

Breast Carcinoma in Thyroid Cancer Survivors

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Abstract: Women with a history of thyroid carcinoma have a greater than expected risk of developing breast carcinoma. This risk is most pronounced in premenopausal white women, who have received treatment for thyroid cancer. We report two patients with well differentiated thyroid cancer on follow up developing carcinoma breast, one patient 22 years and the other developing breast cancer 7 years after treatment for carcinoma thyroid. Both patients were detected at an early stage and were treated with curative intent. Both patients show no evidence of disease at the last follow up. Because this risk is appreciable throughout the lifetime of the individual, lifetime monitoring and breast cancer screening are important for all female patients with thyroid carcinoma.

Keywords: Breast Carcinoma; Thyroid cancer; Second malignant neoplasm; Chemotherapy; Radiotherapy.

INTRODUCTION

Breast carcinoma and thyroid carcinoma are two malignancies that occur most commonly in women. The occurrence of breast and thyroid cancers may be linked genetically or hormonally [1].

Standard treatment of differentiated thyroid cancer involves surgery with elective radioactive iodine-131 treatment [RAI] in an individualized approach [2]. Use of RAI improves the disease free and overall survival in patients with well differentiated thyroid carcinoma [3, 4]. Although RAI is primarily concentrated in the thyroid, exposure of other tissues that have sodium/iodine transporter like breast can also occur. Researchers have noticed cases of non-synchronous second primary malignancies [NSSPM] along the follow-up of non-familial DTC. The relationship between RAI-131 and oncogenic effects are suggested by recent studies with DTC patients treated with RAI-131 [5, 6]. We report cases of two women who are thyroid cancer survivors developing breast cancer on follow up period.

CASE SUMMARY**Case 1**

A 38 year old lady presented to us with history of painless swelling in the front of neck for 2 years and she had undergone hemi-thyroidectomy for the same. Histopathological examination was suggestive of papillary carcinoma thyroid following which she underwent completion thyroidectomy. Post-operative low dose iodine 131 scan which showed residual thyroid tissue and radioiodine ablation was done subsequently. Patient was put on calcium, vitamin D and levothyroxine supplementation and was under regular follow up. She had five yearly low dose iodine

131 scans, all were negative. After a disease free survival of 22 years she presented with left sided breast lump. On examination patient had a 3 x 2 x 1cm mass in the upper inner quadrant of left breast with mobile 2 x 1cm left axillary lymph node. Mammogram showed an irregular marinated soft tissue mass lesion the upper inner quadrant of left breast 2.6 x 2.4 cm with left axillary lymph nodes (BIRADS 5) (Figure 1a). Chest X-ray and ultra-sonogram of abdomen were negative for metastasis. Patient underwent left breast conservation surgery with axillary clearance which showed whitish growth of size 2 x 2 x 1.5cm. Histopathology examination showed infiltrating ductal carcinoma, grade II, six out of twenty seven lymph nodes showing metastasis with extracapsular extension (pT1N2M0, stage IIIA). Immunohistochemistry revealed estrogen receptor (ER) diffuse strong positivity (Allred score 8), progesterone receptor (PR) diffuse strong positivity (Allred score 7) and Her-2/neu protein negative (Score 0). She received adjuvant chemotherapy FEC X 3 cycles (5 fluorouracil 500mg/m² day1, epirubicin 100 mg/m² day 1, cyclophosphamide 500mg/m² day 1) followed by docetaxel x 3 cycles (100mg/m²) every 3 weekly. After chemotherapy patient was started on adjuvant radiotherapy 40 gray in 15 fractions and a tumor bed boost of 10 Gy in five fractions. Patient had vitamin D level of 52 ng/ml which was adequate but baseline bone mineral density scan showed a T score of -2.7 suggestive of osteoporosis. She was started on letrozole,

adjuvant endocrine treatment along with calcium, Zoledronic acid once in 6 months for osteoporosis. Patient is now asymptomatic at 3 months follow up.

Case 2

40 year old female was evaluated for diffuse thyroid swelling and imaging was suggestive of multi nodular goitre. Post op histopathology report revealed a 1.5*1 cm (T1) papillary carcinoma in background of multi nodular goitre. Post op patient was put on calcium, vitamin D and thyroxine supplementation and was under regular follow up. Eight years later the patient developed pain and lump in the left breast. On examination a 2*2 cm lump was found at 12 O'clock position which was mobile (cT1N2M0). Mammography scattered benign appearing calcifications in left breast

and ultrasound correlation revealed irregular hypo-echoic area in 12 O clock of size 21*12 mm (Figure 1b). Biopsy was suggestive of infiltrating ductal carcinoma, estrogen receptor (ER) positivity (Allred score 7), progesterone receptor negative (Allred score 0) and Her-2/neu protein negative. Patient underwent left modified radical mastectomy and axillary clearance. Post op histopathology report showed fibromatoid changes papillomas and an invasive focus. Fifteen lymph nodes were removed of which one were positive (pT1N1M0). The patient was started on adjuvant chemotherapy AC X 4 cycles (Doxorubicin 60 mg/m² day 1, cyclophosphamide 600mg/m² day 1) followed by docetaxel x 4 cycles (100mg/m²) every 3 weekly. After completion of chemotherapy patient is planned for adjuvant tamoxifen.

