

Breast Carcinoma Metastasis to Thyroid Gland Masquerading as Nodular Goitre: A Case Report

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ABSTRACT

Thyroid gland, despite being a highly vascular organ, is an extremely unusual site for metastasis from primary carcinoma like breast. We, hereby, report a case of metastatic lesion in the thyroid with breast carcinoma as a primary, in a 55-year-old postmenopausal female. The metastatic focus had masqueraded as nodular goitre, thereby, creating diagnostic difficulty. The case was suspected on Fine Needle Aspiration (FNA) and confirmed by immunocytochemistry on cell block with progesterone and Her2neu positivity. Also, we have attempted to review the literature reporting similar occurrences. Although breast cancer is less frequent to metastasize to thyroid, it is advised to always exclude metastasis from breast carcinoma especially if new thyroid lesions occur in patients with this malignancy. Such cases create diagnostic dilemma on cytology due to morphologic similarities between primary and metastatic thyroid lesions. Cell block is a crucial technique where ancillary techniques like immunocytochemistry can be applied and help in early and timely diagnosis, hence, rendering better prognostic outcome.

Keywords: Breast carcinoma, Cell block, Her 2 neu, Immunocytochemistry, Invasive ductal carcinoma, Progesterone, Synchronous, Thyroid gland

CASE REPORT

A 55-year-old, female presented with the chief complaints of left breast lump since four months with history of significant weight loss and loss of appetite. She had menarche at 13 years of age with history of menorrhagia. She had tuberculosis 20 years back for which she had taken full ATT course. There was no family history of breast carcinoma or oral contraceptives intake. The patient had a past history of thyroid swelling since 10 years previously diagnosed as nodular goiter with clinical hypothyroidism and was undergoing Eltroxin therapy for the same. No history of dysphagia, dyspnoea, voice change, constipation, diarrhoea tremors or palpitation was present. No family history of thyroid disorder present. On examination, ill-defined lump was present involving upper outer quadrant of left breast, measuring 3.5×3 cm, with restricted mobility. There was no peau de orange but nipples were retracted. A lymph node measuring 1×1 cm was present in the left axilla. Right breast and axilla were without any abnormality. Midline thyroid swelling measured 3×2.5 cm with a nodular surface, extending more towards left-side, firm and moved with deglutition. Ultrasound of thyroid swelling was suggestive of heteroechoic lesion in left lobe of thyroid with increased vascularity.

CT Neck showed a heterogeneously enhancing lesion measuring 21×27 mm. CT breast showed multiple enhancing lesions. CT scan showed a sclerotic foci in L3 vertebral body [Table/Fig-1] and an enlarged mediastinal paraortic lymph node.

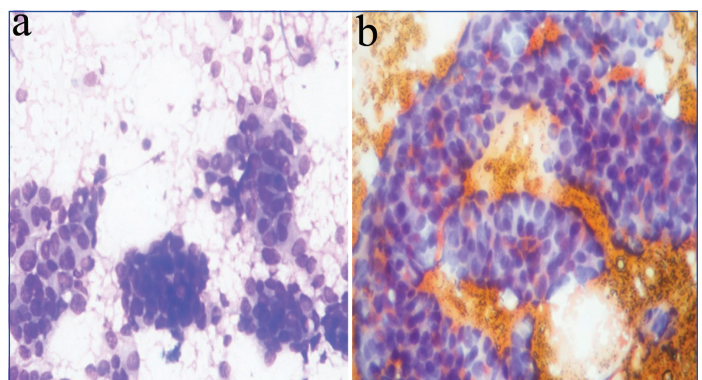
Fine Needle Aspiration Cytology (FNAC) of breast lump was performed. Cytopathological report showed hypercellular smears comprising of moderately pleomorphic malignant ductal epithelial cells lying in clusters as well as papillae, having moderate amphophilic cytoplasm with hyperchromatic nuclei and occasional nucleoli, admixed with stromal fragments [Table/Fig-2,3].

Cytology of lymph node showed similar morphology [Table/Fig-4].

Provisional diagnosis of Infiltrating duct carcinoma of left breast with involvement of left axillary lymph node was suggested which was later confirmed by histopathology of breast biopsy and the patient was planned for modified radical mastectomy to address left-side breast cancer. Cell block was made from the FNA aspirate from breast lump and showed malignant ductal epithelial cells with similar



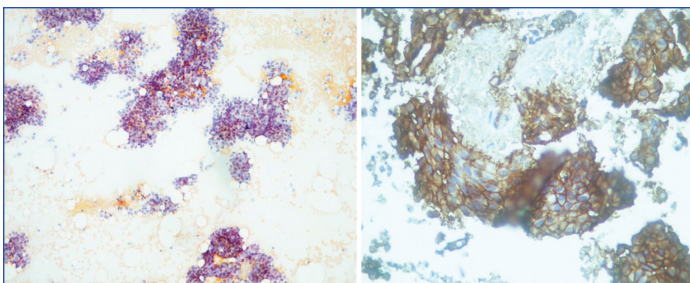
[Table/Fig-1]: CT scan image showing a sclerotic foci in L3 vertebral body and thyroid gland.



