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Case report

METASTASIS OF BREAST CANCER TO THE THYROID GLAND

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Abstract

Metastases to the thyroid gland from nonthyroidal malignant tumors are rare but significant. They are often asymptomatic, indicating advanced-stage primary tumors and poor prognosis. Although infrequently, breast cancer (BC) can metastasize to the thyroid gland. We present the case of a 56-year-old woman with a history of BC who presented with a nodular goiter. Physical examination and imaging revealed a thyroid nodule and cervical lymph nodes with suspicious features. Fine-needle aspiration biopsy (FNAB) confirmed the presence of atypical epithelial cells in the thyroid nodule and lymph nodes. Further evaluation, including positron emission tomography, histological biopsy, and immunohistochemistry, supported the diagnosis of metastatic BC to the thyroid gland. Due to the local extent of the disease, total thyroidectomy was not feasible. The treatment with ribociclib and letrozole was initiated, but unfortunately, the patient had an unfavorable progression with the development of metastasis in the nervous system. Metastatic carcinoma to the thyroid gland is rare but has increased due to improved diagnostic techniques. BC can metastasize to the thyroid. Diagnosis involves imaging, FNAB, and immunohistochemistry. Treatment options include surgery, radiotherapy, and chemotherapy, but the prognosis is generally poor.

Key words: metastasis, breast cancer, thyroid gland, thyroid neoplasms

Resumen

Metástasis de cáncer de mama en glándula tiroides

Las metástasis en la glándula tiroides a partir de tumores malignos no tiroideos son raras pero significativas. A menudo son asintomáticas, lo que indica tumores primarios en etapas avanzadas y un mal pronóstico. Aunque infrecuentemente, el cáncer de mama puede metastatizar en la glándula tiroides. Presentamos el caso de una mujer de 56 años con antecedente de cáncer de mama que consultó por bocio nodular. El examen físico y las imágenes revelaron un nódulo tiroideo y ganglios linfáticos cervicales con características sospechosas. La punción aspiración con aguja fina confirmó la presencia de células epiteliales atípicas en el nódulo tiroideo y los ganglios linfáticos. Una evaluación adicional, que incluyó tomografía por emisión de positrones, biopsia histológica e inmunohistoquímica, respaldó el diagnóstico de cáncer de mama metastásico en la glándula tiroides. Debido a la extensión local de la enfermedad, no fue factible realizar una tiroidectomía total. Se inició el tratamiento con ribociclib y letrozol, pero desafortunadamente la paciente tuvo una progresión desfavorable con el desarrollo de metástasis en el sistema nervioso. El carcinoma metastásico en la glándula tiroides es raro, pero ha aumentado debido a las técnicas de diagnóstico mejoradas. El cáncer de mama puede metastatizar en la tiroides. El diagnóstico implica imágenes, punción aspiración con aguja fina e inmunohistoquímica. Las opciones de tratamiento incluyen cirugía, radioterapia y quimioterapia, pero el pronóstico generalmente es desfavorable.

Palabras clave: metástasis, cáncer de mama, glándula tiroides, neoplasias tiroideas

Metastases to the thyroid gland originate from nonthyroidal malignancies. This condition is rare, with a reported incidence of 0.36%

