

Thyroid metastases from breast cancer: A report of two cases and a literature review

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Abstract. Breast cancer is the most common malignant tumor in women worldwide. Common sites of distant metastasis include bone, liver, brain and lung, while metastasis to the thyroid is relatively rare. The present study aimed to investigate the clinical characteristics, diagnostic challenges and treatment strategies of breast cancer metastasis to the thyroid through two case reports and a structured literature review. Clinical data from 2 patients with breast cancer who developed thyroid metastasis after surgery were retrospectively analyzed. A structured literature search was conducted in PubMed for reports published between January 2010 and December 2025. In total, 44 cases of breast cancer metastasis to the thyroid, including the 2 cases reported in the present study, were reviewed for pathological characteristics, immunohistochemical profiles, ultrasonographic findings and treatment approaches. For variables with missing information, analyses were performed using only cases with available data as the denominator. Both patients experienced recurrence after initial treatment for breast cancer. Case 1 presented with diffuse thyroid involvement and cervical lymphadenopathy, whereas Case 2 presented with a focal thyroid nodule in the setting of widespread metastatic disease. Fine-needle aspiration, histopathological examination and immunohistochemical analysis supported the diagnosis of metastatic breast carcinoma. Invasive ductal carcinoma was the most frequently reported histological type. Among cases with available data, estrogen positivity was observed in 23 of 32 cases (71.9%), and progesterone receptor positivity was observed in 21 of 32 cases (65.6%). Ultrasonographic information was available for 39 cases: 23 cases (59.0%) showed a focal nodular pattern, and 16 cases (41.0%) showed diffuse parenchymal involvement. Microcalcifications were reported in 12 of the 16 diffuse cases (75.0%). Thyroid metastasis from breast cancer is rare

and may mimic primary thyroid malignancy. Accurate diagnosis requires integration of the patient's oncological history, imaging findings, cytological or histopathological examination, and immunohistochemical profile. Increased clinical awareness and targeted thyroid evaluation may facilitate timely diagnosis in patients with thyroid-related symptoms, palpable cervical abnormalities, suspicious imaging findings, cervical lymphadenopathy or established metastatic disease.

Introduction

According to the latest data released by the International Agency for Research on Cancer of the World Health Organization, breast cancer has become the most common malignant tumor among women globally (1). The most frequent sites of distant metastasis are bone, liver, brain and lung, whereas metastasis to the thyroid gland is uncommon (2). The thyroid is a highly vascularized endocrine organ with unique tissue characteristics, including high blood flow and iodine concentration, which have been proposed as potential factors contributing to its relatively low susceptibility to secondary malignancies (3). Secondary thyroid cancers usually originate from primary tumors in the kidney, gastrointestinal tract, lung or skin, with only a minority arising from breast cancer (4).

Secondary malignancies of the thyroid are uncommon. Reported rates of thyroid metastasis vary considerably among clinical studies and autopsy studies, with autopsy studies reporting an incidence of 1.25-24%; breast cancer accounts for a variable proportion of thyroid metastases across published studies (5,6). The mechanisms underlying the relative rarity of thyroid metastasis remain incompletely understood. Despite the rich vascular supply of the thyroid, rapid arterial blood flow, high oxygen tension and iodine-rich conditions have been proposed to create an unfavorable environment for metastatic implantation, whereas pre-existing thyroid abnormalities may potentially alter the local microenvironment and facilitate metastatic colonization (3,5,7,8). No well-established patient-level risk factors specific to breast cancer metastasis to the thyroid have been identified. Clinically, thyroid metastasis may present as a focal nodule, diffuse gland enlargement, cervical lymphadenopathy or an incidental imaging abnormality. Diagnosis generally relies on integration of the previous oncological history, imaging, cytological or histological examination and immunohistochemical profiling (5,6).

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Prognosis is influenced primarily by the biological behavior of the primary tumor and the extent of systemic metastatic disease; selected patients with isolated thyroid metastasis may benefit from local treatment, whereas systemic therapy is generally favored in patients with disseminated disease (5,6).

Due to the lack of specific clinical or imaging features, differentiating between primary thyroid cancer and metastatic breast cancer presents notable diagnostic challenges (5). Immunohistochemistry remains a reliable method for distinguishing these two entities. The present study reports 2 cases of breast cancer metastasizing to the thyroid and integrates them with a structured literature review to summarize clinical characteristics, diagnostic considerations and therapeutic strategies.

Case reports

Case 1. In December 2016, a 48-year-old woman was diagnosed with right-sided breast cancer and underwent modified radical mastectomy with axillary lymph node dissection at Weifang People's Hospital (Weifang, China). Pathological examination revealed grade II invasive ductal carcinoma (IDC) with ductal carcinoma *in situ* (~10%), measuring 3x2.5x1.4 cm, with perineural invasion, lymphovascular emboli and nipple involvement. Axillary lymph nodes showed metastasis (8/20). Immunohistochemistry revealed: Estrogen receptor (ER; 3+, 95%), progesterone receptor (PR; 2+, 30%), HER2 (2+, fluorescence *in situ* hybridization non-amplified), Ki-67 (30%), cytokeratin 5/6 (CK5/6; focal +) and E-cadherin (+). Histopathological and immunohistochemical examinations were performed as part of routine diagnostic procedures in the hospital pathology department. Owing to the retrospective nature of the present study and the long interval since some of the original examinations, complete technical details of the historical immunohistochemical procedures, including antibody catalogue numbers, dilutions, incubation conditions and detection-system parameters, could not be fully retrieved from the archived laboratory records. The immunohistochemical results for both cases reported in the present study were obtained from the available pathology reports and archived clinical records.

The patient received four cycles of epirubicin (90 mg/m² i.v., d1, q3w) plus cyclophosphamide (600 mg/m² i.v., d1, q3w) followed by four cycles of docetaxel (100 mg/m² i.v., d1, q3w), radiotherapy (total dose 50 Gy in 25 fractions over 5 weeks) and long-term endocrine therapy with anastrozole (1 mg once daily) from June 2017 to April 2025 (94 months), followed by regular follow-up.

During routine follow-up in April 2025, the patient had no clinically notable local compressive symptoms, such as dysphagia, dyspnea or hoarseness. Detailed thyroid function test results were not available in the archived medical records. Thyroid and cervical lymph node ultrasonography revealed diffuse thyroid parenchymal changes with multiple punctate hyperechoic foci and bilateral cervical lymphadenopathy. Some cervical lymph nodes showed loss of the normal fatty hilum and punctate hyperechoic foci. The largest left cervical lymph node measured 7.1x4.7 mm, and the largest right cervical lymph node measured 10.6x5.6 mm (Fig. 1A). Fine-needle aspiration of the bilateral thyroid lobes and cervical lymph

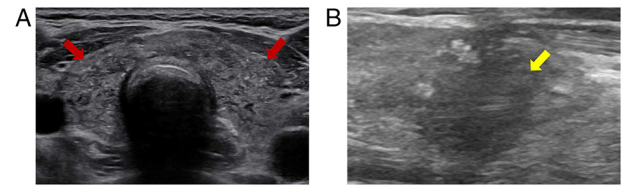


Figure 1. Ultrasonographic findings of the thyroid in 2 patients with breast cancer metastasis. (A) Patient 1: Color Doppler ultrasonography showing diffuse thyroid parenchymal changes with multiple punctate hyperechoic foci (red arrows). (B) Patient 2: Color Doppler ultrasonography of a solid nodule in the lower pole of the right thyroid lobe, demonstrating punctate hyperechoic foci within the lesion (yellow arrow).