[Table/Fig-2]: a) Fine Needle Aspiration Cytology (FNAC) from breast lump showing moderately pleomorphic malignant ductal epithelial cells lying in clusters, having moderate amphophilic cytoplasm with hyperchromatic nuclei and occasional nucleoli. (MGG, 400X); b) Fine Needle Aspiration Cytology (FNAC) from breast lump showing malignant ductal epithelial cells lying in papillary formation. (Papanicolaou, 400X).

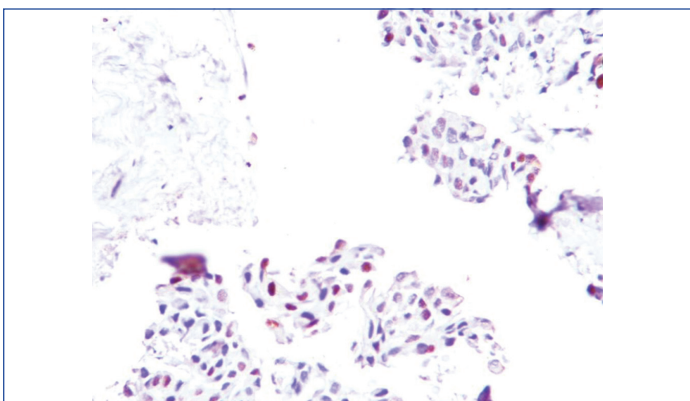
morphology. immunocytochemistry on cell block revealed that the tumour was Oestrogen receptors (ER)-negative, Progesterone Receptor (PR)-positive and Her-2/Neu-Positive [Table/Fig-4,5].

The tumour was assigned grading as T4bN1M0 and BIRADS IVB [1] on radiology. immunocytochemistry profile of the tumour was ER-negative, PR-positive, Her-2/Neu-Positive. FNAC from clinically evident thyroid swelling was suggested from our side and showed malignant epithelial cells of similar morphology as that of the breast lump [Table/Fig-6,7].

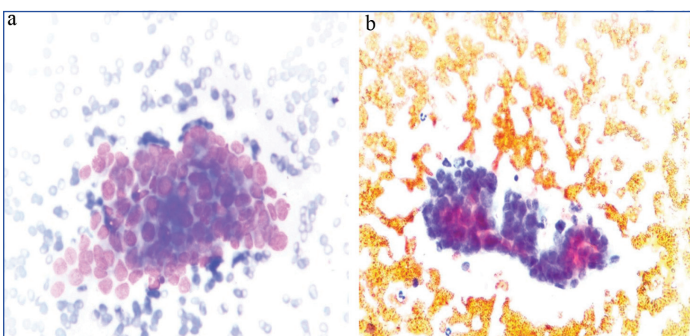


[Table/Fig-3]: Cytology of lymph node showing malignant epithelial cells of similar morphology. (Papanicolaou, 200X).

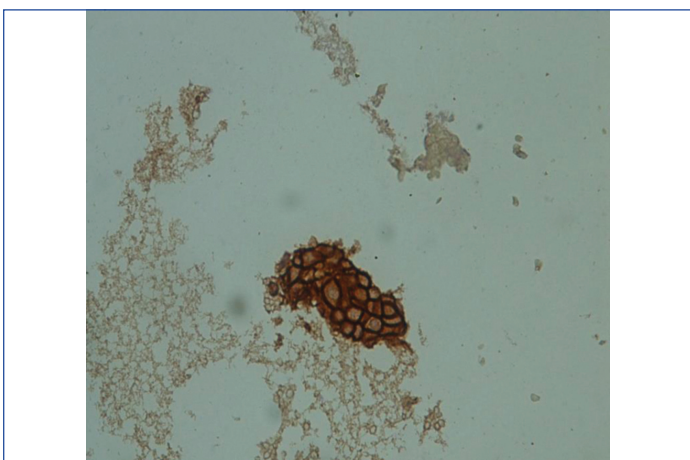
[Table/Fig-4]: Her2Neu positivity in the cell block made from FNA aspirate from breast swelling (400X). (Images from left to right)



[Table/Fig-5]: Progesterone positivity in the cell block made from FNA aspirate from breast swelling (400X).



