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ORIGINAL ARTICLE

Is There any Association between Thyroid Autoimmunity and Breast Cancer?

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ABSTRACT

Background: The relationship between thyroid autoimmunity and breast cancer is a challenging subject. We aimed to investigate this association in women with breast cancer.
Methods: In this descriptive study, 41 women with newly diagnosed breast cancer before receiving any pharmacologic treatment and 38 healthy age-matched women were enrolled. Anti TPO Ab(anti-thyroid peroxidase antibodies), FT4(free thyroxine), T3(triiodothyronine) and TSH (thyroid-stimulating hormone) were measured in both groups.
Results: The mean±SD ages in patients with breast cancer and the control group were 41.71±1.73 and 40.03±1.74 years, respectively (P=0.496). There was no statistically significant difference between the mean values of FT4 and T3 in patients with breast cancer (P=0.447) and the control group (P=0.534). The mean TSH level in patients with breast cancer was 4.9±1.7 µIU/ml which was significantly higher than healthy women (1.79±0.15 µIU/ml, P=0.004). The frequency rate of the increased Anti TPO Ab levels (higher than 35 IU/ml) in women with breast cancer was 22% which was significantly higher than the control group (%0, P=0.002), while no statistically significant difference was found between the mean Anti TPO Ab levels between the two groups (61.07±29.73 versus 9.78±0.78, P=0.21). Four cases of subclinical and/or overt hypothyroidism were found in women with breast cancer.
Conclusion: Based on our findings breast cancer patients have higher rates of thyroid autoimmunity. Measurement of FT4 and T3 in all women with breast cancer is not recommended but measurement of TSH and Anti TPO Ab levels seem reasonable.

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Introduction

Breast cancer (BC) is one of the most prevalent malignancies worldwide and also Iran.[1,2] A variety of hereditary, environmental, reproductive and hormonal factors have been proposed in the pathogenesis of BC; although in most of cases the exact etiologic factor has not been well understood.[1,3,4] The relationship between thyroid autoimmunity and BC is a challenging subject. The findings of some studies were in favor of this association but others did not support this idea.[5-8] We designed this study in order to investigate the association between thyroid autoimmunity and BC.

Patients and Methods

In this descriptive study, 41 women aged 20-70 years with newly diagnosed BC who had been referred to the Oncology Clinics of Urmia city or those who had been admitted to Emam Khomeini Hospital of Urmia and had not taken any chemo-radiation therapy previously were enrolled. 38 age-matched healthy women who did

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not have any history of thyroid or breast diseases were selected as the control group. Subjects with history of nephrotic syndrome, liver or renal failure, hysterectomy, oophorectomy, thyroidectomy or previously known thyroid diseases and those who had received levothyroxine, anti-thyroid drugs, Tamoxifen and other hormonal drugs were excluded.

The study was approved by the Ethic Committee of Urmia University of Medical Sciences. In all subjects after obtaining written informed consent, venous blood samples were taken and free thyroxine(FT4), T3(triiodothyronine) and TSH (thyroid-stimulating hormone) were analyzed by ELISA(enzyme-linked immunosorbent assay) method (Pishtazteb kite, Tehran, Iran). Anti TPO Ab was measured using ELISA method (Monoind kite, USA). The normal range of Anti TPO Ab was less than 35 IU/ml and levels higher than 35 IU/ml were in favor of thyroid autoimmunity. The reference ranges of FT4, T3 and TSH hormones were 0.7-1.8 ng/dl, 0.8-2.1 ng/ml and 0.3-5.5 µIU/ml respectively. Postmenopausal women had not menstruated for at least six months prior to the study.

The patients' information including demographic findings, menopausal status and laboratory tests results were recorded and data were analyzed using SPSS software, version 16. Also, *t*, Mann-Whitny U, Fisher, and Pearson's Chi-square tests were used as appropriated. P<0.05 was considered as significant.

Results

The mean±SD aged of patients with BC and the control group were 41.71±1.73 and 40.03±1.74 years, respectively (P=0.496). As shown in Table 1, 36.8% of patients with BC and 41.46% of healthy women were in the postmenopausal state (P=0.674). There were no significant differences between the mean values of FT4 and T3 in patients with BC (P=0.447) and the control group (P=0.534). The mean±SD TSH level in patients with breast cancer was significantly higher than healthy women (4.9±1.7 µIU/ml *vs.* 1.79±0.15 µIU/ml, P=0.004).

The percentage of women with abnormal TSH levels including higher than 5.5 µIU/ml and lower than 0.3 were 9.8% and 2.4% respectively in patients with BC, whereas no woman with abnormal TSH level was found in the control group (P=0.084).

The frequency rate of the increased Anti TPO Ab levels (higher than 35 IU/ml) in women with breast cancer was 22% which was significantly higher than healthy women (%0, P=0.002) but no statistically significant difference was found between the mean values of Anti TPO Ab between patients with BC and the control group (61.07±29.73 versus 9.78±0.78, P=0.21).