nodes revealed malignant cells (Fig. 2). Fine-needle aspiration smears were prepared and stained with hematoxylin and eosin (H&E) and Papanicolaou stain according to the routine cytopathology procedures of the hospital pathology department. As these examinations were performed as part of routine clinical diagnostic practice, the original detailed fixation and staining-protocol records were not retained and could not be retrospectively retrieved. No mutation was detected in BRAF exon 15 using amplification refractory mutation system-PCR. Core needle biopsy of the right thyroid lesion confirmed malignancy. Immunohistochemical staining (Fig. 3) showed ER (3+, 90%), PR (2+, 15%), HER2 (2+, equivocal), GATA-binding protein 3 (GATA3; +), thyroid transcription factor-1 (TTF-1; -), thyroglobulin (TG; focal +), calcitonin (-), CD56 (-) and Ki-67 (55%). The focal TG staining was interpreted cautiously because it may have originated from entrapped non-neoplastic thyroid follicles rather than metastatic tumor cells. Taken together with the clinical history of the patient and the remaining immunophenotypic findings, the lesion was diagnosed as metastatic breast carcinoma involving the thyroid.

Restaging examinations, including bone scintigraphy, cranial MRI, and contrast-enhanced CT, showed no additional metastatic sites beyond the thyroid and cervical lymph nodes. Following multidisciplinary team discussion, thyroid and cervical lymph node involvement was considered a manifestation of recurrent hormone receptor-positive breast cancer after adjuvant endocrine therapy. Because the patient had no clinically notable local compressive symptoms, systemic endocrine-based therapy was considered an appropriate initial management strategy, and immediate thyroid surgery was not recommended. Systemic treatment with dalpiciclib (125 mg p.o. q.d.; d1-21, q4w) plus fulvestrant (500 mg i.m., cycle 1 d1, d15, then d1 q4w) was initiated in April 2025 as first-line systemic treatment for recurrent metastatic disease and was ongoing at the time of manuscript preparation. Follow-up ultrasonography in June 2025 showed an interval decrease in the thyroid and cervical lymph node lesions, including a reduction in the largest left cervical lymph node from 7.1x4.7 to 7.1x3.0 mm. In view of the continued absence of local symptoms and the observed radiological disease control, systemic treatment and surveillance were continued. The treatment timeline is shown in Fig. 4A.

Case 2. A 40-year-old woman was diagnosed with right-sided breast cancer in March 2013. The original 2013 pathology report and immunohistochemical images could not be retrieved

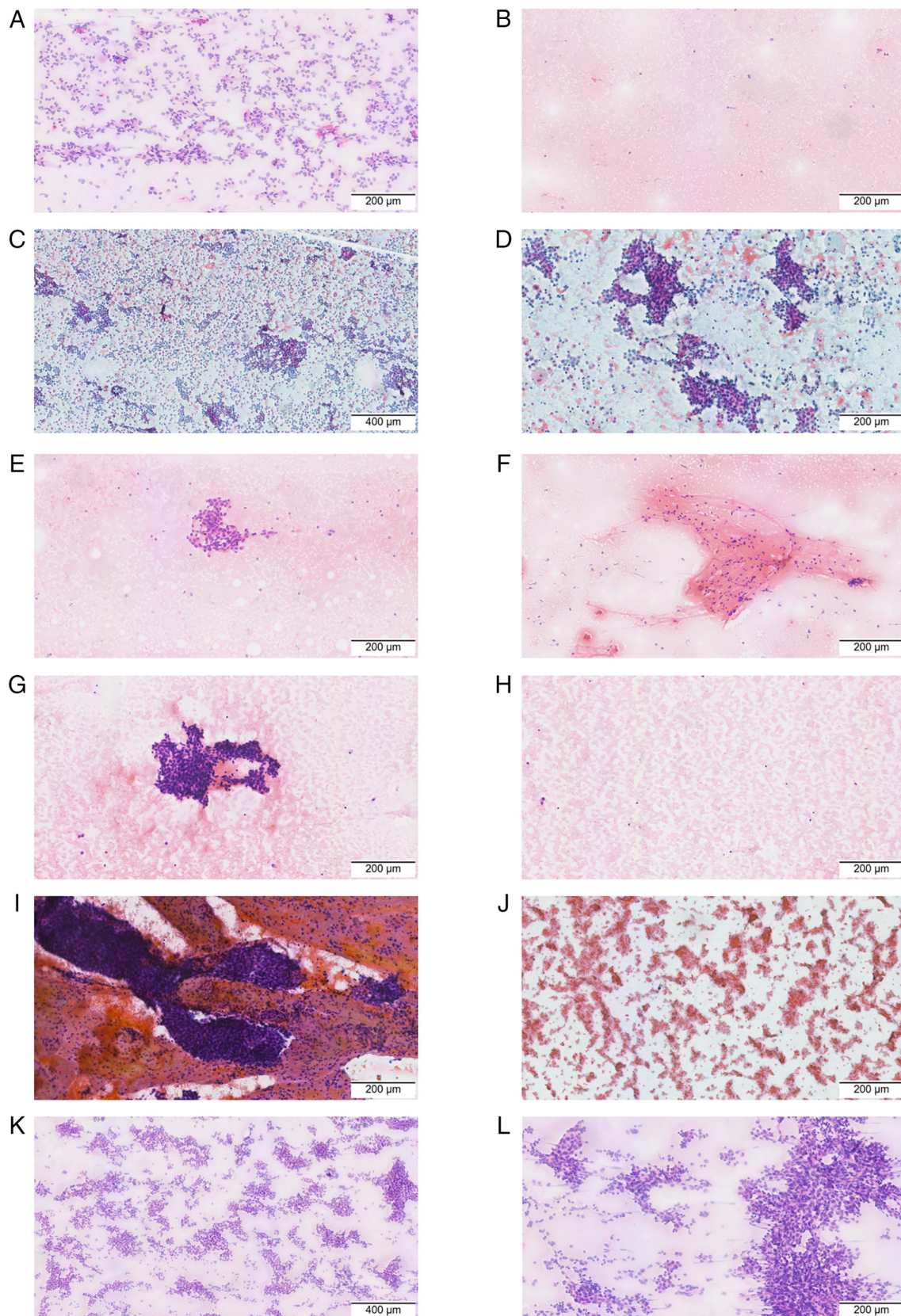


Figure 2. Cytological findings from fine-needle aspiration smears of bilateral thyroid lobes and bilateral cervical lymph nodes in patient 1. (A) H&E staining in the positive area of the left thyroid lobe. Scale bar, 200 μ m. (B) H&E staining in the negative area of the left thyroid lobe. Scale bar, 200 μ m. (C) Papanicolaou staining of the left thyroid lobe positive area. Scale bar, 400 μ m (no negative area observed in this region). (D) Higher-magnification view of the Papanicolaou staining in the same left thyroid lobe. Scale bar, 200 μ m. (E) H&E staining of the positive area of the left cervical lymph node. Scale bar, 200 μ m. (F) H&E staining of the negative area of the left cervical lymph node. Scale bar, 200 μ m. (G) H&E staining of the positive area of the right thyroid lobe. Scale bar, 200 μ m. (H) H&E staining of the negative area in the right thyroid lobe. Scale bar, 200 μ m. (I) Papanicolaou staining of the positive area in the right thyroid lobe. Scale bar, 200 μ m. (J) Papanicolaou staining in the negative area of the right thyroid lobe. Scale bar, 200 μ m. (K) H&E staining of the positive area in the right cervical lymph node. Scale bar, 400 μ m (no negative area observed in this region). (L) Higher-magnification view of the same right cervical lymph-node. Scale bar, 200 μ m. H&E, hematoxylin and eosin.