[Table/Fig-6]: a) Fine Needle Aspiration Cytology (FNAC) from thyroid swelling showing malignant epithelial cells of similar morphology as that of the breast lump. (MGG, 400X). b) Fine Needle Aspiration Cytology (FNAC) from thyroid swelling showing malignant epithelial cells of papillary morphology. (Papanicolaou, 400X).



[Table/Fig-7]: Her 2 Neu positivity demonstrated in tumour cells in the cell block made from FNA aspirate from thyroid swelling (400X).

Cell block made from thyroid swelling aspirate yielded malignant epithelial cells of similar morphology as breast lump. On immunocytochemistry, PR and Her2Neu was positive, TTF-1 was negative [Table/Fig-7]. TTF-1 was done retrospectively on cell block made from FNA aspirate obtained from breast swelling and was negative.

Thus, confirming it to be metastatic foci from breast tumour. The patient was planned for surgery followed by adjuvant chemotherapy consisting of 5-Fluorouracil, Epirubicin and Cyclophosphamide regimen (FEC) regimen and Hormonal therapy targeting PR and Her2Neu receptor. However, she subsequently developed widespread metastasis to lung, bones and uterus and later succumbed to the disease.

DISCUSSION

Thyroid gland is a highly vascular organ with a vascular supply close to 4 to 6 mL/1 g tissue/min, which is second only to the adrenal gland [2,3]. Despite this, metastasis from primary carcinoma to thyroid gland is not a common occurrence. Infact out of all thyroid malignancies, only about 2-3% is metastatic in origin [4]. The incidence of metastasis to the thyroid gland in a autopsy series has varied from 1.25% to 24% [5]. Metastasis to the thyroid gland is more commonly found in females with a female to male ratio of 1.13:1 and a mean age within the sixth or seventh decade of life [3].

Around 80% of thyroid metastasis are metachronous with mean intervals from as little as 2.3 years in head and neck cancer to as long as 21 years in the case of foregut neuroendocrine tumours. Other metachronous tumours present varying levels of delay with a mean of 9.4 years in renal cell carcinoma primaries and 48.2 months in breast primary malignancies [6]. Thus, by the time, primary breast tumour metastasizes to thyroid gland, it is usually accompanied by involvement of other metastatic sites by the tumour [3], and hence, renders poorer prognosis for such patients. Slightly differing from this, in our case, the primary was quick to involve the thyroid gland synchronously along with vertebral bone, sparing the other sites, that too in a short span of four months only.

This highlights the significance of timely and correct identification of metastatic malignancies to thyroid, so that early treatment is ensured to such patients, hence leading to a better prognostic outcome.

Metastasis may present as single or multiple nodules in the thyroid gland, while sometimes present as enlarged nodular goiter or thyroiditis [7]. A small subset of patients has shown an incidentally detected thyroid lesion on imaging studies [8]. Patients with metastatic lesion presented pressure symptoms, hoarseness, dysphagia, stridor, dyspnea, etc., [3]. However, our case lacked these clinical symptoms despite quick metastasis.

Talking about thyroid metastasis from breast, approximately 16.0 to 32.0% cases are seen in postmortem examinations, out of which, only 4.0-9.0% cases has been reported in the literature [8,9].

Thus, thyroid metastases from breast cancer is not a common phenomenon with a quoted range of prevalence from 3% to 34% [6] but routine use of FNA could help detect it more frequently [10]. Infact, on the other hand, breast cancer is more likely to metastasizes to bone, lungs, pleura, liver and brain, as compared to the thyroid gland [11].

A correlation has also been observed between breast cancer and non-malignant thyroid disease. Giani C et al., revealed that the overall prevalence of thyroid disease (including nontoxic goiter and Hashimoto's thyroiditis) in breast cancer patients was higher than in the control group in a study conducted in 1996 [12]. Previous studies have also shown that preexisting thyroid disease (i.e., multinodular goiter and thyroid nodules) may have facilitated the metastases to the thyroid gland [12]. Our patient had a long history of goiter with hypothyroidism, which may have provided a nidus for the metastasis to thyroid. Non toxic goiter and anti-thyroid peroxidase autoantibodies have been found more than twice as common in the breast carcinoma patients compared than in controls [13].

