimoto (HT, *Hashimoto thyroids*), a u 200 (40%) chorobę Gravesa (GD, *Graves disease*). U pacjentów z GD stwierdzono statystycznie wyższą częstość występowania guzków tarczycy (37%) w porównaniu z pacjentami z HT (24,3%) ($p < 0,001$). Wykonano BAC 149 guzków, w 37,8% (76 z 200) przypadków z GD i w 24,3% (73 z 300) z HT. Wyniki badania cytologicznego: cytologia niediagnostyczna (19,4%), guzki łagodne (73,8%), guzki złośliwe (2%) i guzki o pośredniej złośliwości (4,5%). Spośród 55 pacjentów z GD i 32 z HT, u których wykonano tyroidektomię totalną, stwierdzono podobną częstość występowania raka tarczycy — u pacjentów z GD (n = 3, 5,5%), a u pacjentów z HT (n = 2, 6,3%) ($p > 0,05$).
Wnioski: Zaobserwowano wyższą częstość występowania guzków tarczycy u pacjentów z GD w porównaniu z pacjentami z HT. Natomiast charakterystyka guzków i wyniki BAC nie różniły sie w obu typach ATD. **(Endokrynol Pol 2010; 61 (6): 658–664)**

Słowa kluczowe: *guzki tarczycy, zapalenie tarczycy Hashimoto, choroba Gravesa*

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Introduction

The autoimmune thyroid diseases Hashimoto's thyroiditis (HT) and Graves' disease (GD) are the most common organ-specific autoimmune diseases. Hashimoto's thyroiditis occurs as a result of autoimmune inflammation of the thyroid gland. It has a chronic course and is usually associated with hypothyroidism. In physical examination, moderate enlargement of the thyroid gland and, in many cases, the clinical features of hypothyroidism, are observed. Anti-thyroglobulin antibodies (Tg-Ab) and anti-thyroid peroxidase autoantibodies (TPO-Ab) are positive [1]. Nodular goitre is reported in 14–42% of cases [2, 3]. The rate of papillary thyroid cancer in patients with HT is reported to be higher than among the general population [4–9]. The etiological relation between papillary thyroid cancer and HT is still controversial. Whether thyroiditis is induced by neoplasm, or whether thyroiditis promotes development of thyroid cancer, is still unclear. Although, in some articles, cancer development on the basis of thyroiditis is reported to be high, it is generally believed that lymphocytic thyroiditis is not a pre-malignant lesion [7, 10, 11].

The characteristics of GD are hyperthyroidism, goitre, ophthalmopathy and dermatopathy. These features can be seen in several combinations and in different frequencies. In GD, the thyroid nodule is common and it carries a risk for thyroid cancer. In some studies, thyroid cancer accompanying GD is shown to have a more aggressive course than the carcinoma occurring in patients with non-immune hyperthyroidism and euthyroidism; however, its pathogenesis is not well described [12, 13].

In Western countries, the prevalence of thyroid nodules ranges between 4 and 7% although this rate is up to 50% in autopsies and most nodules have a benign nature. In studies, between 1% and 7.3% of nodules have been found to be malignant [14–17].

We have found no study in the literature that presents the nodule frequencies in patients with autoimmune thyroid diseases and compares the features of these nodules in HT and GD. Therefore, we aimed to compare the frequency of thyroid nodules in both autoimmune diseases (HT and GD) and the ultrasonographic features of the thyroid nodules accompanying these diseases.

Material and methods

Study design and patients

Data in relation to 300 HT and 200 GD patients admitted to the thyroid polyclinic at Ankara Numune Research and Training Hospital, Division of Endocrinology and Metabolism, between December 2005 and May 2009 was evaluated retrospectively. Diagnosis of GD was performed on the basis of diffuse goitre accompanying thyrotoxicosis signs and symptoms, elevated radioactive iodine thyroid uptake (RAIU), elevated circulating anti-TSH receptor autoantibodies (TRAb) and the presence of biochemical hyperthyroidism. To differentiate between patients with toxic multinodular goitre and toxic adenoma, RAIU and thyroid scintigraphy were performed after detailed thyroid ultrasonography (US). Patients were diagnosed as HT if they had TPO-Ab or Tg-Ab positivity along with clinical or subclinical hypothyroidism. Other than that, heterogeneous parenchymal appearance, which was consistent with thyroiditis in terms of ultrasonographic aspects, was taken into account and patients who had not had L-thyroxin therapy were included in the study.

