



Metachronous Invasive Breast Carcinoma and Papillary Thyroid Carcinoma with Axillary Caseating Granulomatous Lymphadenitis – A Rare Case Report

T Mitila¹, Shobini Vishali V M^{2*}, Vimal Chander³, Muthuvel E⁴

^{1,2}Final year Postgraduate, ^{3,4}Professor,

Dept. of Pathology, Saveetha Medical College, Chennai

***Corresponding Author:**

Shobini Vishali V M

Final year Postgraduate, Dept. of Pathology, Saveetha Medical College, Chennai

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Abstract

Metachronous primary cancer is defined as a second primary cancer developing 6 months or more after the primary cancer diagnosis. The most commonly occurring second primary malignancy in breast cancer patients is thyroid cancer. The linkage between thyroid and breast disorders are based on hormonal and cellular receptor mechanisms. Thyroid hormones have been found to stimulate cell proliferation in breast tissue, enhance the estradiol-mediated effects on cell proliferation, promote growth and induce the expression of progesterone receptors by mimicking the effects of estradiol. This rare case combines the presence of metachronous breast and thyroid cancers, with an additional finding of Hashimoto thyroiditis, along with axillary caseating granulomatous lymphadenitis.

Keywords: Metachronous carcinoma, Breast, Thyroid, Hashimoto, Axillary lymph node, Granulomatous lymphadenitis

Introduction

Globally, breast cancer (BC) and thyroid cancer (TC) are two of the most common malignancies among women.[1] Multiple primary cancers are generally defined according to the criteria of Warren and Gates as follows: 1) each tumor must have clear evidence of malignancy on histologic examination, 2) each tumor must be geographically separate and distinct, and 3) the possibility of a metastatic lesion having spread from a prior cancer must be excluded.[2] Patients with metachronous cancer are defined as those diagnosed with a second cancer 6 months or more after the primary cancer diagnosis.[1] Breast cancer and thyroid cancer can develop synchronous or metachronous in patients and that the rate of occurrence is higher than expected by chance.[3] The breast and thyroid are hormone-responsive organs and are subject to hypothalamus–pituitary–glandular axis regulation.[4] This rare case combines the presence of metachronous breast and

thyroid cancers, with an additional finding of Hashimoto thyroiditis, along with axillary caseating granulomatous lymphadenitis.

Case Report

A 64-year-old female presented with complaints of hard swelling in the left breast for 10 years with no family history of breast cancer. Local examination revealed a 3.5x2 cm hard lump in the upper inner quadrant of left breast and a mobile node of size 1x1 cm in the left axilla. Mammogram showed a BIRADS-5 lesion which was ill-defined, moderately dense and radio opaque with adjacent spiculations and architectural distortion.

Due to a long history of illness, the patient underwent PET- CT scan and an incidental 2 cm hypodense nodule in the left lobe of thyroid, suspicious of malignancy was noted. Subsequently, fine needle

aspirations of left breast lump and left lobe of thyroid confirmed the malignancies. The patient was taken up for a concurrent left modified radical mastectomy and total thyroidectomy. Histopathological analysis identified a grade 2 (Nottingham histologic score), ER, PR positive and Her 2 neu negative Invasive breast cancer of no special type, which according to the TNM staging system, was classified pathologically as a pT2pN2a lesion. Additionally, axillary lymph node sent for nodal metastasis

evaluation revealed a caseating granulomatous inflammation which was negative for acid fast bacilli on Ziehl Neelson staining. Microscopic examination of total thyroidectomy specimen showed classical features of Oncocytic subtype of papillary thyroid carcinoma, with a concurrent chronic lymphocytic thyroiditis characteristic of Hashimoto disease. It was classified as pT2N0 disease using the 8th AJCC/TNM staging system for thyroid cancer.

