

# Synchronous papillary thyroid carcinoma and breast ductal carcinoma

## A rare case report and literature review

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### Abstract

**Background:** The incidences of both thyroid cancer and breast cancer have been rising in recent years; however, it is very rare to find a single person with both of these cancers. Only a few cases of synchronous thyroid and breast cancer have been published, and even fewer cases have been reported in older patients (>60 years).

**Case summary:** The current study presents a case of synchronous papillary thyroid carcinoma and breast ductal carcinoma in an elderly patient. The patient first underwent a mastectomy and axillary lymphadenectomy in our department, followed by a total thyroidectomy and lymphadenectomy of the left lateral region of the neck 1 month later. Postoperative pathological examination identified invasive ductal carcinoma of the breast and papillary carcinoma of the thyroid. Over almost half a year of follow-up, the patient has exhibited no evidence of recurrence or metastasis, as demonstrated by careful ultrasound examinations. Herein, we not only report this case but also present a systematic review of the causes, diagnosis, and treatment of synchronous breast and thyroid cancer.

**Conclusion:** Although synchronous primary tumors of the thyroid and breast are very rare, they remain a possibility; therefore, more attention should be paid to these cases.

**Abbreviations:** CK = cytokeratin, ER = estrogen receptor, FAD = flavin adenine dinucleotide, FNA = fine needle aspiration, GCDFP = gross cystic disease fluid protein, HBME = human bone marrow endothelial, Her = human epidermal growth factor receptor, NAD = nicotinamide adenine dinucleotide, PR = progesterone receptor, TG = thyroglobulin, TTF = thyroid transcription factor.

**Keywords:** breast, case report, ductal carcinoma, papillary, thyroid carcinoma

## 1. Introduction

Although differentiated thyroid and breast cancer carry a lower risk of death or disease recurrence than other malignancies, their incidences have been steadily increasing for at least 2 decades<sup>[1]</sup>, and they have become the most common malignancies in females.<sup>[2,3]</sup> However, synchronous (diagnosed at the same time) neoplasms of the thyroid and breast are rare in the clinic. The first

report on this dual malignancy was written by Billroth in 1889.<sup>[4]</sup> According to the guidelines<sup>[5,6]</sup>, these 2 malignancies can be synchronous but should not be metachronous. Neither tumor should arise as a metastasis from the other nor the tumors should be separate from each other in terms of their microscopic and morphologic features, which means that they cannot have metastasized from another site. According to the guidelines, the incidence of a second primary tumor in cancer patients is approximately 10%<sup>[5,7]</sup>; however, it is rather rare for a patient to have a diagnosis of synchronous neoplasms of the thyroid and breast. Herein, we report a rare case of a 61-year-old female who was diagnosed with synchronous primary papillary thyroid carcinoma and breast ductal cancer. We also attempted to elucidate the underlying mechanisms of synchronous primary papillary thyroid carcinoma and breast ductal cancer and to systematically review some unsystematic theories regarding their development, diagnosis, and treatment that have been proposed in previous studies.<sup>[8,9]</sup>

## 2. Case presentation

In March 2015, a 61-year-old, postmenopausal female with a mass in her right breast that was found incidentally underwent a right breast mass excision and biopsy at her local hospital. However, the diagnosis could not be confirmed due to limitations regarding clinician experience and equipment; therefore, the patient, along with a paraffin-embedded tissue sample, was admitted to the Department of Pathology at our hospital (West

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China Hospital of Sichuan University, Chengdu, China). Immunohistochemistry revealed that she had primary breast infiltrative ductal carcinoma comprising tumor cells that were P63(–), S-100(–), cytokeratin (CK) 5/6(–), estrogen receptor (ER) (+, strong, 90%), progesterone receptor (PR)(+, strong, 90%), human epidermal growth factor receptor (Her)-2(0), and KI-67(25%). As a result, the patient elected to undergo radical operative therapy, although there were no signs of tumor recurrence in the right breast or metastasis to the lymph nodes. Accordingly, we performed a right mastectomy and right axillary level I lymphadenectomy in our department. No obvious tumor targets were found in the resection specimen.