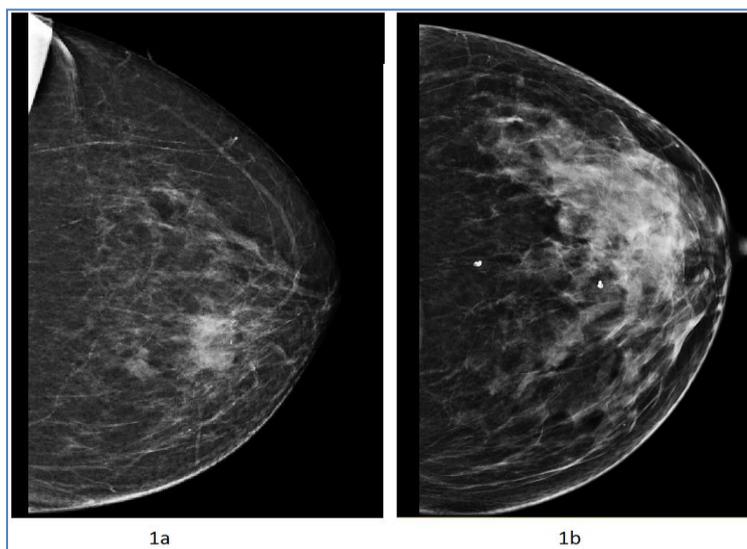


Fig-1: Mammogram showing 1a, irregular marginated soft tissue mass lesion of size 2.6 x 2.4 cm (Case 1) and 1b showing, scattered benign appearing calcifications (Case 2)

DISCUSSIONS

One of the most frequently reported concerns of cancer survivors is fear of recurrence [7]. It has been described an increased risk among DTC survivors for secondary malignancies of salivary glands, stomach, breast, central nervous system, colorectal, prostate, genitourinary tract, kidney, adrenal gland, bone and joints, soft tissue sarcoma and haematological cancers [8]. Breast cancer is one of the most common secondary cancers in female thyroid cancer patients. According to a recently published meta-analysis, the incidence of secondary primary breast cancer [SPBC] in thyroid cancer survivors was increased by a standardized incidence ratio of 1.25 (95% confidence interval 1.17–1.32) on the basis of pooled data from six studies of 60490 thyroid cancer survivors [8]. The likely possibilities for the increased risk of second primary breast cancer in DTC survivors include exposure to ionizing radiation from radioiodine therapy (RAI) genetic predisposition [9, 10]. Rubino and cols. described a linear dose-response relationship among RAI-131 and the occurrence of leukemia and some

specific solid malignancies (colorectal, salivary glands, bone, soft tissue cancer), with no association with others solid malignancies (breast, kidney, central nervous system) [11].

The association between thyroid carcinoma and breast carcinoma in women was first recognized in 1966 [12]. The authors reported that among 92 women with thyroid carcinoma, 8 later developed breast carcinoma. A retrospective study recently performed at the University of Texas MD Anderson Cancer Center suggested that an increased risk exists for women with an index thyroid carcinoma to develop subsequent breast carcinoma [13]. Another study by Chen et al suggest that the greatest risk for women with primary thyroid carcinomas to develop secondary breast carcinomas is with young adult women and a latency of 5 to 20 years [14].

The main factor which may contribute to the development in second cancers in thyroid cancer survivors is the exposure to radioactive iodine used for

diagnostic and therapeutic purpose [5]. Usually the second malignancy occurring in patients with thyroid cancer are solid tumors and as other radiation induced second malignancies they occur after a latent period of 2-3 years [1]. The risk is also higher for younger patients being treated for thyroid cancers. One of our patients had radioactive iodine treatment while other patient with low risk thyroid cancer did not receive it. Both the patients were diagnosed with thyroid cancer at young age (38 and 40 years).

Although there are guidelines for breast cancer screening of patients of lymphoma who received mediastinal radiation, there are no formal recommendations for breast cancer screening in thyroid cancer survivors who have received radioactive iodine therapy. The thyroid cancer survivors develop breast cancer at a younger age and chance of survival improves with screening which helps in early diagnosis of breast cancer. Screening should be advised thyroid cancer patients as the survival of thyroid cancer has improved over the years.

CONCLUSION

Thyroid cancer survivors are at an increased risk of developing second primary breast cancer. Because this risk is appreciable throughout the lifetime of the individual, lifetime monitoring and cancer screening are important for all female patients with thyroid carcinoma. Early diagnosis and treatment is key to cure in such patients.

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