

PREOPERATIVE Ac ANTI-THYROGLOBULIN COULD BE A POTENTIAL RISK FACTOR FOR DIFFERENTATED THYROID CANCER

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Abstract

Hashimoto thyroiditis (HT) is an autoimmune disease and the most common cause of hypothyroidism. It is characterized by the presence of thyroid antibodies (Tg Ab and TPO Ab).

Material and Methods: In a retrospective study we analyzed the date of 201 patients, who underwent total thyroidectomy during a period from January 2013 until February 2016. Tg Abs was measured in all patients before surgery.

Results: Females were 84.5%; males 15.4%; 57.7% with benign pathology and 42.2% with malignant pathology. Papillary thyroid cancer (PTC) accounted for the vast majority of the differentiated thyroid cancer (DTC) diagnoses (95.1%, n=79). There was no difference in the sex ratio between patients with benign tumors or DTC (p=0.66). Patients with DTC were relatively younger (43.2 ± 14.9 versus 48.4 ± 13.6 yr; p=0.760) and had higher preoperative median TSH levels (2.42 mIU/L versus 1.38 mIU/L; p<0.028) than those with benign nodule. Solitary nodules were more common in patients with DTC (40.4%) compared to patients with benign nodules (19.4%; p<0.001). Patients with TgAb concentration more than 115 IU/mL were more common in DTC group than in benign nodule group (28.2% versus 13%, p<0.007), suggesting that elevated Tg Ab may associate DTC. The prevalence of DTC was significantly associated with TgAb ≥ 115 IU/mL (OR=2.8), compared with TgAb < 115 IU/mL group.

Conclusions. Elevated serum TgAb level was associated with an increased risk of TC in patients with TN. We can conclude that high serum TgAb levels may serve as a predictive marker for DTC.

Key words: Hashimoto thyroiditis, papillary thyroid cancer, ac anti-Thyroglobulin

Introduction:

Thyroid cancer accounts for 1% of all type of cancer but it's the most common

endocrine tumor (1). Differentiated thyroid cancer which includes papillary and follicular type is the prevalent form (over 90

%) of all thyroid tumors (2). Both types of DTC as normal thyroid follicular cell have expression for TSH receptor, thyroid peroxidase (TPO), and thyroglobulin (Tg) which serves as autoantigens. Hashimoto's thyroiditis (HT) or chronic lymphocytic thyroiditis, it's an autoimmune disease (3). It is characterized by the presence of thyroid antibodies (Tg Ab and TPO Ab), widespread lymphocytic infiltration with consequences hypothyroidism due to destruction of follicular cells (4). The prevalence of Tg Ab in patient diagnosed with DTC varies from 8-36% and its approximately 2-fold higher in DTC compared with general population 24,9% vs.10,1% respectively (5-7). The prevalence of Tg Ab increase with age and females and is higher in papillary versus follicular thyroid cancer (8). Since Tg Ab has a strong correlation with lymphocytic thyroiditis, a correlation between HT and DTC has been proposed and confirmed by a lot of meta-analysis (9-11). Kim et al reported that in patients with thyroid nodules (TN) the presence of Tg Ab can be a risk factor for thyroid cancer independent from Hashimoto Thyroiditis (12). Although the positivity for thyroid antibody strongly correlates with histologic result for HT (6, 7, 13). So we decided to perform this retrospective study to investigate if the preoperative level of Tg Abs has any predictive value for preoperative malignancy and can we use the Tg Ab as a tumor marker. Because Tg Abs has been proposed by others as an alternative tumour marker but has been contested by others (14,15)

Material and Methods

These is a retrospective study of a total of 201 patients; 170 (84.5%) were females and 31 (15.5%) were males who underwent total or near total thyroidectomy during a period from January 2013 until February 2016 and whose Tg Ab were measured in all patients before surgery. TgAb assay were recorded as "positive" or "negative" based

on a titer above or below the cut-off of the specific assay used in our hospital. Inclusion criteria were: all patients over 16 years old, Tg Ab measured preoperatively, performed total or near total thyroidectomy. The histopathological evaluation of thyroid specimens is done according to the World Health Organization guidelines by our pathologist present at our hospital. Our database included: age, gender, solitary versus multinodular goiter, TSH, Tg Ab measured preoperatively and pathology report.

Thyroid Profiles:

Thyroid profiles included the serum level of thyroid stimulating hormone (TSH) and Tg Ab measured at fasting state before thyroidectomy at American Hospital 2. Serum were detected using ELECSYS 2010 ROCHE, for TSH reference range was 0,27-4,2 μ IU/ml. Tg Ab reference range was <115 IU/mL. We used the reference range as cutoff for considering positive or negative.

Histopathology: All section was fixed in 10 % formalin and was sent for microscopic evaluation. After the histopathology result of 201 patients, 85 with malign pathology and 116 with benign nodules were assessed.

