



A Diagnostic Conundrum of Solitary Thyroid Nodule in Breast Cancer-Second Primary or Metastasis? A Case Report with Review of Literature

Nisha Prasannan¹; Paul Augustine^{2*}; Rexeena V Bhargavan²

¹Fellowship in Breast Surgical Oncology, Associate Consultant, GG Hospital, Thiruvananthapuram, Kerala, India.

²Department of Surgical Services, Regional Cancer Centre, Thiruvananthapuram, Kerala, India.

*Corresponding Author(s): Paul Augustine

Additional Professor, Department of Surgical Services,
Regional cancer centre, Thiruvananthapuram-695011,
Kerala, India.

Tel: 9447220035; Email: augustpaul@gmail.com

Abstract

The rising incidences of breast and thyroid cancer in women has resulted in them becoming among the commonest malignancies in females [1]. The common sites of metastasis from breast cancer are lymph nodes, bones, lungs and liver. Metastases to the thyroid gland from a non-thyroid primary are uncommon and are mostly from the kidney, followed by gastrointestinal tract, lungs, skin, and rarely breast [2]. Synchronous primary tumors of the thyroid and breast are also very rare in clinical practice. This a first case report of a patient with breast cancer which metastasis to the pre-existing solitary thyroid nodule and review of literature of the role of thyroidectomy in this scenario.

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Case report

A 40-year-old premenopausal lady presented with complaints of gradually increasing painless lump in the right breast of 5 months duration. She also had complaints of neck swelling for the past 5 years for which she had been investigated 5 years ago with ultrasound and FNAC and was diagnosed as a benign lesion. She was on regular follow-up for the same with regular clinical examination and ultrasound evaluation with her physician. The lesion was gradually increasing in size as per the ultrasound neck with an ultrasound 2 months prior reporting a solitary thyroid nodule in the left lobe of the thyroid of size 32x32x30mm with calcification and bilateral benign cervical lymph nodes. A Fine Needle Aspiration Cytology (FNAC) of the

thyroid nodule was suspicious of papillary carcinoma thyroid. At that review she complained to her doctor about the right breast lump. An FNAC from the breast lump was suspicious for carcinoma. She was referred to our centre for further management.

Her history and all reports were reviewed at our centre. On examination she had a cT1N1M0 lesion in the right breast with a solitary nodule in the left lobe of the thyroid. A bilateral mammogram (Figure 1) reported a 13x13mm BIRADS5 lesion at 10 o clock position in the right breast with significant right axillary lymph nodes; left breast and axilla were normal. Core needle biopsy from the right breast lesion was reported as infiltrating

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ductal carcinoma grade 3 with perineural tumor infiltration and intermediate grade ductal carcinoma *in situ*. The Oestrogen Receptor (ER) and Progesterone Receptor (PR) Allred scores were both 8/8 and human epidermal growth factor receptor2 (HER) was negative. On ultrasound of the neck a 18x15mm significant node was detected in the right supraclavicular fossa (Level 5). Fine needle aspiration cytology was done from thyroid and right supraclavicular lymph node; which was consistent with adenocarcinoma, showing cells with papillary pattern. Immunohistochemistry (IHC) also could not confirm the primary or metastatic status of the thyroid lesion. Nor could it specify if the supraclavicular node was a metastasis from the thyroid or breast. A CT neck, thorax and abdomen and bone scan were done which reported the same findings with no distant metastasis. A multidisciplinary tumor board discussion concluded that there were two differential diagnosis, two synchronous primaries in the breast and thyroid with supraclavicular node metastasis from either of the 2 or breast cancer with supraclavicular and thyroid metastasis which can be considered oligometastatic. Hence it was decided to proceed with primary surgery of the right breast with left hemithyroidectomy and right supraclavicular lymph node biopsy. She underwent right modified radical mastectomy (patient preference) along with left hemithyroidectomy and excision of right supraclavicular lymph nodes. Histopathological examination revealed invasive carcinoma breast of size 3x2x1cm with perineural invasion and foci of necrosis. Right axillary clearance upto level 3 had 20 lymph nodes, all showing metastatic adenocarcinoma; Right supraclavicular node biopsy reported metastasis from adenocarcinoma breast .The left hemithyroidectomy also showed adenocarcinoma .IHC was done to ascertain whether the thyroid lesion was a primary or metastasis from breast. In the thyroid specimen (Figures 2,3,4) thyroid Transcription Factor-1 (TTF-1) was negative, ER and GATA3 were moderate positive which were suggestive of metastasis from breast carcinoma. MDT decided to consider this as an oligometastatic disease and continue the treatment with curative intent.