Figure 1: a) Mammogram of left breast.

b) USG-guided FNAC of left lobe of thyroid swelling.

c) FNAC of left breast swelling showing features positive for malignancy. (H&E x20)

d) FNAC of left lobe thyroid swelling showing features of papillary thyroid carcinoma. (H&E x40)

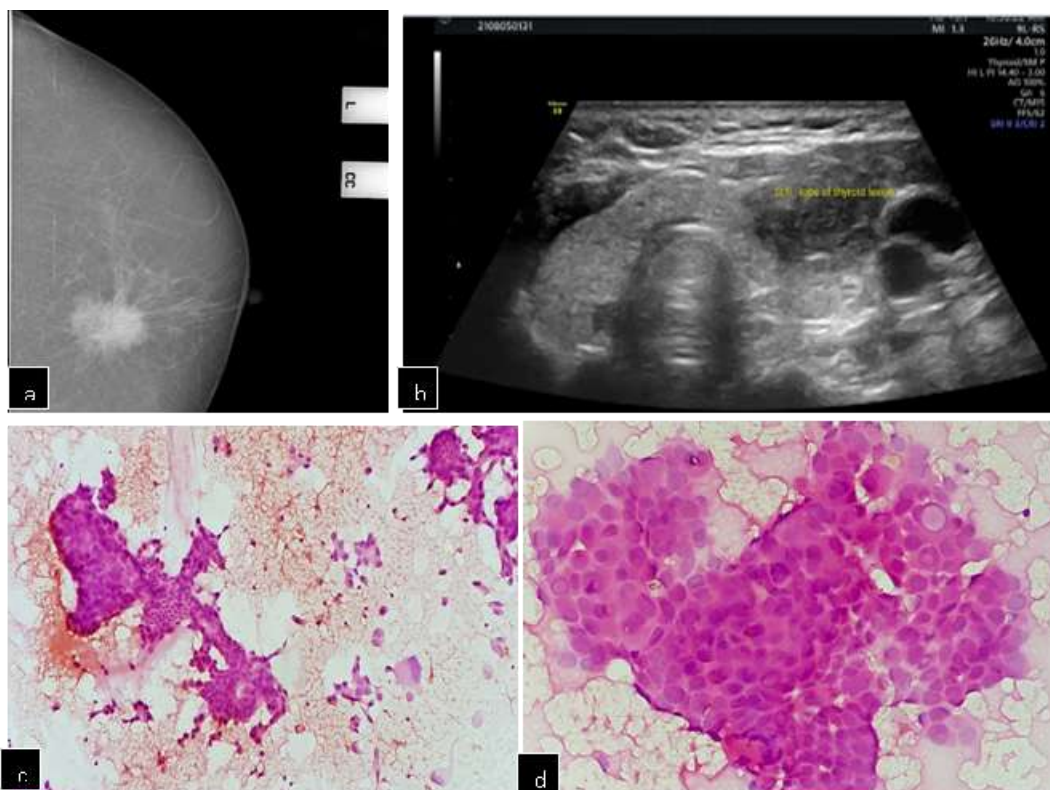


Figure2: a) Gross image of MRM.

b) Gross image of total thyroidectomy.

c) Cords and nests of tumor cells. (H&E x10)

d) Cords and nests of polygonal tumor cells with abundant cytoplasm and vesicular nuclei. (H&E x40)

e) Tumor cells infiltrating the lymph node. (H&E x20)

