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CASE REPORT

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Occult breast cancer metastasis to the thyroid gland: Case report

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Abstract

Thyroid metastases of occult breast cancer are very rare. A 48-year-old female patient presented with chronic bone pain, bone, liver and thyroid nodules, and pleural effusion. Histopathological result of the thyroid showed poorly differentiated papillary thyroid carcinoma. However, clinical laboratory and immunohistochemistry studies showed breast origin of the thyroid lesion.

KEYWORDS

immunohistochemistry, occult breast cancer, thyroid metastasis

1 | INTRODUCTION

Breast cancer is the most prevalent cancer in women and is associated with cancer-related causes of most deaths in females. It commonly metastasizes to the bone, lungs, pleura, liver, brain, and seldom thyroid gland. Despite the thyroid gland is a highly vascularized organ, secondary malignancies metastasizing to the thyroid are very rare.[1] Thyroid metastasis commonly originates from kidney, gastrointestinal tract, lungs, breast, and skin.[2]

Cancer of unknown primary site is explained as secondary lesions without any detectable primary tumor at the time of diagnosis. One example of this situation is occult breast cancer (OBC); occult breast cancer is described as metastasis to the axillary lymph nodes or distant organs without any primary breast lesion on clinical and radiological examination. These cases include 0.3%–1.0% of all breast cancer patients and fortunately potentially respond to treatment.[3]

Since the treatment plan of primary and secondary malignancy of the thyroid differs considerably and could affect prognosis and survival, achieving a precise diagnosis of thyroid malignancy is of utmost importance. Here, we present a rare case of a patient with metastatic lesions in the thyroid gland originated from breast; however, no evident primary breast lesion had been detected previously.

2 | CASE REPORT

A 48-year-old female patient presented with a history of chronic bone pain underwent a spinal MRI and bone scan that revealed widespread bone metastases and cervical mass which raised the suspicion of thyroid origin in spine MRI. Metastatic workup showed diffuse sclerotic infiltrative bone lesions involving the scanned skeleton, including the spine, sternum, ribs, and pelvic bones with the evidence of multiple healed pathological fractures at posterior ribs. Further evaluation revealed multiple nodules in the thyroid and right upper lobe consolidation of lung without nodule or mass, right-sided pleural effusion, and two poorly enhancing lesion in left lobe of liver suggestive of atypical metastasis. In mammography and sonography of breast and axillae, no obvious breast mass and suspicious axillary lymphadenopathy in both axillae were detected. Thyroid mass core needle biopsy results

raised suspicion of follicular neoplasm or medullary carcinoma. Total thyroidectomy without cervical lymph node dissection was performed. The pathological diagnosis was poorly differentiated papillary thyroid carcinoma (PTC) infiltrating the thyroid capsule and three adjacent lymph node metastases. Fine needle aspiration cytology of the pleural fluid showed excessive shedding of malignant follicular cells with even abortive micro-acinar and papillary formations, consistent with malignant metastatic PTC. Laboratory studies showed a low level of thyroid-stimulating hormone, low T4, and a mild increase in liver enzymes. CEA was normal. However, CA15-3, CA-125, and CA19-9 showed elevation with a significant increase in CA15-3. Due to para-clinical suspicion of breast cancer (considerable elevated CA15-3), dissimilar results between core needle biopsy and total thyroidectomy and poorly differentiated tumor cells without definite nuclear features of PTC in thyroid mass slides, microscopic slides were reviewed and immunohistochemical (IHC) evaluations were requested. IHC studies performed on tissue blocks, showed non-diagnostic TG staining, TTF-1 negativity, Ki-67 positivity in 40% of cells (Figure 1), GATA3 positivity, ER positivity (Allred score 7/8, strongly positive in 60% of cells), PR negativity (Allred score 0/8) and HER-2/neu score 2+ (equivocal, incomplete, moderate membranous staining in 30% of cells) (Figure 2). TTF1 is mainly positive in lung neoplasms, thyroid neoplasms, and CNS tumors. GATA3 is mostly positive in breast cancer, urothelial carcinoma, choriocarcinomas, and renal cell carcinoma. ER is generally positive in breast carcinoma, endometrial and ovarian carcinoma, and bladder neoplasms. According to positivity of GATA3 and ER and negativity of TTF1, the results were more related to breast origin and the diagnosis of occult metastatic breast carcinoma to the thyroid was made.

The patient is currently receiving chemotherapy drugs (Herceptin, Carboplatin-Taxol, and Zolena), and symptoms including bone pain, dyspnea, and pleural effusion have been improved.

