BREAST CANCER AND FAMILY HISTORY FOR BREAST CANCER IN PATIENTS WITH DIFFERENTIATED THYROID CARCINOMA

DİFERANSİYE TİROİD KANSERLİ HASTALARDA MEME KANSERİ VE MEME KANSERİ İÇİN AİLE HİKAYESİ

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ABSTRACT

INTRODUCTION: The risk for breast cancer in patients with thyroid cancer has been investigated in previous studies, and has been found to be increased. In this study, we present a retrospective analysis of patients with differentiated thyroid carcinoma in respect to breast cancer and family history of breast cancer.

METHODS: We conducted a retrospective study involving 455 patients who were diagnosed as having differentiated thyroid carcinoma between January 2009 and March 2016.

RESULTS: The majority of the patients were female (403, 88.6 %). The mean age at diagnosis was 45.5 ± 12.8 years (range, 10-81 years). We detected that 0.7 % of patients with thyroid cancer had breast cancer and 13.4 % of patients had a family history of breast cancer within 3 generations of the proband. There were no significant differences between family history of breast cancer and sex, age at diagnosis, pathologic types, and radioiodine therapy.

CONCLUSION: In the literature, there are many clinical, epidemiologic, and experimental studies that show an association between thyroid cancer and breast cancer. Our study is the first report to show history of breast cancer and family history of breast cancer as 0.7 % and 13.4 % in this particular group of Turkish patients with differentiated thyroid cancer.

Key words: *Breast cancer, thyroid cancer, family history for breast cancer.*

ÖZET

AMAÇ: Tiroid kanserli hastalarda meme kanseri riskini araştıran ve artış olduğunu gösteren çalışmalar mevcuttur. Bu çalışmada, diferansiye tiroid kanserli vakalarda meme kanseri varlığı ve ailede meme kanseri hikayesinin varlığı retrospektif olarak araştırıldı.

YÖNTEM: Ocak 2009 - Mart 2016 tarihleri arasında diferansiye tiroid kanseri tanısı alan 455 hastanın retrospektif olarak değerlendirilmesi yapıldı.

BULGULAR: Hastaların çoğunluğu kadındı (403, %88.6). Tanı sırasındaki ortalama yaş 45.5 ± 12.8 yıl (dağılım 10-81 yıl) idi. Tiroid kanserli hastaların %0.7'sinin meme kanseri olduğunu ve %13.4 'ünde ailede geriye doğru 3 kuşakta meme kanseri öyküsü olduğunu tespit ettik. Ailede meme kanseri öyküsü ile cinsiyet, tanı yaşı, patolojik alt tipler ve radyoiyot tedavisi arasında anlamlı fark saptanmadı.

SONUÇ: Literatürde tiroid kanseri ile meme kanseri arasında ilişki olduğunu gösteren bir çok klinik, epidemiyolojik ve deneysel çalışma bulunmaktadır. Çalışmamız, diferansiye tiroid kanserli Türk hasta grubunda meme kanseri öyküsü ve ailede meme kanseri öyküsünü sırayla %0.7 ve%13.4 olarak gösteren ilk rapordur.

Anahtar Kelimeler: *Meme kanseri, tiroid kanseri, ailede meme kanseri hikayesi*

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INTRODUCTION

Differentiated thyroid carcinoma is the most common endocrine malignancy and its incidence is increasing worldwide (1, 2). Differentiated papillary and follicular histologies account for approximately 90% of thyroid carcinoma cases and have 5-year and 10-year survival rates of 95-97 % (3). It is well known that thyroid carcinoma is sex biased and it mostly affects the female population. In the literature, breast cancer is the most frequently diagnosed malignancy in women (4). The association between the incidence of thyroid cancer and breast cancer has been reported previously. The risk for breast cancer in patients with thyroid cancer has been investigated in many studies (5-8), and has been found increased. The possible causes for the increased risk of breast cancer in patients with thyroid cancer remain unclear. The cause may include various factors such as exposure to ionizing radiation from radioiodine (RAI) therapy, genetic predisposition, and hormonal or environmental factors (9-12). In this study, we present a retrospective analysis of 455 patients with differentiated thyroid carcinoma in respect to breast cancer and family history of breast cancer.

