

(CASE REPORT)



## Metastatic breast cancer to thyroid gland: Case report

Manouchehr Aghajanzadeh <sup>1</sup>, Hamid Saeidi Saedi <sup>2,\*</sup>, Pedram Talebi <sup>3</sup>, Hadi Hajizadeh Fallah <sup>3</sup>, Zeinab Aghzadeh <sup>3</sup>, Ehsan Hajipour Jafroudi <sup>4</sup>, Omid Mosafae Rad <sup>1</sup> and Mohay Farzin <sup>5</sup>

<sup>1</sup> Department of Thoracic and General Surgery, Guilan University of Medical Sciences, Rasht, Iran.

<sup>2</sup> Department of oncology, Guilan University of Medical Sciences, Rasht, Iran.,

<sup>3</sup> Department of Pathology, Guilan University of Medical Sciences, Rasht, Iran.

<sup>4</sup> Inflammatory Lung Diseases Research Center, Department of Internal Medicine, Razi Hospital, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran.

<sup>5</sup> Department of physiology, Razi Clinical Research Development Center, Guilan University of Medical Sciences, Rasht, Iran.

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### Abstract

**Introduction:** 1.4–3% of malignant solid tumors metastases to the thyroid gland and these events are rare. When metastatic cancers present to thyroid gland, ultrasound images mimic of the thyroid parenchyma, and diagnosis is difficult. Breast cancer rarely metastasizes to the thyroid gland.

**Case:** A 48-year-old woman was referred to endocrinologist clinic for enlargement of thyroid gland (goiter) with breast cancer history. Physical examination show multinodular goiter. Lymph nodes of cervical region were enlarged. Thyroid ultrasound (US) showed a multinodular goiter with maximum nodule size of 4 cm at the right thyroid lobe. This nodule was isoechoic and cystic degeneration areas with few coarse calcifications. There was a hypoechoic nodule up to 20 mm in left lobe, without any enlarged lymph nodes in the left cervical region. Thyroid and parathyroid hormone levels were normal. Cervical CT scan showed an enlarged thyroid gland and lymph nodes. An US-guided FNA was performed at the largest right and left thyroid lobe nodules, showed thyroid malignancy (Bethesda IV). The patient was monitored by US and thyroid hormone testing. Total thyroidectomy was performed. Histopathological examination revealed the presence of neoplastic infiltration of the right and left lobes with morphological and immunohistological characteristics compatible with breast tissue origin: CK7 focally positive, CK20(-), TTF1(-)GATA-3(+),GCDFP15(-),Mammaglobin (-)PAX 8 (-),Chromogranin (-),Ki67 (15-20),ER (+),PR (+) Her -2 (-) .

**Conclusion:** Metastases should be rolled out in a patient with breast cancer history and thyroid gland enlargement. FNA had been performed in the larger and calcified nodule that had the most suspicious. After total thyroidectomy, primary or secondary thyroid cancer could be diagnosed according to permanent pathology and immunohistology findings.