Patient received adjuvant chemotherapy (6 cycles of docetaxel) and radiation to the chest wall and supraclavicular fossa. Presently the patient is on endocrine therapy (aromatase inhibitor - post radio ablation of the ovaries) and she is clinically stable.

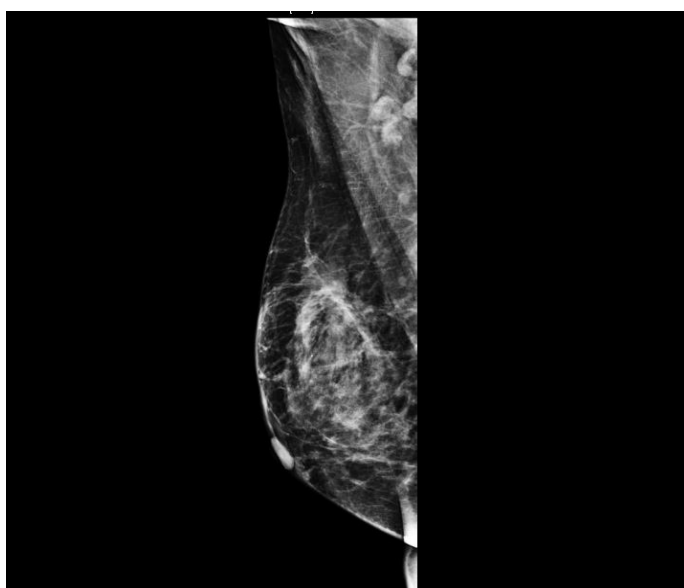


Figure 1: Mammogram showing the BIRADS5 lesion in the right breast.

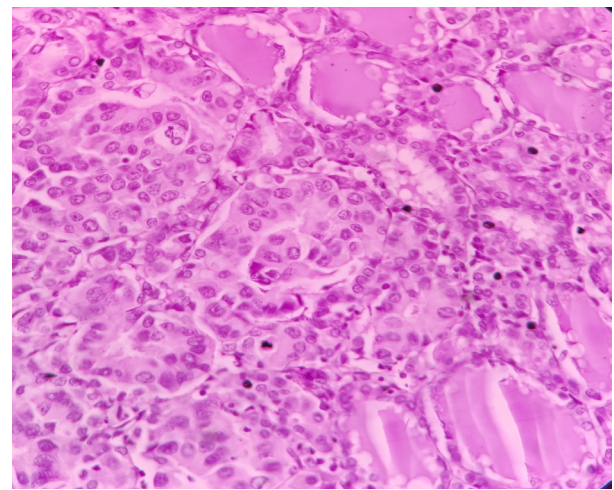


Figure 2: Section from thyroid showing an infiltrating neoplasm composed of sheets of malignant cells with pleomorphic vesicular nucleus (H&Ex400).