The histopathological results of 55 GD and 32 HT patients, on whom total thyroidectomy had been carried out, were included in our study.

Indications for surgery were: preference of patient, compressive symptoms, severe ophthalmopathy, patients whose US revealed features that needed investigation, large goitre, failure, and/or serious side effects of antithyroid drugs including agranulocytosis and hepatotoxicity.

Ultrasonography

Ultrasonographic examinations of the patients were performed in our clinic by an endocrinologist, using the LOGIQ 3 (General Electric Healthcare, Waukesha, Wisconsin, USA) US equipment and an 11 MHz linear probe.

The sizes of the thyroid lobes as well as characteristics of thyroid parenchyma and nodules were noted. Ultrasonography-guided biopsy (fine needle aspiration biopsy, or FNAB) was used for nodules greater than 1 cm in diameter and for nodules < 1 cm with suspicious US findings (e.g. a hypoechogenic nodule in association with punctuated calcification and/or intranodular vascularity and/or irregular borders).

The results of the cytology were categorised as non-diagnostic (ND), benign, malignant or indeterminate. A second biopsy was performed if the FNAB result was ND-FNAB. Total thyroidectomy was performed on the patients whose FNAB result was malignant, indeterminate or ND-FNAB twice.

Laboratory assays

Serum thyroid-stimulating hormone (TSH), free triiodothyronine (fT_3), free thyroxine (fT_4), TRAb, TPO-Ab and Tg-Ab levels were assayed. Serum TSH, fT_3 and fT_4 levels were evaluated using the Abbott Architect 2000 device and Chemiluminescence Microparticle Immunoassay (CMIA) method. Serum Tg-Ab (normal

Table I. *Characteristics of the patients with autoimmune thyroid diseases*
Tabela I. *Charakterystyka pacjentów z autoimmunologicznymi chorobami tarczycy*

	Hashimoto's thyroiditis (n = 300)	Graves' disease (n = 200)	p
Age (years)	41.4 ± 13.3	43.9 ± 14.3	NS
TSH [μIU/mL]	13.0 ± 23.9	0.2 ± 0.6	< 0.001
fT_3 [pg/mL]	2.5 ± 0.5	7.8 ± 7.7	< 0.001
fT_4 [ng/dL]	0.8 ± 0.3	2.0 ± 1.2	< 0.001
TPO-Ab [IU/L]	315.5 ± 451.2	206.7 ± 262.1	0.004
Tg-Ab [IU/L]	431.7 ± 775.8	326.6 ± 736.2	NS
Presence of thyroid nodule (%)	73 (24.3)	76 (37.8)	< 0.001
Number of thyroid nodules	0.2 ± 0.5 (0–3)	0.5 ± 0.9 (0–5)	< 0.001
Mean nodule volume [cm^3]	0.33 (0.01–2.81)	1.77 (0.01–49.9)	NS
Thyroid volume [cm^3]	14.01 ± 13.0	26.3 ± 18.5	< 0.001
Tumour diameter [cm^3]	0.7 ± 0.3	0.5 ± 0.3	NS
Rate of malignancy	2	3	
In all patients (%)	0.6	1.5	NS
In nodules of patients who underwent total thyroidectomy (%)	6.3	5.5	

fT_3 — free triiodothyronine; fT_4 — free thyroxine; Tg-Ab — anti-thyroid thyroglobulin antibodies; TPO-Ab — anti-thyroid peroxidase autoantibodies; TSH — thyroid-stimulating hormone; NS — not significant

range < 50 IU/mL) and TPO-Ab (normal range < 10 IU/mL) values were evaluated through immunoradiometric assay (IRMA) methods (ICN Pharmaceuticals, USA). Anti-TSH receptor antibodies in patients were measured using a radioreceptor assay (Radim, Italy). The normal range for TRAb in our laboratory was found to be < 9 U/L (9–14 U/L borderline, > 14 U/L positive). TSH levels lower than 0.34 μIU/mL were accepted as hyperthyroidism and TSH levels over 5.60 μIU/mL were accepted as hypothyroidism.