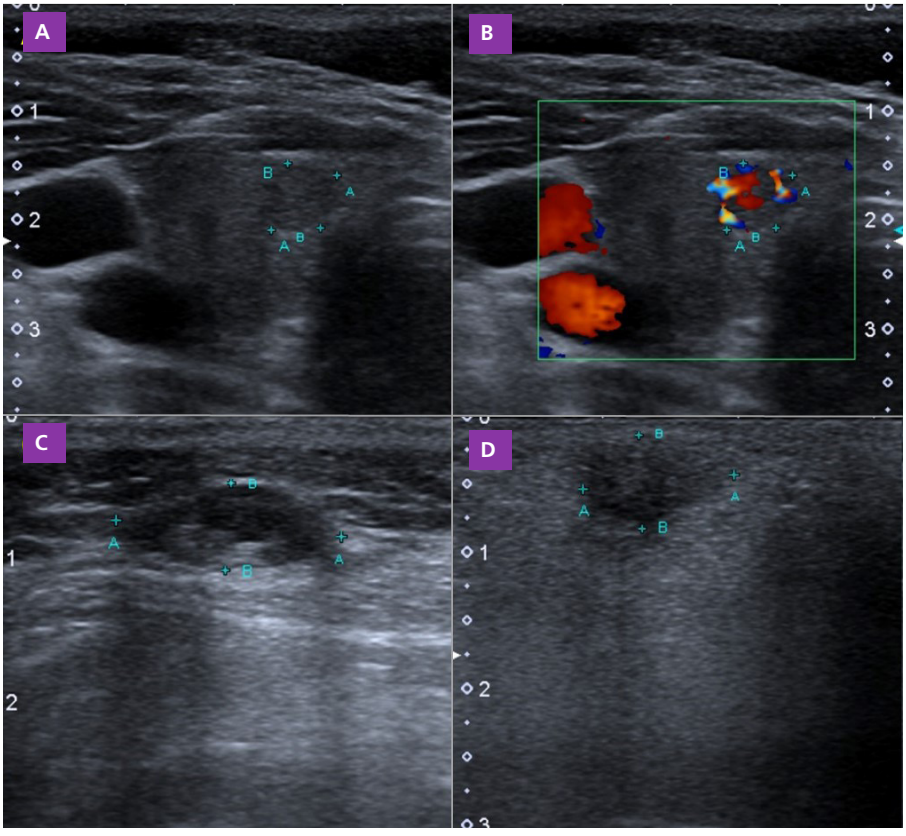
among all cases of thyroid malignancy[1]. However, postmortem studies have shown a higher incidence[2]. In most cases, thyroid metastases are asymptomatic and are only discovered incidentally during follow-up or autopsy[3]. The prognosis is generally poor as it typically indicates advanced-stage primary tumors. In this case report, we present the diagnosis and treatment of a patient with a metastasis in the thyroid from breast cancer (BC).

Clinical case

A 56-year-old woman with a medical history of obesity, hypertension, and type 2 diabetes presented with a nodular goiter and spinal pain, with an intensity level of 7 out of 10. Five years earlier, she had been diagnosed with breast cancer (BC) and underwent a left mastectomy and axillary lymphadenectomy. The histopathology results revealed a 10 cm invasive ductal carcinoma, classified as poorly differentiated (G3), with concurrent metastasis to the lymph nodes on the same side (T3N2M0). The cancer was found to be estrogen receptor (ER) positive (90%), progesterone receptor (PR) positive (85%), human epidermal growth factor receptor 2 (HER2) positive confirmed with FISH, and Ki-67>14%. After the surgery, the patient underwent adjuvant treatment which included chemotherapy with doxorubicin, cyclophosphamide, and paclitaxel, regional radiotherapy, one year of trastuzumab, and hormonal therapy with tamoxifen.

The patient had regular chest, abdomen, and pelvis computed tomography scans every 3 months for disease surveillance. No evidence of disease was detected in these images after five years of follow-up, when a 10 mm thyroid nodule on the right lobe and lymph nodes in the laterocervical region were identified. Thyroid ultrasound showed an 8 by 7 mm hypoechoic solid nodule with ill-defined margins and mixed vascularity (Fig. 1A and Fig. 1B), and two lymph nodes identified, one measuring 11 by 7 mm in the left retroauricular region and another in the posterior right neck region (Fig. 1C and Fig. 1D). During the evaluation of spinal pain, a magnetic resonance

Figure 1 | Sonographic findings. A: Hypoechoic nodular in the right thyroid lobe, with a size of 8 by 7 mm, hypoechoic, with partially defined borders and no halo. B: Doppler examination revealed both peripheral and central vascularization. C: Lymph node image measuring 16 x 6 mm in the topography of the posterior region of the neck, to the right of the midline. D: Lymph node image measuring 11 x 7 mm in the left retroauricular topography



imaging of the spine was performed, revealing osteolytic lesions in the vertebral bodies. Fluorine-18 positron emission tomography (18F-PET) scan showed hypermetabolic supradiaphragmatic lymph nodes, osteolytic lesions, and a hypermetabolic thyroid nodule on the right lobule.

A fine-needle aspiration biopsy (FNAB) of the right thyroid nodule was performed, which reported atypical epithelial cell clusters with moderate nuclear atypia, occasional molding, and overlap, hyperchromasia, nuclear membrane irregularity, and eosinophilic cytoplasm (Bethesda V) (Fig. 2A). The FNAB of the lymph node showed low cellular yield with isolated clusters of epithelial cells with a high nuclear/cytoplasm ratio, moderate nuclear pleomorphism, hyperchromasia and molding, and eosinophilic cytoplasm (Fig. 2B). The determination of thyroglobulin in the needle wash was negative. The thyroid function tests were normal.