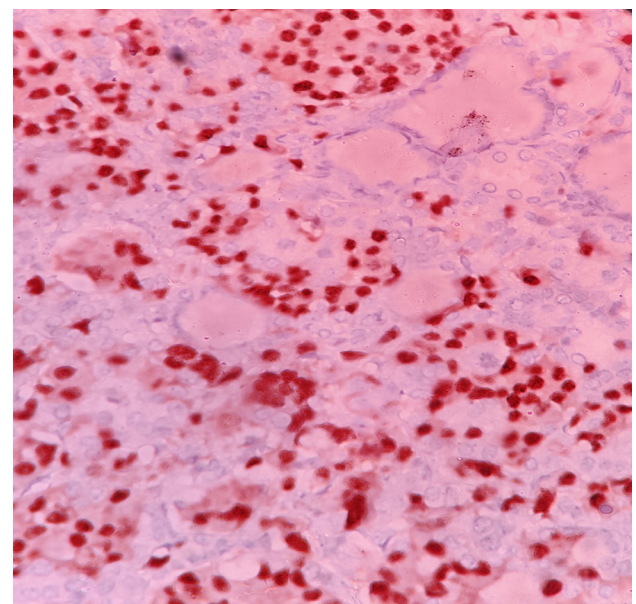


Figure 3: Neoplastic cells are positive for GATA3 (IHCx400).

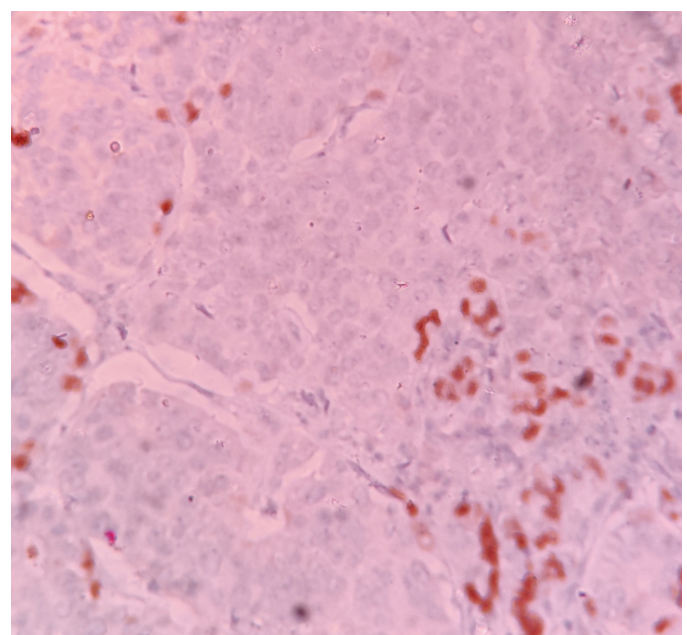


Figure 4: Thyroid follicular cells are positive for TTF1, neoplastic cells are negative for TTF1 (IHCx400).

Discussion

Breast cancer is the most common malignancy among women [1]. Thyroid cancer is the most common endocrine malignancy with a rising incidence. Individuals with breast cancer have been found more likely to develop primary thyroid cancer, possibly due to some common risk factors (genetic, lifestyle, diet habits, hormonal, menstrual, and reproductive factors) [2]. Therefore, an individual presenting with both thyroid and breast malignancy is more likely to have primary cancer of thyroid and breast, rather than breast metastases to the thyroid. Thyroid metastasis is uncommon and breast derived thyroid metastasis is relatively rare [3]. Up to 80% of thyroid metastases 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 tumors [4]. In the breast primary malignancies, the interval for thyroid metastasis is a median of 48.2 months [4]. Most reports of metastases to the thyroid are solitary with Surov and colleagues reporting that thyroid metastases were solitary in 76% of patients in their study [5]. However, in the retrospective study by Hegerova et al. they found that 79% of their patients had evidence of other metastases at the time of diagnosis of thyroid metastases, which may suggest that investigations are needed to rule out other sites of metastasis [6].

Fine Needle Aspiration Cytology (FNAC) is the investigation of choice in the work-up of thyroid nodules and it reportedly has an accuracy of over 90% in the diagnosis of secondary tumors of the thyroid [7]. Unfortunately, as in the case presented, metastatic breast carcinoma involving the thyroid may morphologically mimic primary thyroid malignancy on Fine-Needle Aspiration (FNA) and secondary malignancies of the thyroid may be misdiagnosed.