Review of literature showed that there is increased risk of thyroid cancer in patients with breast cancer. In a study by Park JS et al.,

Study (Y)	No of cases	Age (yr)	Gender	Histological type of breast cancer	Timefor metastasis (mnth)	Metastases elsewhere	Intervention
Wang M et al., [20], (2020)	1	58	F	Mucinous	156	Nil	Thyroidectomy
Durmo R et al., [21], (2019)	1	72	F	Invasive ductal	----	Lumbar vertebrae and left iliac bone	NA
Ghias AF et al., (2019) [22]	1	67	F	Invasive ductal	24	Brain	Lobectomy
Pensabene M et al., [23] (2018)	1	6	F	Invasive lobular	18	Bone	Hemithyroidectomy
Inic Z et al., (2018) [4]	1	28	F	Lobular	60	Right cervical lymph nodes	TT, cervical lymph node dissection
Bourcier K et al., (2018) [24]	1	54	F	Invasive lobular	0	Left supraclavicular and cervical lymph nodes	TT and cervical lymph node dissection
Plonczak AM et al., (2017) [6]	1	62	F	Invasive ductal	144	Lung and bone, bilateral cervical lymph nodes	TT and cervical lymph node dissection
Zhou L et al., (2017) [25]	8	55.37	F	Invasive ductal, medullary and poorly differentiated	6 to 121	Chest wall, lung, supraclavicular, axillary, cervical and mediastinal lymph nodes	Surgery and chemotherapy
Our study (2023)	1	55	F	Invasive ductal	4 months	Vertebral bone, later to lung and uterus	Planned for Mastectomy with Thyroidectomy with CT and HT

[Table/Fig-8]: Studies reporting metastasis from Breast cancer to thyroid gland in past five years.

sonographic screening for thyroid cancer in females undergoing concomitant breast sonography showed a significantly higher incidence of thyroid cancer in the breast cancer group than those without it [14]. Vice versa is true as well i.e., an increased incidence of breast carcinoma was seen in young adult women who had a history of thyroid cancer in a study done at the MD Anderson Cancer Center [15].

Common genetic and hormonal changes have been involved in the pathogenesis of breast and thyroid cancer especially in postmenopausal women. TSH receptors are present abundantly in breast tissue [16], while oestrogen may influence the development, physiology and pathology of thyroid glands [17]. Higher levels of ERs were also found in neoplastic than in normal thyroid tissues [18]. In a study, it was stated that Cowden's disease, a rare genetic syndrome, had increased the risk of both

breast and follicular thyroid cancers [19] and led to sequential occurrence of these two cancers. Thus, coexistence of two primaries in both breast and thyroid should always be considered a probability and should be ruled out.

Some of the studies have specified the histological type of metastatic breast carcinoma [20-25]. Most commonly reported histological type to metastasize to thyroid is invasive ductal carcinoma [Table/Fig-8]. However, Loo CK and Burchett IJ showed neuroendocrine breast carcinoma to be the origin of the metastatic thyroid lesion [26]. Our patient falls in the NOS category, with molecular classification- Luminal type B. As presence of two primaries should always be considered as a possibilities. To confirm the thyroid metastases from the breast cancer, immunocytochemistry panel comprising of MGB2, CEA, ER, PgR, HER2 have been the most useful [20].

IHC staining proves very useful in differentiating between primary thyroid tumours and metastatic lesions in thyroid. In case of primary thyroid tumour, IHC staining for thyroglobulin (TG), Thyroid Transcription Factor 1(TTF-1) or calcitonin is positive. Thyroglobulin (may be spuriously positive due to the permeating colloid. On the contrary, CKMNF 116, Cytokeratin 7 (CK7), Carcinoembryonic Antigen (CEA) and Mammoglobin 2(MGB2) are specific and sensitive markers and should be positive in breast cancer metastatic to thyroid. In addition, Oestrogen and PRs (ER,PgR) as well as Herceptin Receptor (HER2) might be evaluated in metastatic breast cancer [18]. Immunocytochemistry profile of the tumour in our patient was ER-negative, PR-positive, Her-2/Neu-Positive.

CONCLUSION(S)

The metastasis to thyroid gland from breast as primary carcinoma in our case occurred in a short span of time and by the time it was diagnosed it had not metastasized elsewhere except L3 vertebrae.

The thyroid swelling did not cause significant symptoms and had masqueraded as multinodular goitre, which could have delayed the diagnosis. Thyroid metastases from breast cancer is an uncommon phenomenon but knowledge of such occurrences, clinicoradiological correlation, routine use of FNA and thorough cytopathological examination could help detect it more frequently and is very crucial for making the correct and timely diagnosis. To conclude, in a case of new thyroid lesion, it is suggested to always exclude metastasis of breast carcinoma especially in patients with former history of this malignancy.

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