**Keywords:** Secondary malignancy; Thyroid; Breast cancer; Metastasis.

### 1. Introduction

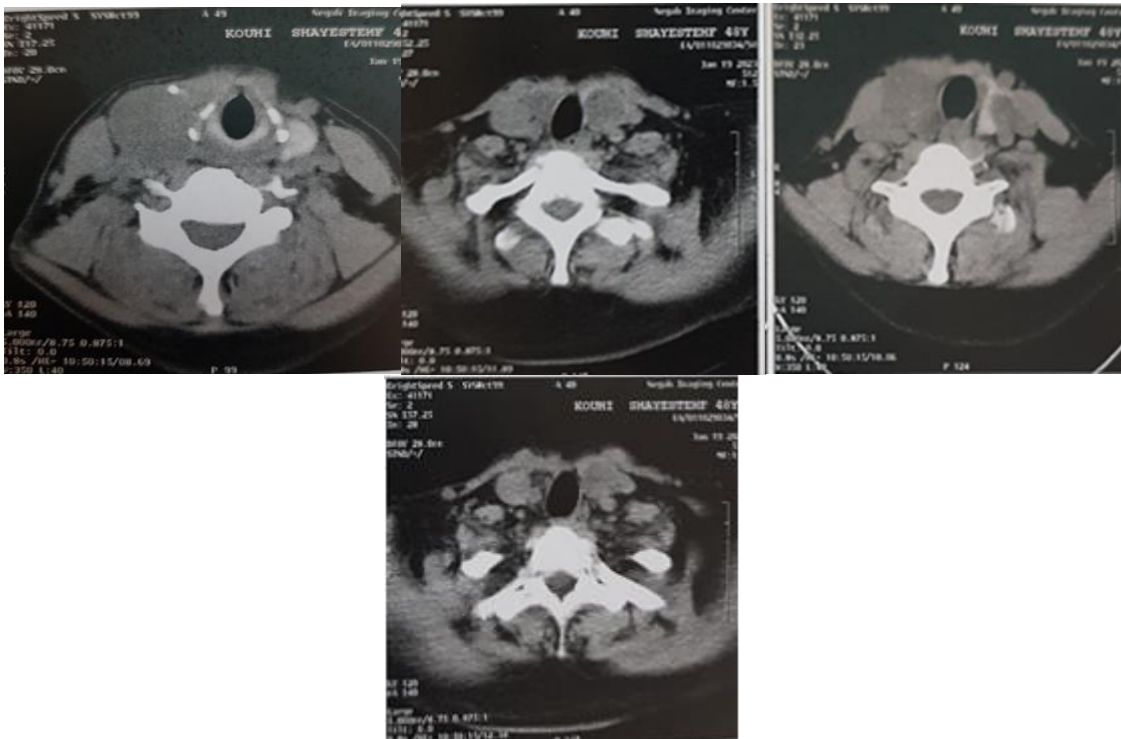
Although the thyroid gland vascularity is high, secondary malignancy and metastasizes to the thyroid, occurs infrequently. Only 1%-3% of thyroid cancers are metastatic [1, 2]. However, in an autopsy series reports, suggest that metastases to thyroid gland are possible more common than primary thyroid carcinoma [3]. Metastases to thyroid gland usually originate from renal cell carcinoma, or malignant tumors of the gastrointestinal tract, lungs, breast, and skin [4, 5]. More common and importantly problem in these cases are diagnosis challenges. There are major problem in the

\* Corresponding author: Hamid Saeidi Saedi

treatment of primary and metastatic thyroid cancer (7, 8). Therefore, a correct diagnosis before surgery is a major problem for oncologists and surgeons. In addition, patients with history of breast cancer, metastatic to the thyroid gland usually present with of a new or enlarging thyroid nodule [6]. In Thyroid metastases from breast cancer, lymph nodes enlargement of cervical region is rare (9). Here, we report a case of thyroid metastasis from left invasive breast ductal carcinoma which operated eight years ago, FNA showed thyroid malignancy (Bethesda IV). After near total thyroidectomy, definitive diagnosis was metastasis from breast cancer.

## 2. Case report

A 48-year-old woman was admitted to endocrinology clinic for thyroid enlargement and cervical palpable lymph nodes. Eight years ago, she was diagnosed with left breast invasive ductal carcinoma with, and treated by breast preserver surgery. and axillary lymph node dissection. Her mastectomy specimen showed a grade II invasive ductal carcinoma. After the surgery, she received chemotherapy, radiotherapy and herceptin immunotherapy for 12 months. The patient had no significant personal or family history of cancer. Physical examination of thyroid showed multinodular goiter with lymph node enlargement. The thyroid tests show euthyroid state, and during the disease course, there were not patient complains of heat, palpitation, sweating, and hand shaking. Ultrasonography (US) revealed solid, hypoechoic thyroid nodules with lymph node enlargement . Computed tomography of the neck and thyroid showed right and left thyroid nodules and multiple right cervical lymph nodes with homogenous enhancement. Contrast-enhanced CT showed homogenous enhancement. Ultrasonography of the thyroid and neck showed left and right lobes; solid, hypoechoic thyroid nodules with irregular margins. Right side cervical lymphadenopathy was diagnosed in neck ultrasonography evaluation. Fine needle biopsy was carried for the right and left enlarged thyroid lobes. Report of pathology showed malignancy of thyroid (Bethesda IV).Immunohistochemical analysis revealed positive for thyroglobulin (TG), estrogen receptor (ER), and progesterone receptor (PR) and negative for human epidermal growth factor receptor 2 (Her-2).