3 | DISCUSSION

Occult breast cancers are rare. Most patients were 50 years old or older. OBC often presents with nonspecific symptoms in the absence of any breast abnormality, which could make the diagnosis challenging. Furthermore, it usually metastasizes to the axillary lymph nodes at the time of diagnosis. Despite its rarity, other metastatic sites include bone, liver, lymphatic system, skin, orbits, bone marrow, lung, and spleen.[4] In this case, no suspected axillary lymphadenopathy was detected, except some benign looking lymph nodes.

Till date, this is the second case of a metastatic cancer of the thyroid gland arising from breast tissue without any background of breast cancer diagnosis priorly. Bourcier et al was the first one who reported metastatic cancer of the thyroid originated from breast without any diagnosis of breast cancer earlier. Although thyroid metastasis from breast cancer is rare, several cases of metastatic disease of the thyroid from breast have been reported in the literature.[5]

The thyroid gland is rich in blood supply, though it is uncommon site of metastases.[6] In the autopsy

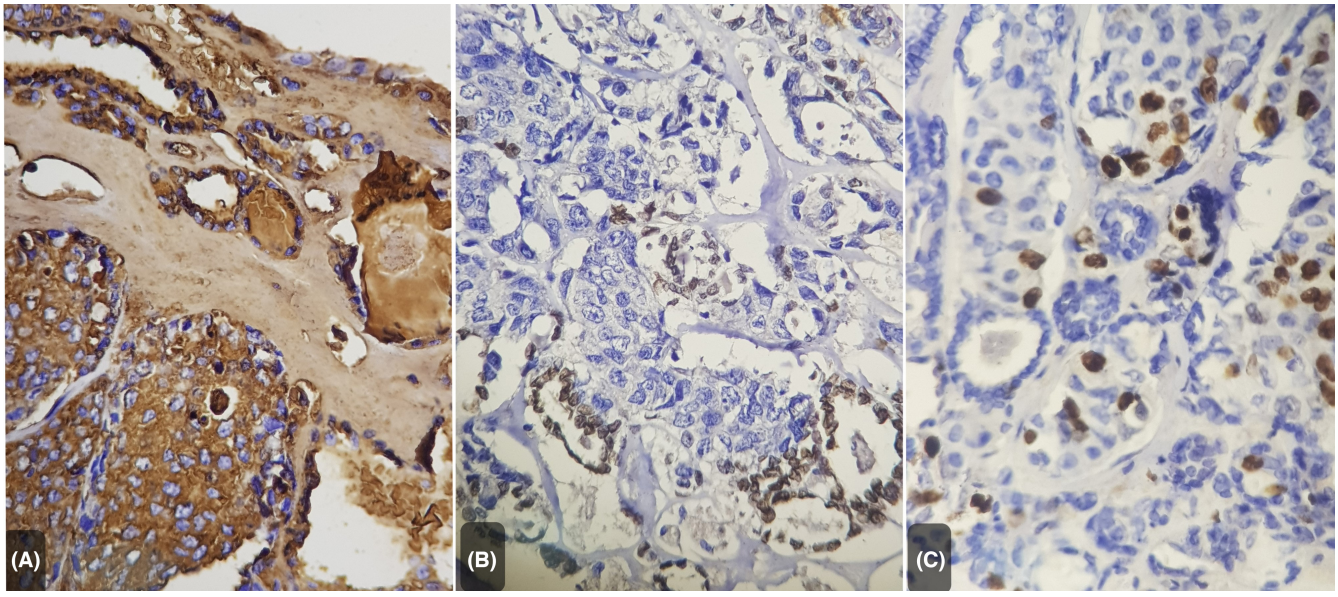

FIGURE 1 Immunohistochemical staining showed non-diagnostic TG (A), TTF-1 negativity in tumor cells (B) and Ki-67 positivity in 40% of malignant cells (C)