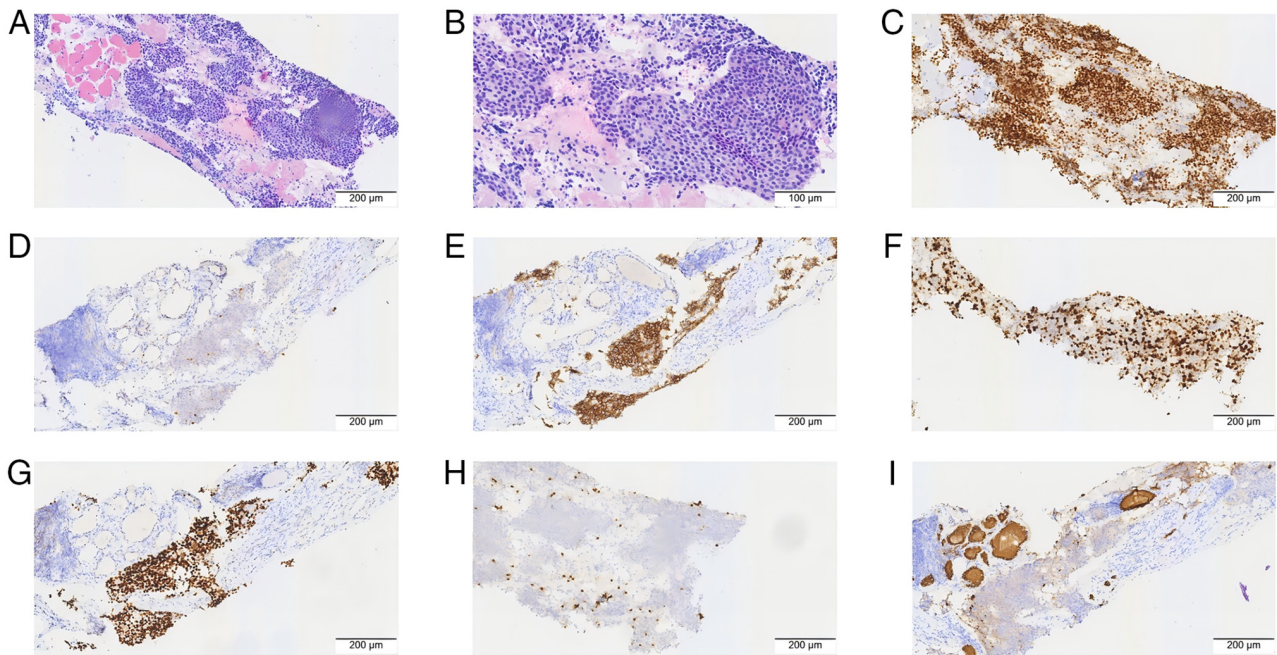


Figure 3. Histopathological and immunohistochemical findings from the core needle biopsy of the right thyroid lesion in patient 1. (A) H&E staining. Scale bar, 200 μ m. (B) H&E staining. Scale bar, 100 μ m. (C) Estrogen receptor strongly positive (3+, 90%). Scale bar, 200 μ m. (D) Progesterone receptor moderately positive (2+, 15%). Scale bar, 200 μ m. (E) HER2 equivocal (2+). Scale bar, 200 μ m. (F) Ki-67 labeling index: 55% positive tumor nuclei. Scale bar, 200 μ m. (G) GATA-binding protein 3 positive. Scale bar, 200 μ m. (H) Thyroid transcription factor-1 negative. Scale bar, 200 μ m. (I) Focal thyroglobulin staining. Scale bar, 200 μ m. H&E, hematoxylin and eosin.

because of the long interval since diagnosis; therefore, the historical pathological and immunohistochemical information described below was obtained from the available archived clinical record. After four cycles of neoadjuvant chemotherapy with docetaxel, doxorubicin and cyclophosphamide, they underwent modified radical mastectomy and axillary lymph node dissection in June 2013. The available clinical record documented invasive breast carcinoma with mixed ductal and lobular components; no metastasis was found in axillary lymph nodes (0/10). Immunohistochemistry revealed: ER (+), PR (+), HER2 (-), Ki-67 (10%), E-cadherin (-) and p120 (+). The patient received four cycles of adjuvant docetaxel plus cyclophosphamide chemotherapy (TC), radiotherapy, and 5 years of tamoxifen as endocrine therapy.

In July 2022, the patient developed multiple bone metastases and was treated with letrozole (2.5 mg p.o. q.d.) plus palbociclib (125 mg p.o. q.d., d1-21, q4w) as first-line therapy. Due to disease progression in June 2024, they switched to alpelisib (300 mg p.o. q.d., continuous) plus fulvestrant (500 mg i.m., cycle 1 d1, d15, then d1 q4w) as second-line treatment, but the regimen was discontinued after 21 days because of severe rash and secondary diabetes. Subsequently, the patient enrolled in a clinical trial receiving fulvestrant (500 mg i.m., cycle 1 d1, d15, then d1 q4w) combined with a novel targeted agent (CDK4/6 inhibitor) and denosumab (120 mg s.c. q4w) for ~11 months, until June 2025.

During follow-up in June 2025, ultrasonography revealed a solid nodule in the lower pole of the right thyroid lobe, classified as Chinese Thyroid Imaging Reporting and Data System category 4C (9), with punctate hyperechoic foci and multiple enlarged bilateral cervical lymph nodes (Fig. 1B). Detailed information regarding thyroid-related symptoms

and thyroid function test results was not available in the archived medical records. Fine-needle aspiration identified malignant cells morphologically consistent with lymph node biopsy specimens (Fig. 5); BRAF mutation was absent. Right cervical lymph node biopsy confirmed metastatic carcinoma. Immunohistochemical analysis of the right cervical lymph node specimen (Fig. 6) showed ER (1+, 35%), PR (2+, <1%), HER2 (IHC score 1+, classified as HER2-negative), GATA3 (+), TG (-), TTF-1 (-), paired box gene 8 (PAX8; -) and CK7 (+). Due to the morphological concordance between the thyroid aspirate and the cervical lymph node specimens, together with the breast cancer history and the immunophenotype of the lymph node metastasis of the patient, the thyroid lesion was diagnosed as metastatic breast carcinoma.

Restaging PET/CT demonstrated hypermetabolic lesions involving the bilateral cervical lymph nodes, bones, left adrenal gland and right thyroid lobe, consistent with widespread metastatic disease. Due to the presence of widespread extra-thyroid metastatic disease and progression after multiple lines of endocrine-based therapy, thyroid surgery was not considered likely to provide meaningful survival or disease-control benefit. Systemic treatment was therefore prioritized. Following further disease progression during endocrine-based therapy, treatment was changed to exemestane (25 mg p.o. q.d.), everolimus (10 mg p.o. q.d.) and abemaciclib (150 mg p.o. b.i.d.) in July 2025. Disease progression with liver metastasis occurred in September 2025, and the patient was then switched to nab-paclitaxel (200 mg i.v., d1, q3w) plus cisplatin (30 mg i.v., d1-3, q3w) chemotherapy. At the time of manuscript preparation, the patient remained on this treatment. The treatment timeline for the patient is shown in Fig. 4B.