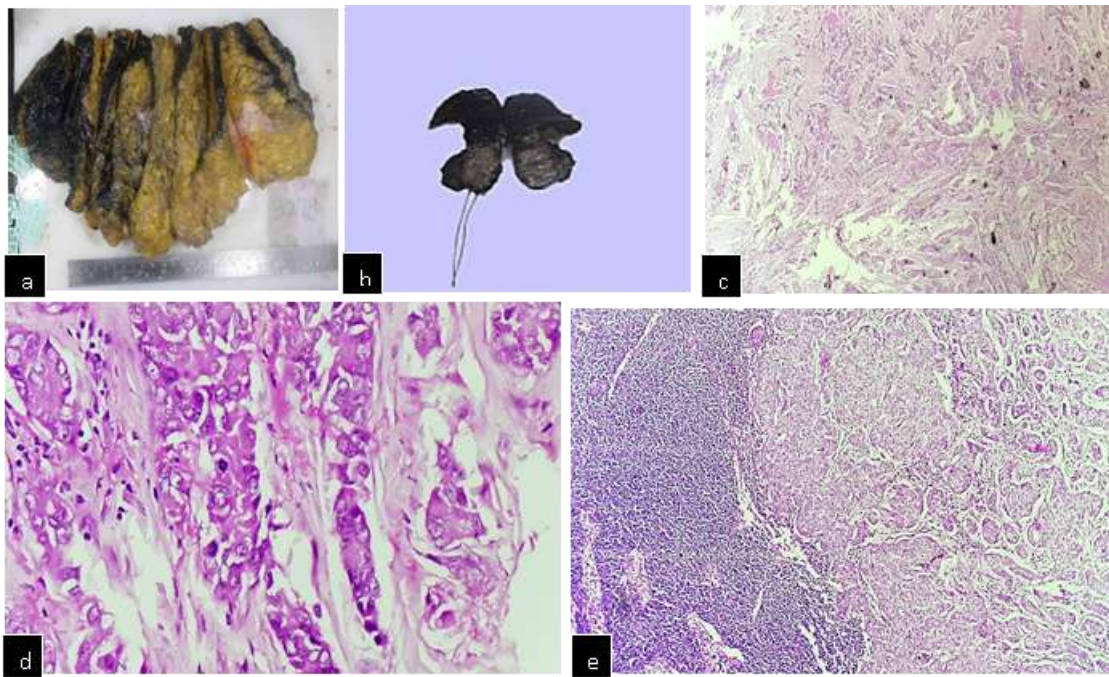
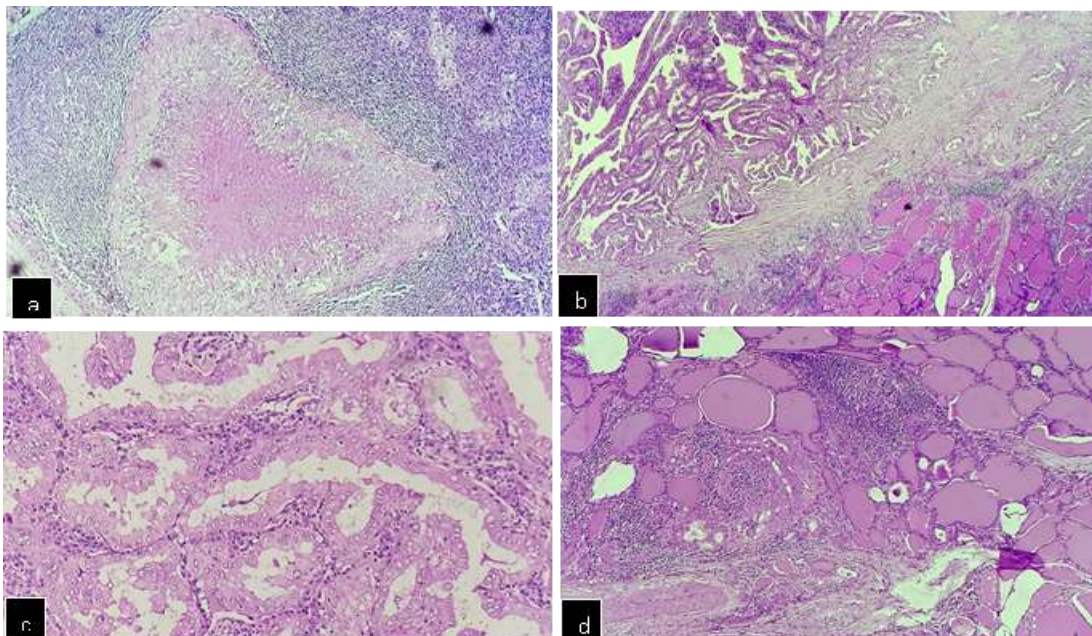