Table 2 shows the percentage of subjects with normal, increased and decreased concentrations of FT4 and TSH in patients with BC (P=0.168) and healthy women (P=0.084). Among the four patients with BC with high TSH levels, two cases of subclinical hypothyroidism (increased TSH and normal FT4 levels) and two cases of overt hypothyroidism (increased TSH and low FT4 levels) were detected. All patients in both groups had normal T3 levels.

Discussion

In this study, although the mean values of thyroid hormones (FT4 and T3) and Anti-TPO Abs did not differ in women with BC and healthy controls, the prevalence of elevated Anti-TPO Ab (more than 35 IU/ml) was significantly higher in women with BC. Women with BC had higher TSH titers than healthy women. We also found four patients with hypothyroidism (subclinical and/

Table 1: Demographic characteristics and thyroid function tests of women with breast cancer and healthy women

Variable	Patients with breast cancer (n=41)	Healthy women (n=38)	P value
Age (years)	41.71±1.73	40.03±1.74	0.496
Menopause (%)	14(36.8%)	17(41.46%)	0.674
TSH (µIU/ml)	4.9±1.7	1.79±0.15	0.004
FT4 (ng/dl)	1.23±0.04	1.27±0.03	0.447
T3 (ng/ml)	1.16±0.04	1.13±0.04	0.534
Anti TPO Ab (IU/ml)	61.07±29.73	9.78±0.78	0.21
Anti TPO>35 IU/ml	9(22%)	0(0%)	0.002

Data are expressed as mean ± SE (Standard error), FT4 (free thyroxine), T3 (triiodothyronine), TSH (thyroid-stimulating hormone), Anti TPO Ab (anti-thyroid peroxidase antibodies)

Table 2: Comparing thyroid function tests between women with breast cancer and healthy women

Variable		Breast cancer (n=41)	Control group (n=38)	P value
TSH	Increased	4(9.8%)	0(0%)	0.084
	Decreased	1(2.4%)	0(0%)	
	Normal	36(87.8%)	38(100%)	
FT4	Increased	0(0%)	0(0%)	0.168
	Decreased	2(4.9%)	0(0%)	
	Normal	39(95.1%)	38(100%)	

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or overt) in patients with BC.

While limited studies did not find any association between thyroid autoimmunity and BC[6,9,10] growing evidence has demonstrated this relationship.[11-16]In a study by Jiskra and co-workers, the prevalence of increased levels of Anti-TPO Abs and anti thyroglobin antibodies (Anti Tg Abs) were significantly higher in women with breast cancer compared to those women with colorectal malignancies and women without cancer.[14]

In a prospective study by Giani and colleagues, the researchers found that the prevalence of thyroid diseases especially Hashimoto thyroiditis and nontoxic goiter was significantly higher in women with BC compared with healthy women. However they did not find any significant difference between mean values of FT4, FT3 and TSH in women with BC and the control group.[11]

In another study by Turken and colleagues, although no significant difference was seen in mean FT4, FT3, TSH levels and Anti Tg Abs between women with BC and healthy controls, the mean Anti-TPO Abs levels was significantly higher in patients with BC. Higher frequency of autoimmune thyroiditis and goiter was also found in patients with BC.[8]

Gogas and colleagues also found higher incidence of thyroid autoimmunity in patients with BC.[13]

Giustarini et al observed significant relationship between BC and thyroid autoantibodies and they recommended evaluation of autoimmune thyroid diseases in patients with nodular breast disease before surgery for earlier diagnosis and treatment of hypothyroid state.[12]

Studies by Rasmusson[15] and Shering[16] and co-workers have also supported the hypothesis of relationship between thyroid autoimmunity and breast cancer.

In some studies BC patients with increased TPO Abs had favorable outcome.[17] Although the precise mechanism by which thyroid autoimmunity plays a role in BC pathogenesis is unknown, but similar abilities of thyroid follicles and breast epithelial cells for concentration of iodine via natriume iodide symporter expression, existence of TSH receptors in the breast tissue, interaction of thyroid autoantibodies with receptors of breast neoplasms and thyroid releasing of some hormonal and growth factors that affect mammary glands are some possible explanations.[11,13,14,18]

Jiskra and colleagues suggested that increased iodine intake in breast tissue stimulates thyroid autoantibodies and has a favorable influence on patients survivals and response to treatment. In their study TSH levels greater than 3.5 mIU/l were associated with lower carcinoembryonic antigen levels in patients with BC.[14]

One of the limitations of this study was the small sample size and we cannot definitely support the association between thyroid dysfunction and breast cancer.

Conclusion

Based on our result, thyroid autoimmunity may be associated with breast cancer and women with BC have higher rates of positive Anti TPO Abs compared to healthy women. We do not recommend routine measurement of FT4 and T3 in BC patients, but measurement of TSH and Anti TPO Ab levels seems reasonable in these individuals for earlier discovering of autoimmune thyroid dysfunction. We also suggest further research to investigate the role of thyroid autoantibodies in predicting breast cancer outcome.

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Conflict of Interest: None declared.

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