Since the diagnosis was not clear, a multidisciplinary decision was made to proceed with a total thyroidectomy, which could not be performed due to the local extent of the disease. A biopsy was performed, which reported extensively compromised thyroid parenchyma by an invasive, poorly differentiated adenocarcinoma composed of solid nests with scarce glandular structures and perineural permeation (Fig. 2C). Immunohistochemistry analysis revealed that the tumor cells exhibited positivity for GATA3 and estrogen receptor (ER), while they were negative for thyroid transcription factor 1 (TTF-1) and thyroglobulin. Additionally, the HER2 score was negative (score 0). These results were consistent with metastatic BC, with no evidence of primary thyroid malignancy.

The decision was made to initiate systemic treatment with ribociclib, letrozole, and pamidronate, which was well-tolerated. Unfortunately, the patient experienced an unfavorable progression with the development of metastasis in the nervous system. As a result, she is currently undergoing whole brain radiation therapy.

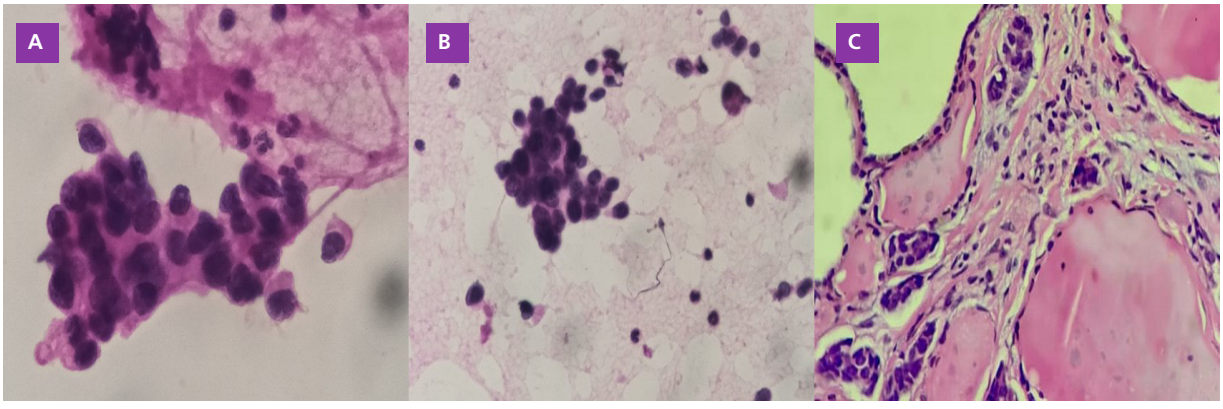
The patient signed the correspondent Informed consent.

Discussion

Although the thyroid gland receives a high blood supply (4 to 6 ml/min/g), metastatic carcinoma to the thyroid is a rare occurrence and typically originates from primary tumors in the kidney, gastrointestinal system, lungs, skin, and rarely, the breast[4]. Metastatic BC often targets bones and internal organs such as the lungs, brain, and liver[5,6]. Thyroid metastasis from BC accounts for only 7.8% of all metastatic neoplasms in the thyroid gland[7]. However, its incidence has increased due to improved diagnostic imaging techniques. Furthermore, BC and differentiated thyroid cancer are the most prevalent malignancies among women and endocrine cancers, respectively. Therefore, the simultaneous occurrence of these two cancers in the same patient should raise suspicion of synchronous primary cancers, while a metachronous one suggests a metastasis.

The clinical presentation of thyroid metastasis is variable. It often manifests as a palpa-

Figure 2 | Cytological and histological biopsy. A: Thyroid nodule fine-needle aspiration biopsy (FNAB) (HE; 40X) cluster of atypical epithelial cells, exhibiting poorly developed acidophilic cytoplasm, hyperchromatic nuclei, overlapping with irregular contours, mild anisocariosis, and occasional small nucleoli. C: Cervical lymph node FNAB (HE: 60X): cluster of atypical epithelial cells showing similar characteristics to those observed in B and C. Histologic biopsy (HE: 40X): Thyroid parenchyma is observed with follicles lined by low cuboidal epithelium and colloid content. The stroma shows infiltration of atypical epithelial cells grouped in nests and cords with limited tendency to form ductal structures



ble neck mass, but can also lead to symptoms such as dysphagia, hoarseness, dysphonia, and pain due to local invasion. However, many cases are asymptomatic and are discovered incidentally during follow-up studies of patients with previously diagnosed malignant neoplasms[3]. In our case, the metastasis was discovered incidentally as there were no accompanying symptoms.