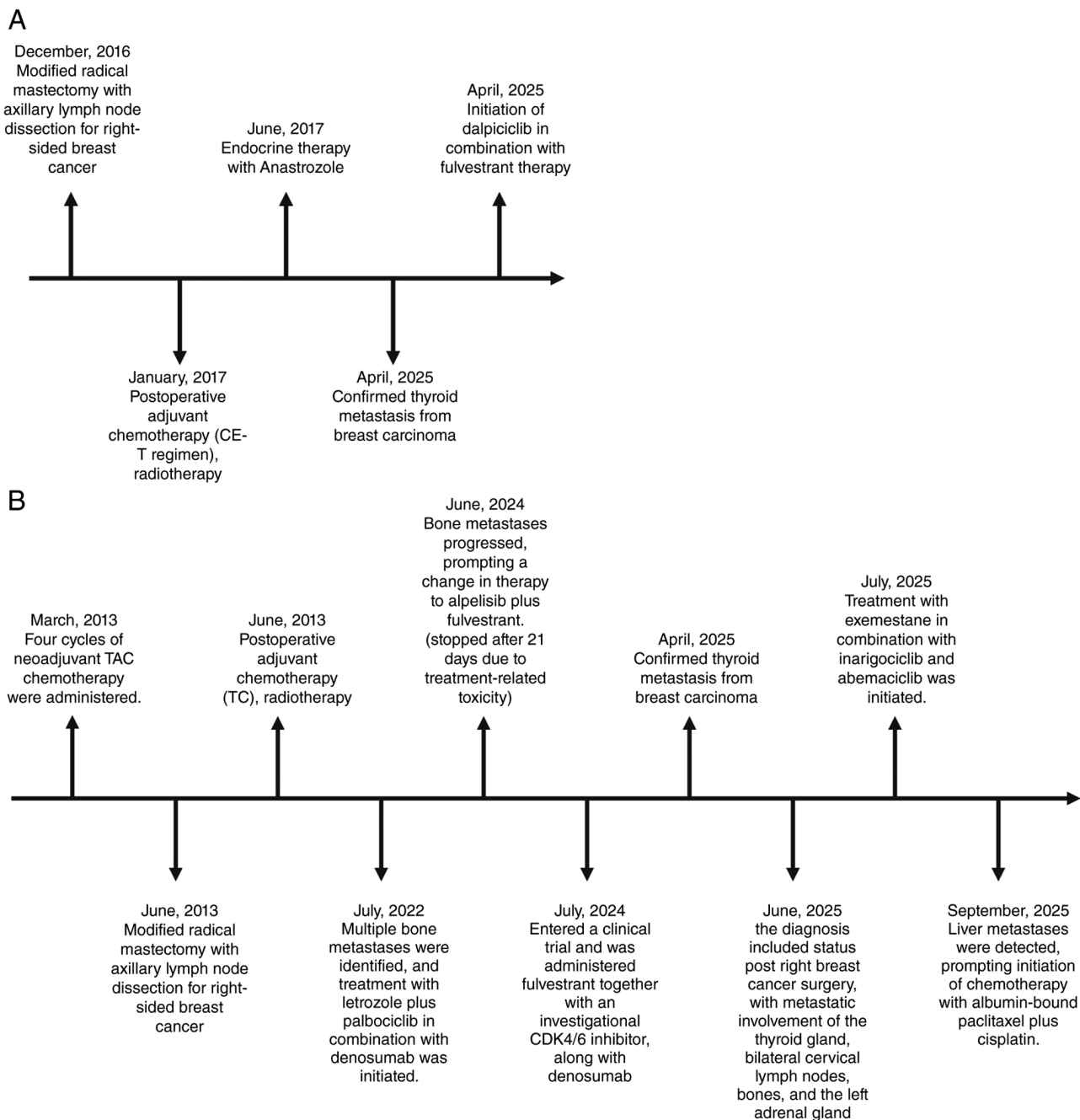


Figure 4. Clinical course and treatment timelines of 2 patients with breast cancer. (A) Patient 1: Timeline illustrating the clinical course from initial breast cancer diagnosis to subsequent detection of thyroid metastasis. (B) Patient 2: Timeline illustrating the clinical course from initial breast cancer diagnosis to multiple subsequent episodes of disease progression.

Literature review

A structured literature search was conducted in PubMed (<https://pubmed.ncbi.nlm.nih.gov/>) to identify reports published between January 1, 2010 and December 31, 2025. The search was last updated on August 6, 2026. The following search strategy was used: ('Breast Neoplasms' [Mesh] OR 'breast cancer' [Title/Abstract] OR 'breast carcinoma' [Title/Abstract] OR 'mammary carcinoma' [Title/Abstract]) AND ('Thyroid Neoplasms/secondary' [Mesh] OR 'thyroid metastasis' [Title/Abstract] OR 'thyroid metastases' [Title/Abstract] OR 'thyroid gland metastasis' [Title/Abstract] OR 'thyroid gland metastases' [Title/Abstract] OR 'metastasis

to the thyroid' [Title/Abstract] OR 'metastases to the thyroid' [Title/Abstract] OR (('Thyroid Gland' [Mesh] OR thyroid [Title/Abstract]) AND (metastasis [Title/Abstract] OR metastases [Title/Abstract] OR metastatic [Title/Abstract])). No article-type or relative publication-date filters were applied.

Reports were eligible if they described ≥ 1 patient with pathologically confirmed breast cancer metastasis to the thyroid gland and provided extractable case-level clinical information. Reports of thyroid malignancies metastatic to the breast, metastases from non-breast primary tumors, articles without individual patient data, duplicate reports and reports lacking sufficient evidence of thyroid involvement were excluded.