Figure 3: a) Caseating granulomatous inflammation of axillary lymph node. (H&E x20)
b) Thyroid follicles with adjacent papillary neoplasm. (H&E x10)
c) Papillary architecture of oncocyctic tumor cells. (H&E x40)
d) Hashimoto thyroiditis showing extensive lymphocytic infiltrate. (H&E x20)



Discussion

Dual malignancy was first reported by Billroth in 1889.[5] In the study by Piek *et al*, the incidence of TC among 318,002 women with BC (BC-TC) was

0.1% (423 patients) with a standardized incidence ratio of 1.86.[3] The higher incidence of thyroid cancer in women could possibly be due to the expression of functional estrogen receptor, which

participates in cellular processes that contribute to the enhanced mitogenic, migratory, and invasive potential of thyroid cells.[6] Breast tissue also has receptors of thyroid stimulating hormone, which alone or in combination with estrogen can promote the onset of breast cancer.[4]

Levels of thyroid-stimulating hormone are associated with the onset of primary thyroid cancer. Thyrotropin, thyroxin, and thyroid antibodies also promote the occurrence and development of primary thyroid cancer and breast cancer.[4] Thyroid tissue is also shown to contain estrogen and progesterin receptors, and these hormones can promote proliferation of thyroid cells and carcinogenesis of differentiated thyroid carcinoma. Papillary thyroid carcinoma shows significantly higher expression rates of estrogen receptor α and progesterin receptor than the other types of thyroid tumors. Iodine deficiency may stimulate the gonadotrophin secretion and cause DNA damage in the thyroid gland and promote cancer and then result in a hyperestrogenic state, which further predisposes to both cancers.[4]

Multiple studies have found RET/PTC gene rearrangements in up to 95% of the pure Hashimoto's thyroiditis cases, which is highly specific for papillary thyroid carcinoma. In addition, molecular expression patterns of PTC and subsets of Hashimoto's thyroiditis show similarities. Because of the close relationship between these entities, it has been debated as to whether Hashimoto's thyroiditis is a premalignant state of PTC.[7] The oncocytic subtype of PTC is a rare subtype accounting for 1–11% of all PTC cases, characterized by higher incidence of local invasion, cervical lymph node metastases and resistance to radioactive iodine therapy. Hence, they are associated with a higher recurrence rate and shorter disease-free survival.[8]

A granulomatous reaction is regarded as an immune mechanism against infection, non-neoplastic, and neoplastic conditions.[9] In patients with malignancy, the most frequent granuloma-associated conditions are tumor-related, tuberculosis, sarcoidosis, and infections, such as fungal infections. Tumor-related granulomatous reaction most probably represents an immunological, mediated antitumor response of macrophages activated by T-lymphocytes.[10]

Warthin was the first to report the unique coexistence of tuberculosis and breast cancer in 1899.[11]

Axillary lymph nodes should be carefully observed during breast surgery in patients with breast cancer living in populations with high TB prevalence because these lymph nodes might be TB lymphadenitis clinically imitating breast cancer, which should never be disregarded.[9] Microscopic detection of AFB by ZN staining is often not sensitive enough to confirm a histopathological diagnosis. PCR-based assays are relatively sensitive and rapid in the detection of *M. tuberculosis*. [10]

Conclusion:

Co-occurrence of primary cancers of the thyroid and breast may be associated by endocrine hormone interactions and congenetic oncogenes, which may serve as novel targets for cancer prevention and therapy. Preoperative assessment of thyroid gland by physical examination is mandatory in patients diagnosed with breast cancer and if clinically negative for thyroid pathology, radiological evaluation can be performed for them. Treatment for both cancers can be safely performed at the same time.

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