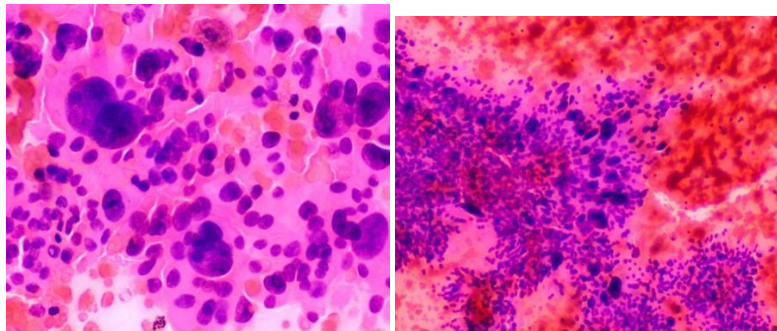
**Figure 1** Computed tomography of the thyroid and neck showed thyroid nodules and cervical lymph nodes with homogenous enhancement pattern

There was no obvious bone and brain metastasis in the whole-body bone scan and MRI. Total thyroidectomy and neck lymph node dissection were performed for this patient. Postoperative pathology showed extensive intravascular infiltration and nerve infiltration of breast invasive ductal carcinoma in the bilateral thyroid tissue and cervical lymph nodes. The results of immunohistochemistry indicated the following: origin [CK7 focally positive,CK20(-),TTF1(-)GATA-3(+),GCDFP15(-),Mammaglobin(-)PAX8(-),Chromogranin(-),Ki67(15-20),ER(+),PR(+),Her -2(-) .One month after surgery, the patient was referred to oncologist for postoperative treatment. Breast ultrasound examination was

performed and was normal, after a 5-monthes follow-up, no recurrence and distant metastasis was identified. FNA cytological smears from the bilateral thyroids with the same cell characteristics revealed scattered to clustered, round or elongated malignant cells with abundant cytoplasm enlarged irregular nuclei, coarse chromatin and nucleoli of varying sizes.



**Figure 2** Ultrasonography of neck: In the thyroid, there were multiple hypoechoic areas, which had unclear boundary, and a number of small spots with strong echo and showed a number of hypoechoic areas with clear boundaries and unclear internal structures, some of which contained multiple small spots with strong echo.



**Figure 3** FNA cytological smears from the bilateral thyroids with the same cell characteristics revealed scattered to clustered, round or elongated malignant cells with abundant cytoplasm enlarged irregular nuclei, coarse chromatin and nucleoli of varying sizes.

Immunohistochemical findings, after the thyroedectomy indicated the following: CK7 focally positive, CK20 (-), TTFI (-) GATA-3 (+), GCDP15 (-), Mammaglobin (-) PAX 8(-), Chromogranin (-), Ki67 (15-20), ER (+), PR (+) Her -2(-). This findings consistent with breast carcinoma within thyroidal paranchimal .In the thyroid, there were multiple hypoechoic areas, which had unclear boundary, and a number of small spots with strong echo.

### 3. Discussion

The thyroid blood circulation is high (about 560 ml/100 g tissue/min). Metastatic carcinoma to the thyroid gland is rare and the underlying causes for this rarity event are unknown [1 -2]. Clinically, thyroid metastasis misdiagnosis is high, because are because the metastases size are small and not to detect easily [3]. Over all, Thyroid metastatic carcinoma is very rare, especially from breast cancers [2]. Fine-needle aspiration cytology (FNAC) is a sensitive and specific method for diagnosis of thyroid metastasis [11, 10]. Fine-needle aspiration biopsy (FNA) is an indispensable test in assessing the nature of a nodular lesion of thyroid, especially in patients with a history of a malignant neoplasm (11, 12). The sensitivity and specificity of FNA in the diagnosis of thyroid metastases is estimated at 94% and 100%, respectively [6-12]. The most common site of breast metastases are bones (21.9%) and lungs (19%), lymph nodes, liver and brain [5, 6, 7, 8]. Although thyroid gland, blood flow is very high, breast cancer metastasis is very rare [5, 6]. Metastatic tumors of the thyroid constitute from 0.3% to 2.2% of all malignant tumors of the thyroid gland [6, 7, 14, and 15]. Most of them are metastases of kidney clear cell carcinoma (22%) and lung cancer (22%). Metastatic carcinoma of the large intestine, esophagus, larynx, neuroendocrine carcinomas and sarcomas are found less frequently [8, 9, 14]. Metastasis of breast cancer accounts for between 3% reports [15]. Metastatic thyroid carcinoma should be differentiated from primary thyroid carcinoma (1, 2, 3). Previous studies have revealed that the incidence of thyroid carcinoma in breast