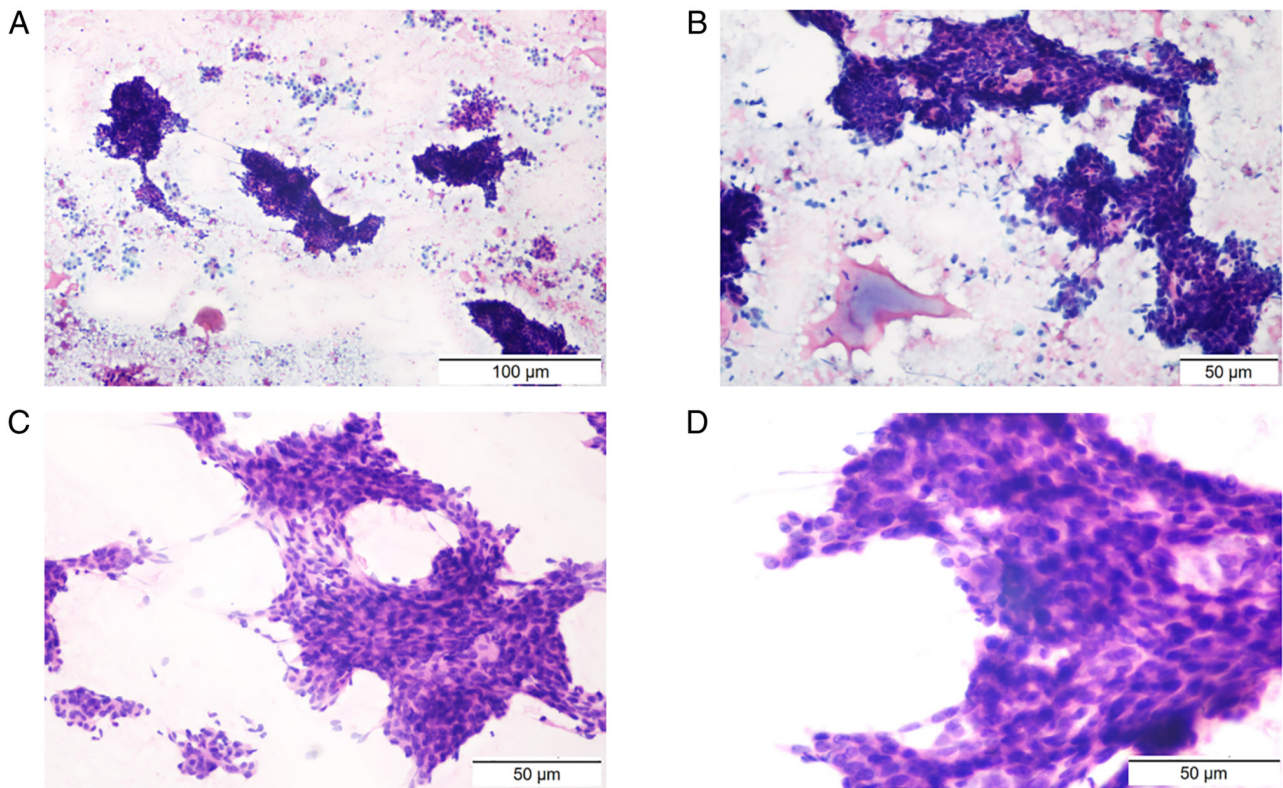


Figure 5. Cytological findings from fine-needle aspiration smears of a C-TIRADS 4C nodule in the right thyroid lobe and bilateral cervical lymph nodes in patient 2. (A) H&E staining of the right thyroid lobe, C-TIRADS 4C nodule. Scale bar, 100 μm . (B) Higher-magnification view of the same right thyroid lobe, C-TIRADS 4C nodule. Scale bar, 50 μm . (C) H&E staining of the left cervical lymph node. Scale bar, 50 μm . (D) H&E staining of the right cervical lymph node. Scale bar, 50 μm . H&E, hematoxylin and eosin.

The database search, screening of titles, abstracts and full texts, reviewing of eligibility, and checking extracted data were performed by two authors. Any disagreements were resolved through discussion and consensus. Data were extracted into a standardized table, including publication year, patient age, breast cancer histological type, receptor status, interval between the initial diagnosis of breast cancer and thyroid metastasis, other involved or metastatic sites, ultrasonographic findings, and treatment. When the same patient appeared to have been reported in more than one publication, only the report containing the most complete information was retained. Variables that were not reported were recorded as 'not reported' and excluded from the denominator for the corresponding percentage calculation.

Receptor status was recorded as reported in each source publication. Because the specimen source was not consistently specified, receptor status was analyzed at the case level. When discordant receptor results were reported among different specimens from the same patient, the case was classified as positive if at least one reported specimen was positive. Ultrasonographic findings were categorized as focal nodular or diffuse parenchymal patterns according to the descriptions in the source publications. Microcalcifications were counted only when explicitly reported.

Discussion

In the present structured literature review, 44 cases of breast cancer metastasis to the thyroid, including the 2 cases

reported in the present study, were evaluated (5,10-42; Table I). The mean patient age was 55.9 years, with a range of 34-82 years. IDC was the most frequently reported histological type. Among the 32 cases with available ER data, 23 were ER-positive (71.9%), while 21 of the 32 cases with available PR data were PR-positive (65.6%). Cases in which receptor status was not reported were excluded from the corresponding denominator. These findings indicate that hormone receptor-positive tumors accounted for a substantial proportion of the reported cases. However, in the absence of a comparator population, these descriptive data do not establish that hormone receptor-positive breast cancers have a specific propensity to metastasize to the thyroid.

Ultrasonographic information was available for 39 cases. A focal nodular pattern was reported in 23 cases (59.0%), whereas diffuse parenchymal involvement was reported in 16 cases (41.0%). Among the 16 cases with diffuse involvement, 12 (75.0%) exhibited microcalcifications. The metastatic distribution, ultrasonographic patterns and treatment approaches of the included cases are summarized in Table II. The 2 patients in the present study demonstrated these two principal patterns: Diffuse thyroid involvement with punctate hyperechoic foci in Case 1 and a focal thyroid nodule with punctate hyperechoic foci in Case 2. Nevertheless, neither the nodular nor the diffuse pattern is specific for metastatic disease, and punctate echogenic foci may also be observed in primary thyroid malignancies. These ultrasonographic findings should therefore be interpreted in combination with the oncological history of the patient, pathological findings and systemic disease status.