Statistical analysis: All continuous data were expressed as mean \pm standard deviation (SD). For categorical variables we used the chi-square test (χ^2) or Fisher's exact test. P value <0.05 were considered statistically significant.

Result:

Patient characteristics.

We investigated retrospectively 201 patients; 170 (84.5%) were females and 31 (15.5%) were males with mean age 45.6 ± 13.95 SD years with range (16-76).

Postoperative histopathologic diagnoses:

Postoperative histopathologic diagnoses are listed in table 1. From 201 patients 116 (57.7%) were diagnosed with benign tumors, and the remaining 85 (42.2%) were diagnosed with malignant pathology. PTC

accounted for the vast majority of the DTC diagnoses (95.1%, n =79). There was no difference in the sex ratio between patients with benign tumors and patients with DTC (97/19 for benign and 73/12 for malignant p=0.66). Patients with DTC were relatively

younger (43.2 ± 14.9 versus 48.4 ± 13.6 yr; $p=0.760$) and had higher preoperative median TSH levels (2.42 mIU/L versus 1.38 mIU/L; $p < 0.028$) than those with benign nodules.

Tab 1. Histopathological diagnosis and distribution according to the age and gender

Histopathologic diagnoses	Age	Gender	
	Year \pm SD (range)	Female n=170 (84.5 %)	Male n=31 (15.5%)
MNG	48.7 ± 13.6 (18-76)	77(84.6%)	14(15.3%)
Follicular adenoma	42.55 ± 12.3 (16-60)	19(86.3%)	3 (13.7%)
Graves Disease	2 ± 1	1 (50%)	1(50%)
Sub acute thyroiditis	41	0 (100%)	1 (100%)
Papillary thyroid cancer	43.2 ± 14.2 (16-71)	68 (85.8)	11(14.2%)
Follicular thyroid cancer	47.14 ± 17 (24-63)	4(100%)	0
Medullary thyroid cancer	51.5 ± 0.35 (51-52)	1 (50%)	1 (50%)

Solitary nodules were more common in patients with DTC (34/84, 40.4%) compared with patients with benign nodules (22/113, 19.4%; $p < 0.001$). These data suggest a higher risk of DTC in individuals with a solitary nodule. We also found that patients with TgAb concentration more than 115 IU/mL were more common in DTC group than in benign nodule group (28.2% versus 13%, $p < 0.007$), suggesting that elevated Tg Ab may associate DTC See tab 2. We than

calculated if the TgAb might be independent risk predictors for DTC. Binary logistic regression analysis (including gender, age, nodule type, serum TSH, TgAb ≥ 115 IU/mL) was conducted, and the odds ratio (OR) in favor of having DTC was calculated. As shown in Table 3, the prevalence of DTC was significantly associated with TgAb ≥ 115 IU/mL (OR=2.8, compared with TgAb < 115 IU/mL group).

Tab 2. Comparison of age, gender, positive serum Tg and solitary/multinodularity in benign versus malign pathology.

	Benign pathology Nr 116	Malign pathology Nr 85	P value
Age	47.3 ± 13.6	43.5 ± 14.9	0.918
Gender f/m	97/19	73/12	0.66
Positive Tg Ab	15 (13%)	24 (28.2%)	0.007
Solitary versus multinodularity	22/113	34/85	0.004
TSH	1.38	2.42	0.028

Discussion:

Conducting this retrospective study of 201 patients who underwent thyroidectomy we can say that the prevalence of DTC was higher in patients with elevated Tg Ab over 115 IU/mL. And further analysis revealed that Tg Ab over 115 might be a predictive risk factor for DTC independent of other risk factor like increased TSH, solitary versus multinodularity or decreased age. Azizi et al in a retrospective study suggested that the association between Hashimoto disease and thyroid cancer is antibody specific, serum TgAb concentration was elevated above the normal range in 20.6% (n=48) of the TC patients as compared with 10.17% (n=182) of the patients with benign nodule ($p < 0.0001$). In agreement with it, we also observed that elevated TgAb concentration is associated with high prevalence of DTC (28.2% versus 13%) (16). Many clinical factor like decreased of age, male, nodule size, single nodule, are recognized as risk factor for TC (17-19). We also observed that single nodule were more prevalent in TC than benign pathology, we didn't find any differences in DTC related to gender. Patients with DTC were relatively younger (43.2 ± 14.9 versus 48.4 ± 13.6 yr; $p = 0.760$) but it didn't reach statistically significant differences. Boelaert K et al reported for the first time that the risk of diagnosis of malignancy raises in parallel with the serum TSH concentration at presentation. In our study we reported that patients with DTC had higher mean level of TSH than patients with benign pathology (2.42 mIU/L versus 1.38 mIU/L; $p < 0.028$).

In conclusion we can conclude that high serum TgAb levels may serve as a predictive marker for DTC. Our data in agreement with other study suggests that elevated TgAb along with other risk factors, such as decreased age, single nodule, and elevated

TSH level, may provide useful information for the diagnosis and prognosis of DTC.

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