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Analysis of Incidental Thyroid Cancers in Surgically Treated Toxic Goiter Patients

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ABSTRACT

Differentiated Thyroid Cancer (DTC) is the most common endocrine cancer and the frequency of DTC detection in histopathological examinations in thyroid surgeries performed for non-cancer indications is increasing. The aim of this study is to investigate the rate of incidentally detected thyroid cancer in patients who underwent surgery for toxic goiter in our clinic.

Histopathological data of patients who underwent surgery with a diagnosis of toxic goiter were retrospectively reviewed. Patients were divided into 3 groups as toxic adenoma (TA), toxic multinodular goiter (MNG) and Basedow-Graves disease. The presence of malignancy and clinicopathological features were investigated

RESULTS: 84% of the cases were female and 16% were male, and the mean age was 43. 202 (65%) of the toxic goiter cases had TMG, 8 (3%) had TA, and 101 (32%) had Graves' disease. Histopathologically, the malignant/benign ratio was 65 (21%) / 246 (79%). Malignancy was detected in 3 of the 15 patients with a family history of thyroid cancer

Incidental thyroid cancer was detected in 65 (21%) of the patients with toxic goiter. Thyroid carcinoma was present in 45 (22%) of the patients with toxic MNG, 1 (12.5%) of the patients with TA and 19 (19%) of the patients with Graves. Histopathological examination revealed 62 papillary (38 microcarcinoma), 2 Non-invasive Follicular Thyroid Neoplasm with Papillary-like Nuclear Features (NIFTP) and 1 medullary microcarcinoma. The incidence of incidental thyroid cancer in the patients with toxic goiter treated with surgery was found to be consistent with the literature.

Keywords: Thyroid cancer, thyroid surgery, Graves' disease, toxic goiter, toxic adenoma

Introduction

Thyroid cancers constitute the most common endocrine cancer group and constitute approximately 95% of all endocrine cancers, and their frequency is increasing (1, 2). Toxic goiter is a common health problem in the world with a prevalence of up to 1.3% (3, 4). Historically, there was a belief that toxic goiter provided protection against the development of thyroid cancer (5, 6). The frequency of DTC in the hyperthyroid population has been reported as 0.027%, 1.63% and 3%, which are much lower than the rates seen in the population with general thyroid pathology (7, 8). Current studies indicate that malignancy rates in patients with toxic goiter are higher than previous reports (18.3%-42.8%) (9-11)(10-12). In this study, we aimed to contribute to the literature by sharing our incidental cancer results in patients who underwent surgery with a diagnosis of toxic goiter in our clinic.

Material and Methods

Patients who underwent thyroid surgery due to toxic goiter between January 2014 and October 2020, aged between 18 and 80, at the Department of General Surgery of Yüzüncü Yıl University Faculty of Medicine, were screened and patients who underwent bilateral total thyroidectomy and unilateral thyroidectomy (Hemithyroidectomy) were included in the study. Patients were divided into 3 groups as TA, Toxic MNG and Graves disease. Cases for which histopathological results were not reached were excluded from the study. The malignancy rates of patients with toxic goiter were compared with the data of patients with nontoxic goiter treated with surgery during the same period. The study was initiated with the decision number 11 dated 30.09.2020 of the Van YYU Faculty of Medicine Clinical Research Ethics Committee.

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Table 1: Demographic and Pathologic Characteristics of Cases

	Toxic MNG	Graves' disease	Toxic Adenoma	Total
Age, mean	47	37	37	
Gender				
Female	173	80	8	261
Male	29	21	0	50
PATHOLGOY				
Malignant	45(%22)	19(%19)	1(%12,5)	65(%21)
niftp	1		1	2
mkc	28	10		38
tpc	16	8		24
Medüller mkc		1		1
Benign	157(%78)	82(%81)	7(%87.5)	246(%79)
FNAB				
Yes	41	2	2	45
No	161	99	6	266
Total	202(%65)	101(%32)	8(%3)	311(%100)

Niftp: Noninvasive follicular neoplasm with papillary-like nuclear features, Mkc: Microcarsinom, Tpc: Thyroid papiller carsinom

Statistical Analysis: Descriptive statistics for the continuous variables were presented as Mean and Standard while count and percentages for categorical variables. Chi-square test was performed to determine the relationship between categorical variables. Statistical significance level was considered as 5% and SPSS (ver: 21) statistical program was used for all statistical computations.

