Synchronous Papillary Thyroid Carcinoma and Breast Ductal Carcinoma: A Case Report

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Abstract
Breast cancer was the most frequent cause of cancer-induced death among middle-aged (20-59) women in the last decade. In contrast, the incidence rates of thyroid cancer have begun to stabilize in recent years. The synchronous neoplasms of thyroid and breast cancers are very rare in clinical settings. The current study presented a case of synchronous Papillary Thyroid Carcinoma (PTC) and breast ductal carcinoma in a 37-year-old woman. It is proposed that the mechanism of these synchronous primary tumors is associated with an interaction between the breast and thyroid hormonal responses. It is essential to examine breast tissue in patients with thyroid carcinoma or vice versa. In our case, although axillary sentinel lymph node was free from the tumor, cervical lymph nodes were involved by breast carcinoma; suggesting the importance of cervical examination in breast cancer patients.

Introduction
Breast cancer is the most prevalent cause of cancer-induced death in middle-aged (20-59) women in the last decade. The incidence rate of breast cancer has slightly increased from 2005 to 2014 [1]. In contrast, the incidence rate of thyroid cancer has begun to stabilize in recent years. This is in the wake of changes in clinical practice guidelines that include more conservative indications for biopsy and the reclassification of noninvasive follicular thyroid neoplasm with papillary-like nuclear features [2].

The incidence of purely synchronous lesions (diagnosed concurrently) in patients with cancer is approximately 9% [3]. Overall synchronous neoplasms of thyroid and breast cancer are very rare in clinical settings. There appears to be an increased risk of breast cancer in women with thyroid cancer; however, it is unclear whether this

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is due to screening bias, Radioactive Iodine (RAI) therapy, or other factors [4].

A population-based retrospective cohort analysis was conducted by Chen and associates. Accordingly, they identified that females with a history of thyroid carcinoma present an increased risk of developing breast cancer, particularly premenopausal Caucasian females [5].

The breast and the thyroid are endocrine organs, i.e. involved in hormonal responses. Thus, the mechanism of these synchronous primary tumors is associated with an interaction between the breast and thyroid hormonal responses [6]. Wang et al. reported that RET/PTC kinase is not only a proto-oncogene highly-expressed in Papillary Thyroid Carcinoma (PTC), but also involved in breast cancer growth, prognosis, and tamoxifen resistance; thus, there seems to be a correlation between these cancers in oncogenesis [7].

Few articles provided case reports of synchronous thyroid and breast cancer. Thyroid cancer in one case report was an incidental finding in an 18F-FDG PET-CT study conducted in a search for occult breast cancer [8]. Liliu et al. also reported the case of a 41-year-old female exhibiting synchronous primary cancers of the thyroid and breast [6].

Another case was reported in 2017 by Zhong et al.; she was a 61-year-old female who was diagnosed with synchronous primary PTC and breast ductal cancer [9]. Here, we reported a rare case of a 37-year-old Iranian woman who was diagnosed with synchronous primary PTC and breast ductal cancer.

Case Presentation

In September 2018, a 37-years-old female was admitted to Sina Hospital in Tehran City, Iran. She was admitted following the thyroid nodule fine-needle aspiration and breast sonography at her local hospitals. The patient presented no medical history; however, she had a family history of thyroid cancer (her mother).

The first chief complaint was feeling a mass in her neck. All thyroid function tests were normal. She underwent cervical sonography in May 2018 which indicated multiple thyroid nodules in both lobes with a maximum diameter of 17 mm in the left lobe and multiple reactive-like right cervical lymph nodes. Then, in June 2018, she underwent the fine-needle aspiration of the right thyroid firm nodule, i.e. reported as suspicious for PTC (Bethesda V). At that time, she had finished the lactation period and noticed that her right breast is remaining to enlarge.

The workup ultrasound breast sonography revealed one lobulated well-defined lesion M: 19 × 17 mm in the right breast; 7 o’clock, no axillary lymphadenopathy. Mammography (Figure 1) was then performed for the patient; accordingly, it reported an irregular bordered mass in the upper outer quadrants of the right breast (BIRADS 4c). Next, the patient underwent breast lesion

Figure 1. The mammography images of the right breast, showing an irregular outline mass in the UOQ of the right breast.
core needle biopsy in our center and specimen submitted to our pathology department which reported an invasive ductal carcinoma (nuclear grade II).

After her admission to our hospital, such workups as cervical sonography were repeated. The related data reported further details. We noticed that some lymph nodes were solid-cystic with a maximum diameter of $15 \times 8$ mm in the right side, zone IV, suggestive of lymphadenopathy in the field of PTC, also some right supraclavicular lymphadenopathy with hypo echo pattern and a maximum diameter of $16 \times 8$ mm in the field of breast cancer. She was concurrently operated in the surgery department of Sina Hospital (Tehran, Iran) for total thyroidectomy and right lymph node dissection zone (II-V) as well as breast mass lumpectomy. During operation, the frozen section study of axillary sentinel lymph nodes was performed, in which all three lymph nodes were free from tumor.

The macroscopic and microscopic examination of all specimen’s revealed the invasive ductal carcinoma of the right breast, NOS type (Figure 2) M:3.5 $\times$ 2.5 in greatest dimensions with Nottingham score II/III and free margins plus multifocal PTC of the right and left lobes; classic and follicular variant (Figure 3) with the greatest dimension of 1.3 in the right lobe (PT2), 11 out of 14 dissected lymph nodes (right, level II-V) were involved by the breast carcinoma and one lymph node (level II-IV) was involved by thyroid carcinoma (Figure 4). Breast cancer cells immunohistochemistry study on metastatic lymph node indicated ER+, PR+, and GCDFP-15+ (Figure 5).