MATERIALS and METHODS

Study Population

We conducted a retrospective study involving 455 patients who were diagnosed as having differentiated thyroid carcinoma between January 2009 and March 2016. No patients had a history of thyroid or neck surgery for non-thyroidal cancer or neck irradition. Medical records, radiologic and pathologic reports were analyzed. Papillary thyroid carcinomas measuring 10 mm or less in diameter were classified as papillary thyroid microcarcinoma (PTMC). Data points collected included: age at diagnosis (≥45 vs. < 45 years), sex, family history of both breast and thyroid cancer, preoperative clinical suspicion of cancer in ultrasonography (USG) findings, pathologic types, tumor size, multifocality, chronic lymphocytic thyroiditis, extrathyroidal extension, central or lateral lymph nodes with metastatic carcinoma, distant metastasis, type of surgery (thyroidectomy with or without central lymph node dissection), RAI treatment, thyroid-stimulating hormone (TSH), thyroglobulin (TG), thyroid globulin antibody (TGAb), and thyroid peroxidase antibody (TPOAb). Tumor size was defined as the largest dimension. Multifocality was defined as greater than 1 focus of tumor within the thyroid.

Statistical Analysis

Statistical analyses were performed using SPSS version 18.0 (SPSS Inc., Chicago, IL, USA). Data with normal distribution are expressed as mean ± SD and were compared using t-test. Categorical variables are expressed as percentage and were compared using the Chi-square test or Fisher's exact test, as appropriate. Non-parametric variables were analyzed using the Mann-Whitney U test. In the statistical analyses, $p<0.05$ value was considered significant.

RESULTS

The study population included 455 patients, the majority of whom were female (403, 88.6 %). The mean age at diagnosis was 45.5 ± 12.8 years (range, 10-81 years) and 240 patients (52.7 %) were aged ≥ 45 years. **Table 1** lists the demographic characteristics of the study population.

We detected that 0.7 % patients with thyroid cancer had breast cancer, and 13.4 % patients had a family history of breast cancer within 3 generations of the proband. In three patients who had both thyroid and breast cancer, two had primary breast cancer first followed by thyroid cancer, and one had primary thyroid cancer first followed by breast cancer. In addition, among these three patients, two had a family history of breast cancer, one had an aunt with breast cancer, and the other had a sister with breast cancer. There were no significant differences between family history of breast cancer and sex, age at diagnosis, pathologic types, and RAI therapy.

Table 1 Patient Characteristics

Variable	N=455
Sex (n, %)	
Female	403, 88.6
Male	52, 11.4
Age at diagnosis (mean±SD)	45.5 ± 12.8
Age (n, %)	
< 45 years	215, 47.3
≥ 45 years	240, 52.7
Follow-up time (months)	1-264 (24)
Pathologic types (n, %)	
Papillary carcinoma (PTC)	191, 42.0
Papillary microcarcinoma (PTMC)	229, 50.3
Follicular carcinoma (FC)	15, 3.3
WDTN-UMP[1]	6, 1.3
PTC and FC	5, 1.1
PTMC and WDTN-UMP	5, 1.1
PTMC and FC	3, 0.7
PTC and WDTN-UMP	1, 0.2
Second primary malignancy (n,%)	
Breast cancer	3, 0.7
Renal cell cancer	2, 0.4
Colon cancer	2, 0.4
Endometrial cancer	1, 0.2
Parathyroid cancer	1, 0.2
Family history of breast cancer (n, %)	61, 13.4
Family history of thyroid cancer (n, %)	41, 9.0
RAI therapy (n, %)	
Absent	119, 26.2
Present	336, 73.8

[1]WDTN-UMP: Well-differentiated thyroid neoplasms of uncertain malignant potential.

Among 455 patients with differentiated thyroid cancer, we evaluated 186 patient's long-term follow-up data **(Table 2).**

Table 2 Clinicopathologic Characteristics and Long-term Follow-up Results of 186 Patients with Differentiated Thyroid Cancer