Statistical analysis

Data analysis was performed using Statistical Package for Social Sciences (SPSS) version 13.0 software (SPSS Inc., Chicago, Illinois, USA). Metric discrete variables were shown as mean ± standard deviation, and percentages were used for categorical variables. Chi-square tests were used to assess the statistical significance of differences between groups in the frequency distribution of categorical variables. Medians were compared using the Mann Whitney U test when the number of independent groups was two. Differences between the medians of more than two groups were evaluated using the Kruskal Wallis test. A p value less than 0.05 was considered to be statistically significant.

Results

Three hundred out of 500 patients with ATD had HT and 200 had GD. Of the 300 patients with HT, 90% (270) were female and the mean age was 40 (20–65 years) while 65% (130) of 200 GH patients were female and the mean age was 44 (22–68 years). The mean thyroid volume of the GD patients was statistically significantly higher than that in the patients with HT [14.01 ± 13.0 cm^3 in HT; 26.3 ± 18.5 cm^3 in GD ($p < 0.001$)].

Thyrotropin level in patients with HT was 13.0 ± ± 23.9 μIU/mL, while it was 0.2 ± 0.6 μIU/mL in patients with GD. Free T3 level was 2.5 ± 0.5 pg/mL in HT and 7.8 ± 7.7 pg/mL in GD. Free T4 level was 0.8 ± ± 0.3 ng/dL in HT and 2.0 ± 1.2 ng/dL in GD ($p < 0.001$ for all) (Table I).

A thyroid nodule was found in 24.3% of the 300 patients with HT (n = 73) and in 37.8% of the 200 patients with GD (n = 76). The frequency of thyroid nodules was statistically significantly higher in GD ($p < 0.001$). Thyroid nodule number was statistically significantly higher in GD ($p < 0.001$) (Table I).

Thyroid cancer was observed in 0.6% of patients with HT (n = 2), and in 1.5% of GD patients (n = 3). However, there was no statistically significant difference regarding thyroid cancer frequency between HT and GD ($p > 0.05$). Besides, given the cases on which total thyroidectomy was carried out, the incidence of thyroid carcinoma was similar between patients with GD (3 out of 55, 5.5%), and patients with HT (2 out of 32, 6.3%) ($p > 0.05$).

The characteristics of the thyroid nodules in HT and GD patients are presented in Table II. In 73 of the pa-

Table II. *Selected ultrasonographic features in thyroid nodules according to autoimmune thyroid diseases*
Tabela II. *Wybrane cechy ultrasonograficzne guzków tarczycy w obu rodzajach ATD*

	Hashimoto's thyroiditis (n = 73)	Graves' disease (n = 76)	p
Structure (%)			
Solid	67 (91.8)	64 (84.2)	
Cystic	4 (5.5)	10 (13.2)	0.306
Mixed	2 (2.7)	2 (2.6)	
Echogenity (%)			
Hypoechoic	28 (38.4)	25 (32.9)	
Isoechoic	18 (24.7)	12 (15.8)	0.006
Hyperechoic	14 (19.1)	6 (7.9)	
Mixed	13 (17.8)	33 (43.4)	
Microcalcification (%)	13 (17.8)	8 (10.5)	0.179
Shape irregularity (%)	3 (4.1)	2 (2.6)	0.708
AT ≥ 1 (%)	15 (20.5)	12 (15.8)	0.618
LA/SA < 1.5 (%)	36 (49.3)	43 (56.6)	0.527

AT — anteroposterior diameter to transverse diameter ratio; LA/SA — long axis to short axis ratio

tients with nodular variant of HT, 91.8% of the thyroid nodules were solid, 5.5% were cystic and 2.7% had both solid and cystic components. In 76 GD patients with thyroid nodules, 84.2% of the thyroid nodules were solid, 13.2% were cystic and 2.6% had both solid and cystic components. No statistically significant difference was observed when HT and GD were compared regarding the structure of the thyroid nodule ($p > 0.05$).