cancer patients is 1.34%, and the incidence of breast cancer in thyroid carcinoma patients is 1.07% [5]. Papillary, follicular and medullary carcinomas of thyroid have a complex pathological pattern. Cytology alone is difficult to differentiate the metastatic carcinomas from primary carcinomas [3, 8]. In such situation, immunohistochemistry and molecular analysis may play an important role (8, 17). In our case, thyroid FNA specimen cells showed malignant carcinoma. Routine tests during and after oncological treatment, play a key role in the early detection of breast cancer recurrence. Ultrasound and fine-needle aspiration biopsy have a very important role in true diagnosis (18, 19). Symptoms such as dysphagia, hoarseness, a rapidly growing tumor on the neck are observed in 21.9%–85% of breast cancer to thyroid [9, 11]. Asymptomatic metastases are detected accidentally in routine examinations during and after oncological treatment [9, 18]. The other diagnostic methods include neck ultrasound and PET-CT using 18F-FDG [19, 21]. The latter not performed in our patient. PET-CT is characterized by very high sensitivity in diagnosing metastatic changes [13, 16, 19, 21]. In most cases, the metastatic nodule is single, rarely multiple or disseminated [8, 10, 14].]. Surgical treatment of patients with thyroid metastases involves total or subtotal thyroidectomy or lobectomy and has a proven effect on extending survival(13,16) The choice of surgical method depends on the number and metastases distribution in the gland, although recurrent metastases in thyroid tissue preserved after incomplete resection are described in patients with a generalized cancer [13,16,18,19,11]. Overallly, isolated thyroid metastases have a poor prognosis in patients with breast cancer and it is the first announcement of cancer dissemination [22, 23]. In our patient with multiple thyroid nodules, it was decided to remove total thyroidectomy and central cervical lymphadenectomy. [8, 9, 13, 16, 12]. The choice of surgical method depends on the number and distribution of metastases in the gland, although recurrent metastases in thyroid tissue preserved after incomplete resection are described in patients with a generalized cancer [13, 16, 17, 18]. In patients without any metastases or with surgical resectable metastases eligible, the procedure is performed with the intention of complete resection (18). In other cases, the indication for thyroidectomy is a rapidly growing tumor mass, which may cause swallowing and breathing difficulty due to pressure effects on the esophagus and trachea In this case, the patient developed bilateral thyroid metastasis eight years after breast cancer diagnosis and treatment. Common risk factors for breast cancer metastasis include tumor size, histologic grade, nodal stage and receptor status. In addition, breast cancer molecular type plays a role in metastasis [22, 23]. The previous study has demonstrated that various breast cancer subtypes show a strong correlation to site-specific metastasis patterns (18). This case was ER (+), PR (+) and HER2 (-) and may highly express certain proteins to adapt to the thyroid microenvironment to initiate thyroid or other organ metastasis [18]. While isolated metastatic lesions in the thyroid gland, except for cases of rapidly growing tumors causing compression of the cervical organs, do not seem to have much clinical significance on their own, they are extremely important in oncological practice, as they mostly constitute the first manifestation of tumor recurrence (4, 8, 12). In summary, breast cancer metastases to the thyroid gland can present many years after the primary cancer treatment. Cytological morphology and immunohistochemistry can help distinguish primary and secondary tumors. Thyroidectomy is the best method for definitive diagnosis and treatment.

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#### 4. Conclusions

Routine tests during and after oncological treatment is very important key in the early breast cancer metastases detection. Cervical lymph nodes examining and thyroid are very important. In patient with breast cancer if thyroid was enlarged, ultrasound and fine-needle aspiration biopsy can detect the diagnosis. If definitive diagnosis was metastases, patient refer to oncologist for metastatic work up evaluation, but as our patient, if diagnosis was not definitive, thyroidectomy performed to detect primary or metastatic disease.

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#### Compliance with ethical standards

##### *Acknowledgments*

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##### *Disclosure of conflict of interest*

No conflict of interest to be disclosed.

##### *Statement of ethical approval*

The study was performed in accordance with the declaration of Helsinki and approved by the Ethics Committee of Guilan by IR.GUMS.REC.1402.431. Guilan University of Medical Sciences, Iran.

### Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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