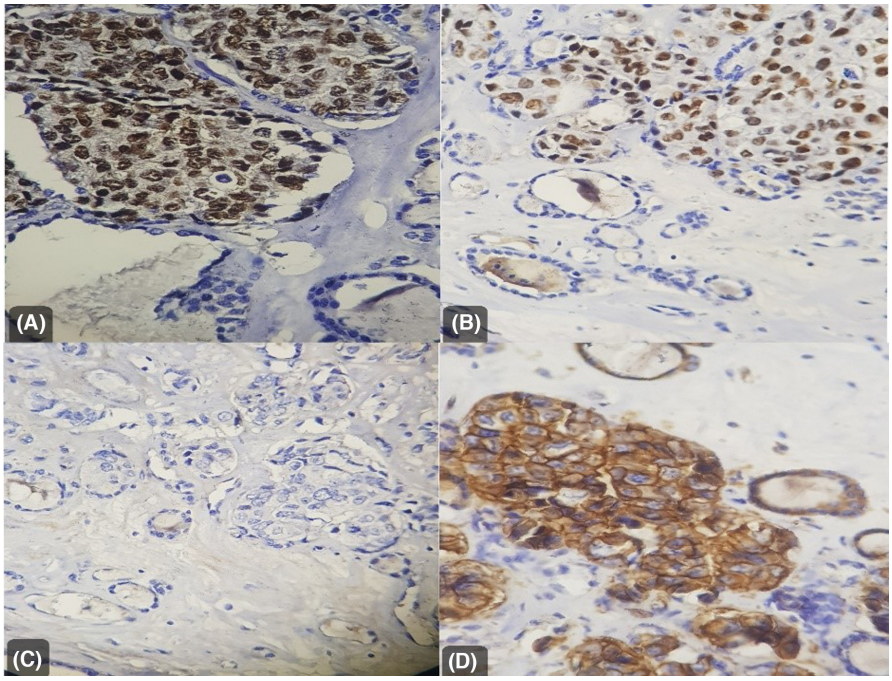

FIGURE 2 Tumor cells expressed nuclear positivity for GATA-3 (A) and ER (B), negativity for PR (C), and HER-2/neu score 2+, immunohistochemistry (D)

examinations, the incidence of metastasis accounts for 2% of all cases[7]; this paradox is justified by a combination of fast blood circulation preventing tumor cell adhesion, and high oxygen saturation and iodine content inhibiting tumor cell growth.[6]

Chung et al. suggested that nearly half of metastases to the thyroid took place in abnormal thyroid glands affected by primary thyroid neoplasia, goiter, or thyroiditis, this vulnerability may justified due to lack of blood supply resulting in reduced oxygen and iodine levels; however, metastatic disease appears to affect otherwise normal thyroid glands at an equal likelihood.[8]

Thyroid metastasis usually occurs in the advanced stages and is often (up to 80%) asynchronous as in this patient.[8]

Metastasis has similar radiologic features to those described for both benign and malignant thyroid diseases.[9] Most of the lesions are solitary than diffuse or multiple,[10] heterogeneous, and hypoechoic.[9] Therefore, evaluation by the use of fine-needle aspiration (FNA) can help distinguish it, because based on studies, FNAB has more than 90% accuracy for the diagnosis of a secondary tumor of the thyroid.[1] Metastatic ductal breast carcinoma involving the thyroid may morphologically imitate primary thyroid malignancy on fine-needle aspiration, and secondary malignancies of the thyroid may be misdiagnosed.[11]

Since prognosis and treatment plan of secondary and primary thyroid malignancies thoroughly differ, making a precise diagnosis is very important to pathologists,[5] in our case, pathologists reported poorly differentiated PTC after thyroidectomy. Immunohistochemistry (IHC) analyses helped to reveal that lesions were breast in origin.

TTF-1 has nuclear positivity in follicular and parafollicular cells of the thyroid, and thyroglobulin (TG) is a specific marker of thyroid differentiation. The most prevalent immunohistochemical prognostic and therapeutic markers of breast cancer include ER, PR, HER-2, and P-53. Nuclear staining of GATA-3 can differentiate metastatic urothelial and breast carcinoma from many other metastatic carcinomas. When considering breast cancer metastasis, GCDFP-15 and mammaglobin are other potentially useful markers of breast origin, though they are less sensitive than GATA3.[11] Interestingly, a study of 25 patients with metastatic breast cancer reported that ER-positive tumors metastasized more frequently to the thyroid and parathyroid glands than ER-negative tumors, perhaps reflecting tissue differences in hormone-binding receptors.[12] In our case, IHC study showed strong GATA-3 and ER positivity and TTF-1 negativity that was more compatible with metastatic breast carcinoma. As previously mentioned, it is noticeable that, in this case, patient had no history of protuberance or mass in her breast and only laboratory tests revealed the breast origin of thyroid metastases, so, these statements suggest rarity of our case.

4 | CONCLUSION

A history of malignancy elsewhere should raise the index of suspicion of metastatic disease with any nonspecific symptoms such as bone pain as same as present case. Occult breast cancer should be considered as primary source of metastases, especially in females. Immunohistochemical markers are of great importance to

identify origin of malignancy, even if obvious mass is not found in the primary organ.

AUTHOR CONTRIBUTIONS

MG reviewed pathologic and IHC slides and made the diagnosis and contributed in writing the manuscript. FN provided patient's history and documents and performed treatment process. PV reviewed slides and took the pathological slide's photographs, wrote the manuscript, and was submitter. All authors read and approved the final manuscript.

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CONFLICT OF INTEREST

Non declared.

DATA AVAILABILITY STATEMENT

Most of the data are available in Reza radiotherapy and oncology center and Ghaem hospital of Mashhad.

CONSENT

Written informed consent was obtained from the patient

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