When we investigated the echogenicity of the thyroid nodules of 73 patients with HT, 38.4% was hypoechoic, 24.7% were isoechoic, 19.1% were hyperechoic and 17.8% had a mixed echogenicity; while of 76 GD patients, 32.9% were hypoechoic, 15.8% were isoechoic, 7.9% were hyperechoic and 43.4% had a mixed echogenicity. No statistically significant difference was observed between the thyroid nodules of mixed echogenicity in patients with GD and HT ($p > 0.05$).

While microcalcifications were found in 17.8% and nodular shape irregularity was found in 4.1% of nodular patients with HT, the rates in nodular GD were 10.5% and 2.6%, respectively. There was no statistically significant difference between HT and GD regarding the presence of microcalcification and shape features ($p > 0.05$). Malign nodules in GD patients were hypoechoic and they consisted of microcalcification; a halo was not observed in any of the patients. While shapes were regular in two of the malign nodules, shape irregularity was existent in one of the malign nodules. Malign nodules in patients with HT showed mixed echogenicity. Microcalcifications were observed in one of the malign nodules. The shapes of both malign nodules were regular and a halo was existent. While long axis to short axis (LA/SA) ratio was < 1.5 in four of the malign nodules, anteroposterior diameter to transverse diameter ratio (AT) was ≥ 1 in both of the malign nodules in the patients with GD. On the other hand, AT was ≥ 1 in one of the malign nodules in patients with HT.

Though the number of nodules positively correlated with age, TSH level and tumour diameter showed a positive correlation in malign patients (Table III).

In patients with GD, there was no significant difference between TRAb positive and negative individuals regarding the number of nodules, volume of nodules, presence of nodules and ultrasonographic features of the nodules (Table IV).

Fine needle aspiration biopsy outcomes of the nodular patients with HT were 76.3% benign, 13.6% non-diagnostic, 6.7% indeterminate and 2.7% malignant, while the rates in patients with nodular GD were found to be 72.4%, 23.7%, 2.6% and 1.3%, respectively. Those patients with inadequate FNAB for the second time in a row were referred for surgery.

Discussion

Clinical and ultrasonographic characteristics of HT reflect diffuse goitre, although nodular goitre is not infrequently observed in these patients. Studies on HT have reported a nodular goitre rate of 14-42% [2, 3, 18, 19].

In HT, if a nodular lesion is observed, FNAB should be performed [20]. Rates ranging between 0.3% and 58% have been reported on the co-existence of papillary thyroid cancer and HT [4–9]. This very wide range can be attributed to ethnic and geographical features, gender, theselection of patients referred for thyroidectomy and differences in histopathological comments in the stud-

Table III. *Correlation coefficients and levels of significance between the level of change in terms of age, thyroid function, autoantibodies and tumour diameter*

Tabela III. *Współczynniki korelacji i poziomy znamienności statystycznej różnic w zakresie wieku, czynności tarczycy, przeciwciał i wymiarów guza*

	Number of nodules		Tumour diameter	
	Rho	p	Rho	p
Age	0.161	< 0.001	–0.532	0.357
TSH	–0.098	0.029	0.968	< 0.001
fT_3	0.016	0.720	–0.308	0.614
fT_4	0.003	0.938	–0.130	0.835
TPO-Ab	0.010	0.837	–0.383	0.617
Tg-Ab	0.036	0.432	0.966	0.034
Number of thyroid nodules	–	–	–0.183	0.769
Thyroid volume	0.229	< 0.001	–0.369	0.548
Tumour diameter	–0.183	0.769	–	–

fT_3 — free triiodothyronine; fT_4 — free thyroxine; Tg-Ab — anti-thyroid thyroglobulin antibodies; TPO-Ab — anti-thyroid peroxidase autoantibodies; TSH — thyroid-stimulating hormone

Table IV. *Comparison of ultrasonographic and histopathological features according to TRAb results*

Tabela IV. *Porównanie cech ultrasonograficznych i histopatologicznych w zależności od wyniku TRAb*