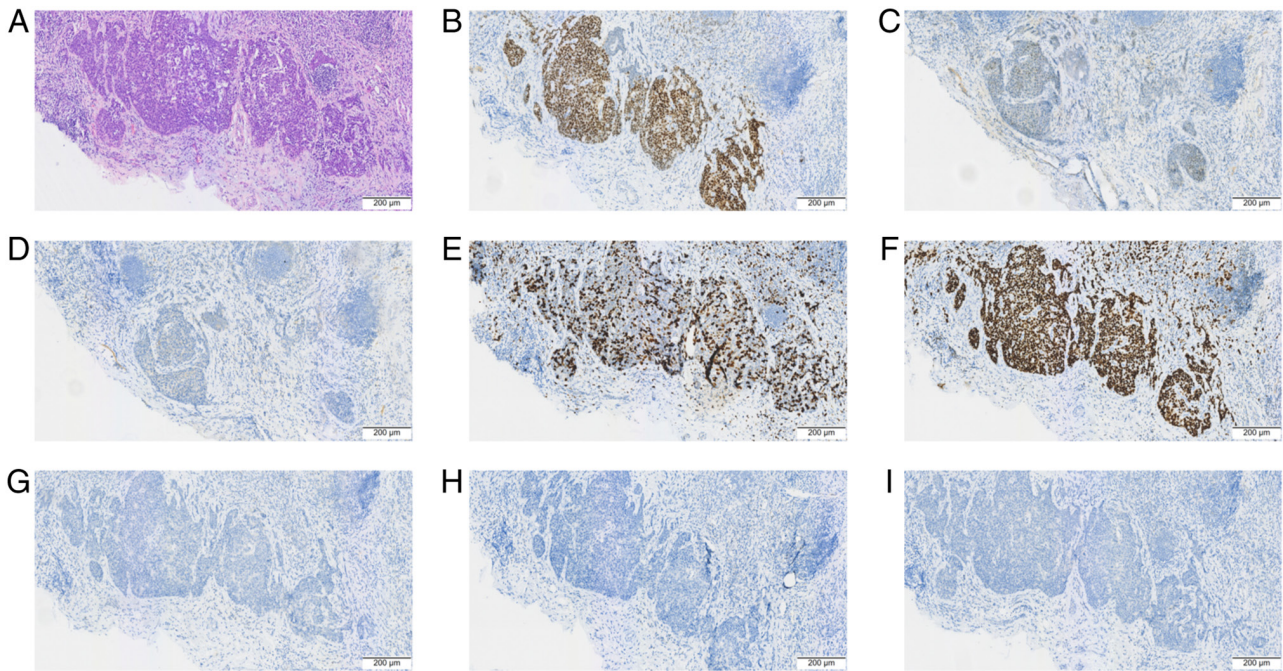


Figure 6. Histopathological and immunohistochemical findings of the right cervical lymph node biopsy from patient 2. (A) Hematoxylin and eosin staining. Scale bar, 200 μ m. (B) Estrogen receptor, weakly positive (1+, 35%). Scale bar, 200 μ m. (C) Progesterone receptor, moderately positive (2+, <1%). Scale bar, 200 μ m. (D) HER2 immunohistochemical score 1+ (HER2-negative). Scale bar, 200 μ m. (E) Ki-67 labeling index: 45% positive tumor nuclei. Scale bar, 200 μ m. (F) GATA-binding protein 3 positive. Scale bar, 200 μ m. (G) Thyroid transcription factor-1 negative. Scale bar, 200 μ m. (H) Thyroglobulin, negative. Scale bar, 200 μ m. (I) Paired box gene 8, negative. Scale bar, 200 μ m.

Potential routes of breast cancer metastasis to the thyroid include hematogenous dissemination and retrograde lymphatic spread. The thyroid is highly vascularized, yet clinically detected metastases to this organ remain uncommon. It has been proposed that rapid arterial blood flow, high oxygen tension and a relatively high iodine concentration may create a microenvironment that is unfavorable for the implantation and growth of circulating tumor cells (7). Pathological alterations of the thyroid gland have also been proposed to modify this environment and potentially increase susceptibility to metastatic colonization (8,43). However, these hypotheses are based primarily on clinical observations and theoretical considerations, and direct mechanistic evidence remains limited. The proposed microenvironmental suppression of thyroid metastasis should therefore be regarded as speculative.

Estrogen can influence thyroid physiology through interactions with the hypothalamic-pituitary-thyroid axis, thyroxine-binding globulin and ER signaling in thyroid tissue (44-47). However, these physiological interactions do not establish a causal mechanism linking estrogen signaling to thyroid-specific metastasis. The predominance of hormone receptor-positive tumors in the reported cases should therefore be interpreted as a descriptive clinical observation rather than evidence of a hormone-mediated thyroid tropism.

Breast cancer metastasis to the thyroid may present as a thyroid nodule, diffuse thyroid enlargement, a neck mass, dysphagia, dyspnea or hoarseness, but it may also be detected incidentally in asymptomatic patients. The radiological appearance may closely resemble that of a primary thyroid malignancy (10,48). When thyroid involvement is clinically suspected, ultrasonography is a useful initial imaging modality

for characterizing thyroid and cervical lymph node abnormalities (48). Targeted thyroid evaluation may be appropriate in patients with breast cancer with thyroid-related symptoms, palpable cervical abnormalities, suspicious incidental imaging findings, cervical lymphadenopathy or established metastatic disease. However, the available case-report-level evidence does not support routine thyroid ultrasound screening for all breast cancer survivors.

Distinguishing metastatic breast carcinoma from a primary thyroid malignancy requires integration of the clinical history, tumor morphology and immunohistochemical profile of the patient. Primary thyroid carcinomas may display adenocarcinoma-like architecture, while metastatic breast carcinoma may show acinar, trabecular or solid growth patterns that overlap with those of primary thyroid tumors (11). Breast-derived tumors commonly express markers such as ER, PR, GATA3 and gross cystic disease fluid protein-15, whereas thyroid-derived tumors generally express TTF-1, PAX8 and TG (49,50). Nevertheless, no single immunohistochemical marker should be interpreted in isolation. In Case 1, focal TG staining may have reflected entrapped non-neoplastic thyroid follicles rather than TG expression by metastatic tumor cells. The combined findings of GATA3 and hormone receptor positivity, together with TTF-1 negativity and the previous breast cancer history, supported a breast origin. In Case 2, GATA3 positivity and negative staining for TTF-1, PAX8 and TG similarly supported metastatic breast carcinoma. HER2 results should also be interpreted according to established criteria: An immunohistochemical score of 1+ is classified as HER2-negative, whereas a score of 2+ is equivocal and requires confirmatory *in situ* hybridization to determine HER2 amplification status.

Table I. Demographic, histological and receptor characteristics of 44 cases of breast cancer metastasis to the thyroid included in the present analysis.

First author, year	Age, years	Breast cancer histology	ER	PR	HER2	Interval, months	(Refs.)
Present study, Case 1	56	IDC	Positive	Positive	Primary: IHC 2+, FISH non-amplified; thyroid metastasis: IHC 2+ (equivocal)	100	-
Present study, Case 2	52	Mixed IDC/ILC	Positive	Positive	Primary: Negative; cervical LN metastasis: IHC 1+ (HER2-negative)	147	-
Jbali <i>et al</i> , 2025	63	ILC	Positive	Negative	Negative	25	(12)
He <i>et al</i> , 2025	34	IDC	Positive	Positive	Negative	97	(13)
Gvazava <i>et al</i> , 2025	63	IDC	Positive	Positive	Negative	179	(14)
Guan <i>et al</i> , 2025	55	IDC	Positive	Positive	Negative	100	(15)
Gao <i>et al</i> , 2025	41	IDC	Positive	Positive	Negative	96	(10)
Yousaf <i>et al</i> , 2025	47	Invasive breast carcinoma	NR	NR	NR	0	(16)
Ramírez Stieben <i>et al</i> , 2024	56	IDC	Positive	Positive	Positive	60	(19)
Patrizio <i>et al</i> , 2023	71	IDC	Positive	Positive	Negative	216	(5)
Hoshi <i>et al</i> , 2023	58	IDC	Positive	Positive	Negative	156	(17)
Bai <i>et al</i> , 2023	35	IDC	Negative	Negative	Positive	60	(18)
Zhang <i>et al</i> , 2022	46	NR	NR	NR	NR	24	(20)
Yang <i>et al</i> , 2022	62	IDC	Negative	Negative	Positive	60	(21)
Wen <i>et al</i> , 2022	49	IDC	Positive	Positive	NR	42	(22)
Gharib <i>et al</i> , 2022	48	NR	NR	NR	NR	0	(23)
Celik <i>et al</i> , 2022	78	IDC with neuroendocrine differentiation	Positive	Negative	Negative	0	(24)
Yu <i>et al</i> , 2021	59	IDC with IMPC component	Positive	Positive	Negative	60	(25)
Wang <i>et al</i> , 2021	54	IDC	Negative	Negative	Positive	22	(26)
Kiziltan <i>et al</i> , 2021	82	IDC	Positive	Positive	Negative	144	(27)
Jung <i>et al</i> , 2021	59	IDC	NR	NR	NR	180	(28)
Zhang <i>et al</i> , 2020	38	IDC	Negative	Negative	Positive	24	(29)
Wang <i>et al</i> , 2020	58	Mucinous carcinoma with IDC	NR	NR	NR	156	(30)
Lee <i>et al</i> , 2020	64	IDC	Positive	Positive	NR	5	(31)
Raveendrannair <i>et al</i> , 2019	36	IDC	NR	NR	NR	0	(32)
Pakuła <i>et al</i> , 2019	66	Invasive breast carcinoma	NR	NR	NR	240	(33)
Durmo <i>et al</i> , 2019	72	IDC	Positive	Positive	Negative	NR	(34)
Pensabene <i>et al</i> , 2018	64	ILC	Positive	Positive	Negative	6	(35)
Zhou <i>et al</i> , 2017	48	Invasive breast carcinoma	Negative	Positive	Positive	87	(36), Case 1
Zhou <i>et al</i> , 2017	59	IDC	Negative	Negative	NR	27	(36), Case 2
Zhou <i>et al</i> , 2017	57	Signet-ring cell carcinoma	Positive	Negative	NR	108	(36), Case 3
Zhou <i>et al</i> , 2017	67	IDC	Negative	Negative	NR	71	(36), Case 4
Zhou <i>et al</i> , 2017	48	IDC	Negative	Negative	NR	121	(36), Case 5