Thyroid primary and metastasis have similar symptoms, examination findings and radiological appearance. Imaging like CT scan may demonstrate diffuse calcification or invasion of surrounding tissues in the thyroid which points towards primary lesion. Disseminated metastasis may also arise from either primary. Biopsy and IHC from both lesions can be helpful however in our scenario it did not contribute to the solution. The accuracy of US-guided biopsy for diagnosis of thyroid mets is reported to be 90.8% to 91.2% [8]. However, some thyroid metastatic carcinomas can still have similar morphological features to those of primary thyroid cancer by biopsy, including papillary, follicular, and myeloid structures. On these occasions, immunohistochemical staining, such as for Thyroglobulin (TG), calcitonin, GATA3, Paired box gene 8 (PAX8), and Thyroid Transcription Factor-1 (TTF-1), is helpful in distinguishing between primary thyroid cancer and mets. TG is the only specific marker for malignant tumors of thyroid origin and can confirm the non-medullary carcinoma of the thyroid containing a follicular structure [9]. TTF-1 regulates the transcription of specific genes in thyroid follicular cells and activates the transcription of TG and thyroid peroxidase genes in thyroid cancer cells [10]. However, TTF-1 has no specificity because it can also be found in lung cancer, and PAX8 can also be found in kidney cancer and gynaecological tumors [11]. GATA3, ER, PR, and HER-2 are markers for breast cancer, and the positive staining for E-cadherin supports the catheter phenotype. ER positive breast cancer often metastasizes to the thyroid gland and parathyroid glands, while PR positivity tends to metastasize to the myocardium, gastrointestinal tract, or urinary tract epithelium [11].

The clinical conundrum of our patient was deepened by the fact that the thyroid nodule was present more than 4 years be-

fore the breast lump appeared. This led to the probability that the 2 lesions are more likely to be 2 separate primary lesions than metastasis. Also the supraclavicular node and breast lesion were on the ipsilateral side and the thyroid lesion on the contralateral side. So the suspicion was more towards an cT-1N3M0 breast malignancy with a primary thyroid malignancy. A hemithyroidectomy was planned as it would be both diagnostic and may also be therapeutic for the patient even if primary or metastatic. A second surgery for the thyroid maybe necessary as per the final histopathology report. With this plan our patient with breast metastasis to the thyroid and supraclavicular lymph nodes, was managed with a hemithyroidectomy. The final histopathology of the breast axilla, supraclavicular node and the thyroid was adenocarcinoma which on further IHC was confirmed to be metastasis from the breast. She was staged as pT2N3CM1 invasive ductal carcinoma of the right breast, ER, PR positive, HER negative. The good biology of the breast carcinoma with an oligometastatic disease limited only to the thyroid as per the workup resulted in treatment with curative intent for this patient. She received adjuvant chemotherapy and radiotherapy and is now on endocrine therapy for 3 months and asymptomatic.

Isolated thyroidectomy has been proposed in previous studies as a local disease control option to palliate and prevent the potential morbidity of tumor extension related to the airway. It has been also suggested that this may be beneficial for a selected group of patients with clinically significant and relatively isolated metastatic disease of the thyroid especially from a renal primary; however, in the absence of prospective trials this is at best speculative. Our report adds to the increasing evidence supporting the role of metastasectomy in oligometastatic breast cancer. It is too early in the treatment of the patient to predict any survival benefit. Long term survival data of such anecdotal cases should contribute to the management of such rare situations.

Conclusion

Thyroid metastasis from breast cancer is rare. It should be differentiated from synchronous thyroid cancer which is also rare. If thyroid is the only site of metastasis in breast cancer in good biology patients, a thyroidectomy and therapy with curative intent can be considered.

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