Variable	N=186
Sex (n,%)	
Female	160, 86.0
Male	26, 14.0
Age at diagnosis (mean±SD)	46.4 ± 13.2
Age (n,%)	
< 45 years	86, 46.2
≥ 45 years	100, 53.8
Body mass index (kg/m²)	28.9 ± 5.1
Diabetes mellitus (n, %)	37, 19.9
Clinical suspicion on preoperative USG (%)	37.1
Second primary malignancy (n, %)	
Breast cancer	1, 0.5
Renal cell cancer	2, 0.5
Colon cancer	2, 0.5
Family history of breast cancer (n, %)	17, 9.1
Family history of thyroid cancer (n, %)	19, 10.2
Preoperative TSH level (μU/mL)	0.01-27.3 (1.6)
Pathologic types (n, %)	
Papillary carcinoma (PTC)	74, 39.8
Papillary microcarcinoma (PTMC)	98, 52.7
PTMC and FC	3, 1.6
WDTN-UMP	1, 0.5
PTC and FC	1, 0.5
PTC and WDTN-UMP	1, 0.5
PTC variant (%)	
Follicular	19.4
Classic	18.8
Tumor size (cm)	0.1-6.8 (0.9)
Presence of multifocality (n, %)	44.1
Presence of extrathyroidal extension (n, %)	4.8
Presence of chronic lymphocytic thyroiditis (%)	36.6
Surgical treatment (n, %)	
Total or near-total thyroidectomy	185, 99.5
Lobectomy	1, 0.5
Central lymph node dissection	54, 29.0
Lateral lymph node dissection	7, 3.8
RAI therapy (n, %)	
Absent	55, 29.6
Present	131, 70.4
Postoperative permanent hypoparathyroidism (n, %)	20, 10.8
Distant metastasis (n, %)	1, 0.5
Lymph node metastasis (n, %)	20, 10.8
Follow-up time (months)	1-264 (21.5)

Of all 186 patients, 61 (32.8 %) had lymph nodes removed, 15 (24.5 %) had central lymph node metastasis only, and 5 (8.2 %) had both central and lateral lymph node metastasis. According to the clinicopathologic characteristics and long-term follow-up period there was no differences among patients with and without family history of breast cancer in either the univariate or multivariate logistic regression analyses.

DISCUSSION

In this study, 0.7 % of the patients with thyroid cancer were diagnosed as having second primary breast cancer. We also found that 13.4 % of the patients with thyroid cancer had a family history of breast cancer. As reported, there are many clinical, epidemiological, and experimental studies that show an association between thyroid cancer and breast cancer (7, 13-15). Moreover, an increased risk of thyroid cancer was reported in individuals with history of breast cancer (15-17). An et al. (7) reported that 4.3 % of patients with thyroid cancer and 2.6 % of those with breast cancer were diagnosed as having second primary or concomitant breast cancer and thyroid cancer, respectively. Another study by Zhang et al. (15) showed that the overall risk of occurrence of a second primary thyroid cancer or breast cancer was highly elevated in patients with breast cancer or thyroid cancer.

Several recent studies concluded that thyroid cancer and breast cancer are closely related; however, the exact mechanisms that bind thyroid cancer and breast cancer have not yet been clearly identified. Nielsen et al.(18) reviewed thyroid cancer and breast cancer survivors received an increased surveillance in the form of clinical examinations and imaging, and it may be that the increase in surveillance is responsible for the higher rates of thyroid cancer or breast cancer detection. Previous studies also suggested a role for hormone receptors in the molecular pathogenesis of thyroid cancer. Estrogen, progesterone, and androgen receptors have been shown to be expressed in both normal and malignant thyroid tissue (19). Additionally, estrogen receptor levels are significantly higher in thyroid cancer compared with normal thyroid tissue (20). In our study, we did not the evaluate the hormone receptor situation in our three patients with thyroid and breast cancer and 67 family members with breast cancer.

In the literature, many previous studies demonstrated an increased prevalence of autoimmune thyroid disease in patients with breast cancer (21-23). Our study also investigated the presence of lymphocytic thyroiditis in patients with thyroid cancer. We were unable to detect a significant association between lymphocytic thyroiditis and family history for breast cancer using both univariate and multivariate analyses. Additionally, we observed that there was no significant association between the prevalence of anti-TPOAb and family history of breast cancer in patients with thyroid cancer.

Obesity has been associated with increased incidence of thyroid and breast cancer (18, 24). In our study, the majority of patients were overweight with a mean body mass index (BMI) of 28.9 ± 5.1 kg/m². We were unable to detect a significant difference between BMI and family history of breast cancer.

Some treatment characteristics affect the risk profiles for developing subsequent primary breast or thyroid cancer such as RAI therapy. An increased risk of second primary malignancy after RAI treatment has been reported (25). Lin et al. (26) showed that patients with thyroid cancer treated with RAI had a significantly increased risk of breast cancer compared with controls. In our study, 73.8 % patients were treated with RAI and we were unable to detect a correlation between second primary breast cancer and RAI treatment.

This study has limitations. Evidence derived from a retrospective cohort study is generally lower in statistical quality because of many biases and the necessary adjustments for confounding factors.

CONCLUSION

Our study is the first report to show the history of breast cancer and family history of breast cancer as 0.7 % and 13.4 % in this particular group of Turkish patients with differentiated thyroid cancer. We still need further studies to identify a subgroup of patients with higher risk of breast cancer in patients with thyroid cancer.

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