Preoperative examination, which included a color Doppler ultrasound examination of the neck (neck ultrasound was routinely performed to detect neck lymph node metastasis, especially supraclavicular lymph node metastasis), indicated that there were multiple nodes in the middle left lobe of the thyroid with aspect ratios (vertical/transverse diameters)  $\geq 1$ , irregular shapes, and unclear boundaries, as well as multiple nodes of hypoechoic intensity, solid nodules, and calcifications. Additionally, the ultrasound elasticity imaging score was 5, and the strain ratio was 37.33. These 2 scores were used to identify benign or malignant tissue. Contrast-enhanced ultrasonography demonstrated homogeneous enhancement. The above-mentioned findings were detected in multiple lymph nodes in the left neck area (area IV), and the diameter of the largest mass was  $32 \times 23 \times 22$  mm (the mass exhibited irregular margins, solid nodules, and calcification). Preoperative CT of the chest and a bonescan ruled out any metastasis. For further diagnosis, preoperative fine needle aspiration (FNA) biopsy of a nodule in the left lobe of the thyroid and the left supraclavicular lymph nodes was performed. A follow-up pathology examination demonstrated the following: (gross cystic disease fluid protein) GCDFP15(–), Calectin-3(+), CK19(+), human bone marrow endothelial (HBME)-1(+), thyroglobulin (TG)(+), and thyroid transcription factor (TTF)-1(+), thereby confirming the diagnosis of thyroid papillary carcinoma in the left supraclavicular lymph nodes. The patient then underwent a total thyroidectomy + a double-sided region VI lymphadenectomy + a lymphadenectomy of the left lateral region of the neck. Intraoperatively, a tumor was found to be located in the left lobe of the thyroid and to have invaded the left belt-shaped muscle, and multiple lymph nodes with diameters ranging from 0.3 to 3.5 cm were noted in the left lateral region of the neck. A postoperative histological examination confirmed the diagnosis of thyroid papillary carcinoma with left supraclavicular and left lateral neck region lymph node metastasis.

The patient refused any chemotherapy or radiotherapy after surgery, but she accepted TSH suppressive therapy with levothyroxine (100  $\mu$ g, once per day) continuously. For the last 6 months, the patient has been followed with scheduled color Doppler ultrasounds, thyroid function tests, and periodic tumor marker monitoring, and no evidence of recurrence or metastasis has been observed thus far.

### 3. Discussion

Breast carcinoma and thyroid carcinoma are the 2 most common malignancies that occur in women. However, synchronous primary tumors of the thyroid and breast are very rare in clinical practice. Dual malignancy was first reported by Billroth in 1889.<sup>[4]</sup> Recently, concern about the risk of developing 2 primary tumors synchronously has increased. Previous studies have mainly focused on possible increases in the incidence of

contralateral breast carcinoma. However, the risk of concurrent thyroid carcinoma among women with breast cancer has not been explored in recent years.<sup>[10]</sup> 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 and that the incidence of other malignancies is higher in patients with thyroid cancer than in patients without thyroid cancer<sup>[11]</sup>, findings consistent with the current guidelines.<sup>[5]</sup>

A previous study revealed that a history of any thyroid disorder or subsequent treatment was not associated with an increased risk of developing breast cancer. However, this study revealed that parous females with a history of thyroid cancer exhibited an increased risk of developing breast cancer.<sup>[12]</sup> The presence of breast cancer did not increase the risk of thyroid cancer. It is well known that the use of radiotherapy to treat cancer may increase the risk of developing a second malignancy. For breast carcinoma, the most common risk factor for a second soft tissue sarcoma is postoperative radiotherapy, especially radiotherapy targeting the thyroid, which is very sensitive to radiation. Although the breast and thyroid are both endocrine organs, there is no evidence of a relationship between these organs with respect to the development of simultaneous breast and thyroid cancer. Liu et al<sup>[9]</sup> performed a literature review to elucidate the mechanism underlying the development of synchronous breast and thyroid cancer and focused on thyroid hormones. He proposed mechanisms underlying the activation of associated oncogenes, such as a sodium iodide symporter that acts as a potential co-passageway and facilitates thyroid and breast cancer development.<sup>[13,14]</sup> Additionally, previous studies have suggested that amplified levels of nuclear protein 1<sup>[15]</sup>, retinoid-inducible nuclear factor,<sup>[16]</sup> and nuclear receptor coactivator<sup>[17]</sup> in the breast served as potential oncogenic coactivators of and biomarkers for thyroid and breast cancers. Furthermore, it has been reported that the risk of synchronous thyroid and breast cancer is associated with Cowden syndrome and Cowden-like syndrome, which usually cause multiple cancers via flavin adenine dinucleotide (FAD)/nicotinamide adenine dinucleotide (NAD)-dependent destabilization of P53.<sup>[18]</sup>