	TRAb+ (n = 166)	TRAb– (n = 34)	p
Number of thyroid nodules	0.49 (0–3)	0.24 (0–2)	0.117
Mean nodule volume [cm^3]	0.45 (0.11–1.61)	1.9 (0.01–49.92)	0.666
Thyroid volume [cm^3]	26.93 (1.29–141.41)	22.95 (7.69–51.11)	0.254
Malignancy (%)	2 (3.1)	1 (9.1)	1.000

ies [6, 21]. Nevertheless, it is accepted that the incidence of papillary thyroid cancer is higher in patients with HT compared to the general population [7, 8]. In our study, a thyroid nodule was found in 24.3% of HT patients, though thyroid cancer was observed in only 0.6%. Besides, when the cases on which total thyroidectomy was carried out were evaluated, it was observed that 6.3% of the cases had thyroid cancer. The fine needle aspiration biopsy outcomes of 73 patients with the nodular variant of HT were found to be benign in 76.3%, non-diagnostic in 13.6%, indeterminate in 6.7% and malignant in 2.7%. The incidence of thyroid cancer was lower than in the literature on patients with HT in our series, because the rates of thyroid cancer in previous studies were generally obtained from the data of patients who had undergone thyroidectomy. The rate of thyroid cancer in cases on which total thyroidectomy was carried out, made us think that the rate of thyroid cancer would be higher when all cases were subjected to surgery. Our aim was not to determine the prevalence of thyroid cancer, but rather to compare the frequency of thyroid nodules, cytology results and nodule features. A study which aims to reveal the frequency of thyroid cancer in ATD patients would of course require a method that investigates the histopathological outcomes of the patients who had undergone total thyroidectomy.

Long-term studies, including series with a large number of patients, suggest that recurrence of thyroid cancer and metastasis are observed less frequently and the term of survival is longer in patients with HT and this has been attributed to the lymphocytic response that limits the growth and metastasis potential of the tumour [6, 7, 21]. Our study found a relation between TSH levels and the diameter of a tumour. Fiore et al. found a direct relationship between TSH levels and the risk of papillary thyroid carcinoma in patients with thyroid nodular disease [22]. In the above-stated study, no relation was found between thyroid autoimmunity and the risk of thyroid cancer. Similarly, Haymart et al. states that incidence of thyroid cancer correlates with higher TSH independently of age [23]. Besides, in this study,

researchers have found that higher TSH is associated with extrathyroidal extension of this disease. In GD, the rate of thyroid nodules is almost three times higher than in the general population and the risk of thyroid cancer rises in patients with nodular GD [24]. The frequency of nodules varies between 15% and 45% in GD [24–28]. The risk of carcinoma in a thyroid nodule of GD is higher than in other nodular thyroid disease [24]. Pathogenesis in relation to the development of a thyroid nodule in GD is unclear and the cause of the increase in the rate of thyroid cancer is still being debated [29]. Although one study found thyroid cancer to be at a rate of 9% in patients operated for GD [30], this high incidence of carcinoma has not been reproduced in other studies. The risk of thyroid carcinoma ranges between 0% and 9.8% in GD [24]. For example, in a study performed on 468 GD patients, the frequency of nodules was 12.6%, the risk of thyroid cancer in nodules was 10% and the risk of thyroid cancer for all patients was 1.3% [29]. In one study, a thyroid nodule was found in 25% of 557 patients and thyroid cancer was found in 15% of thyroid nodules and in 3.8% of all patients [31].

In our study, 37.8% of 200 GD patients had thyroid nodules and 1.5% had thyroid cancer. When the cases on which total thyroidectomy had been carried out were evaluated, it was observed that 5.5% of the cases had thyroid cancer. The high frequency of thyroid nodules may be attributed to iodine deficiency in our society. Although iodine deficiency has improved since 1998, when iodine prophylaxis was initiated, moderate to severe iodine deficiency still exists in 27.8% of our population [32].

In terms of the surveys, which were performed prior to (1997) the iodine prophylaxis and in its early years, this rate was 58% and 38.9%, respectively.