Results

The total number of cases was 311 and female/male ratio was 261(83.92%)/50(16.08%) (Table 1). The cases were between 18-80 years and the mean of age was 43.03(Table 1). According to preoperative USG and laboratory data, 202 (65%) of the cases were toxic MNG, 8 (3%) were TA and 101 (32%) were Graves' disease. The malignant/benign ratio of toxic goiter cases was 65(21%) / 246(79%) (Table 1). The malignant/benign ratio in non-toxic MNG was 374(49%) / 395(51%) (Table 2). Thyroid carcinoma was present in 45 (22%) of toxic MNG patients, 1 (12.5%) of TA patients, and 19 (19%) of Graves patients (Table 1).

Histopathologically, cancer cases were observed to have 62 papillary carcinomas (38 microcarcinomas), 2 Non-invasive Follicular Thyroid Neoplasm with Papillary-like Nuclear Features (NIFTP) and 1 medullary microcarcinoma case (Table 1). Malignancy was found in 10% of males and 23% of females (Table 3). Malignancy was found in 20% under 50 years of age and 23% over 50 years of age (Table 5). There was no history of preoperative RAI or neck radiation. Malignancy was detected in 3 of 15 patients with a family history of thyroid cancer.

Discussion

In earlier studies, the frequency of cancer in patients with toxic goiter was reported to range between 0.15% and 3% (7, 8, 12, 13). These findings led to the belief that toxic goiter might provide some protection against thyroid cancer, explaining its lower incidence in this group. (5, 6). When we look at current data, there are different malignancy rates in hyperthyroid cases such as 5.8% (14), 8.3% (15) , 6.5% (16), 13.3% (17), 21.1% (18) and 22% (19). In our series, we found micro + macrocarcinoma to be 21% and macrocarcinoma to be 8%. There are many reasons why the malignancy rates in old and current data are so different. The surgical methods performed may cause different results. Because in the past, more conservative surgeries were performed whereas today, total or near-total thyroidectomy surgeries were performed, which affects the incidence of cancer. Nowadays, histopathological examinations performed by taking more sections and using different staining techniques also affect cancer incidence rates.

Histopathological findings of non-toxic goiter and toxic goiter can be compared, while in some

Table 2: Distribution of Toxic and Non-Toxic Goiter

	Toxic Goiter	Non-Toxic Goiter
Mean age	45	46
Gender		
Female	261	652
Male	50	117
Pathology		
MALIGNANT	65(%21)	374(%49)
niftp	2	14
mkc	38	147
tpc	24	197
Medüller mkc	1	
Squamous cell carcinoma		1
Medullary carcionma		6
Follicular carcinoma		6
Lymphoma		2
Anaplastic carcionma		1
BENİNG	246	395
FNAB		
yes	45	488
no	266	281

Table 3: Distribution of Toxic Goiter According To Gender

	Toxic MNG		Graves' disease		Toxic adenoma		Total		Total
Gender	Malignant	Benign	Malignant	Benign	Malignant	Benign	Malignant	Benign	
Male	2	27	3	18	0	0	5(%10)	45(%90)	50
Female	43	130	16	64	1	7	60(%23)	201(%77)	261
Total	45	157	19	82	1	7	65	246	311
p value	0,031		0,551		0,999		0,039		

publications it is seen that malignancy rates are close to each other. Also it is seen that there are more publications reporting higher malignancy rates in non-toxic goiter. Cerci et al. reported similar malignancy rates of 9% in toxic goiter and 10.58% in non-toxic goiter (6). In a meta-analysis, the rate of malignancy in toxic goiter was higher than expected, but the rates were lower compared with nontoxic goiter (20). Very different malignancy rates have been reported in non-toxic goiter. Ali et al. reported it as 15%(21), Naeem et al. reported it as 31.8%(22). The malignancy rate for toxic goiter was 21% and simultaneously 49% for nontoxic goiter in our study. The difference was statistically significant. The reason for this difference is that the indication for surgery in toxic goiter is usually toxic picture, while surgery in nontoxic goiter is usually due to malignancy or suspicion of malignancy.