The patient was referred to a surgeon and oncologist for continued treatment. The treatment program included chemotherapy, radiotherapy, and iodine therapy.

**Discussion**

Breast carcinoma and thyroid carcinoma are the two most common malignancies that occur in women. Breast cancer is the most frequent second primary cancer among thyroid cancer survivors, followed by renal cell cancer [10].

The analysis of the USA National Cancer Institute's Surveillance, Epidemiology, and End Results data has
demonstrated that the incidence of thyroid cancer is higher in patients with a pre-existing malignancy than in patients without a preexisting malignancy. Furthermore, the incidence of other malignancies is higher in patients with thyroid cancer, compared to patients without thyroid cancer. Reports suggested that a unidirectional or bidirectional association may exist between thyroid and breast cancer [11].

Wang et al. reported that RET/PTC kinase is not only a proto-oncogene highly-expressed in PTC, but also is involved in breast cancer growth, prognosis, and tamoxifen resistance; thus, there seems to be a correlation between these cancers in oncogenesis. They demonstrated that RET/PTC kinase is a critical regulator for the proliferation of ER-positive breast cancer cells. Accordingly, RET/PTC kinase may serve as a novel prognostic biomarker and therapeutic target for the prevention and treatment of ER-positive breast cancer [7]. This therapeutic target can be a better immunotherapeutic intervention in patients with synchronous PTC and breast carcinoma with RET/PTC kinase.

Conclusion

In the presented case, although the breast mass was located in the upper outer quadrant of the right breast, and sentinel axillary lymph nodes were free from the tumor; however, the patient had right cervical lymph nodes metastasis by breast cancer cells. Thus, physicians should pay attention to the examination of the neck and cervical region for lymphadenopathy in patients with breast cancer. The synchronous primary tumors of the thyroid and breast are very rare, but they remain a possibility; therefore, more attention should be paid to these cases.

Ethical Considerations

Compliance with ethical guidelines

All ethical principles are considered in this article. The patient was assured about the confidentiality of her information.

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Conflict of interest

The authors declared no conflict of interest.

References

[1] Seigel R, Miller K, Jemal A: Cancer Statistics 2018. CA: A Cancer Journal for Clinicians. 2018; 68(1):7-30. [DOI:10.3322/caac.21442] [PMID]

[2] Morris LG, Tuttle RM, Davies L. Changing trends in the incidence of thyroid cancer in the United States. JAMA Otolaryngol Head Neck Surgery. 2016; 142(7):709-11. [DOI:10.1001/jamaoto.2016.0230] [PMID] [PMCID]

[3] Bittorf B, Kessler H, Merkel S, Brückl W, Wein A, Ballhausen WG, et al. Multiple primary malignancies: An epidemiological and pedigree analysis of 57 patients with at least three tumours. European
Journal of Surgical Oncology. 2001; 27(3):302-13. [DOI:10.1053/ ejso.2001.1112] [PMID]

[4] Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Niki- forov YE, et al. 2015 American Thyroid Association Management Guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: The American Thyroid Association Guidelines task force on thyroid nodules and differentiated thyroid cancer. Thyroid. 2016; 26(1):1-133. [DOI:10.1089/thy.2015.0020] [PMID] [PMCID]

[5] Chen AY, Levy L, Goepfert H, Brown BW, Spitz MR, Vassilopoulou- Sellin R. The development of breast carcinoma in women with thyroid carcinoma. Cancer. 2001; 92(2):225-31. [DOI:10.1002/1097- 0142(20010715)92:2<225::aid-cncr13113>3.0.co;2-b] [PMID]

[6] Liu L, Shi J, Mao F, Wei J, Fu D, Zhang J. Synchronous primary cancers of the thyroid and breast: A case report and review of the literature. Oncology Letters. 2015; 9(1):351-4. [DOI:10.3892/ol.2014.2625] [PMID] [PMCID]

[7] Wang C, Mayer JA, Mazumdar A, Brown PH. The rearranged during transfection/Papillary Thyroid Carcinoma tyrosine kinase is an estrogen-dependent gene required for the growth of estrogen receptor positive breast cancer cells. Breast Cancer Research and Treatment. 2012; 133(2):487-500. [DOI:10.1007/s10549-011-1775-9] [PMID] [PMCID]

[8] Banzo J, Ubieto MA, González C, Razola P, Tardín L, Andrés A, et al. Papillary Thyroid Carcinoma synchronous with breast cancer: An incidental finding in an (18) F-FDG PET-CT study carried out in a search for occult breast cancer. Revista Española de Medicina Nuclear e Imagen Molecular. 2012; 31(4):213-5. [DOI:10.1016/j.remn.2011.11.009] [PMID]

[9] Zhong J, Lei J, Jiang K, Li Z, Gong R, Zhu J. Synchronous Papillary Thyroid Carcinoma and breast ductal carcinoma: A rare case report and literature review. Medicine (Baltimore). 2017; 96(7):e6114. [DOI:10.1097/MD.0000000000006114] [PMID] [PMCID]

[10] Garner CN, Ganetzky R, Brainard J, Hammel JP, Berber E, Siperstein AE, et al. Increased prevalence of breast cancer among patients with thyroid and parathyroid disease. Surgery. 2007; 142(6):806-13. [DOI:10.1016/j.surg.2007.07.024] [PMID]

[11] Van Fossen VL, Wilhelm SM, Eaton JL, McHenry CR. Association of thyroid, breast and renal cell cancer: A population-based study of the prevalence of second malignancies. Annals of Surgical Oncology. 2013; 20(4):1341-7. [DOI:10.1245/s10434-012-2718-3] [PMID]