In Chen's retrospective cohort analysis<sup>[19]</sup>, it was discovered that females with a history of thyroid carcinoma, particularly premenopausal Caucasian females, have an increased risk of developing breast cancer. However, the patient in the present case is a Xanthoderm, postmenopausal female. As shown in Table 1, most cases of synchronous breast and thyroid cancer occur in Xanthoderm, postmenopausal women; however, there is no clear or accurate evidence indicating whether differences in morbidity according to race or pre- or postmenopausal status exist.<sup>[20]</sup>

Accurate diagnosis is a very difficult but important task for clinical surgeons, who must differentiate between the diagnosis of synchronous breast and thyroid cancer and the development of either as a result of metastasis from a primary tumor involving the other, that is, thyroid cancer arising from breast cancer metastasis or breast cancer arising from thyroid cancer metastasis. The most important and difficult diagnosis is the diagnosis of lymph node metastasis. FNA of targets and lymph nodes is the best and first approach for making this diagnosis.<sup>[21,22]</sup> Van et al<sup>[11]</sup> assessed data from the American Cancer Society and discovered that thyroid cancer in female patients led to a 0.67-fold increase in the subsequent development of breast cancer, but thyroid cancer in males led to a 29-fold increase in the subsequent development of breast cancer. Moreover, breast cancer in female patients led to a

Table 1 Patients with synchronous primary cancers of the thyroid and breast.										
Case report	Year of publication	Age	Gender	Country	Race	Pre- or postmenopausal	Pathological examinations	Metastasis	Follow-up	Outcome at time of report
Liu (9)	2015	41	F	China	Xanthoderm	Premenopausal	Papillary carcinoma of the thyroid and invasive ductal carcinoma of the breast	No metastasis	2 years	No recurrence or metastasis
Kim (8)	2013	70	F	Korea	Xanthoderm	Postmenopausal	Papillary carcinoma of the thyroid and invasive ductal carcinoma of the breast, adenocarcinoma of the pancreas and a gastrointestinal stromal tumor	Unknown	8 months	Deceased
Ghosh (4)	2014	61	F	India	Unknown	Postmenopausal	Anaplastic carcinoma of the thyroid with ductal carcinoma of the breast	Metastasis to the lung and left axillary lymphadenopathy	Unknown	Unknown
Agarwal (19)	2007	50	F	India	Unknown	Postmenopausal	Papillary carcinoma of the thyroid and infiltrating ductal carcinoma of the breast	No metastasis	Unknown	Unknown
Our present case	2015	61	F	China	Xanthoderm	Postmenopausal	Papillary carcinoma of the thyroid and invasive ductal carcinoma of the breast	Left supraclavicular lymph nodes	0.5 years	No recurrence or metastasis

F = female.

2-fold increase in the subsequent diagnosis of thyroid cancer, whereas breast cancer in male patients led to a 19-fold increase in the subsequent diagnosis of thyroid cancer. These data may have important implications for patient follow-up and screening after primary cancer treatment. However, surgeons should be aware of not only a second cancer when following up a primary cancer but also a synchronous cancer, such as a synchronous papillary thyroid carcinoma or breast ductal carcinoma, both of which occurred in our present case. However, regarding the present case, we cannot speculate on whether the thyroid or breast cancer developed first based on depth of invasion or tumor size because papillary thyroid carcinoma and breast ductal carcinoma are minimally invasive and grow slowly. However, we can speculate that the papillary thyroid carcinoma was the first cancer to develop and that the breast cancer was the second cancer to develop based on the fact that the thyroid cancer exhibited poorer TNM staging than the breast cancer and left neck lymph node metastasis. If papillary thyroid carcinoma and breast ductal carcinoma are detected synchronously, the breast ductal carcinoma should be resected upon the exclusion of medullary or anaplastic thyroid carcinoma because breast ductal carcinoma is more likely to present with distant metastasis and to have a poorer prognosis.<sup>[4]</sup>

In conclusion, although synchronous primary tumors of the thyroid and breast are very rare, our case presentation and review have reminded us of the possibility that breast and thyroid cancer can occur synchronously. However, more studies in this field are needed to confirm our results.

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