Table I. Continued.

First author, year	Age, years	Breast cancer histology	ER	PR	HER2	Interval, months	(Refs.)
Zhou <i>et al</i> , 2017	52	IDC	Positive	Positive	Positive	6	(36), Case 6
Zhou <i>et al</i> , 2017	69	Invasive breast carcinoma	NR	NR	NR	57	(36), Case 7
Zhou <i>et al</i> , 2017	43	Medullary carcinoma	Negative	Negative	NR	82	(36), Case 8
Plonczak <i>et al</i> , 2017	62	IDC	Positive	Positive	Negative	144	(37)
Magers <i>et al</i> , 2016	37	IDC	Positive	Positive	Positive	72	(11)
Liu <i>et al</i> , 2014	47	IDC	Left breast: Positive; right breast: Positive	Left breast: Positive; right breast: Negative	Left breast: Positive; right breast: Negative	48	(38)
Nguyen <i>et al</i> , 2013	67	Invasive breast carcinoma	NR	NR	NR	48	(39)
Lacka <i>et al</i> , 2012	54	ILC	NR	NR	NR	168	(40)
Cihan <i>et al</i> , 2011	70	IDC	Positive	Positive	Negative	18	(41)
Skowrońska-Józwiak <i>et al</i> , 2010	49	ILC	NR	NR	NR	0	(42), Case 1
Skowrońska-Józwiak <i>et al</i> , 2010	65	Invasive breast carcinoma	NR	NR	NR	48	(42), Case 2

All patients were female. Age refers to age at diagnosis of thyroid metastasis. Interval refers to the time from the initial diagnosis of breast cancer to the diagnosis of thyroid metastasis; an interval of 0 months indicates synchronous diagnosis of primary breast cancer and thyroid metastasis. Receptor status was recorded as reported in the source publications and analyzed at the case level. When discordant receptor results were reported across different specimens from the same patient, the case was classified as positive if at least one reported specimen was positive. HER2 IHC scores of 0 or 1+ were classified as negative, whereas an IHC score of 2+ was considered equivocal unless confirmatory *in situ* hybridization results were available. ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; FISH, fluorescence *in situ* hybridization; NR, not reported; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; IMPC, invasive micropapillary carcinoma.

Management of breast cancer metastasis to the thyroid should be individualized according to the extent of metastatic disease, local symptoms, tumor biology, expected survival, available systemic treatment options and multidisciplinary assessment. Thyroid surgery may be considered in selected patients with isolated or oligometastatic thyroid involvement, technically resectable disease or clinically notable local compressive symptoms (5,7,8,51,52). By contrast, for patients with widespread extra-thyroid metastases, systemic therapy generally takes priority because local thyroid surgery is unlikely to control the overall disease course. In Case 1, thyroid and cervical lymph node involvement occurred without evidence of additional distant metastases. The patient had no clinically notable local compressive symptoms. Following multidisciplinary discussion, endocrine-based systemic therapy with dalpiciclib and fulvestrant was selected as the initial treatment rather than immediate thyroid surgery. Subsequent ultrasonography demonstrated a reduction in the thyroid and cervical lymph node lesions, supporting continued systemic treatment and surveillance. In Case 2, thyroid involvement occurred in the setting of extensive metastatic disease

involving the cervical lymph nodes, bones, and left adrenal gland, with subsequent liver progression. In this context, thyroid surgery was unlikely to provide meaningful overall disease-control or survival benefit, and systemic therapy was therefore prioritized. These contrasting cases illustrate that the decision to perform thyroid surgery should consider local symptoms, disease distribution, anticipated benefit from systemic treatment and multidisciplinary assessment rather than thyroid involvement alone.

Several limitations should be acknowledged. First, the present analysis was based predominantly on published case reports and small case series, which are susceptible to publication and selection bias and may not represent the full clinical spectrum of breast cancer metastasis to the thyroid. Second, clinical, pathological, ultrasonographic and treatment data were incompletely reported in several published cases. Detailed thyroid function test results were not available in the archived medical records of either patient, and detailed thyroid-related symptom documentation was unavailable for Case 2. For Case 2, the original pathology report and immunohistochemical images from the initial breast cancer diagnosis

Table II. Metastatic distribution, ultrasonographic findings and treatment.

First author, year	Other involved or metastatic sites	Ultrasonographic pattern	Reported treatment following diagnosis of thyroid metastasis	(Refs.)
Present study, Case 1	Cervical LNs	Diffuse parenchymal; punctate echogenic foci	Fulvestrant plus dalpiciclib	-
Present study, Case 2	Cervical LNs, bone, left adrenal gland	Focal nodular; punctate echogenic foci	Exemestane, everolimus, and abemaciclib; after progression, nab-paclitaxel plus cisplatin	-
Jbali <i>et al</i> , 2025	Supraclavicular LNs, cervical LNs	Focal nodular	Radioactive iodine; radiotherapy; chemotherapy; endocrine therapy	(12)
He <i>et al</i> , 2025	Supraclavicular LNs, cervical LNs	Diffuse parenchymal	Surgery; endocrine therapy; targeted therapy; levothyroxine replacement therapy	(13)
Gvazava <i>et al</i> , 2025	Bone, mediastinal LNs	Diffuse parenchymal	Surgery; endocrine therapy; targeted therapy	(14)
Guan <i>et al</i> , 2025	Axillary LNs, lung, bone	Diffuse parenchymal; microcalcifications	Endocrine therapy; targeted therapy	(15)
Gao <i>et al</i> , 2025	None	Focal nodular	Surgery; endocrine therapy; targeted therapy	(10)
Yousaf <i>et al</i> , 2025	Axillary LNs, cervical LNs, mediastinal LNs	NR	NR	(16)
Patrizio <i>et al</i> , 2023	Liver, bone, peritoneum, infraclavicular LNs, paratracheal LNs	Focal nodular; microcalcifications	Surgery; chemotherapy; levothyroxine replacement therapy	(5)
Hoshi <i>et al</i> , 2023	Cervical LNs	Focal nodular	Surgery	(17)
Bai <i>et al</i> , 2023	Pleura, chest wall, lung (carcinomatous lymphangitis), left breast, pancreas, adrenal glands, stomach	Diffuse parenchymal; microcalcifications	Chemotherapy; targeted therapy	(18)
Ramírez Stieben <i>et al</i> , 2024	Supradiaphragmatic LNs, bone, liver	Focal nodular	Surgery; chemotherapy; targeted therapy	(19)
Zhang <i>et al</i> , 2022	Axillary LNs, brain	Diffuse parenchymal	Chemotherapy; targeted therapy	(20)
Yang <i>et al</i> , 2022	Cervical LNs	Focal nodular; microcalcifications	Chemotherapy; targeted therapy	(21)
Wen <i>et al</i> , 2022	Cervical LNs, mediastinal LNs, bone	Diffuse parenchymal; microcalcifications	Chemotherapy	(22)
Gharib <i>et al</i> , 2022	Liver, bone, lung, pleura	NR	Chemotherapy; targeted therapy	(23)
Celik <i>et al</i> , 2022	Bone, lung, mediastinal LNs	NR	Endocrine therapy	(24)
Yu <i>et al</i> , 2021	Cervical LNs, mediastinal LNs	Focal nodular; microcalcifications	Surgery; chemotherapy; targeted therapy	(25)
Wang <i>et al</i> , 2021	Cervical LNs, chest wall	Diffuse parenchymal; microcalcifications	Chemotherapy; targeted therapy	(26)
Kiziltan <i>et al</i> , 2021	Bone, mediastinal LNs	Focal nodular; microcalcifications	Chemotherapy	(27)
Jung <i>et al</i> , 2021	Bone, mediastinal LNs, paraaortic area	Focal nodular	Chemotherapy	(28)
Zhang <i>et al</i> , 2020	None	Focal nodular	Surgery	(29)
Wang <i>et al</i> , 2020	None	Focal nodular	Surgery	(30)
Lee <i>et al</i> , 2020	None	Diffuse parenchymal; microcalcifications	Surgery	(31)
Raveendrannair <i>et al</i> , 2019	Lung	NR	Surgery	(32)