Ultrasound is the preferred imaging modality for evaluating thyroid diseases, including thyroid metastasis. Metastasis in the thyroid can be classified into two categories based on ultrasound findings: (1) diffuse type, and (2) nodular type[8]. In our case, the metastasis appeared as a hypoechoic nodule with ill-defined margins and without microcalcifications.

Compared to conventional computed tomography scans, 18F-PET is more sensitive in diagnosing tumors. Metastases to the thyroid gland typically exhibit focal single nodular uptake, multiple discrete nodular uptakes, or diffuse uptake/infiltration on 18F-PET imaging. The standardized uptake value in these cases can range between 3.9 and 42[9]. In our patient, we identified a hypermetabolic nodule with a standardized uptake value of 5.0.

Respect to FNAB, less than 0.2% reveal BC metastasis and determining the origin of the primary metastatic cancer can be challenging[10]. FNAB samples from thyroid metastatic disease originating from BC typically exhibit malignant epithelial cells with enlarged nuclei, irregular nuclear contours, and the absence of intranuclear grooves and pseudoinclusions[10]. In our case, the FNAB of the thyroid revealed atypical epithelial cells with moderate nuclear atypia, hyperchromasia, irregular nuclear membranes, and eosinophilic cytoplasm (Fig. 2A).

Immunohistochemistry analysis is useful for distinguishing between primary and secondary thyroid tumors. Primary tumors show positive staining for markers like thyroglobulin, TTF-1, and PAX8[11], while secondary thyroid malignancies are negative for these markers. BC-derived tissues are characterized by markers such as ER, PR, HER2, GATA3, and GCDFP15[12]. However, the lack of these markers does not preclude a mammary origin, given that a subset of tumors –specifically the triple-negative ones– exhibit negligible expression of ER, PR, and HER2, often accompanied by reduced GATA3 expression. Furthermore, GCDFP15 demonstrates limited expression in non-luminal tumors[13]. In the presented case, immunohistochemistry analysis of the surgical biopsy confirmed the BC origin of the lesion by showing positive staining for ER and GATA3, and negative staining for thyroglobulin and TTF1. Finally, a discordance in HER2 expression is observed in the thyroid metastasis relative to the primary BC in our patient. Receptor discordance was defined as a change in ER, PR, or HER2 status (in any direction) between the primary tumor and the metastasis, with a HER2 discordance rate of 10% (range 0-40%). The prognosis of patients exhibiting altered HER2 expression would likely be less favorable compared to those with unaltered HER2 expression. This could potentially be attributed to inadequate administration of appropriate anti-HER2 therapy in cases of altered HER2 expression[14].

The ductal type is the most common histology observed in BC cases with metastasis to the thyroid gland[3], as seen in our patient. Metastasis to the thyroid gland is typically metachronous, occurring on average 70 to 180 months after the primary diagnosis of BC. In our case, the patient developed thyroid metastasis 60 months after the BC diagnosis.

The treatment of secondary thyroid neoplasms primarily involves surgery, radiotherapy, and chemotherapy. Thyroidectomy is considered a more effective treatment option compared to radiotherapy and chemotherapy[2]. However, patients with widespread metastasis of malignant tumors often do not meet the criteria for surgical intervention[15]. In our patient, a multidisciplinary team decided to perform a total thyroidectomy; however, it was not feasible due to locoregional invasion of the disease. Nonetheless, the procedure was valuable in confirming the breast origin of the neoplasm.

Finally, the presence of thyroid metastasis from BC is an unfavorable prognostic factor for long-term survival. Approximately 35% to 80% of patients with thyroid metastatic cancer exhibit multi-organ metastasis, resulting in a poor prog-

nosis[3]. Our patient with BC metastasis to the thyroid, presented concurrent lung, lymphatic, and bone metastatic lesions.

In conclusion, we present a rare but increasingly recognized case of BC metastasis to the thyroid gland. It emphasizes the importance of considering metastasis in thyroid nodule diagnosis, particularly in patients with a history of BC. Multidisciplinary collaboration is crucial for optimal management.

Conflict of interest: None to declare

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