In our study, similar to patients with HT, GD patients had a lower frequency of thyroid cancer compared to the literature, because thyroidectomy was not performed on all cases, since our primary aim was not to detect the rate of cancer. Thyroid microcarcinomas are found in 5% to 36% of adults at autopsy. Clinically detectable thyroid carcinomas constitute less than 1% of all human cancers, while the annual incidence rate in various parts of the world ranges from 0.5 to 10 cases per 100,000 [33]. The possibility of a bias related to the pathological examination of the excised thyroid is supported by studies in which the incidence of carcinoma can be compared between patients with GD who have undergone thyroidectomy and those who have not.

A possible role of TRAb in the development and progression of thyroid cancer was suggested on the basis of in vitro experiments and confirmed in clinical studies [26, 34–37]. At this point, we cannot make any conclusion on the basis of our series. We did not consider the possible relationship between TRAb levels and the presence of nodules in patients with GD, and found no significant increase of TRAb levels preceding or accompanying the growth of nodules.

Today, like all diseases, ATDs can be diagnosed earlier, thanks to a wide distribution of thyroid clinics, as well as better access to molecular and ultrasonographic examinations. Therefore, in these groups of patients, exposure time to abnormal TSH levels previously blamed for pathogenesis (high in HT and low in GD) is shorter. Similarly, early diagnosis and removal of TRAb source by early thyroidectomy in GD patients might result in less thyroid gland stimulation causing malignancy.

While there are studies in which solid structure is reported as a weak indicator of malignancy in thyroid nodules (since most benign nodules are of solid structure) some other publications report it as a strong indicator of malignancy [38–41]. In our study, 91.8% of the nodules in HT patients, and 84.2% of the nodules in GD patients, had solid structure. While malign nodules in GD patients had solid structure, the nodules in HT patients had mixed structure.

In previous studies, hypoechoic ultrasonographic appearance in thyroid nodules was significantly associated with malignancy [39–42]. Thyroid nodules of GD patients had a higher rate of mixed echogenicity when compared to those of HT patients. However, hypoechoic pattern was found to be similar in both diseases (HT 38.4% and GD 32.9%). As mixed echogenicity did not predict malignancy, it was suggested that there was no significant difference between these two diseases. In these groups of patients, ultrasonographic characteristics of the benign and malign nodules could not be specified as the number of malign cases was limited. While a hypoechoic pattern was observed in the malign nodules of GD patients, mixed echogenicity was observed in the malign nodules of HT patients.

In many studies, microcalcifications in thyroid nodules have been associated with malignancy [38, 43, 44]. We detected microcalcifications in 17.8% of the nodules of HT patients and 10.5% of the nodules of GD patients. Malign nodules in Graves' patients consisted of microcalcifications. One of the malign nodules in HT patients had microcalcifications.

Spherical shape was independently correlated with the risk of malignancy. In various studies, this feature has been evaluated on the basis of LA/SA or AT ratio. A long to short axis ratio greater than 2.5 was 100% predictive of a benign process, although it was present in only 4% of our cohort [45]. A long axis/short axis ratio (LA/SA) of < 1.5 was associated with malignancy in subcentimeter thyroid nodules [39]. Long axis to short axis ratio was found to be < 1.5 in 49.3% of the nodules in HT patients and 56.6% of the nodules in GD patients.

LA/SA ratio was < 1.5 in 4 of the malign nodules. It is reported that an AT rate of ≥ 1.0 is a very good predictor of the risk of thyroid cancer in thyroid nodules [46]. In GD patients, there is a relation between thyroid cancer and US features such as microcalcification, hypoechoic feature, shape irregularity and an A/T rate of ≥ 1 [47]. AT was found to be ≥ 1 in 20.5% of the nodules in HT patients and 15.8% of the nodules in GD patients. Although the rates of spherical shapes in all nodules were similar, AT was found to be ≥ 1 in both malign nodules in Graves' patients. On the other hand, AT was ≥ 1 in one of the malign nodules in HT patients.

Conclusions

Our study found a higher frequency of thyroid nodules in GD patients compared to HT patients. However, mean thyroid nodule volume and cytological results of the nodules were similar. Ultrasonographic features of the nodules were generally similar, although mixed echogenicity was found to be more frequent in GD patients. We have concluded that there is a need for large scale studies, in which frequency of thyroid nodules is compared between individuals with Graves' disease and Hashimoto's thyroiditis.

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