Table II. Continued.

First author, year	Other involved or metastatic sites	Ultrasonographic pattern	Reported treatment following diagnosis of thyroid metastasis	(Refs.)
Pakuła <i>et al</i> , 2019	None	Focal nodular; calcifications	Surgery; chemotherapy; endocrine therapy	(33)
Durmo <i>et al</i> , 2019	Bone	Focal nodular	NR	(34)
Pensabene <i>et al</i> , 2018	None	Focal nodular; calcifications	Surgery; endocrine therapy	(35)
Zhou <i>et al</i> , 2017	Chest wall	Diffuse parenchymal; microcalcifications	Chemotherapy	(36), Case 1
Zhou <i>et al</i> , 2017	Chest wall	Diffuse parenchymal; microcalcifications	Chemotherapy	(36), Case 2
Zhou <i>et al</i> , 2017	Lung, supraclavicular LNs	Diffuse parenchymal; microcalcifications	Chemotherapy	(36), Case 3
Zhou <i>et al</i> , 2017	Axillary LNs	Diffuse parenchymal; microcalcifications	Chemotherapy	(36), Case 4
Zhou <i>et al</i> , 2017	Lung	Focal nodular	Surgery	(36), Case 5
Zhou <i>et al</i> , 2017	None	Focal nodular	Surgery	(36), Case 6
Zhou <i>et al</i> , 2017	None	Diffuse parenchymal; microcalcifications	Surgery	(36), Case 7
Zhou <i>et al</i> , 2017	Cervical LNs, mediastinal LNs	Diffuse parenchymal; microcalcifications	Chemotherapy	(36), Case 8
Plonczak <i>et al</i> , 2017	Lung, bone	Focal nodular	Surgery; endocrine therapy	(37)
Magers <i>et al</i> , 2016	Brain, bone	NR	NR	(11)
Liu <i>et al</i> , 2014	Cervical LNs	Diffuse parenchymal; microcalcifications	Targeted therapy	(38)
Nguyen <i>et al</i> , 2013	None	Focal nodular	NR	(39)
Lacka <i>et al</i> , 2012	Supraclavicular LNs, bone, adrenal gland	Focal nodular	Surgery; levothyroxine replacement therapy	(40)
Cihan <i>et al</i> , 2011	Bone, liver	Focal nodular	Radiotherapy; chemotherapy	(41)
Skowrońska-Jóźwiak <i>et al</i> , 2010	None	Focal nodular; calcifications	Surgery; levothyroxine replacement therapy	(42), Case 1
Skowrońska-Jóźwiak <i>et al</i> , 2010	Lung, pleura	Focal nodular; calcifications	NR	(42), Case 2

'None' indicates that the source publication explicitly reported no additional involved or metastatic site, whereas NR indicates that the relevant information was not reported. Other involved or metastatic sites were recorded as described in the source publications; for the present cases, sites identified at the diagnosis of thyroid involvement are listed. Treatment categories were expanded to avoid ambiguous single-letter abbreviations. Levothyroxine replacement therapy refers to thyroid hormone replacement therapy and is distinct from endocrine therapy for breast cancer. Ultrasonographic findings were categorized as focal nodular or diffuse parenchymal patterns according to the descriptions in the source publications, and microcalcifications were recorded only when explicitly reported. LN, lymph node; LNs, lymph nodes; NR, not reported.

in 2013 could not be retrieved because of the long interval since diagnosis and the limited availability of historical archived materials. Therefore, the historical histological and immunohistochemical information for the primary breast tumor was extracted from the available archived clinical record rather than verified by direct review of the original pathology materials. Percentage calculations were therefore based only on cases for which the relevant variable was available, and cases with unreported data were excluded from the corresponding denominator. Third, the structured literature review was based on a PubMed search and did not include a formal risk-of-bias or quality appraisal; therefore, it should not be interpreted as a PRISMA-compliant systematic review. Finally, the included

cases covered the period from 2010 to 2025, during which systemic treatment for metastatic breast cancer evolved substantially with the introduction of CDK4/6 inhibitors, PI3K inhibitors and antibody-drug conjugates. Differences in treatment era, therapeutic availability, disease burden and follow-up duration limit direct comparisons of management strategies and clinical outcomes across the reported cases.

In conclusion, thyroid metastasis from breast cancer is rare and may present as either focal nodular or diffuse thyroid involvement. Because its clinical and imaging findings overlap with those of primary thyroid malignancies, diagnosis should be based on integration of the oncological history, imaging findings, cytological or histopathological examination, and

immunohistochemical profile of the patient. Clinicians should maintain appropriate awareness of possible thyroid involvement in patients with breast cancer with thyroid-related symptoms, cervical abnormalities, suspicious imaging findings or established metastatic disease. Treatment should be individualized according to the extent of disease, local symptoms, tumor biology, patient condition and multidisciplinary assessment. The available evidence does not support routine thyroid screening for all breast cancer survivors.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

YL conducted the database search and screened the titles, abstracts, and full texts. WW reviewed the eligibility decisions and checked the extracted data. YL designed the study and wrote the manuscript. YL and WW confirmed the authenticity of all the raw data. YL and WW gathered medical pictures and examined patient information. YL and WW contributed to the study's conceptualization, general design and quality assurance. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

The present study was approved by the Ethics Committee of Weifang People's Hospital (approval no. KYLL20251226-2).

Patient consent for publication

Written informed consent was obtained from both patients for the publication of these case reports and the accompanying images.

Competing interests

The authors declare that they have no competing interests.

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