According to subgroup analyses, malignancy rates in Graves' disease patients are seen as different values such as 6.5% (23), 12% (24), 3.8% (16) and 16% (19). There are current data indicating that thyroid cancer associated with Graves' disease is more aggressive (23, 25, 26). In our series, the micro and macrocarcinoma rate was 18.8% and the macrocarcinoma rate was 7.9%.

Cappelli reported a malignancy rate of 4.4% (23), Giles 12% (16) and Alvarez 50% for toxic adenoma, (19). In our series, the malignancy rate was found to be 12.5%. Cappelli reported a malignancy rate of 3.9%, Terzioğlu 5%, and Alvarez 24% for toxic MNG, (14, 23). In our series, the rate of malignancy was found to be

Tablo 4: Distribution of Toxic Goiter According To Age

	Toxic MNG		Graves' disease		Toxic Adenoma				Total
Age group	Malignant	Benign	Malignant	Benign	Malignant	Benign	Malignant	Benign	
Age 50 and under	27	87	12	73	1	4	40(%20)	164	204
Over 50 years old	18	70	7	9	0	3	25(%23)	82	107
Total	45	157	19	82	1	7	65	246	311
p value	0,584		0,005		0,686		0,439		

Tablo 5: Distribution According To The Presence of Toxic Goiter FNAB

	Toxic MNG		Graves' disease		Toxic Adenoma		Total	
FNAB	Malignant	Benign	Malignant	Benign	Malignant	Benign	Malignant	Benign
Yes	17	24	1	1		2	18(%40)	27(%60)
No	28	133	18	81	1	5	47(%18)	219(%82)
Total	45	157	19	82	1	7	65	246
p value	0,001		0,555		-		0,001	

22%. When subgroup analyses were examined, it was observed that our results were consistent with the literature.

Although it has been reported in the literature that male gender is a risk factor in toxic goiter (27), we found a higher rate of malignancy in female gender in toxic goiter patients and this difference was statistically significant (p=0.039).

Higher malignancy rates have been reported in toxic goiter patients aged 50 and over (16). In our study, when patients were divided into groups as over and under 50 years of age, malignancy rates were found to be 23% in those over 50 years of age and 20% in those under 50 years of age, as shown in Table 4. Although there was a significant difference (p=0.006) for Graves in the statistical analysis, no significant difference (p=0.439) was found in terms of age in the total of toxic goiter patients.

FNAB is a routine procedure that should be performed within the indication. Şahin and colleagues reported that they performed FNAB routinely and were able to diagnose all micro+macrocarcinomas preoperatively [28]. In our series, FNAB was applied to only 43 patients, and regardless of cytopathology, the malignancy rate was found to be 40% in individuals who underwent FNAB and 18% in individuals who did not undergo FNAB, and the difference was found to be statistically significant (p=0.001).

In conclusion, although the incidental malignancy rates in toxic goiter cases are lower compared to non-toxic goiter, they are higher than expected. In our study, our malignancy rates are consistent with the literature. We identified cases that underwent FNAB, female gender, and age over 50 as risk factors for malignancy. Our study showed that surgical treatment should be prioritized in patients with toxic goiter who have an indication for FNAB. More research is needed in this area to evaluate the different risks in patients with toxic goiter in more detail.

Conflicts of Interest: The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Patient Permission/Consent Declaration: Verbal consent was obtained from the cases included in the study by calling the contact numbers registered in the system.

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